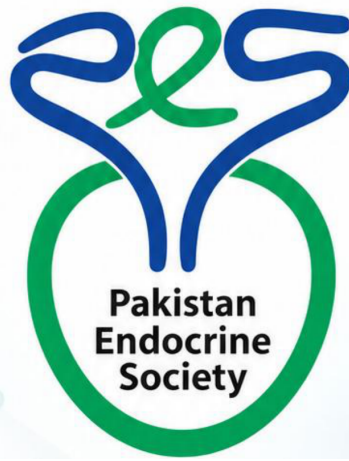




Pakistan **Endocrine** Case Collection

2026

6th Edition



Pakistan Endocrine Society

Advancing endocrine practice through clinical learning

Founded in 2001, the Pakistan Endocrine Society brings together clinicians working to advance the practice and science of endocrinology in Pakistan. Its educational meetings and continuing medical education programmes support professional learning and improved standards of care.

The sixth edition of the Pakistan Endocrine Case Collection presents 21 reports spanning paediatric, thyroid, adrenal, pituitary and metabolic disease. These cases offer opportunities for bedside reasoning, teaching and discussion among trainees and practising clinicians.

Acknowledgements

The Pakistan Endocrine Society thanks Getz Pharma for its technical support and assistance in preparing this booklet.

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President's message



Dr Ali Asghar

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Consultant Endocrinologist

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President, Pakistan Endocrine Society

As-Salam-o-Alaikum,

With gratitude to Almighty Allah, the Pakistan Endocrine Society presents the sixth edition of the Pakistan Endocrine Case Collection (PECC 2026). Through the dedication of our members, this initiative has grown into an academic tradition that records endocrine practice in Pakistan.

The 21 cases in this edition reflect a broad range of clinical presentations. They bring together histories, examinations, investigations, management and discussion from our clinics and wards, offering practical material for clinical learning.

Medical education shapes judgement, attitudes and standards of care as well as knowledge and skill. These reports encourage clinicians to recognise patterns, question initial assumptions and revisit a diagnosis when the clinical course does not fit. I hope the collection will support general physicians, postgraduate trainees and endocrine fellows, and stimulate discussion in teaching sessions and journal clubs.

I appreciate the colleagues who submitted their cases, and Dr Tahir Ghaffar, Dr Urooj Lal Rehman, Dr Gohar Khan, Dr Rab Nawaz, Dr Sidra Lodhi, Dr Zarin Kiran, Dr Saira Bashir and Dr Rimsha Azhar for their work in preparing this edition. I also acknowledge the successive editors and office bearers whose vision has sustained PECC across its editions.

May Allah reward everyone who contributed and grant us the strength to continue learning, teaching and serving our patients.

Chief editor's message



Dr Ibrar Ahmed

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Past President, Pakistan Endocrine Society

As-Salam-o-Alaikum,

With gratitude to Almighty Allah, I present the sixth edition of the Pakistan Endocrine Case Collection on behalf of the editorial board.

These 21 reports reflect the curiosity, perseverance and clinical judgement required in endocrine practice. They describe rare genetic disorders, difficult diagnostic pathways and presentations in which a familiar clinical label required reassessment.

The aim of this collection is to present the contributors' clinical experiences clearly and consistently. A uniform format supports comparison and discussion, while distinguishing documented findings from suspected diagnoses and investigations that remain outstanding.

I encourage colleagues to record their cases while the details are fresh, obtain informed consent, protect patient confidentiality and retain complete investigation and follow-up records. A clear clinical lesson gives each report value for the next reader.

I thank Dr Gohar Khan for leading the preparation of this edition, and my fellow editors Dr Tahir Ghaffar, Dr Rab Nawaz, Dr Sidra Lodhi, Dr Hina Sattar, Dr Zarin Kiran, Dr Saira Bashir and Dr Rimsha Azhar for their commitment. I am grateful to Dr Ali Asghar, President of the Pakistan Endocrine Society, and the Society's office bearers for their support.

Submissions are welcome for the seventh edition. We look forward to your contributions.

Preface



Dr Gohar Khan

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“The value of experience is not in seeing much, but in seeing wisely.” These words by Sir William Osler, one of history’s most revered physicians, perfectly encapsulate the spirit of this booklet. In the vast and rapidly evolving landscape of medical science, progress depends on discerning evaluation and a rigorous commitment to truth. The sixth edition of PECC stands as a testament to this collective wisdom.

We extend our deepest gratitude to our distinguished authors for sharing their groundbreaking research and to our publisher for providing a platform through which to share it. We are especially indebted to our Editorial Board and Reviewer Panel. Through their collaborative expertise, meticulous evaluation and academic stewardship, they transform observations into clinical insights and uphold the highest standards of scientific integrity and excellence.

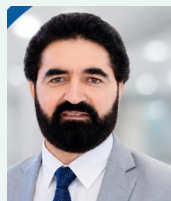
I would like to congratulate the entire PES family, especially Dr Ibrar Ahmed, for his consistent efforts to create an environment in which colleagues and junior clinicians can learn, acquire evidence-based knowledge and skills, develop leadership qualities and contribute to the advancement of endocrinology in Pakistan. These efforts are truly the need of the hour. I also congratulate him and the entire team on publishing this edition of PECC, which will benefit endocrine fellows, internal medicine residents, family physicians, medical specialists and endocrinologists alike.

Last but certainly not least, I would like to extend my heartfelt congratulations to Dr Ali Asghar, President of the Pakistan Endocrine Society (PES), for his visionary leadership. I also thank him for the guidance, encouragement and support that led to the successful publication of this booklet.

Looking ahead, this collection of cases does more than document past triumphs; it serves as a clinical compass for the future. As precision medicine, artificial intelligence and genomics reshape endocrinology, the insights compiled within these pages will lay the groundwork for the next generation of patient care. We hope this volume inspires emerging clinicians to push the boundaries of innovation and helps Pakistan remain at the forefront of global endocrine health in the years to come.

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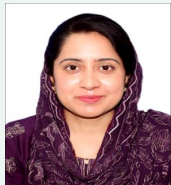
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CASE REPORT 01

An Interesting Case of an Infant with Two Rare Genetic Diagnoses in a Consanguineous Setting

Dr Shafaq from Islamabad

Abstract

A seven-month-old boy from a consanguineous family was evaluated following a sibling's neonatal death. Metabolic abnormalities were interpreted by the submitting author as suggestive of cystathionine beta-synthase deficiency, while a reported heterozygous CACNA1H variant and raised aldosterone suggested familial hyperaldosteronism type IV. Hypertension persisted despite spironolactone. The case highlights the need to confirm each diagnosis independently when metabolic and endocrine abnormalities coexist.

Keywords: genetic disorders; cystathionine beta-synthase deficiency; CACNA1H; familial hyperaldosteronism; childhood hypertension

Introduction

Consanguinity increases the risk of genetic disorders in general and autosomal recessive disorders in particular. A family history of neonatal death from unexplained metabolic acidosis further raises red flags for inborn errors of metabolism. Meanwhile, germline variants in CACNA1H are associated with early-onset familial hyperaldosteronism type IV manifesting as mild primary aldosteronism and childhood hypertension.

Case presentation

A seven-month-old boy was born at term by spontaneous vaginal delivery to first-cousin parents. An older sibling had died in the early neonatal period. Vitamin B6 and folic acid were started. Baseline tests, including lactate, were within the reported reference range, apart from ammonia of 88.8 micromol/L. Amino acid profiling showed raised methionine and cystathionine; the submitting author interpreted this as suggestive of cystathionine beta-synthase deficiency. The full metabolic profile, total homocysteine and CBS molecular findings were not available. Genetic testing reportedly identified a heterozygous germline CACNA1H variant associated with familial hyperaldosteronism type IV, with aldosterone reported as 52.5 (unit not supplied). Exact variant classification, renin and numerical blood pressure readings were not provided. Growth and development were described as normal. Examination was unremarkable except for hypertension, which persisted despite spironolactone and remained under monitoring.

Conclusion

This case describes an infant with a reported CACNA1H-associated aldosteronism phenotype and a possible coexisting metabolic disorder. The family history warranted integrated metabolic and genetic assessment. Available biochemical data do not independently establish cystathionine beta-synthase deficiency; confirmation requires review of the original metabolic and genetic results. Persistent hypertension required ongoing treatment and follow-up.

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CASE REPORT 02

A Boy with Growth Failure, Short Stature and Micropenis: A Rare Presentation of KATNIP Gene Mutation

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Abstract

A boy evaluated at six months for micropenis, growth failure and dysmorphic features developed central hypothyroidism and growth hormone deficiency by three years. MRI showed pituitary dysgenesis and the molar tooth sign, while reported KATNIP genetic testing supported Joubert syndrome. Levothyroxine, growth hormone and a short testosterone course were followed by improved growth and penile length. The case demonstrates that pituitary deficits can emerge over time in a child with syndromic features.

Keywords: Joubert syndrome; KATNIP; pituitary dysgenesis; growth failure; micropenis

Introduction

Joubert syndrome (JS) is a rare, genetically heterogeneous neurodevelopmental disorder characterized by the "molar tooth sign" on brain MRI, resulting from midbrain-hindbrain malformation. Clinically, JS presents with developmental delay, hypotonia, abnormal eye movements, and distinctive physical features such as a broad forehead, arched eyebrows, ptosis, hypertelorism, low-set ears, triangular-shaped mouth, and sometimes polydactyly. Multi-organ involvement is common, affecting the eyes (e.g., coloboma, retinal dystrophy), kidneys (nephronophthisis, polycystic kidney disease), liver (hepatic fibrosis), skeleton, and endocrine system. Over 35 genes, including AHI1, CEP290, TMEM67, NPHP1, RPGRIP1L, and KATNIP, have been identified, most with autosomal recessive inheritance, classifying JS as a ciliopathy. Although primarily neurological, endocrine abnormalities such as multiple pituitary hormone deficiency (MPHD) are rare, reported in fewer than 5% of cases, with only a handful of documented reports. Early recognition of both neurological and systemic features, including subtle endocrine dysfunction, is critical for timely intervention and optimal outcomes.

Case presentation

A 6-month-old male presented to the endocrine clinic with micropenis and poor weight gain. He was born full-term via cesarean section due to PROM and fetal distress, with an immediate cry and a birth weight of 2.5 kg. Development was unremarkable until 2 months of age, after which the parents noticed failure to gain weight. There was no history of seizures, prolonged jaundice, apnea, infections, lethargy, or constipation. Family history was unremarkable, and the child was the fourth product of a non-consanguineous marriage. On examination, weight and length were both below the 3rd percentile. Dysmorphic features included a broad prominent forehead, right eye ptosis and squint, and polydactyly of the right hand. Genital examination revealed a micropenis (SPL 1.5 cm), hypoplastic scrotum with few rugosities, and bilaterally palpable testes. Developmentally, the child had no neck holding at 6 months.

Investigations

Initial investigations showed normal renal function, normal cell counts, and no abnormalities on pelvic ultrasound or karyotype (46, XY). Hormonal evaluation including cortisol, ACTH, testosterone, and thyroid function was initially normal. The hCG stimulation test showed an adequate testosterone response, ruling out primary hypogonadism. By age 3, the patient continued to exhibit severe growth retardation, developmental and speech delay, and persistent micropenis. Repeat investigations revealed central hypothyroidism (low FT4, low TSH), growth hormone deficiency (markedly reduced IGF-1 and IGFBP-3), with normal cortisol and ACTH levels. MRI brain with pituitary protocol revealed ectopic posterior pituitary, absent pituitary stalk, and small sella, consistent with pituitary dysgenesis. Re-evaluation of MRI identified the molar tooth sign, suggestive of Joubert syndrome, which was confirmed by genetic testing showing a KATNIP gene mutation (autosomal recessive inheritance). The diagnosis of Joubert syndrome with multiple pituitary hormone deficiency (MPHD) was made.

Management and follow-up

The patient was started on thyroxine (50 mcg daily), recombinant growth hormone (Norditropin 0.025 mg/kg/day), and testosterone injections (50 mg IM monthly × 3 doses). Follow-up showed improvement in growth velocity (6 cm/year), penile length (SPL 4 cm), and weight gain of 4 kg. Hormonal profiles including thyroid function, IGF-1, cortisol, and bone age were regularly monitored, and the patient remains under ongoing endocrine follow-up.

Discussion

Joubert syndrome is a rare neurodevelopmental disorder characterized by the molar tooth sign on MRI and commonly presents with developmental delay and dysmorphic features. Although primarily neurologic, endocrine involvement, such as multiple pituitary hormone deficiency (MPHD), can occur due to structural pituitary abnormalities. This case demonstrates the importance of considering central hypothyroidism, growth hormone deficiency, and hypogonadotropic hypogonadism in syndromic children with growth failure and micropenis. Early diagnosis and appropriate hormone replacement led to significant clinical improvement. Genetic confirmation and MRI findings support the diagnosis, highlighting the need for multidisciplinary care in Joubert syndrome.

Conclusion

In a child with syndromic features, growth failure and micropenis, evolving pituitary hormone deficiencies should prompt reassessment of neuroimaging and consideration of an underlying ciliopathy. In this case, recognition of pituitary dysgenesis and the molar tooth sign, followed by genetic confirmation of a KATNIP mutation, supported the diagnosis of Joubert syndrome with multiple pituitary hormone deficiency. Hormone replacement was followed by improvement in growth and penile length.

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CASE REPORT 03

hypercalcaemia, Parathyroid Adenoma and Papillary Thyroid Carcinoma

Anam Fatima; Saira Bashir; Gohar Khan

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Abstract

A 45-year-old woman presenting with pancreatitis was found to have severe PTH-dependent hypercalcaemia. Parathyroid scintigraphy localized a left parathyroid adenoma, while neck ultrasonography unexpectedly identified suspicious thyroid nodules; cytology and subsequent histopathology confirmed papillary thyroid carcinoma. Combined total thyroidectomy and left parathyroidectomy were performed, followed by calcium replacement and thyroid cancer surveillance. The case illustrates the value of systematic thyroid evaluation during the work-up of primary hyperparathyroidism.

Keywords: primary hyperparathyroidism; parathyroid adenoma; papillary thyroid carcinoma; hypercalcaemia

Case presentation

A 45-year-old woman with type 2 diabetes mellitus and hypertension was admitted with epigastric pain and vomiting and treated for pancreatitis. Investigation identified severe hypercalcaemia, which was initially managed in hospital before endocrine outpatient review.

At endocrine outpatient review, the history was revisited with particular attention to symptoms, causes and associations of hypercalcaemia. On detailed history, she informed us about the constipation and intermittent abdominal pains for last six to eight months, general body aches, weakness and fatigue. There was no history of chronic kidney disease, chronic granulomatous disease, or substantial use of antacids, calcium, vitamin D, lithium, diuretics, or any other over-the-counter, herbal, or homeopathic treatments. Moreover, there was also no history of any noteworthy weight loss, cough or haemoptysis, headaches, flushing, palpitations, episodic hypertension, visual problems, or seizures. Family history was also insignificant for hyperparathyroidism, pheochromocytoma, medullary thyroid carcinoma, and pancreatic tumours.

After detailed examination, BMI was 27 kg/m², BP 130/80 mmHg, pulse 84/min, RR 16/min, and she was afebrile. There was also no neck swelling, lymphadenopathy, pedal oedema, or other significant findings on general physical assessment and examination. Chest, CNS and cardiovascular examinations were unremarkable. Abdomen was soft with moderate epigastric tenderness.

hypercalcaemia was confirmed, and a workup was initiated to find out the cause of hypercalcaemia. Parathyroid hormone (PTH) was elevated on repeated measurement, establishing PTH-dependent hypercalcaemia. Neck ultrasonography and parathyroid scintigraphy were planned. Parathyroid scintigraphy demonstrated a left parathyroid adenoma.

Interestingly, ultrasound neck also revealed multiple thyroid nodules that were not clinically palpable. The nodules were suspicious of TI-RADS 4 category. FNAC of suspicious thyroid nodule was subsequently performed and it revealed papillary thyroid carcinoma.

In view of the concomitant left parathyroid adenoma and papillary thyroid carcinoma, total thyroidectomy and left parathyroidectomy were planned. Histopathological examination of the thyroid specimen confirmed papillary thyroid carcinoma, classic variant. The patient was subsequently followed with thyroid malignancy surveillance, including serial thyroglobulin, anti-thyroglobulin antibody, TSH and ultrasound neck assessment.

Investigations

The initial laboratory evaluation demonstrated significant hypercalcaemia, while renal and hepatic parameters remained within their stated reference ranges. Normal albumin further supported the significance of the elevated measured calcium level.

Calcium concentrations

Calcium was markedly elevated at admission and remained elevated after discharge. Before surgery, calcium had decreased to 10.5 mg/dL, indicating substantial biochemical improvement following initial management prior to definitive surgical treatment.

Postoperative investigations

Post-operative investigations showed hypocalcaemia and elevated TSH. Thyroglobulin remained within the stated reference range, while anti-thyroglobulin antibodies were elevated, necessitating continued biochemical and imaging surveillance during follow-up.

Parathyroid scintigraphy showed evidence of a left parathyroid adenoma. Ultrasound neck demonstrated a multinodular goitre including several TR4 moderately suspicious nodules and one TR1 benign nodule. FNAC and histopathology subsequently confirmed papillary thyroid carcinoma, classic variant (THY5 malignant). The final diagnosis was papillary thyroid carcinoma and left parathyroid adenoma.

Management and follow-up

The patient underwent total thyroidectomy and left parathyroidectomy on 5 August 2025.

Post-operatively, calcium replacement was initiated, and she was referred to oncology and nuclear medicine for further management. A diagnostic radioactive iodine

scan was planned four weeks after surgery. The scan demonstrated residual disease, and radioactive iodine ablation was planned.

The patient was started on thyroxine, with a plan to withhold it one month before ablation.

Thyroglobulin and anti-thyroglobulin antibody levels were advised four weeks after surgery. Ongoing follow-up includes thyroglobulin levels, neck ultrasound and TSH monitoring.

Discussion

This case illustrates an important diagnostic sequence in a patient presenting with significant hypercalcaemia, ultimately leading to the identification of a left parathyroid adenoma coexisting with papillary thyroid carcinoma (PTC). The initial presentation was dominated by epigastric pain and vomiting, for which the patient was initially managed as a case of pancreatitis. The subsequent discovery of marked hypercalcaemia prompted further endocrine evaluation. Serum calcium was 15.9 mg/dL at admission and remained elevated at 14 mg/dL after discharge, despite preserved renal function and normal albumin levels.

The subsequent workup focused on determining the underlying cause of PTH-dependent hypercalcaemia. Parathyroid scintigraphy localized a left parathyroid adenoma. During the accompanying evaluation of the neck, ultrasonography unexpectedly revealed multiple thyroid nodules that were not clinically palpable. Several nodules were classified as TI-RADS 4 and therefore underwent fine-needle aspiration cytology (FNAC). Cytological examination was suggestive of papillary thyroid carcinoma, which was subsequently confirmed on histopathological examination following surgery.

The coexistence of a parathyroid adenoma and PTC presented an additional diagnostic and therapeutic challenge. Definitive treatment consisted of total thyroidectomy and left parathyroidectomy. Following surgery, serum calcium decreased to 7.7 mg/dL, necessitating calcium replacement. The postoperative thyroid profile showed an elevated TSH of 13 mU/L. Thyroglobulin was 1.15 ng/mL, while anti-thyroglobulin antibodies were elevated at 156 IU/mL. Subsequent

radioactive iodine imaging demonstrated residual disease, for which radioactive iodine ablation was planned, with continued biochemical and imaging surveillance.

The reported prevalence of thyroid carcinoma among patients with hyperparathyroidism varies considerably across published studies, ranging from 2.8% to 47.1%, with PTC being the predominant histological subtype. Several studies have reported an association between primary hyperparathyroidism and PTC, although the underlying mechanism remains incompletely understood.

PTC has also been reported in patients with both primary and secondary hyperparathyroidism, frequently presenting as papillary thyroid microcarcinomas. Although many of these lesions are small, some may demonstrate clinically relevant or aggressive pathological features. These findings support careful evaluation of the thyroid gland during the assessment and surgical management of patients with hyperparathyroidism.

This case highlights the importance of comprehensive neck imaging in patients undergoing evaluation for primary hyperparathyroidism, particularly because clinically silent thyroid nodules may coexist with parathyroid disease. In the present patient, thyroid ultrasonography performed as part of the preoperative neck evaluation led to the detection of otherwise non-palpable thyroid nodules, ultimately resulting in the diagnosis of PTC. A subsequent review of the literature demonstrated a documented association between parathyroid adenoma and PTC, emphasizing the importance of maintaining clinical vigilance for concomitant thyroid pathology in patients with hyperparathyroidism.

Conclusion

This case demonstrates how investigation of significant PTH-dependent hypercalcaemia led to the diagnosis of a left parathyroid adenoma and unexpectedly revealed coexisting papillary thyroid carcinoma, highlighting the importance of careful evaluation of every patient to look for the hidden associated disease.

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CASE REPORT 04

Five Years of Pain, One Missed Clue: A Diagnostic Journey

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Abstract

A 51-year-old woman had five years of severe recurrent abdominal pain, vomiting, systemic symptoms and nalbuphine dependence. Repeated gastrointestinal investigations and cholecystectomy did not relieve symptoms, which were subsequently attributed to substance dependence and psychiatric illness. Reassessment identified hypercalcaemia up to 13.2 and PTH 217 (reference 15-68), with units not provided. Imaging showed a parathyroid adenoma. Parathyroidectomy was followed by improved pain, function and reduced analgesic requirements. The case highlights the risk of attribution bias and the value of metabolic reassessment.

Keywords: primary hyperparathyroidism; hypercalcaemia; abdominal pain; parathyroid adenoma

Case presentation

A 51-year-old female presented with a long-standing history of recurrent severe abdominal pain over five years, associated with vomiting, generalised body aches, and mood disturbances. During this period, she developed dependence on nalbuphine for pain control.

She was repeatedly treated for acute pancreatitis and chronic biliary pain, ultimately undergoing cholecystectomy without symptomatic relief. Additionally, she underwent two upper gastrointestinal endoscopies, both of which were inconclusive.

Despite persistent and debilitating symptoms, her clinical picture was increasingly attributed to drug-seeking behaviour and possible somatization. This led to psychiatric admission for suspected substance dependence and depressive symptoms. Notably, a comprehensive metabolic evaluation had not been performed during prior healthcare encounters.

Investigations

During a subsequent evaluation, a more holistic approach was undertaken. Investigations revealed:

Persistent hypercalcaemia up to 13.2 (unit not supplied).

PTH was 217 (reference 15-68; unit not supplied).

These findings were diagnostic of primary hyperparathyroidism.

Further imaging confirmed the presence of a parathyroid adenoma.

Retrospective review of her clinical course suggested that her recurrent abdominal pain, generalised body aches, and neuropsychiatric symptoms were manifestations of prolonged untreated hyperparathyroidism.

Management and follow-up

The patient underwent definitive surgical management with parathyroidectomy. Following surgery, she experienced:

Marked improvement in abdominal pain

Resolution of systemic symptoms

Significant reduction in analgesic requirements

Her overall functional status improved considerably, with decreased reliance on healthcare services.

Discussion

This case illustrates the diagnostic challenges posed by the overlap between endocrine disorders and substance dependence.

Primary hyperparathyroidism is an endocrine disorder characterized by inappropriate secretion of parathyroid hormone leading to hypercalcaemia and multisystem involvement. It classically presents with "stones, bones, abdominal groans, and psychic overtones," reflecting renal, skeletal, gastrointestinal, and neuropsychiatric manifestations (1). However, its protean clinical features often lead to delayed or missed diagnosis, particularly when symptoms overlap with more common gastrointestinal or psychiatric conditions.

Gastrointestinal manifestations include recurrent abdominal pain, nausea, vomiting, constipation, and pancreatitis (2,3). neuropsychiatric symptoms such as fatigue, mood disturbances, and cognitive impairment are also well documented and may be misinterpreted as primary psychiatric illness (1,2). In this case, the patient's chronic abdominal pain and vomiting led to repeated hospitalizations, extensive gastrointestinal evaluation, and even cholecystectomy without symptomatic relief.

A key diagnostic challenge was the coexistence of nalbuphine dependence, which contributed to attribution bias and labeling of the patient's symptoms as drug-seeking behaviour or somatization. Such bias may delay appropriate investigation of organic pathology and result in prolonged morbidity (5). Chronic pain itself, when inadequately treated, may also contribute to opioid dependence, further complicating clinical interpretation.

hypercalcaemia plays a central role in symptom generation, causing gastrointestinal dysmotility, constipation, abdominal discomfort, and in some cases pancreatitis (3,4). Neurocognitive effects may further contribute to functional decline and increased analgesic use. In this patient, persistent symptoms likely reflected long-standing untreated hypercalcaemia.

This case underscores the importance of early metabolic evaluation in patients with unexplained chronic abdominal pain and neuropsychiatric features. A simple serum calcium test, if performed earlier, could have prevented years of diagnostic delay and unnecessary interventions.

Definitive surgical management resulted in marked symptomatic improvement, highlighting the reversible nature of the condition when appropriately diagnosed.

Conclusion

Primary hyperparathyroidism should be considered in patients presenting with recurrent, unexplained abdominal pain, neuropsychiatric symptoms, and especially when hypercalcaemia is present. Early recognition and appropriate evaluation can prevent unnecessary procedures, reduce morbidity, and avoid mislabeling patients with psychiatric or substance use disorders.

Learning points

- In patients with chronic, unexplained pain and frequent healthcare utilization, it is crucial to reassess the diagnosis and consider underlying metabolic or endocrine disorders.
- A comprehensive and empathetic approach can uncover reversible causes and significantly alter patient outcomes.

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CASE REPORT 05

Persistent TSH Suppression Following Total Thyroidectomy in Refractory TRAb-Negative Hyperthyroidism: A Diagnostic Dilemma

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Abstract

Persistent suppression of thyroid-stimulating hormone (TSH) following total thyroidectomy is uncommon and presents a diagnostic challenge, particularly when structural imaging demonstrates no residual thyroid tissue. Potential explanations include prolonged hypothalamic-pituitary suppression, residual functioning thyroid tissue, ectopic thyroid hormone production, or assay interference. We report a rare case of refractory TRAb-negative hyperthyroidism characterized by discordant radionuclide imaging, failure of repeated radioactive iodine (RAI) therapy, and persistent postoperative TSH suppression despite apparent complete thyroid ablation.

Keywords: hyperthyroidism; TSH suppression; thyroidectomy; diagnostic dilemma

Case presentation

A 34-year-old man presented with palpitations and marked weight loss from 110 kg to 81 kg.

Initial biochemical evaluation demonstrated severe thyrotoxicosis with TSH 0.0008 (unit recorded as mIU/mL; original laboratory report unavailable) (0.4-4.2), total T3 753.81 ng/dL (70-204), and T4 >30 µg/dL (4.6-10.5). Thyrotropin receptor antibodies (TRAb) were negative. Radioiodine uptake imaging demonstrated diffuse increased uptake consistent with diffuse toxic goitre. However, Tc-99m thyroid scintigraphy showed minimal thyroid uptake (0.1%), with tracer activity predominantly within the salivary glands and surrounding soft tissues. The findings were attributed to rapid tracer turnover, a phenomenon rarely reported in severe Graves' disease.

Despite treatment with carbimazole and propranolol, hyperthyroidism remained difficult to control. Two courses of RAI therapy failed to achieve remission. Subsequent I-131 whole-body scintigraphy demonstrated diffuse uptake confined to the thyroid gland without evidence of ectopic iodine-avid tissue. Owing to persistent disease, total thyroidectomy was performed in August 2025. Postoperative ultrasonography did not identify residual thyroid tissue.

Following surgery, the patient developed hypothyroidism and commenced levothyroxine replacement. Six months later, he re-presented with lethargy, body aches, and palpitations.

Thyroid function testing suggested over-replacement, prompting progressive dose reduction and eventual discontinuation of levothyroxine. Surprisingly, repeat testing performed six weeks after complete withdrawal continued to demonstrate suppressed TSH despite normalisation of free thyroxine levels. Repeat ultrasonography again failed to identify residual thyroid tissue, while anti-thyroglobulin antibodies were negative.

Discussion

This case highlights several unusual features, including TRAb-negative Graves'-like hyperthyroidism, marked discordance between radioiodine and Tc-99m imaging, resistance to two courses of RAI therapy, and persistent TSH suppression following total thyroidectomy.

Rapid tracer turnover was proposed in the original account as an explanation for the discordant scans and poor RAI response; the supplied data do not establish this mechanism.

The most significant diagnostic challenge emerged following thyroidectomy. Persistent TSH suppression may reflect delayed recovery of pituitary thyrotrope function after prolonged severe thyrotoxicosis. However, this explanation alone may not fully account for the persistence of normal free thyroxine concentrations following complete withdrawal of levothyroxine replacement. Residual functioning thyroid tissue remains a plausible explanation, particularly because microscopic thyroid remnants may not be detected by ultrasonography alone. Functional radionuclide imaging may be more sensitive for identifying metabolically active residual thyroid tissue.

This case raises important clinical questions regarding the optimal evaluation of persistent TSH suppression after definitive treatment of hyperthyroidism. Should postoperative radionuclide imaging be routinely considered when biochemical findings appear discordant with structural imaging? Can markedly reduced Tc-99m uptake serve as a marker of accelerated iodine turnover and predict failure of radioactive iodine therapy? Finally, how should clinicians distinguish delayed hypothalamic-pituitary recovery from occult residual thyroid function in patients who remain biochemically atypical following apparently complete thyroid ablation?

Conclusion

Persistent TSH suppression after definitive treatment requires serial biochemical review and assessment for delayed pituitary recovery, residual thyroid function and analytical interference. Structural ultrasonography alone does not exclude a microscopic functional remnant. The cause remained unresolved in the supplied record.

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CASE REPORT 06

Refractory hypocalcaemia Due to Hypoparathyroidism Presenting with neuropsychiatric Manifestations and Intracranial Calcification

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Abstract

A patient with refractory hypocalcaemia due to hypoparathyroidism presented with prominent neuropsychiatric manifestations and intracranial calcification. Biochemical evaluation and imaging established the endocrine basis of the presentation. The case emphasizes that chronic hypocalcaemia may present beyond classic neuromuscular symptoms and that recognition of the underlying parathyroid disorder is essential for appropriate replacement and long-term monitoring.

Keywords: hypoparathyroidism; refractory hypocalcaemia; intracranial calcification; neuropsychiatric manifestations

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Case presentation

A 35-year-old male, a known case of schizophrenia for the last 10 years, was referred from the psychiatry ward to the emergency room with generalised tonic-clonic seizures, fever, and ear discharge for one day. He was intubated in the ER and shifted to the MICU. Endocrinology was consulted due to severe hypocalcaemia at presentation.

According to family, behavioural changes started 10 years back when the patient became socially withdrawn and was diagnosed with schizophrenia and managed with antipsychotic therapy. For the last 3 years, he developed generalised tonic-clonic seizures and was started on antiepileptic treatment without workup. Family also noticed a progressive, unsteady gait over the last 2 years, which was attributed to psychiatric illness. There was no history of palpitations, syncope, arrhythmias, cataracts, hair loss, skin or nail changes, or chronic diarrhoea.

Drug history included quetiapine, clonazepam, brivaracetam, divalproex sodium, and eslicarbazepine acetate.

There was no history of neck surgery, thyroid/parathyroid surgery, radiation exposure, or prior hospitalizations. He was the eldest among four siblings and had no clear family history suggestive of an inherited hypocalcemic or syndromic disorder.

On examination at admission, the patient was sedated, intubated, and mechanically ventilated. No dysmorphic features or cataracts were noted. Classical signs of neuromuscular irritability could not be assessed initially due to sedation.

After extubation, the patient remained conscious but disoriented with intermittent irrelevant speech. No obvious focal neurological deficit was identified on gross examination.

Investigations

Initial investigations showed severe hypocalcaemia with serum calcium 4.8 mg/dL (8.5-10.5 mg/dL), elevated phosphate 6.5 mg/dL (2.5-4.5 mg/dL), magnesium 2.53 mg/dL, and low intact parathyroid hormone level 7 pg/mL (15-65 pg/mL), consistent with hypoparathyroidism. Vitamin D level was markedly low at 6 ng/mL. Serum albumin was 3.8 g/dL. Thyroid profile and serum cortisol were within the normal range. Serum ceruloplasmin was normal.

CT brain and MRI brain demonstrated multiple punctate calcific foci scattered bilaterally in cerebral parenchyma, including basal ganglia, consistent with intracranial calcification secondary to chronic hypocalcaemia.

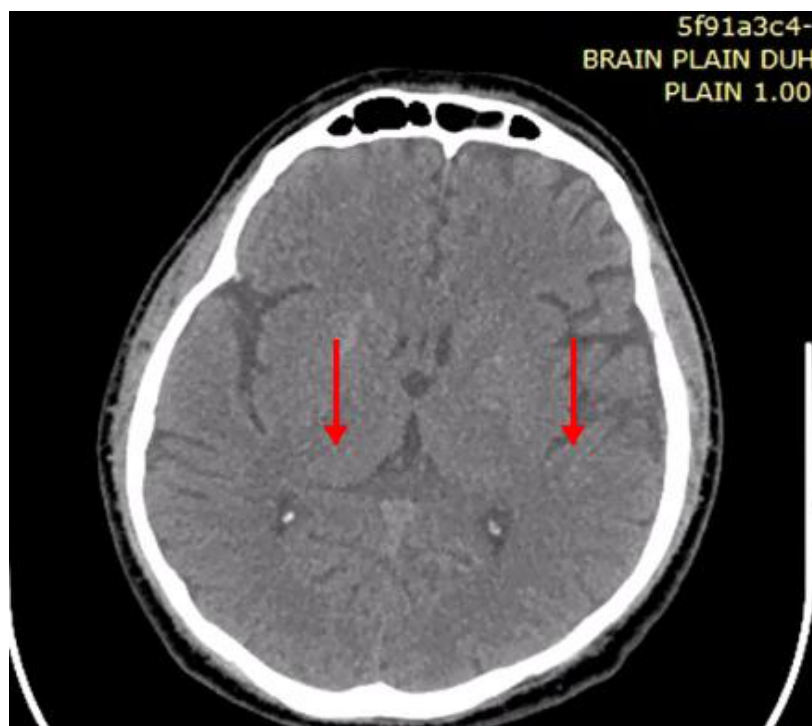


Figure 1. Brain CT showing bilateral intracranial calcification in the reported case.

Management and follow-up

The patient was initially treated with continuous intravenous calcium gluconate infusion, oral alfacalcidol, calcium carbonate with vitamin D supplementation, intramuscular vitamin D replacement, and hydrochlorothiazide.

Subsequently, repeat investigations on 17th March 2026 showed recurrent hypocalcaemia with calcium 6.4 mg/dL and worsening hypomagnesaemia, 1.26 mg/dL, despite ongoing treatment. Although serum magnesium was initially normal, recurrent hypomagnesaemia developed during hospitalization and likely contributed to persistent calcium instability.

Doses of alfacalcidol, calcium supplementation, hydrochlorothiazide, and magnesium replacement were escalated. Following optimization of magnesium replacement and increasing hydrochlorothiazide dose calcium levels became more stable after 28th April 2026, permitting stepwise reduction of therapy to oral magnesium and Caltrate, each recorded as one tablet twice daily (tablet strengths not supplied) by May 2026.

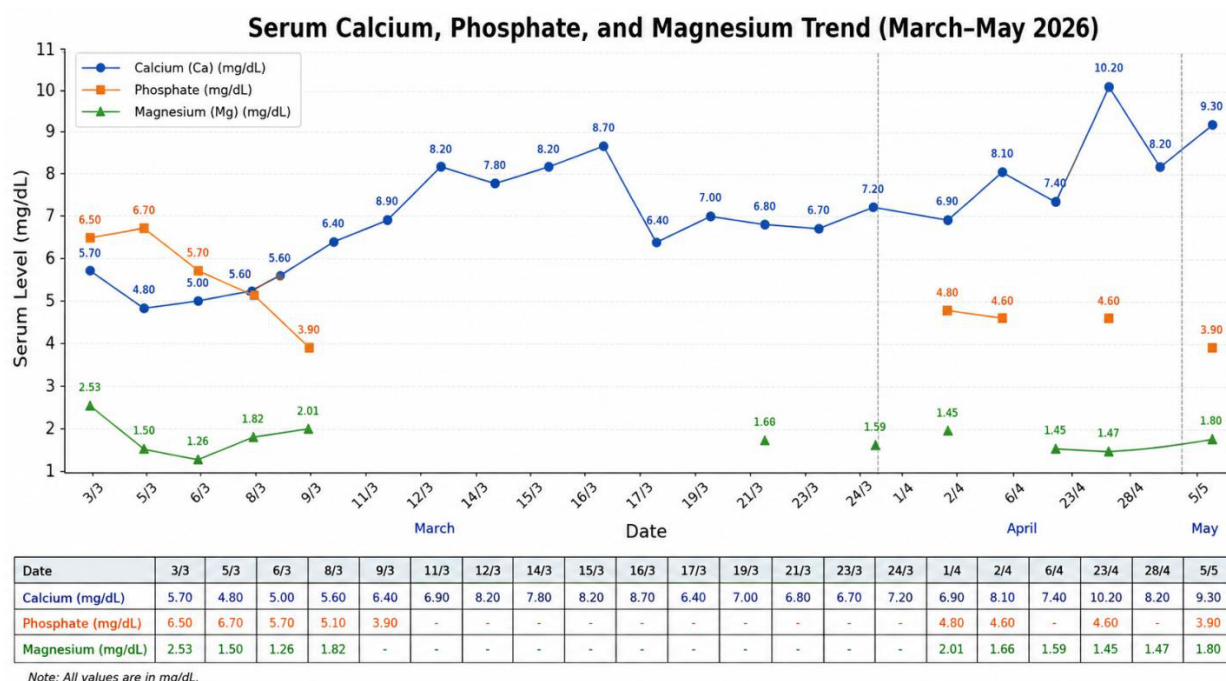


FIGURE 2: Graphical trend analysis demonstrated severe fluctuating hypocalcaemia during the early disease course, associated with recurrent hypomagnesaemia and hyperphosphataemia. Following aggressive magnesium replacement and optimization of calcium/vitamin D therapy, serum calcium levels became relatively stable from late April onward, allowing gradual de-escalation of calcium supplementation."

Discussion

Hypoparathyroidism is an endocrine disorder characterized by hypocalcaemia with inappropriately low or absent parathyroid hormone levels (1). It is considered a rare disorder and may occur secondary to postsurgical causes, autoimmune destruction, genetic abnormalities, infiltrative disorders, or severe magnesium disturbances (2).

Our patient presented with long-standing neuropsychiatric manifestations, including schizophrenia-like symptoms, seizures, gait abnormalities, and intracranial calcifications. Chronic hypocalcaemia is known to cause neuropsychiatric symptoms, extrapyramidal manifestations, seizures, and basal ganglia calcification. The delayed diagnosis in this patient likely contributed to the progression of neurological complications.

The biochemical profile showed severe hypocalcaemia with hyperphosphataemia and low PTH, confirming hypoparathyroidism. The presence of recurrent hypomagnesaemia further complicated management. Magnesium plays a crucial role in PTH secretion and peripheral responsiveness to PTH (3). Persistent hypomagnesaemia can therefore worsen hypocalcaemia and render patients refractory to calcium replacement therapy (4). In this patient, transient improvement in serum calcium was followed by recurrent decline despite aggressive calcium and vitamin D replacement, likely related to ongoing magnesium deficiency.

Conventional treatment of hypoparathyroidism includes oral calcium supplementation together with activated vitamin D analogs such as calcitriol or alfacalcidol. Adequate magnesium replacement is essential (5). Thiazide diuretics may help reduce urinary calcium losses in selected patients. However, some patients remain difficult to control despite optimized conventional therapy (6).

The differential diagnosis in this patient includes autoimmune hypoparathyroidism and genetic causes such as CASR mutation, mitochondrial disorders, or syndromic hypocalcaemia. The presence of bilateral basal ganglia calcification raises consideration of Fahr syndrome secondary to chronic hypocalcaemia. Primary familial brain calcification was considered less likely in view of the biochemical evidence of hypoparathyroidism.

Lack of surgical history and relatively young age raise suspicion for nonsurgical etiologies including autoimmune or genetic hypoparathyroidism (7). Genetic workup may be considered if feasible, particularly in view of refractory disease and neurological manifestations.

Current international guidelines recommend considering recombinant PTH therapy in patients with chronic hypoparathyroidism who remain symptomatic or biochemically uncontrolled despite optimized conventional therapy (8). Indications include persistent symptomatic hypocalcaemia, fluctuating calcium levels, hyperphosphataemia, renal complications, hypercalciuria, reduced quality of life, or the requirement of high doses of calcium and active vitamin D (8).

This case underscores the importance of screening serum calcium in patients presenting with unexplained neuropsychiatric manifestations, seizures, or extrapyramidal symptoms, particularly when associated with intracranial calcification.

Conclusion

Chronic hypocalcaemia due to hypoparathyroidism may present with predominant neuropsychiatric manifestations leading to delayed diagnosis. Refractory hypocalcaemia should prompt evaluation for coexisting hypomagnesaemia, which may impair both PTH secretion and responsiveness to therapy. Early recognition and aggressive correction are essential to prevent irreversible neurological complications.

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CASE REPORT 07

Ectopic ACTH Syndrome

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Abstract

A 33-year-old woman with diabetes, hypertension and overt Cushingoid features was evaluated for ACTH-dependent hypercortisolism. Dexamethasone testing remained unsuppressed, ACTH was elevated, and initial pituitary and cross-sectional imaging did not identify a definitive source. Her course was complicated by acute respiratory deterioration while further localisation was pending. The case illustrates the diagnostic and therapeutic challenges of occult ectopic ACTH syndrome.

Keywords: ectopic ACTH syndrome; Cushing syndrome; hypercortisolism; DOTATATE PET

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Case presentation

A 33-year-old woman with diabetes and hypertension diagnosed six months earlier and untreated compensated hepatitis C for three years presented with one week of high-grade fever and productive cough. Sputum was scant and yellow, with no diurnal variation. She also had breathlessness on minimal exertion.

She reported recurrent chest infections over the preceding year, progressive unquantified weight gain despite a normal appetite, lower back pain, difficulty walking, amenorrhoea and hirsutism for two years. Previous admissions had not led to a detailed endocrine evaluation.

She used hakimi medication after developing these symptoms for pain relief. She denied any headaches, visual changes, chronic pulmonary disease, or allergies.

On examination, her blood pressure was 150/95, with overt Cushingoid features including puffy face with plethora, hirsutism, supraclavicular and dorsocervical fat pads and marked central obesity. She had bruise marks at multiple sites as well as abdominal striae. Also had proximal weakness and spinal tenderness. Her systemic examination was unremarkable.

Overnight, low-dose and high-dose dexamethasone suppression tests showed unsuppressed cortisol, with elevated ACTH supporting ACTH-dependent hypercortisolism. An ectopic case was suspected but remained unconfirmed; pituitary MRI and cross-sectional imaging did not localise a definitive source.

While further investigation was pending, she developed sudden breathlessness and tachycardia requiring intubation. Anticoagulation was started for suspected pulmonary embolism. She was extubated after three days, but worsening biochemical abnormalities limited further treatment and investigation.

Cabergoline 0.5 mg weekly was started as a temporising treatment in the reported case.

DOTATATE PET was pending at the time of reporting.

The treating team planned symptom control while continuing source localisation.

Investigations

Endocrine tests

Test	Result	Interpretation
Overnight Dexamethasone Suppression Test (ODST)	37 µg/dL	Unsuppressed
Low-Dose Dexamethasone Suppression Test (LDDST)	20 µg/dL	Unsuppressed
ACTH	58 pg/mL	Raised
High-Dose Dexamethasone Suppression Test (HDDST)	26 µg/dL	Unsuppressed

Imaging

MRI BRAIN (pituitary protocol): unremarkable

CT CHEST (WITH CONTRAST):

Small nodular opacities (4*5 mm) in posterior segment of rt upper lobe.

A small fibrotic band in post segment of rt lower lobe, findings consistent with acute or chronic pulmonary infection.

CT ABDOMEN AND PELVIS: Hepatomegaly with hepatic steatosis. Mildly enlarged adrenal glands.

Other investigations

General investigation	Result	Endocrine or relevant investigation	Result
Hemoglobin (Hb)	10.2 g/dL	TFT	Normal
WBC Count	8 ×10 ⁹ /L (Neutrophils 90%)	LH	0.9 mIU/mL
Creatinine	0.8 mg/dL	FSH	0.4 mIU/mL
Sodium	142 mmol/L	Testosterone	0.5 ng/mL (Ref: 0.08- 0.4)
Potassium	2.5 mmol/L	Estradiol	26 pg/mL
Total Bilirubin	0.8 mg/dL	Prolactin	23 ng/mL
ALT	303 U/L	DHEA	120 µg/dL (Normal)
AST	110 U/L	BMD T-score (reported)	T-score: -2.6
ALP	800 U/L	Sputum AFB/GeneXpert	Negative
GGT	1400 U/L		
Hepatitis C PCR	Detected		

Investigation	Result
BMD T-score (reported)	-2.6
HbA1c	7.2%
Echocardiography (ECHO)	Ejection Fraction (EF): 45-50%, with diastolic dysfunction

Discussion

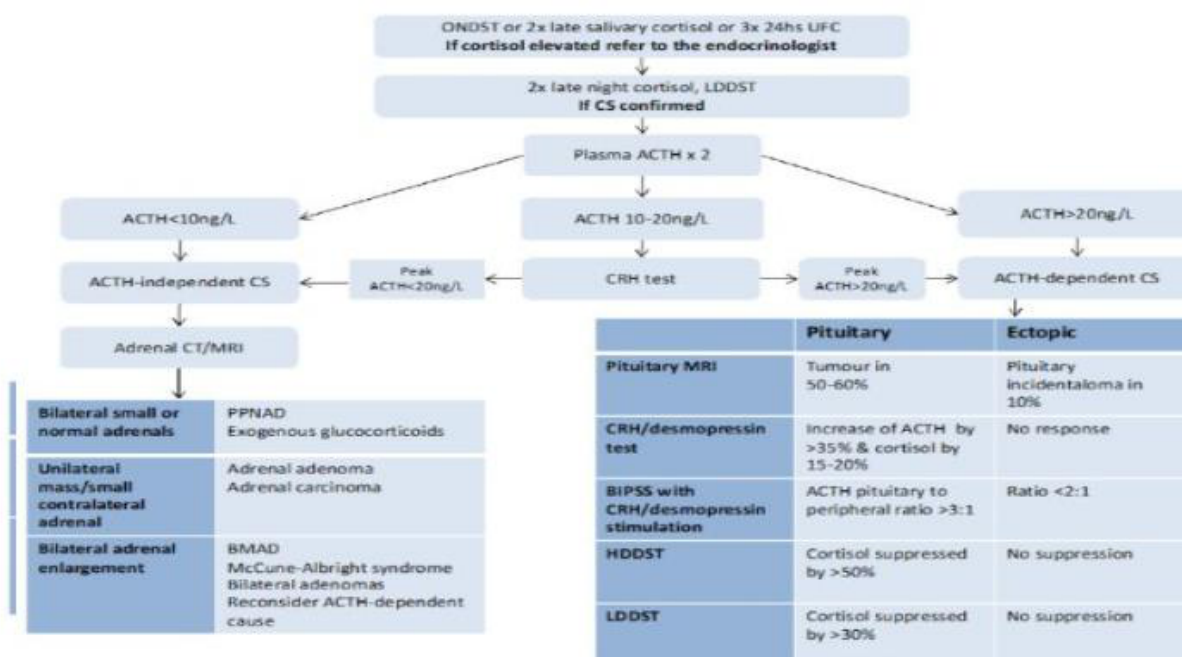
Ectopic ACTH secretion accounts for a subset of ACTH-dependent Cushing syndrome. The lung is a common source; other possibilities include thymic and gastrointestinal neuroendocrine tumours, medullary thyroid carcinoma and pheochromocytoma.

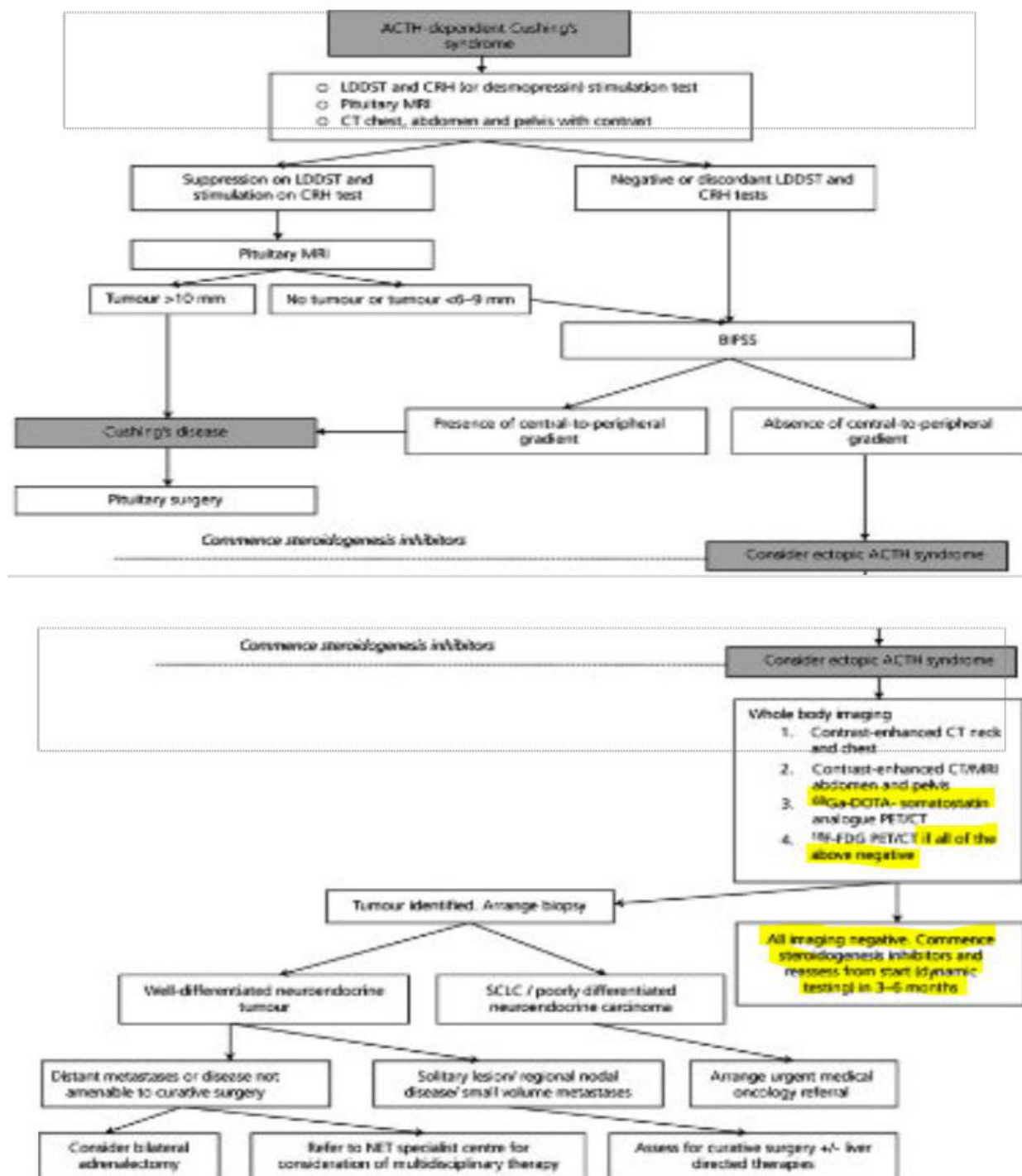
The lung is the most commonly reported site, followed by thymic tumours, medullary thyroid carcinoma, pheochromocytoma, gastrointestinal neuroendocrine tumours and adenocarcinoma.

In thorax now NETS are the most common cause, and being slow growing they may present like classical Cushing Disease rather than the typical, acute and aggressive presentation associated with Ectopic ACTH secreted by malignant tumours.

Lung tumours remain the major occult source, although this may take many years to become apparent.

Diagnostic approach





Management and follow-up

Occult ECS:

Medical therapy combined with continued imaging every 6 to 12 months

ECS with a visible resectable tumour:

Surgery.

Medical treatment with a rapid dose escalation to control severe hypercortisolism while awaiting surgery.

ECS WITH METASTATIC TUMOR:

medical treatment

debulking surgery, ablation techniques, chemotherapy.

Bilateral adrenalectomy.

Conclusion

This patient had ACTH-dependent hypercortisolism with an occult source. Non-suppression on high-dose dexamethasone and negative pituitary MRI do not independently establish ectopic ACTH secretion. Further localisation and control of severe cortisol excess remained priorities; no final source or long-term outcome was supplied.

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CASE REPORT 08

Acromegaly with a Suspected Ectopic Source

Dr Ehtisham**Abstract**

This case examines acromegaly in which the biochemical and clinical phenotype raised concern for a non-pituitary or ectopic source. The diagnostic work-up illustrates the importance of integrating growth hormone/IGF-1 assessment with targeted imaging when the usual pituitary explanation is not established. The report focuses on the localisation challenge and the need for stepwise endocrine evaluation.

Keywords: acromegaly; growth hormone excess; ectopic source; endocrine imaging

Case presentation

A 49-year-old male engineer from Islamabad was referred by a neurosurgical clinic after coarse facial features were noticed during assessment of neck pain.

Neck pain had begun suddenly two weeks earlier, was sharp and non-radiating, worsened with movement and temporarily improved with simple analgesics. There was no preceding trauma or heavy lifting. NSAIDs and muscle relaxants had been prescribed.

He reported longstanding excessive sweating, including in winter, and snoring without frequent nocturnal waking, early morning headache or daytime somnolence. He had not noticed physical changes or an increase in shoe size and did not wear rings.

He denied headache, visual symptoms, joint pain, hand numbness, erectile dysfunction, reduced libido, exertional dyspnoea or orthopnoea. There was no known new diabetes or hypertension.

He reported no altered bowel habit, palpitations, weight change, temperature intolerance, unusual fatigue, polydipsia or polyuria.

On examination

Vitals were normal

BMI was 26.88 kg/m², height 185 cm and weight 92 kg.

He had coarse facial features with prominent eyebrows, cheeks. Prognathism, deep nasal furrows, large nose, increased interdental spaces, enlarged tongue and prominent forehead folds and large lips.

There was no reported visual-field defect or thyroid enlargement.

JVP was not elevated and chest was clear on auscultation.

There was no proximal myopathy or carpal tunnel syndrome.

Investigations

HbA1C 5.6%

TSH 0.82 uIU/ml, FT4 1.4 ng/dL

PROLACTIN 9 ng/mL

(8 am) CORTISOL 11 ug/dL

TESTOSTERONE: 205 ng/dL

IGF-1: 509.90 ng/mL (68 - 225)

OGTT was done

Growth Hormone: 3.89 ng/mL (1 hour) ADULT Male: 0.03 - 2.47

Growth Hormone: 3.25 ng/mL (2 hours)

Second OGTT done a few months back

Growth Hormone: 5.90 ng/mL (1 hour)

Growth hormone: 6.3 ng/ml (2 hours)

MRI PITUITARY FOSSA Partially empty sella with thinned out pituitary gland. No sellar or suprasellar mass. Optic nerve, chiasm and tracts are within normal limits

CT Chest with contrast: Few sub centimetric lymph nodes in mediastinal and hilar region. Gravity dependent bibasilar congestive changes are seen. A nodule is seen in the left lung along the fissure measuring 4.5 mm in image 3-127. Tiny calcified nodules are seen in the right lower lobe in image 3-140 and 3-115. No suspicious pulmonary nodule or focal consolidation seen. Few atelectatic bands are seen in the left inferior lingular segment and in both lower lobes.

CT ABDOMEN AND PELVIS: Mild hepatomegaly with fatty infiltration, prominence of central biliary ducts and CBD, tapering smoothly at the ampulla. Suggestion of subtle density within the distal CBD near the ampulla. Few sub centimetric lymph nodes.

Ga-68-TATE PET-CT Scan DOTA avid lesion in right lung and mild DOTA avid mediastinal lymph nodes concerning for ectopic tumour.

Management and follow-up

The patient was treated with octreotide (Sandostatin), with oncology input to consider resection of the suspected ectopic lesion. A lung lesion associated with ectopic GHRH or, more rarely, GH secretion remained a working hypothesis; tissue confirmation and GHRH measurement were not supplied.

Discussion

Raised IGF-1 and failure of GH suppression supported acromegaly. A pituitary MRI without a visible mass prompted investigation for an ectopic source. DOTATATE avidity identified a possible pulmonary target but did not establish hormone secretion or tumour histology. Ectopic acromegaly is more commonly attributed to GHRH than direct GH secretion; biochemical and pathological confirmation are needed to characterise the source.

Conclusion

Acromegaly with no visible pituitary tumour requires careful source localisation. The suspected pulmonary source in this case remained unconfirmed while medical therapy and multidisciplinary planning continued.

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CASE REPORT 09

Aromatase Deficiency in 46, XX Individuals Mimicking Congenital Adrenal Hyperplasia: Diagnostic Challenges in a Resource-Limited Setting

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Abstract

Background: Aromatase deficiency is a rare autosomal recessive disorder caused by loss-of-function variants in CYP19A1, the gene encoding the enzyme that converts androgens to oestrogens. In 46, XX infants it causes genital virilisation and is easily mistaken for congenital adrenal hyperplasia (CAH). **Case presentation:** We describe two 46, XX patients treated as CAH from infancy. The first, now 19 years 9 months old, had primary amenorrhoea, absent thelarche, FSH 82.2 mIU/L, LH 37.2 mIU/L, estradiol <5 pg/mL, raised androstenedione and a bone age of 11-12 years. The second, an infant, had normal 17-hydroxyprogesterone on follow-up and a homozygous likely pathogenic CYP19A1 variant on genetic testing. **Conclusion:** Aromatase deficiency should be considered in virilized 46, XX infants when CAH biochemistry does not fit. Earlier recognition avoids years of unnecessary glucocorticoid in case labelled as CAH and allows timely oestrogen replacement for growth and bone health.

Keywords: aromatase deficiency; CYP19A1; 46,XX DSD; congenital adrenal hyperplasia; hypergonadotropic hypogonadism

Introduction

Aromatase converts androstenedione and testosterone to estrone and estradiol in gonadal and extra-gonadal tissues. In 46, XX individuals its deficiency causes virilisation in utero and, later, loss of oestrogen feedback on the hypothalamic-pituitary axis, with hypergonadotropic hypogonadism, delayed epiphyseal fusion and primary amenorrhoea. Because the newborn has ambiguous genitalia, the usual first diagnosis is CAH due to 21-hydroxylase deficiency. Normal or suppressed 17-hydroxyprogesterone (17-OHP) and the absence of cortisol deficiency should prompt reconsideration. We report two such patients.

Case presentation

Case 1. A 19-year-9-month-old woman presented with primary amenorrhoea and excessive weight gain. She was born with atypical genitalia, and her mother had virilized during the pregnancy. She was the second child of non-consanguineous parents with no family history of disorders of sex development. Mildly raised 17-OHP and a transient electrolyte disturbance in infancy led to a presumptive diagnosis of CAH, and hydrocortisone and fludrocortisone were started. At six years she had no hyperpigmentation, normal growth, suppressed 17-OHP, normal serum cortisol and delayed bone age, which did not fit classical CAH, and glucocorticoid was gradually withdrawn. Genitoplasty was done at ten years. At twelve she had weight gain and pubic hair but no thelarche, and she was then lost to follow-up. Several gynecologists later labelled her as primary ovarian insufficiency because of markedly raised FSH and LH with low estradiol.

At our centre her height was 165 cm (50th-75th centile), weight 78.8 kg (>90th centile), BMI 29.4 kg/m² (>90th centile) and blood pressure 138/90 mmHg. She was breast Tanner stage 1 with lipomastia, axillary hair stage 3 and pubic hair stage 4, with no hyperpigmentation or clitoromegaly. FSH was 82.2 mIU/L, LH 37.2 mIU/L and estradiol <5 pg/mL. Androstenedione was raised, while testosterone, ACTH, cortisol and 17-OHP were normal. Bone age was 11-12 years at a chronological age of nearly 20. Pelvic ultrasound showed a small uterus and small ovaries bilaterally. Aromatase

deficiency was suspected, genetic testing was advised, and oestrogen replacement was started for pubertal induction.

Case 2. A 46, XX infant of non-consanguineous parents had ambiguous genitalia at birth after an uneventful pregnancy, with no maternal virilisation. There was clitoromegaly, partially fused rugose labial folds and a single perineal opening, with no palpable gonads or hyperpigmentation. 17-OHP and DHEA sulphate were raised, cortisol was borderline low, and ACTH and electrolytes were normal. Ultrasound showed a uterus and both ovaries, and karyotype was 46, XX. Hydrocortisone and fludrocortisone were started for presumed CAH. On follow-up she showed no classical features of CAH, but growth velocity was suboptimal and bone age delayed. A short Synacthen test showed an inadequate cortisol response with normal 17-OHP. Given these discordant results, genetic testing was done and identified a homozygous likely pathogenic CYP19A1 variant. Fludrocortisone was tapered and stopped under monitoring, and glucocorticoid tapering was planned.

Discussion

Without aromatase, androgens accumulate and virilize the 46, XX fetus, and loss of placental aromatase can virilize the mother, as in Case 1. After birth, oestrogen deficiency removes negative feedback on the pituitary, so gonadotropins, particularly FSH, rise with disruption of follicular maturation. The same deficiency delays epiphyseal fusion, which explains a bone age of 11-12 years in a woman of almost 20.

Confusion with CAH is common in the neonatal period. The distinguishing features are normal or suppressed 17-OHP on follow-up, absence of an untreated classical CAH biochemical pattern, and hypergonadotropic hypogonadism with very low estradiol. Ovarian morphology varies, and the absence of large multicystic ovaries does not exclude the diagnosis. Case 1 also shows how the label can shift over the years, from CAH to primary ovarian insufficiency, before a unifying diagnosis is reached.

Early diagnosis avoids prolonged unnecessary glucocorticoid and allows oestrogen replacement at the right time, for secondary sexual development, epiphyseal closure and bone mineral density. Management needs pediatric endocrinology, genetics, gynecology and psychological support.

Conclusion

Aromatase deficiency should be considered in any 46, XX individual with virilized genitalia whose biochemistry does not fit CAH. Hypergonadotropic hypogonadism with very low estradiol and delayed bone age are the key clues, and CYP19A1 testing confirms the diagnosis and guides hormonal management.

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CASE REPORT 10

An Unusually Severe Gestational Transient Thyrotoxicosis in a Singleton Pregnancy

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Abstract

A 30-year-old primigravida at 10 weeks of gestation presented with hyperemesis and marked biochemical thyrotoxicosis without goitre, orbitopathy or TSH-receptor antibodies. Thyroid function normalized rapidly as the vomiting settled, allowing propylthiouracil to be discontinued after 10 days. The case demonstrates that gestational transient thyrotoxicosis can occasionally be biochemically severe and should be distinguished from Graves disease.

Keywords: gestational transient thyrotoxicosis; hyperemesis gravidarum; pregnancy; hCG

Introduction

Graves' disease and gestational transient thyrotoxicosis (GTT) are the two commonest causes of thyrotoxicosis in pregnancy [1]. hCG rises in the first trimester and peaks at about 8-11 weeks. Because it shares its alpha subunit with TSH, it can stimulate the TSH receptor, though far more weakly than TSH. Very high levels, usually with hyperemesis gravidarum (HG), multiple gestation or molar pregnancy, can suppress TSH and raise FT4 [2]. The degree of suppression correlates with hCG: levels above 200,000 IU/L are more likely to suppress TSH, and levels above 400,000 IU/L do so most consistently [2].

Case presentation

A 30-year-old primigravida at 10 weeks' gestation was admitted with progressively worsening nausea and vomiting for five to six weeks, lower abdominal pain, palpitations, dizziness and exertional dyspnoea, and diarrhoea for three days. Despite antiemetics she had poor oral intake and had been unable to gain weight. Before pregnancy she had noticed palpitations, weight loss, weakness, lethargy and fatigue. She had no past medical history and took only prenatal vitamins.

She was given oral and IV fluids and antiemetics in the Emergency Department. Blood pressure was 107/59 mmHg and pulse 116/min, regular. She was mildly restless, with warm moist skin and a mild hand tremor. There was no goitre or orbitopathy.

Haemoglobin was 8.8 g/dL (11-14), WBC $10.1 \times 10^9/L$ (4.6-10.8), platelets $199 \times 10^9/L$ (154-433), sodium 137 mmol/L (136-145), potassium 3.3 mmol/L (3.5-5.1), chloride 104 mmol/L (98-107), creatinine 0.9 mg/dL (0.6-1.1), AST 16 IU/L (13-39) and ALT 22 IU/L (7-52). TSH was <0.005 mIU/L (0.4-4.2), FT4 4.34 ng/dL (0.92-1.68), FT3 6.46 pg/mL and total T4 >24.86 µg/dL (5.5-11). TSH receptor antibodies were <0.8 IU/L (0-1.75). Serum hCG was not measured.

She received IV fluids and ondansetron 4 mg eight-hourly as needed, with improvement in nausea and vomiting; the diarrhoea was considered drug induced. Because of her symptoms before pregnancy, propylthiouracil (PTU) 50 mg twice daily was started with early outpatient review. Ten days later the vomiting had resolved, she had gained 1.5 kg, and she denied tremor, sweating, diarrhoea or palpitations. TSH was 0.5 mIU/L and FT4 0.84 ng/dL, and PTU was stopped with follow-up advised.

Discussion

hCG shares its alpha subunit with TSH and its beta subunit is homologous, so it acts as a weak thyroid stimulator, causing a slight fall in TSH and a slight rise in FT4 and FT3 [2], most evident near the hCG peak at the end of the first trimester [1]. In about 15% of healthy women, TSH falls below the pregnancy-specific range by the end of the first trimester; this is physiological and recovers as hCG declines [3]. Very high hCG concentrations have been associated with suppressed TSH [3], and such levels occur in multiple gestation, HG and gestational trophoblastic disease. Some hCG isoforms have a longer half-life and greater thyrotropic potency, suppressing TSH at lower concentrations [4].

GTT appears at 10-12 weeks with mild symptoms, suppressed TSH and modestly raised FT4, and normally resolves early in the second trimester as hCG falls [5]. Graves' disease, the other main cause, is characterized by goitre, orbitopathy, occasionally dermopathy, and positive TSH receptor antibodies [6]. GTT is often associated with HG, which may involve severe vomiting, weight loss and dehydration and commonly causes hyponatraemia, hypokalaemia, hypochloraemia, alkalosis and abnormal liver tests [5]. Its symptoms overlap with thyrotoxicosis, although sweating, heat intolerance, tachycardia and tremor favour the latter [7].

Our patient had HG with marked thyrotoxicosis, no stigmata of Graves' disease and negative antibodies. The severity, with FT4 more than twice the upper limit and total T4 above the assay range, was uncharacteristic of GTT, which is usually milder. hCG was not measured, so we could not compare her level with those reported in similarly severe cases. Most women with GTT need no antithyroid treatment [5,7]. Beta-blockers for tachycardia, IV fluids, antiemetics and electrolyte correction are appropriate, with thyroid function followed through pregnancy [7].

Conclusion

GTT can occasionally cause severe biochemical thyrotoxicosis with markedly raised FT4 and total T4, particularly with HG. Recognizing its transient nature is important. In this patient, PTU was given for only 10 days because of symptoms before pregnancy, and stopped once thyroid function normalized; symptomatic management was otherwise sufficient.

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CASE REPORT 11

Bilateral Adrenal Nodules with Aldosterone and Cortisol Co-secretion and Uncertain Lateralisation

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Abstract

A patient with bilateral adrenal nodules was found to have biochemical evidence of both primary aldosteronism and mild autonomous cortisol secretion, consistent with a Conn's phenotype. Adrenal venous sampling was technically limited by failed right adrenal vein cannulation, while cortisol co-secretion complicated interpretation. The case highlights the need to integrate biochemical, radiological and multidisciplinary assessment when localisation is uncertain.

Keywords: primary aldosteronism; mild autonomous cortisol secretion; adrenal adenoma; Conn's syndrome; adrenal venous sampling

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Case presentation

A 76-year-old woman with a 55 pack-year smoking history, diabetes mellitus for 16 years, hypertension for 10 years, dyslipidaemia, obstructive sleep apnoea and obesity attended the endocrine clinic for weight management. Her medications were metformin 1 g twice daily, sitagliptin 100 mg daily, a weekly GLP-1 analogue (1 mg) for three years, bisoprolol 5 mg daily, amlodipine/valsartan 10/160 mg daily, doxazosin 2 mg daily, atorvastatin 20 mg at night and inhalers. Blood pressure was 126/64 mmHg, pulse 86/min and BMI 32.8 kg/m², with no clinical features of Cushing's syndrome. All comorbidities were optimally controlled.

An adrenal incidentaloma was found during routine cancer screening in London in 2023, but no work-up was available. CT scans of the chest and abdomen in 2024 and 2025, done for respiratory problems, showed bilateral adrenal nodules: right 1.5 × 1.1 cm (-14 HU) and left 3.2 × 3.2 cm (-86 HU). As these were not adrenal-protocol scans, washout values were unavailable.

The aldosterone-to-renin ratio (ARR) was raised with normal potassium. Two overnight dexamethasone suppression tests and a high-dose test all showed failure of cortisol suppression, with low-normal ACTH, indicating co-secretion of aldosterone and cortisol. Adrenal venous sampling (AVS) was done for lateralization, but the right adrenal vein could not be cannulated. The contralateral ratio suggested suppression of the successfully cannulated left side, with possible right-sided aldosterone excess; this was difficult to interpret given the cortisol co-secretion and discordant imaging. Because the left lesion was twice the size of the right and the left adrenal vein showed markedly raised aldosterone and cortisol, left adrenalectomy was advised. The surgeon's pre-operative CT showed a well-defined mixed-density (fat and soft tissue) right nodule of 1.7 × 1.2 cm (14 HU) in the body and lateral limb, and a well-defined mixed-density left nodule of 3.5 × 3.0 cm with heterogeneous enhancement. Surgery is awaited.

Discussion

Primary aldosteronism (PA) is one of the commonest causes of secondary hypertension and is increasingly recognized in patients with adrenal incidentalomas, in whom guidelines also advise testing for cortisol co-secretion. Mild autonomous cortisol secretion (MACS), previously called subclinical Cushing's syndrome, coexists with PA in a subset of patients. This combination, termed Connshing syndrome, produces a complex phenotype with significant cardiometabolic risk, and localisation is particularly difficult when disease is bilateral.

Our patient had no cushingoid features, yet repeated dexamethasone testing showed failure of suppression with low-normal ACTH, and the ARR was raised with normal potassium. Cortisol co-secretion is reported in 10-20% of patients with PA [1-3] and is linked to more diabetes, obesity, dyslipidaemia, osteoporosis and cardiovascular disease, and to worse cardiac hypertrophy and diastolic dysfunction [4]. Her long-standing metabolic comorbidities may partly reflect chronic mild cortisol excess in addition to aldosterone effects.

AVS remains the gold standard for lateralization, but failed right-sided cannulation is well recognized because of the anatomy. Here the selectivity index confirmed failed right cannulation with successful left cannulation, and the contralateral ratio pointed to a suppressed left gland and an overactive right one. Cortisol hypersecretion, however, alters aldosterone-to-cortisol ratios and lateralization indices. Imaging showed a much larger left lesion, and left adrenal vein aldosterone and cortisol were markedly raised. Such discordance between imaging and AVS has been reported in bilateral disease, especially with cortisol co-secretion or failed cannulation.

Plasma metanephrines, chromogranin A and dopamine have been proposed as alternatives to cortisol for selectivity and lateralization indices [5-7], but were not measured in our case. Metanephrines appear most promising because of their short half-life, almost exclusive (>90%) adrenal production and secretion that is independent of systemic stress [6,7]. In MACS with bilateral adrenal masses, an inter-adrenal cortisol ratio of ≤ 2.0 suggests bilateral cortisol secretion; in our patient it was 7.43.

Normokalaemic PA is increasingly recognized, and relying on serum potassium alone may delay diagnosis. Her blood pressure was also well controlled on several agents, showing that clinically significant PA can exist despite apparent control. Bilateral nodules raise the possibility of bilateral hyperplasia, bilateral adenomas or asymmetric functioning adenomas, which histopathology should clarify. Given her age, metabolic burden, imaging and the unresolved lateralisation of hormone excess, the multidisciplinary team favoured left adrenalectomy.

Conclusion

Adrenal incidentalomas need full hormonal evaluation regardless of phenotype, and cortisol co-secretion should be actively sought in PA because it affects AVS interpretation and perioperative care. With failed cannulation and cortisol co-secretion in bilateral disease, AVS must be read alongside biochemical, radiological and clinical findings, and decisions made jointly by endocrinologists, radiologists and endocrine surgeons. Standardized approaches to AVS interpretation and surgical decision-making in aldosterone- and cortisol-co-secreting tumours are still needed.

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CASE REPORT 12

Hormonal Storm in a Young Female Masquerading as Polycystic Ovarian Disease

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Abstract

A 20-year-old woman initially managed as polycystic ovarian disease developed progressive amenorrhoea, hirsutism, hypertension, proximal weakness and wide purple striae. Imaging revealed a large left adrenal mass with bilateral pulmonary lesions interpreted as metastases, supporting functional adrenocortical carcinoma with multi-hormonal secretion. Her young age and family history raised concern for a hereditary cancer syndrome; neither ACC nor Li-Fraumeni syndrome was genetically or histologically confirmed in the supplied record. Rapidly progressive PCOS-like features should prompt evaluation for adrenal malignancy.

Keywords: adrenocortical carcinoma; virilisation; Cushing syndrome; Li-Fraumeni syndrome; PCOS mimic

Case presentation

A 20-year-old FSc student from Wah Cantt, the youngest of six sisters born to non-consanguineous parents, presented with hypomenorrhoea for six months followed by amenorrhoea for three months, weight gain, hirsutism and frequent falls, especially while climbing stairs. Menarche was at 12 years with regular cycles. She had no significant past medical history and no chronic medication, head trauma or irradiation.

A local gynaecologist had managed her as PCOD with intensive lifestyle modification and metformin 500 mg three times daily for three months. She lost 2 kg, her complexion became fairer and her mood lifted for a few months, which she credited to herbal teas, exercise and treatment. A few weeks later she developed extreme fatigue with frequent falls, and her acne, hirsutism and amenorrhoea worsened.

Her paternal uncle had osteosarcoma of the left knee and died at 37 years, and her mother was recently diagnosed with stage 3 breast cancer at 54 years. A brother died at six months with hydrocephalus that was never investigated.

On examination, BMI was 27 and blood pressure 150/100 mmHg. She had acne, facial hirsutism (Ferriman-Gallwey score 18), wide (1.5-2 cm) purple striae on the abdomen and thighs, and a positive Gowers' sign indicating proximal muscle weakness. No other systemic findings were noted. Hormonal results are shown below.

Ultrasound showed a large left suprarenal mass, and CT of the chest, abdomen and pelvis showed a large left adrenal mass with diffuse bilateral lung metastases.

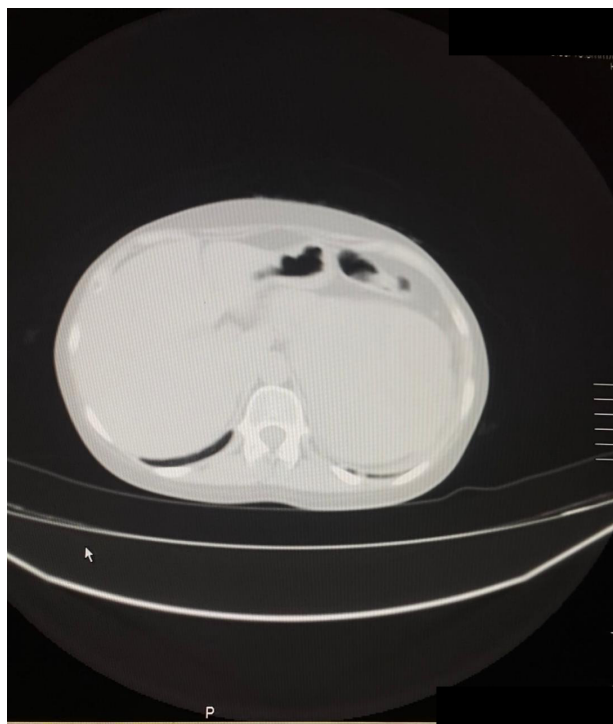


Figure. Abdominal CT from the case record.

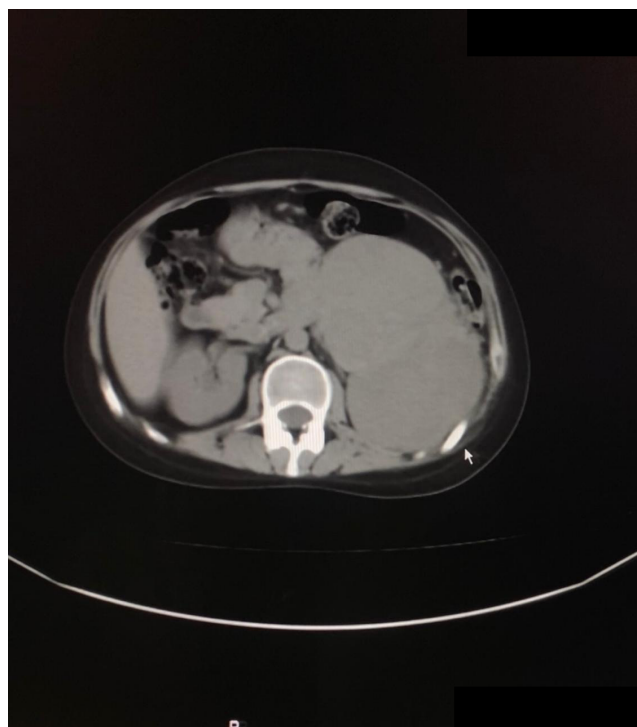


Figure. Abdominal CT showing the reported left adrenal mass.

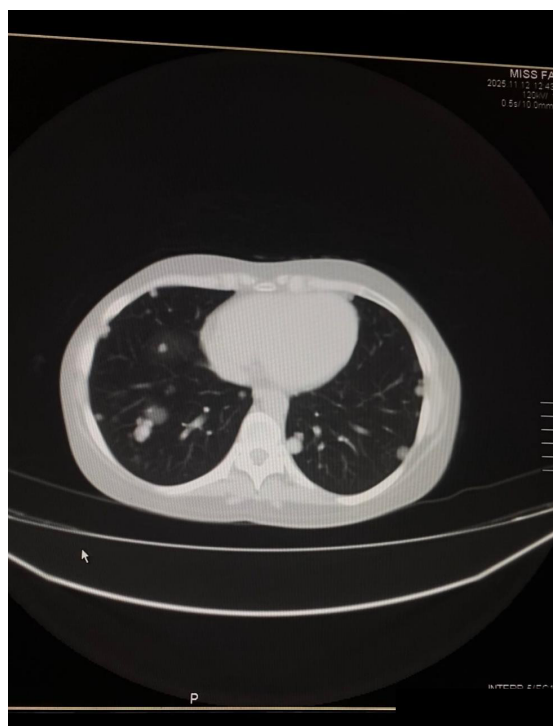


Figure. Chest CT showing the reported pulmonary lesions.

Differential diagnosis

Functional adrenocortical carcinoma (ACC) with multi-hormonal secretion, with suspected underlying Li-Fraumeni syndrome.

Management and follow-up

Treatment, adrenal histopathology, TP53 testing and follow-up outcomes were not supplied. The available record supports suspected functional ACC with pulmonary metastases and possible hereditary predisposition; definitive confirmation remains outstanding.

Discussion

ACC is a rare and highly aggressive malignancy that often presents with hormone excess, particularly in young patients. Tumors secreting glucocorticoids, androgens and mineralocorticoids together produce cushingoid features, virilisation and hypertension, as in this case [1,2]. Mixed secretion explains the coexistence of proximal myopathy, purple striae, hirsutism and metabolic disturbance, a picture that can easily be taken for polycystic ovarian syndrome. The brief improvement in weight, complexion and mood before rapid deterioration added to the confusion.

ACC in a young person should raise suspicion of a hereditary cancer predisposition, most importantly Li-Fraumeni syndrome (LFS), a rare autosomal dominant condition caused by germline TP53 mutations [3]. p53 regulates DNA repair, cell-cycle arrest and apoptosis, and its loss leads to genomic instability and early-onset, multi-organ, aggressive cancers [3,4]. ACC is a core LFS tumour, typically hormone-secreting with rapid progression and early metastasis, as seen here.

ACC at any age is in itself an indication for germline TP53 testing under the revised Chompret criteria [3]. Our patient's family history strengthens the suspicion: osteosarcoma in a paternal uncle at 37, breast cancer in her mother at 54, and an unexplained infant death in a brother. She therefore needs germline TP53 analysis, and genetic counselling should guide any predictive testing of relatives if a pathogenic germline variant is identified. If LFS is confirmed, lifelong surveillance with whole-body MRI and early breast screening is required, and radiation exposure should be avoided where possible because of the risk of radiation-induced cancers. ACC management remains standard (surgery with or

without mitotane and chemotherapy), but radiotherapy is used cautiously in LFS. Multidisciplinary care involving endocrinology, oncology and genetics is essential.

Learning points

- PCOS is common, but a young woman with PCOS-like features whose symptoms progress rapidly, with cushingoid changes and virilisation, needs careful evaluation for adrenal malignancy. The endocrinologist's role is to recognize these red flags and the patterns that do not fit PCOS, and to direct appropriate hormonal assessment and imaging. When there is also a family history of early-onset cancer, hereditary syndromes such as LFS should be actively evaluated, so that both the patient and her family benefit from early screening.

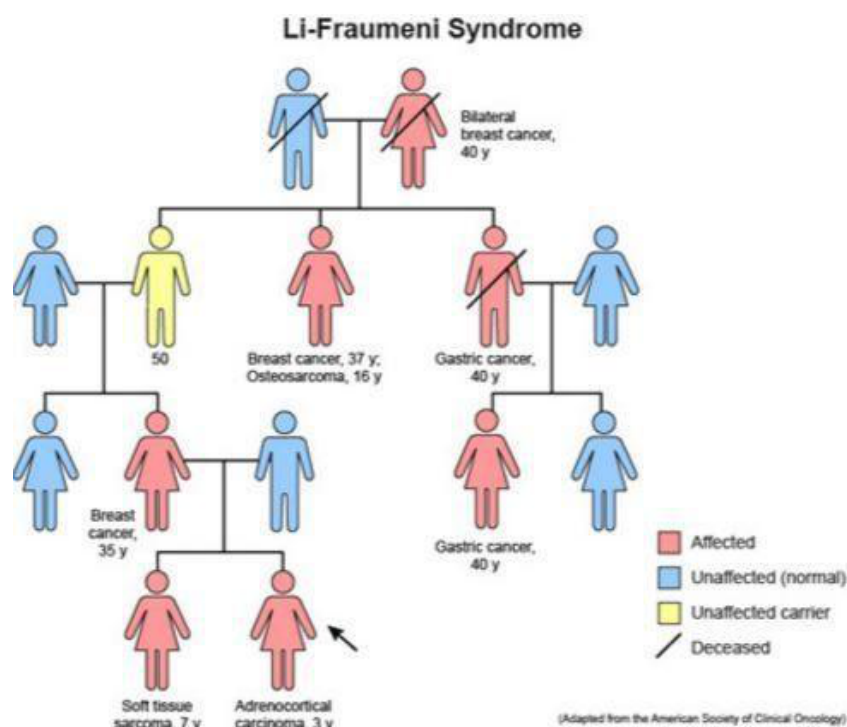


Illustration of Li-Fraumeni syndrome supplied with the report; this is not the patient's pedigree.

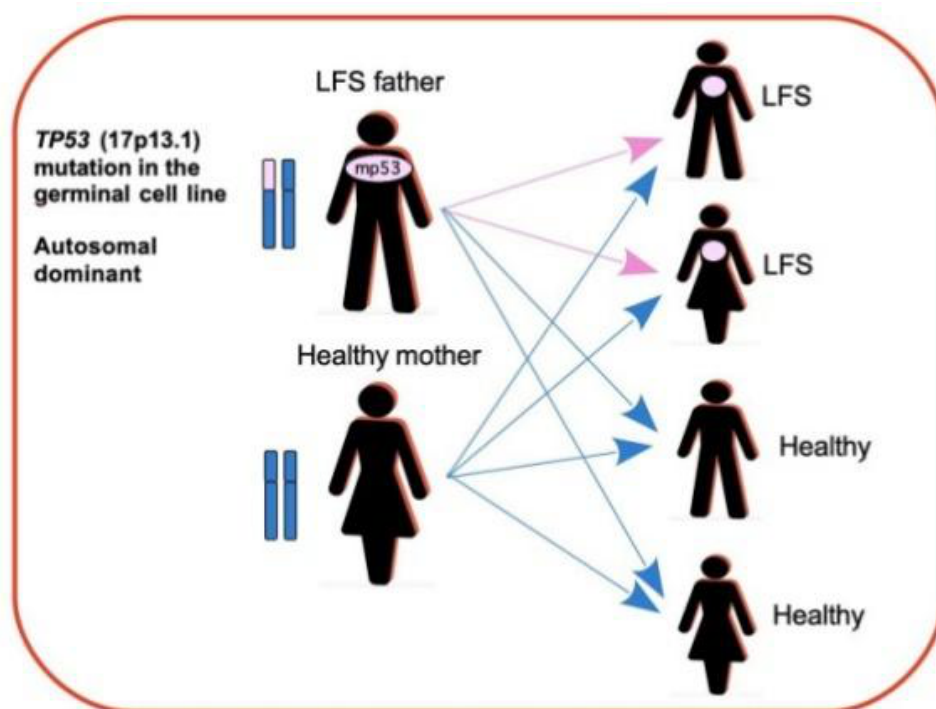


Illustration of Li-Fraumeni syndrome supplied with the report; this is not the patient's pedigree.

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CASE REPORT 13

Primary Adrenal Insufficiency Presenting as Pyrexia of Unknown Origin in a 13-Year-Old Boy

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Abstract

Primary adrenal insufficiency can be difficult to recognize in children when the initial presentation is dominated by prolonged fever and nonspecific constitutional or gastrointestinal symptoms. A 13-year-old boy presented with two months of unintentional weight loss and one month of fever that had not responded to repeated courses of antibiotics. He subsequently developed abdominal pain, vomiting, dehydration and marked postural hypotension. Laboratory evaluation showed severe hyponatraemia (112 mmol/L), hyperkalaemia (6.6 mmol/L), a morning cortisol of 1.8 µg/dL and ACTH >2000 pg/mL. Twenty-one-hydroxylase antibodies were positive, supporting autoimmune primary adrenal insufficiency. Notably, hyperpigmentation and hypoglycaemia were absent. He was treated for adrenal crisis with intravenous hydrocortisone and isotonic saline, followed by oral hydrocortisone and fludrocortisone. At two-week follow-up, symptoms had resolved and blood pressure, serum electrolytes and blood glucose were normal. This case highlights the importance of considering adrenal insufficiency in a child with persistent fever, weight loss, gastrointestinal symptoms, postural hypotension and an electrolyte pattern of hyponatraemia with hyperkalaemia, even when classic cutaneous features are absent.

Keywords: primary adrenal insufficiency; Addison disease; pyrexia of unknown origin; adrenal crisis; hyponatraemia; hyperkalaemia; 21- hydroxylase antibodies

Introduction

Primary adrenal insufficiency is a potentially life-threatening endocrine disorder in which deficient glucocorticoid and mineralocorticoid secretion may present with nonspecific symptoms such as fatigue, weight loss, anorexia, abdominal pain and vomiting [1-3]. In children, fever may occasionally dominate the presentation and lead to an initial search for infectious or inflammatory disease [5,6]. Recognition becomes especially important when constitutional symptoms coexist with postural hypotension, hyponatraemia and hyperkalaemia. Autoimmune adrenalitis can be supported by the presence of 21-hydroxylase autoantibodies [1,7]. We describe a 13-year-old boy whose prolonged febrile illness and progressive deterioration were ultimately explained by autoimmune primary adrenal insufficiency presenting in adrenal crisis.

Case presentation

A 13-year-old boy presented with progressive, unintentional weight loss for two months and fever for one month, without any reported change in diet or physical activity. He had consulted multiple physicians and received several courses of antibiotics without improvement. He was subsequently admitted to a district hospital, where extensive investigations, intravenous fluids and broad-spectrum antibiotics did not establish a diagnosis or reverse his clinical deterioration. He later developed abdominal pain, vomiting and reduced oral intake. There was no history of diarrhoea, haematemesis, melaena, seizures, loss of consciousness, steroid exposure, chronic illness or tuberculosis contact. He and his family did not report increased skin pigmentation or a change in complexion. Past medical, drug, family, birth and developmental histories were unremarkable.

On examination, he appeared ill, weak and dehydrated. Temperature was 99 °F, pulse 100 beats/min and respiratory rate was within normal limits. Blood pressure was 95/70 mmHg supine and fell to 70/50 mmHg on standing. Cardiovascular, respiratory and neurological examinations were unremarkable. Abdominal examination showed diffuse tenderness without guarding or rigidity, with

bowel sounds present. No hyperpigmentation was seen. Testicular volume was 8 mL bilaterally, stretched penile length 7 cm and pubertal staging was G3 P2. Height was 150 cm, weight 39 kg and BMI 17.3 kg/m².

Investigations

Initial investigations showed mild microcytic anaemia and a striking electrolyte disturbance. The infection and inflammatory screen was unrevealing, while endocrine testing demonstrated markedly reduced morning cortisol with an extreme elevation of ACTH. Positive 21-hydroxylase antibodies supported autoimmune adrenalitis. Thyroid function and coeliac serology were normal/negative as reported. Selected results are summarized in Table 1.

Table 1. Key laboratory findings at presentation

Parameter	Result	Reference range / comparator	Interpretation
Haemoglobin	11.8 g/dL	12.6-17.7 g/dL (paediatric range)	Mild anaemia
MCV	75.9 fL	79-97 fL	Microcytosis
Sodium	112 mmol/L	135-145 mmol/L	Severe hyponatraemia
Potassium	6.6 mmol/L	3.5-5.2 mmol/L	Hyperkalaemia
Chloride	86 mmol/L	102-112 mmol/L	Low
Urea	56 mg/dL	11-38 mg/dL	Raised
Random glucose	100 mg/dL	70-140 mg/dL	Normal
CRP	2 mg/L	0-7 mg/L	Not elevated
ESR	15 mm/h	0-15 mm/h	Within stated range
Blood culture	No growth at 5 days	No growth	Negative
Morning serum cortisol	1.8 µg/dL	3-21 µg/dL	Low
ACTH	>2000 pg/mL	7.2-63.3 pg/mL	Markedly elevated
21-hydroxylase antibodies	Positive	Negative	Supports autoimmune adrenalitis
Free T4	1.15 ng/dL	0.93-1.60 ng/dL (paediatric range)	Within stated range
TSH	2.2 mIU/L	0.5-4.3 mIU/L (11-19 y)	Within stated range
tTG-IgA	Negative	<4.0 U/mL	Negative

Abdominal ultrasonography was essentially normal. Thyroid ultrasonography showed normal size and echotexture without a cystic or solid mass. Contrast-enhanced CT of the abdomen demonstrated normal pancreas, spleen and both adrenal glands, with no abdominal lymphadenopathy or free fluid. The overall CT conclusion was an essentially normal study. A normal adrenal appearance on imaging did not exclude autoimmune primary adrenal insufficiency.

Diagnosis

The combination of dehydration, marked postural hypotension, sodium 112 mmol/L, potassium 6.6 mmol/L, morning cortisol 1.8 µg/dL, ACTH >2000 pg/mL and positive 21-hydroxylase antibodies established the diagnosis of autoimmune primary adrenal insufficiency (Addison disease), presenting as adrenal crisis in the setting of a prolonged febrile illness. The negative infection screen and failure to respond to antibiotics prompted reassessment of the original diagnostic approach.

Management and follow-up

The patient was treated promptly for acute adrenal crisis. Hydrocortisone 100 mg was administered intravenously as an initial stress dose, followed by parenteral hydrocortisone at 50 mg/m²/day divided every six hours and adjusted according to clinical response. Rapid volume resuscitation was provided with 0.9% normal saline in 10 mL/kg boluses, repeated as required. Blood pressure, perfusion, urine output, glucose, renal function and serum electrolytes were monitored frequently.

Table 2. Electrolyte response to acute treatment

Electrolyte	At presentation	After treatment	Reference range
Sodium	112 mmol/L	135 mmol/L	135-145 mmol/L
Potassium	6.6 mmol/L	3.6 mmol/L	3.5-5.5 mmol/L
Chloride	86 mmol/L	98 mmol/L	95-110 mmol/L

As haemodynamic status and electrolyte abnormalities improved, intravenous fluids were tapered and discontinued once he was clinically stable and tolerating oral fluids and diet. Parenteral hydrocortisone was progressively reduced and converted to oral replacement.

Table 3. Maintenance replacement regimen

Drug	Dose	Timing
Hydrocortisone	10 mg	7:00 AM
Hydrocortisone	5 mg	12:00 PM
Hydrocortisone	5 mg	4:00 PM
Fludrocortisone	0.1 mg	Once daily

The patient and his father received counselling on strict adherence to glucocorticoid and mineralocorticoid replacement, sick-day rules, stress-dose escalation during intercurrent illness and indications for emergency parenteral hydrocortisone. They were educated about clinical features of under-replacement and over-replacement, and a steroid emergency card was provided. At two-week follow-up he had marked clinical improvement with resolution of presenting symptoms. Serum electrolytes, blood pressure and blood glucose were normal, with no clinical features of glucocorticoid or mineralocorticoid excess or deficiency. He was advised to continue the same replacement regimen with regular endocrinology follow-up.

Discussion

Primary adrenal insufficiency may remain unrecognized because its early manifestations are nonspecific. Fatigue, weight loss, anorexia, abdominal pain and vomiting can be attributed to infection or gastrointestinal disease, while fever itself has been described as an unusual presentation of Addison disease in children [1,2,5,6]. In this patient, repeated antibiotic exposure and an extensive infection work-up delayed the endocrine diagnosis. The subsequent combination of severe postural hypotension, hyponatraemia and hyperkalaemia was a major clue to adrenal failure.

The absence of hyperpigmentation should not provide false reassurance. Although increased pigmentation is traditionally associated with primary adrenal insufficiency, it is not universal. In the paediatric cohort cited in the case, hyperpigmentation was reported in 50.4% of children and in 50% of those with autoimmune adrenal insufficiency [5]. Similarly, hypoglycaemia is not obligatory; this patient had a random glucose of 100 mg/dL. The biochemical pattern of a low morning cortisol with ACTH far above the laboratory upper limit strongly supported a primary adrenal defect [1].

Positive 21-hydroxylase autoantibodies supported autoimmune adrenalitis [1,7]. A normal appearance of the adrenal glands on CT does not exclude this diagnosis. When autoantibodies are negative, alternative causes in boys include X-linked adrenoleukodystrophy, tuberculosis and genetic disorders [1,3,5]. Autoimmune adrenalitis may coexist with autoimmune thyroid disease and diabetes, which should be considered during ongoing surveillance [2,7].

The immediate therapeutic priority in adrenal crisis is glucocorticoid replacement and restoration of intravascular volume. The management in this case followed this principle, with intravenous hydrocortisone and isotonic saline followed by oral hydrocortisone and fludrocortisone once clinical stability was achieved [1,3,4]. Equally important is prevention of future crises through sick-day education, emergency steroid planning and provision of a steroid card.

Conclusion

Autoimmune primary adrenal insufficiency should be considered in children with unexplained prolonged fever, weight loss and gastrointestinal symptoms, particularly when accompanied by postural hypotension, hyponatraemia and hyperkalaemia. Normal glucose and the absence of hyperpigmentation do not exclude the diagnosis. Early recognition and prompt treatment can reverse life-threatening adrenal crisis and prevent recurrent decompensation.

Learning points

- Consider adrenal insufficiency in children with prolonged unexplained fever, weight loss and gastrointestinal symptoms.
- Check serum electrolytes and postural blood pressure early; hyponatraemia with hyperkalaemia should prompt adrenal evaluation.
- Normal glucose and absence of hyperpigmentation do not exclude primary adrenal insufficiency.
- Positive 21-hydroxylase antibodies support an autoimmune cause and should prompt consideration of associated autoimmune disease.
- Sick-day education, emergency hydrocortisone planning and steroid identification are core components of long-term care.

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CASE REPORT 14

Broken Bones and Paralysed Summers: A Decade-Long Masquerade of Familial Distal Renal Tubular Acidosis

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Abstract

Distal renal tubular acidosis (dRTA) is a disorder of urinary acidification that may cause hyperchloraemic metabolic acidosis, hypokalaemia, hypercalciuria, nephrocalcinosis and nephrolithiasis, with chronic acidosis producing substantial skeletal morbidity. A 32-year-old man had generalised bone pain since 2015, recurrent low-trauma fractures of both femora and the left humerus from the age of 27, and recurrent hypokalaemic paralysis that worsened in summer; a brother was similarly affected. He had previously been treated for inflammatory arthritis and had received zoledronic acid. At presentation, bicarbonate was 12.4 mmol/L with pH 7.36, potassium 2.58 mmol/L, phosphate 2.2 mg/dL and alkaline phosphatase 263 U/L; ultrasonography showed bilateral nephrolithiasis with echogenic kidneys. Potassium citrate increased bicarbonate to 15.3 mmol/L and potassium to 3.7 mmol/L within two weeks. The case illustrates that dRTA should be considered in young adults with otherwise unexplained fragility fractures, hypokalaemic paralysis and renal stones, particularly when another family member is affected.

Keywords: distal renal tubular acidosis; hypokalaemic paralysis; osteomalacia; fragility fractures; nephrolithiasis; familial dRTA

Introduction

Renal tubular acidosis comprises a group of disorders in which the kidney cannot maintain acid-base balance despite a near-normal glomerular filtration rate. In proximal (type 2) RTA, bicarbonate reabsorption in the proximal tubule is reduced; in distal (type 1) RTA, the collecting duct cannot secrete hydrogen ions, so urine cannot be acidified below a pH of about 5.5 [1]. Primary dRTA is usually inherited, through autosomal dominant variants in SLC4A1 or autosomal recessive variants in ATP6V1B1, ATP6V0A4 and, more recently described, FOXI1 [2]. Recessive forms present in infancy with failure to thrive, vomiting and, in some, sensorineural deafness, whereas dominant forms are milder and may be recognised only in adolescence or adulthood [2,3].

The clinical burden of dRTA comes from three linked abnormalities: renal potassium wasting, which can cause periodic paralysis; hypercalciuria with hypocitraturia, which leads to nephrocalcinosis and stones; and chronic acidosis buffered by bone, which leads to rickets in children and osteomalacia, bone pain and fractures in adults [1,5]. This report describes an adult in whom these features accumulated over a decade before the unifying diagnosis was made.

Case presentation

A 32-year-old man from District Kohat presented with generalised body aches and bone pain dating from 2015. His first fracture occurred at 27 years of age; thereafter he sustained recurrent low-trauma or spontaneous fractures of both femora, including the trochanteric region, and of the left humerus. These were managed surgically with intramedullary nails and plate fixation. He also reported recurrent episodes of hypokalaemic periodic paralysis, which were more frequent during the summer months. His brother had a similar illness.

During the preceding years, he had consulted several orthopaedic surgeons and rheumatologists. Anterior chest pain had been attributed to costochondritis, and he was prescribed methotrexate and sulfasalazine. Six months before presentation he received zoledronic acid, and he had also taken weekly vitamin D supplementation for three months.

Investigations

Arterial blood gas analysis showed a pH of 7.36 with bicarbonate 12.4 mmol/L, showing markedly low bicarbonate with a near-normal pH; full acid-base interpretation requires pCO₂. Serum potassium was 2.58 mmol/L and sodium 126 mmol/L. Calcium was low-normal at 8.6 mg/dL, phosphate decreased from 2.84 to 2.2 mg/dL, and alkaline phosphatase was elevated at 263 U/L. After vitamin D supplementation, 25-hydroxyvitamin D was 120 ng/mL and intact PTH was suppressed at 12.7 and subsequently 5.86 pg/mL. Blood counts, ESR and CRP were normal; ANA and rheumatoid factor were negative; and thyroid function, cortisol and testosterone were within their reported reference ranges. The spot urine calcium/creatinine ratio was 0.19 mg/mg, at the upper limit of normal. Ultrasound of the kidneys, ureters and bladder demonstrated bilateral renal calculi and echogenic kidneys. Key laboratory and imaging findings are summarised in Table 1.

Table 1. Laboratory and imaging findings, from baseline to specialised investigations

Investigation	Result	Reference range	Interpretation
A. Baseline haematology and inflammatory markers			
Haemoglobin	15.6 g/dL	13-17 g/dL	Normal
Total leucocyte count	7.67 ×10 ⁹ /L	4-11 ×10 ⁹ /L	Normal
Platelets	241 ×10 ⁹ /L	150-400 ×10 ⁹ /L	Normal
ESR	10 mm/1st hour	0-15 mm/1st hour	Normal
C-reactive protein	3.57 mg/L	<5 mg/L	Normal
Random blood glucose	91 mg/dL	<140 mg/dL	Normal
B. Arterial blood gas and serum electrolytes (on admission)			
pH	7.36	7.35-7.45	Near-normal; low bicarbonate
Bicarbonate (HCO ₃ ⁻)	12.4 mmol/L	22-26 mmol/L	Markedly low - metabolic acidosis
Potassium	2.58 mmol/L	3.5-5.1 mmol/L	Severe hypokalaemia
Sodium	126 mmol/L	135-145 mmol/L	Hyponatraemia
C. Bone and liver profile			
Calcium	8.6 mg/dL	8.5-10.5 mg/dL	Low-normal
Phosphate	2.84 → 2.2 mg/dL	2.5-4.5 mg/dL	Low, falling
Alkaline phosphatase	263 U/L	40-129 U/L	Raised
ALT	59.8 U/L	<41 U/L	Mildly raised
Albumin	4.45 g/dL	3.5-5.0 g/dL	Normal
D. Mineral-regulating hormones			
25-OH vitamin D	120 ng/mL	30-100 ng/mL	Raised (after supplementation)

Investigation	Result	Reference range	Interpretation
Intact PTH	12.7 → 5.86 pg/mL	15-65 pg/mL	Low / suppressed
E. Endocrine screen			
TSH	2.61 mIU/L	0.4-4.2 mIU/L	Euthyroid (T3/T4 normal)
Cortisol (random)	13.4 µg/dL	5-25 µg/dL	Adequate
Testosterone	3.57 ng/mL	2.8-8.0 ng/mL	Normal
F. Autoimmune screen			
Antinuclear antibody	Negative	Negative	Negative ANA
Rheumatoid factor	Negative	Negative	Negative rheumatoid factor
G. Urine studies (spot sample)			
Urine calcium	8.94 mg/dL	-	-
Urine creatinine	46 mg/dL	-	-
Urine calcium/creatinine ratio	0.19 mg/mg	<0.20 mg/mg	Upper limit of normal
H. Imaging			
	Left: ≥2 calculi (largest 6 mm, lower pole); right: 5 mm calculus (mid-pole); bilaterally echogenic kidneys	-	Bilateral nephrolithiasis with echogenic kidneys
I. Follow-up after 2 weeks of potassium citrate			
pH	7.39	7.35-7.45	Normal
Bicarbonate (HCO ₃ ⁻)	15.3 mmol/L	22-26 mmol/L	Improving
Potassium	3.7 mmol/L	3.5-5.1 mmol/L	Corrected

Diagnosis

Renal tubular acidosis was diagnosed. The combination of metabolic acidosis, hypokalaemic paralysis, bilateral nephrolithiasis and echogenic kidneys favoured distal RTA. Proximal and mixed (type 3) RTA were considered because of the hypophosphataemia and prominent bone disease.

Management and follow-up

The patient was started on potassium citrate, one tablet three times daily, with weekly serum electrolyte monitoring. At review after two weeks, pH had increased to 7.39, bicarbonate to 15.3 mmol/L and potassium to 3.7 mmol/L. He remained on regular follow-up with titration of alkali therapy.

Discussion

The defining lesion in dRTA is failure of the alpha-intercalated cell to secrete hydrogen ions, through loss of function of the apical H⁺-ATPase or the basolateral chloride-bicarbonate exchanger AE1 [2]. Net acid excretion falls and metabolic acidosis develops. Potassium is lost in the urine, and volume contraction with secondary hyperaldosteronism worsens the loss, which explains both the severe hypokalaemia and the summer clustering of paralysis in this patient, when sweating and dehydration may aggravate kaliuresis [1,3]. Acidosis also increases urinary calcium and reduces urinary citrate, the main natural inhibitor of crystallisation; in alkaline urine, calcium phosphate precipitates readily. Bilateral stones and echogenic kidneys, likely reflecting nephrocalcinosis, therefore favour the distal rather than proximal form [1].

Bone disease is an important but often under-recognised consequence of dRTA in adults. Bone carbonate and phosphate buffer retained acid, osteoclastic resorption increases and mineralisation is impaired, producing osteomalacia with bone pain, elevated alkaline phosphatase and insufficiency fractures [1,5]. The decade of bone pain, fractures from age 27, increased alkaline phosphatase and low phosphate in this patient fit this pattern. The anterior chest pain labelled as costochondritis may have represented osteomalacic pain or a rib pseudofracture. Because a tubular cause was not initially sought, he received methotrexate, sulfasalazine and a bisphosphonate. Bisphosphonates do not correct a mineralisation defect and should not be given until osteomalacia has been excluded or treated.

The distinction between distal, proximal and mixed RTA was the principal diagnostic question. Proximal RTA is self-limiting because, once plasma bicarbonate falls to the lowered renal threshold, the distal nephron can still acidify the urine; serum bicarbonate therefore usually settles at 15-18 mmol/L, stones are uncommon and urinary citrate is preserved [1,5]. Proximal RTA is also seldom isolated in adults and is usually part of Fanconi syndrome with glycosuria, aminoaciduria and phosphaturia. Hypophosphataemia raised that possibility, but phosphate wasting can also occur with chronic acidosis, and zoledronic acid may lower serum phosphate. The suppressed PTH was considered most consistent with the high vitamin D level after supplementation. Mixed (type 3) RTA due to carbonic anhydrase II deficiency typically presents in childhood with osteopetrosis, cerebral calcification and learning difficulty, none of which was present [1]. On balance, bicarbonate 12.4 mmol/L together with stones, nephrocalcinosis and hypokalaemic paralysis favoured dRTA.

An affected brother and presentation in adulthood suggest an inherited, possibly autosomal dominant SLC4A1-related dRTA, although recessive variants can also present late [2,3]. Genetic testing would confirm the diagnosis, facilitate screening of relatives and guide whether audiometry is required. Acquired causes, particularly Sjogren syndrome and other autoimmune disease, were not supported by the negative autoimmune screen. Urine pH, urine anion gap, serum chloride and tubular reabsorption of phosphate were not available; these measurements, with fractional excretion of bicarbonate after alkali loading if uncertainty persists, would strengthen classification.

Alkali therapy is the cornerstone of treatment. Potassium citrate corrects acidosis and hypokalaemia, raises urinary citrate, reduces hypercalciuria and stone formation, and permits bone remineralisation; the dose is titrated toward a normal plasma bicarbonate [3,4]. Long-term follow-up data indicate that well-controlled patients have better growth and renal outcomes, although chronic kidney disease remains common in adults, making sustained adherence important [4]. The rapid rise in bicarbonate and potassium within two weeks in this patient supported both the diagnosis and the need for continued dose titration.

Conclusion

Recurrent fragility fractures, hypokalaemic paralysis and kidney stones in a young adult should prompt assessment of acid-base status and serum potassium before treatment for inflammatory arthritis or osteoporosis is considered. In this patient, suspected familial dRTA provided a unifying explanation for ten years of fractures, paralysis and stones, and potassium citrate began to correct the biochemical abnormalities within weeks. Early recognition may prevent further fractures, preserve renal function and allow affected relatives to be screened.

Learning points

- Consider distal renal tubular acidosis in young adults with the combination of fragility fractures, hypokalaemic paralysis and renal stones.
- A blood gas and serum potassium are inexpensive early investigations that can reveal the acid-base and electrolyte pattern.
- A similarly affected sibling raises the possibility of inherited dRTA and supports consideration of genetic evaluation and family screening.
- Potassium citrate is central to treatment and requires biochemical follow-up with titration of alkali replacement.

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CASE REPORT 15

Parathyroid Carcinoma Presenting as Recurrent, Difficult-to-Localize Hyperparathyroidism: A Multidisciplinary Case

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Abstract

A 46-year-old man with a long history of recurrent renal stones and multiple lithotripsy procedures was evaluated for hyperparathyroidism. An initial PTH of 212 pg/mL led to bilateral inferior parathyroidectomy in March 2019; histopathology favoured adenoma, although hyperplasia could not be excluded, and the patient remained biochemically stable until 2024. Recurrence was subsequently marked by PTH 307 pg/mL with calcium 12 mg/dL, discordant localisation studies, and repeated surgical exploration that did not remove the hyperfunctioning tissue. By January 2026, PTH had risen to 1835 pg/mL and calcium to 15.6-16.8 mg/dL despite a negative parathyroid scan. MRI identified a 7-8 mm exophytic nodule at the lower pole of the left thyroid lobe. Tissue obtained during a planned left hemithyroidectomy was reported as parathyroid carcinoma by two laboratories; intraoperatively the tumour was fixed to skeletal muscle, indicating local invasion. The case illustrates the diagnostic difficulty of recurrent severe hyperparathyroidism when biochemistry, imaging and operative findings remain discordant.

Keywords: parathyroid carcinoma; recurrent hyperparathyroidism; severe hypercalcaemia; parathyroidectomy; non-localizing imaging; multidisciplinary care

Introduction

Recurrent hyperparathyroidism after apparently successful surgery can become a prolonged diagnostic challenge when biochemical severity, localisation imaging and operative findings do not align. The case documents a patient with decades of renal stone disease, an initial operation for presumed benign parathyroid disease, repeated recurrence and failed localisation, and eventual histopathological confirmation of parathyroid carcinoma. The chronology highlights why serial biochemical review and multidisciplinary reassessment become essential when the clinical course no longer fits the original diagnosis.

Case presentation

A 46-year-old man from District Buner had experienced recurrent renal stones since 1997 and had undergone 18 lithotripsy sessions. In 2018, serum PTH was 212 pg/mL and he was referred for endocrine assessment of suspected hyperparathyroidism. He underwent bilateral inferior parathyroidectomy in March 2019. Symptoms improved, and the case record states that PTH and calcium remained normal during a symptom-free period from 2019 to 2024. Histopathology from the first operation favoured parathyroid adenoma, although hyperplasia could not be completely excluded.

In 2024, PTH again increased to 170 pg/mL, prompting repeat biochemical and imaging evaluation. Subsequent PTH was 307 pg/mL with serum calcium 12 mg/dL. Neck ultrasonography was reported as normal, while a parathyroid scan localized a small lesion in the right paratracheal space posterior to the mid/lower pole of the right thyroid lobe. A second operation was performed, but the excised specimen was reported as normal tissue. PTH remained elevated at 357 pg/mL and increased to 456 pg/mL two days later, with persistent calcium of 12 mg/dL.

Repeat ultrasonography then demonstrated small hypoechoic lesions at the inferior pole of the left thyroid lobe and prominent bilateral cervical lymph nodes. A parathyroid scan dated 29 October 2024

localized an adenoma anterolateral to the left thyroid lobe. Surgery was performed in November 2024; however, according to the case account, the surgeon did not identify the adenoma despite exploration. The patient continued to experience constipation, abdominal pain and restlessness, and subsequent ultrasound showed no sonographic evidence of parathyroid tissue.

The patient did not seek further consultation during 2025 because of disappointment with the preceding procedures. On 12 January 2026, self-initiated testing showed PTH 1835 pg/mL and calcium 15.6 mg/dL. A parathyroid scan on 15 January 2026 showed no scintigraphic evidence of adenoma or hyperplasia, while calcium increased to 16.8 mg/dL by 26 January. The case was discussed in an endocrine multidisciplinary forum. MRI of the neck identified a 7-8 mm exophytic nodule along the lower pole of the left thyroid lobe, isointense on T1 and hyperintense on STIR, with a differential diagnosis of parathyroid tissue, exophytic thyroid nodule or lymph node.

Investigations

The key feature was progressive biochemical severity despite repeatedly discordant localisation studies and operative findings. The major events provided in the case record are summarised in Table 1.

Table 1. Chronology of biochemical, imaging and operative findings

Time point	Biochemistry	Localisation or pathology	Clinical action or outcome
2018	PTH 212 pg/mL	Suspected hyperparathyroidism	Endocrinology referral
March 2019	Postoperative PTH and calcium reported normal	Adenoma favoured; hyperplasia not excluded	Bilateral inferior parathyroidectomy; symptom-free until 2024
2024 recurrence	PTH 307 pg/mL; calcium 12 mg/dL	Ultrasound normal; scan localised right paratracheal lesion	Second operation
After second surgery	PTH 357 then 456 pg/mL; calcium 12 mg/dL	Excised specimen reported as normal tissue	Persistent hyperparathyroidism
October-November 2024	Persistent symptoms and raised PTH	Left-sided target on scan; lesion not identified at exploration	Further surgery without reported biochemical resolution
12 January 2026	PTH 1835 pg/mL; calcium 15.6 mg/dL	Repeat localisation requested	Urgent reassessment
15-26 January 2026	Calcium 16.8 mg/dL	Scan negative; MRI showed 7-8 mm left-sided exophytic nodule	MDT discussion and surgery planning
Definitive tissue diagnosis	Not reported	Carcinoma confirmed by two laboratories; fixed to skeletal muscle	Decision to remove remaining tissue despite laryngeal nerve risk

Diagnosis and management

A left hemithyroidectomy approach was selected on the basis of the MRI-localized exophytic lesion. The operation was initially halted when further dissection was judged to carry a significant risk of laryngeal nerve injury, pending tissue diagnosis. Biopsy subsequently confirmed parathyroid carcinoma in reports from both NWGH and Shaukat Khanum laboratories. Following confirmation of malignancy, the team decided to remove the remaining tissue despite the nerve risk. The operative description noted that the tumour was fixed to skeletal muscle, supporting local invasion. The case record does not provide a subsequent calcium/PTH trajectory, oncologic treatment plan or longer-term postoperative outcome.

Discussion

The diagnostic challenge evolved over several years. The first operation in 2019 appeared successful clinically and biochemically, while histopathology favoured adenoma but left hyperplasia in the differential. When hyperparathyroidism recurred in 2024, imaging alternated between right-sided and left-sided targets, and repeat surgery either removed normal tissue or failed to identify the suspected lesion. This created a substantial discordance between the biochemical evidence of disease and the anatomical localisation available to the treating teams.

The severity of the biochemical recurrence became striking in January 2026, when PTH reached 1835 pg/mL and calcium reached 16.8 mg/dL. At that stage, a negative parathyroid scan did not resolve the diagnostic problem. MRI provided a new anatomical target: a 7-8 mm exophytic lesion adjacent to the lower pole of the left thyroid lobe. Histopathological confirmation from two laboratories ultimately established parathyroid carcinoma, while fixation of the tumour to skeletal muscle at surgery indicated locally invasive behaviour in the submitted operative account.

The case therefore illustrates the value of revisiting the working diagnosis when recurrent disease becomes progressively severe and conventional localisation remains inconsistent. It also demonstrates the importance of multidisciplinary coordination between endocrinology, endocrine/ENT surgery, radiology, pathology, oncology and nuclear medicine when further intervention carries substantial anatomical risk.

Conclusion

Recurrent severe hyperparathyroidism after multiple operations requires continued biochemical surveillance and repeated diagnostic synthesis rather than reliance on a single localisation study. In this patient, escalating PTH and calcium, discordant scans and unsuccessful explorations ultimately led to MRI-directed tissue sampling and confirmation of parathyroid carcinoma. The case underscores the role of multidisciplinary decision-making when diagnostic uncertainty and operative risk coexist.

Learning points

- Recurrent hyperparathyroidism should be reassessed when the subsequent biochemical course no longer fits the original benign diagnosis.
- Severe biochemical disease may persist despite negative or conflicting localisation studies.
- When imaging and operative findings are discordant, pathology review and multidisciplinary reassessment can be decisive.
- Operative planning in suspected invasive parathyroid malignancy must balance disease control against the risk to adjacent structures.

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CASE REPORT 16

From Shock to Solution: Unraveling a Hidden Cause of Refractory Supraventricular Tachycardia

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Abstract

A previously well 28-year-old woman presented in haemodynamic collapse after receiving intramuscular ceftriaxone for sore throat and vomiting and was initially treated as anaphylaxis. Eleven hours later she developed haemodynamically unstable supraventricular tachycardia at more than 200 beats/min that failed adenosine 6 mg, 12 mg and 12 mg and required synchronised cardioversion. Echocardiography was normal and troponin elevation was mild and non-ischaemic. One week later she returned with neck and jaw pain, myalgia, irritability and a tender unilateral thyroid swelling. ESR was 66 mm/h, CRP 78.7-88.5 mg/L, TSH 0.005 mIU/L, free T4 4.76 ng/dL and free T3 7.28 pg/mL; TSH-receptor antibodies were negative. Thyroid ultrasound showed unilateral enlargement with hypoechoic heterogeneous change. The case record diagnosed subacute (De Quervain) thyroiditis with thyrotoxicosis as the unifying cause of the arrhythmia. Corticosteroids, propranolol and NSAIDs were used, antithyroid drugs were stopped, and no further SVT was reported during follow-up.

Keywords: De Quervain thyroiditis; subacute thyroiditis; thyrotoxicosis; supraventricular tachycardia; adenosine resistance; cardioversion

Introduction

Thyrotoxicosis can have prominent cardiovascular manifestations, while subacute (De Quervain) thyroiditis may initially present before its classical painful thyroid features are fully apparent. This case was presented as a diagnostic sequence in which an initial episode of shock and an adenosine-resistant supraventricular tachycardia were managed as a primary cardiac problem before the later appearance of painful thyroid inflammation revealed a unifying endocrine diagnosis.

Case presentation

A 28-year-old woman with no known comorbidities developed sore throat and vomiting and received intramuscular ceftriaxone at home. She subsequently presented to the emergency department in collapse, with blood pressure 70/40 mmHg, heart rate 103 beats/min, oxygen saturation 92% on room air and drowsiness while remaining arousable. She was afebrile. The initial working diagnosis was ceftriaxone-associated anaphylaxis with haemodynamic shock, and she was treated with intravenous fluids, corticosteroids and antihistamines, with initial stabilization.

Approximately 11 hours after admission, she developed sudden haemodynamically unstable supraventricular tachycardia with a heart rate above 200 beats/min. Adenosine 6 mg, followed by 12 mg and a second 12 mg dose, did not terminate the arrhythmia. synchronised direct-current cardioversion restored sinus rhythm. Echocardiography showed no structural abnormality and troponin elevation was described as mild and non-ischaemic. She was discharged on propranolol with the arrhythmia aetiology still unclear.

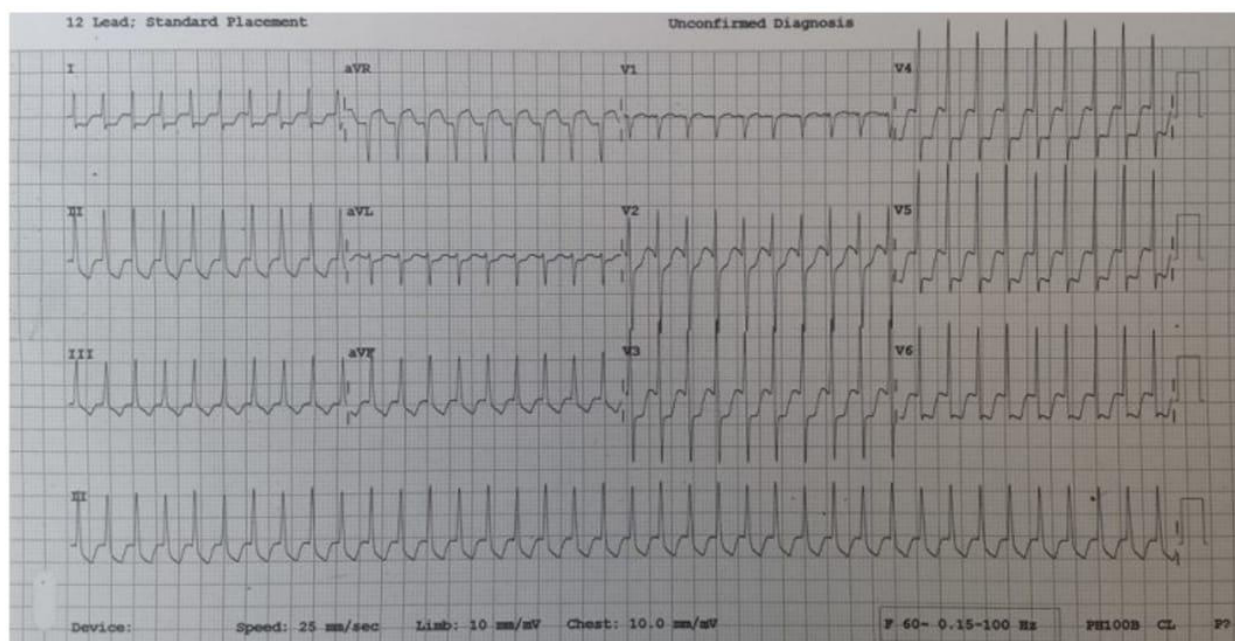


Figure 1. Electrocardiographic tracing reproduced from the case record during the supraventricular tachycardia episode.

One week later she returned with neck pain, jaw pain, myalgia and irritability. Examination disclosed a tender unilateral neck swelling without allergic features. This second presentation prompted reassessment of the original cardiac diagnosis and targeted thyroid evaluation.

Investigations

The cardiac evaluation did not identify structural heart disease. Inflammatory markers were markedly elevated, and thyroid testing demonstrated severe thyrotoxicosis with negative TSH-receptor antibodies. The case record reported unilateral thyroid enlargement with hypoechoic, heterogeneous change on ultrasonography.

Table 1. Key investigations reported in the case

Investigation	Result	Reported interpretation
Echocardiography	Normal	No structural heart disease identified
Troponin	Mildly elevated	Described as non-ischaemic
ESR	66 mm/h	Elevated
CRP	78.7-88.5 mg/L	Markedly elevated
TSH	0.005 mIU/L	Suppressed
Free T4	4.76 ng/dL	Elevated
Free T3	7.28 pg/mL	Elevated
TSH-receptor antibodies	Negative	Used in the presentation to argue against Graves disease
Thyroid ultrasound	Unilateral enlargement; hypoechoic, heterogeneous changes; increased vascularity reported	Supported the submitted diagnosis in the setting of thyroid pain and inflammation

Differential diagnosis

The presentation considered structural heart disease, viral myocarditis, an ion-channel disorder, ceftriaxone anaphylaxis, Graves disease and anxiety/functional SVT. A normal echocardiogram and lack of baseline structural disease argued against a primary structural cause. The initial collapse was considered compatible with a drug reaction, but this did not account for the later adenosine-resistant SVT or painful neck swelling. Graves disease was considered less likely because TSH-receptor antibodies were negative, there was a painful thyroid, unilateral ultrasound change and no ophthalmopathy. The final unifying diagnosis in the case was subacute (De Quervain) thyroiditis with thyrotoxicosis driving the arrhythmia.

Management and follow-up

The acute unstable SVT required synchronised cardioversion after failure of escalating adenosine doses. Once the thyroid diagnosis was established, intravenous corticosteroids were used to treat the inflammatory thyroid process, propranolol was continued for rate control and symptom relief, and NSAIDs were used for pain. Antithyroid drugs were discontinued because the case record classified the thyrotoxicosis as destructive release of preformed hormone rather than increased hormone synthesis. Follow-up documented resolution of neck pain, normalisation of thyroid function toward the expected course and no further SVT recurrence. Thyroid function testing at 4-6 weeks and again at 3-6 months was advised.

Discussion

The case record framed the case around two diagnostic traps. First, the plausible initial diagnosis of anaphylaxis became an anchoring point after haemodynamic collapse. Second, the dramatic SVT shifted attention to the heart even though the echocardiogram was normal and the troponin rise was not considered ischaemic. The painful thyroid syndrome became clinically obvious only one week later, at which point the elevated inflammatory markers, severe thyrotoxicosis and negative TSH-receptor antibodies redirected the diagnostic pathway.

The proposed mechanism was follicular disruption from subacute granulomatous thyroid inflammation, with release of stored thyroid hormone and resulting beta-adrenergic cardiovascular effects. The presentation also proposed that persistent thyrotoxic and inflammatory effects may have sustained an arrhythmogenic substrate despite adenosine. This mechanistic interpretation was used to explain why treating the thyroid process, rather than escalating cardiac-specific therapy alone, was followed by recovery.

A further practical point was the distinction between destructive thyrotoxicosis and increased hormone synthesis. In the management rationale, thionamides were stopped because they inhibit new hormone synthesis and therefore do not address release of preformed hormone from inflamed follicles. Symptom control with beta-blockade and anti-inflammatory treatment was emphasized instead.

Conclusion

A severe arrhythmia may be the first dominant manifestation of an endocrine disorder. In this case, recurrent diagnostic review after a normal structural cardiac assessment and the subsequent appearance of painful thyroid swelling disclosed subacute thyroiditis with thyrotoxicosis. The case emphasizes the value of revisiting an initial diagnosis when the subsequent clinical course no longer fits it.

Learning points

- An initially plausible diagnosis such as drug-related anaphylaxis should be reconsidered when later events are not fully explained by it.
- Thyroid function testing can be clinically important in otherwise unexplained or refractory tachyarrhythmia.

- Painful thyroid swelling, raised inflammatory markers and thyrotoxicosis with negative TSH-receptor antibodies supported the submitted diagnosis of subacute thyroiditis.
- Destructive thyrotoxicosis was treated with anti-inflammatory therapy and beta-blockade rather than continued thionamide therapy in this case.
- Follow-up thyroid testing is important because the course may evolve from thyrotoxicosis toward a hypothyroid phase.

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CASE REPORT 17

Pituitary Macroadenoma Presenting with Hypogonadotropic Hypogonadism and Fertility Concern

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Abstract

A 21-year-old woman presented with a two-year history of headache and secondary amenorrhoea and was diagnosed with a pituitary macroadenoma after approximately one year of symptoms. She had attained menarche at 15 years and had normal secondary sexual characteristics, but fertility and restoration of menstruation became major concerns. She underwent transsphenoidal surgery in June 2025 and later received radiotherapy beginning in February 2026. The postoperative course was complicated by polyuria requiring desmopressin, secondary hypothyroidism requiring levothyroxine and possible secondary adrenal insufficiency treated with prednisone. The case record described clinically evident hypogonadotropic hypogonadism and recommended assessment of LH, FSH, estradiol, prolactin and anti-Müllerian hormone. This case highlights the reproductive implications of a pituitary macroadenoma and the need for long-term surveillance of tumour status, pituitary hormone deficits and fertility goals after surgery and radiotherapy.

Keywords: pituitary macroadenoma; hypogonadotropic hypogonadism; secondary amenorrhoea; fertility; hypopituitarism; transsphenoidal surgery

Introduction

Pituitary macroadenomas may present through mass effect, hormone excess or pituitary hormone deficiency. In young women, suppression of the hypothalamic-pituitary-gonadal axis can lead to amenorrhoea and create important fertility concerns. The case focuses on a young woman whose pituitary tumour, subsequent surgery and radiotherapy were followed by multiple endocrine replacement needs and an ongoing need for reproductive counselling.

Case presentation

A 21-year-old woman presented with headache that had been present for approximately two years. Menarche had occurred at 15 years of age, but she developed menstrual irregularity followed by amenorrhoea for two years from around the onset of her headache. She was diagnosed with a pituitary macroadenoma in 2024, approximately one year after the beginning of symptoms. Secondary sexual characteristics were described as normal, and the patient expressed significant concern regarding restoration of menses and future fertility.

Transsphenoidal surgery was performed in June 2025. The submitted timeline states that radiotherapy began in February 2026. After surgery, she developed symptoms and treatment requirements consistent with broader pituitary dysfunction, including polyuria requiring desmopressin, low blood pressure, hypothyroid symptoms managed with levothyroxine, and treatment with prednisone for possible secondary adrenal insufficiency.

Investigations

MRI of the pituitary was reported as consistent with a pituitary macroadenoma, with mass effect considered a likely contributor to gonadotropin suppression. The presentation emphasized serial MRI surveillance after surgery and radiotherapy together with visual-field assessment. Numerical tumour dimensions, formal visual-field results, histopathology and numerical pituitary hormone concentrations were not included in the case record.

Clinically, hypogonadotropic hypogonadism was considered evident. The presentation also identified secondary hypothyroidism, possible secondary adrenal insufficiency and diabetes insipidus. Further gonadal-axis evaluation was recommended with LH, FSH, estradiol, prolactin and anti-Mullerian hormone to assess the reproductive axis and ovarian reserve.

Table 1. Timeline and endocrine consequences reported in the case record

Time point	Event	Endocrine/reproductive relevance
2023	Onset of headache and menstrual irregularity	Beginning of clinical course leading to tumour diagnosis
2024	Pituitary macroadenoma diagnosed	Mass effect considered relevant to gonadotropin suppression
June 2025	Transsphenoidal surgery	Postoperative endocrine deficiencies subsequently required replacement therapy
Postoperative period	Polyuria, low blood pressure and hypothyroid symptoms	Desmopressin, prednisone and levothyroxine used
February 2026	Radiotherapy initiated	Need for continued tumour surveillance and monitoring for radiation-related hypopituitarism
Ongoing	Amenorrhoea and fertility concern	Reproductive counselling and gonadal-axis assessment recommended

Management and follow-up

Current medications reported in the case record were levothyroxine, prednisone and desmopressin. Regular endocrinology follow-up was advised to assess the adequacy of hormone replacement. Long-term surveillance was planned with serial pituitary MRI, hormonal profiling, assessment for recurrence or progression, monitoring for radiation-related hypopituitarism, and attention to bone health and cardiovascular risk.

Fertility management was presented as a parallel priority. Detailed reproductive counselling was recommended, with consideration of ovulation induction, pulsatile GnRH or gonadotropin therapy, and assisted reproductive techniques according to residual pituitary and ovarian function. Joint follow-up with endocrinology and fertility specialists was emphasized.

Discussion

This case illustrates that pituitary disease in a young woman cannot be considered solely in terms of tumour control. Secondary amenorrhoea was a major presenting feature, and the patient's concern about fertility remained central after surgery. Normal secondary sexual characteristics suggested prior oestrogen exposure, but persistent amenorrhoea and clinically suspected hypogonadotropic hypogonadism raised the question of residual gonadotropin function and the likelihood of spontaneous menstrual recovery.

The postoperative need for desmopressin, levothyroxine and prednisone indicated that endocrine follow-up had to extend beyond the reproductive axis. The case record also highlighted the potential for radiotherapy to further compromise pituitary function, making repeated hormone assessment

important over time. Fertility planning therefore depends not only on the gonadal axis but also on safe and adequate replacement of other pituitary-dependent hormones and ongoing tumour surveillance.

Conclusion

Pituitary macroadenoma in a young woman may present with menstrual disturbance and create long-term reproductive as well as endocrine consequences. Following transsphenoidal surgery and radiotherapy, this patient required multiple hormone replacements and ongoing surveillance. Fertility counselling and assessment of the gonadal axis should remain integrated with tumour follow-up and management of hypopituitarism.

Learning points

- Pituitary tumours may initially present with menstrual abnormalities as well as headache.
- Young women with pituitary disease require explicit discussion of reproductive goals and fertility options.
- Surgery and radiotherapy may be followed by multiple pituitary hormone deficiencies requiring long-term surveillance.
- Fertility planning should be integrated with adequate replacement of thyroid, adrenal and water-balance deficits where present.
- Serial imaging and endocrine review remain important after definitive tumour treatment.

CASE REPORT 18

Thyroid Inferno in Primary Hypothyroidism: A Doppler Pattern Mimicking Graves Disease

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Abstract

Marked thyroid hypervascularity ("thyroid inferno") on Doppler ultrasonography is classically associated with Graves disease but may rarely occur in severe primary hypothyroidism. We report a 30-year-old female physician who presented with six months of fatigue and five months of weight gain, cold intolerance, constipation, menstrual irregularity, and diffuse neck swelling. Laboratory evaluation revealed severe primary hypothyroidism with thyroid-stimulating hormone (TSH) reported as >100, with units unavailable, free thyroxine (FT4) reported as 6.9, with units unavailable, and anti-thyroid peroxidase (anti-TPO) antibodies reported as >1000, with units unavailable. Doppler ultrasonography demonstrated diffuse thyroid enlargement with marked hypervascularity producing a "thyroid inferno" pattern. Thyroid uptake was reported as 6.6%. Despite the Graves-like sonographic appearance, the clinical and biochemical findings supported autoimmune primary hypothyroidism. Levothyroxine was initiated at 1.6 µg/kg/day. At six-week follow-up, thyroid function improved and Doppler hypervascularity had markedly decreased. This case highlights that striking thyroid hypervascularity should be interpreted in conjunction with clinical and biochemical findings rather than as an isolated marker of hyperthyroidism. Measurement of TSH receptor antibodies (TRAb) may be helpful when diagnostic uncertainty persists.

Keywords: primary hypothyroidism; Hashimoto thyroiditis; thyroid inferno; Doppler ultrasound; thyroid hypervascularity; diagnostic pitfall

Introduction

colour Doppler ultrasonography is frequently used to assess thyroid blood flow. The term "thyroid inferno" was first described by Ralls et al. as intense diffuse hypervascularity characteristic of Graves disease. Increased thyroid blood flow has traditionally been regarded as a useful marker of hyperthyroidism and autoimmune stimulation. However, rare reports have documented Graves-like Doppler appearances in patients with biochemical hypothyroidism, creating a potential diagnostic pitfall.

A recent case series by Ushakov described three patients with primary hypothyroidism exhibiting diffuse thyroid hypervascularity despite biochemical evidence of thyroid failure. These observations emphasize that imaging findings should not supersede clinical and laboratory evaluation. We report a patient with severe autoimmune primary hypothyroidism whose Doppler ultrasound demonstrated a classic thyroid inferno pattern that resolved following thyroid hormone replacement.

Case presentation

A 30-year-old female physician (G2P2A0) presented with fatigue of six months' duration and progressive weight gain for five months. She also reported cold intolerance, constipation, menstrual irregularity with menorrhagia, and gradual enlargement of the anterior neck over the preceding several months. There was no history of fever, visual disturbance, headache, postpartum thyroiditis, neck pain, radiation exposure, or use of amiodarone, lithium, iodine-containing medications, biotin supplements, or traditional medicines. There was no known personal or family history of autoimmune disease.

On examination, blood pressure was 120/80 mmHg, pulse 67 beats/min and respiratory rate 16 breaths/min; temperature was normal. The thyroid was diffusely enlarged without palpable nodules or

a bruit. There were no signs of thyroid eye disease. Anthropometric measurements, thyroid grade and a definitive reflex assessment were not available.

Investigations

Baseline investigations were reported as normal apart from microcytic anaemia. Thyroid testing demonstrated a TSH greater than 100, free T4 reported as 6.9 (the unit and reference range were not specified in the case record), and anti-thyroid peroxidase antibodies greater than 1000. Ultrasound of the neck with Doppler demonstrated diffuse thyroid enlargement with marked hypervascularity, described by the presenter as a "thyroid inferno". Thyroid uptake was reported as 6.6%.

Table 1. Key diagnostic findings reported in the case record

Investigation	Result	Clinical interpretation / relevance
CBC	Microcytic anaemia	Only baseline abnormality specifically reported
TSH	>100	Markedly elevated; biochemical hypothyroidism
Free T4	6.9 (unit not stated)	Reported with the hypothyroid biochemical profile; unit/reference range not supplied
Anti-TPO antibody	>1000	Strongly positive
Thyroid ultrasound/Doppler	Diffuse swelling with marked hypervascularity ("thyroid inferno")	Imaging appearance created potential confusion with Graves-like hypervascularity
Thyroid uptake scan	6.6%	Reported in the diagnostic work-up



Figure 1. Colour Doppler image from the case record showing marked diffuse thyroid hypervascularity ("thyroid inferno").

Management and follow-up

The patient was treated with levothyroxine at 1.6 micrograms/kg/day and was asked to return after six weeks. At follow-up, the thyroid profile was reported to be within the normal range, Doppler hypervascularity had settled and thyroid uptake was described as lower-normal.

Discussion

The central teaching point in this case was the discordance between the Doppler appearance and the biochemical diagnosis. A markedly vascular thyroid can visually suggest Graves disease, but this patient had clinical symptoms of hypothyroidism, TSH greater than 100 and strongly positive anti-TPO antibodies. The submitted literature-review slide also referred to a January 2024 report in which three patients with primary hypothyroidism had ultrasound findings resembling those commonly seen in Graves disease.

The case therefore argues against interpreting a single imaging descriptor in isolation. Doppler findings should be integrated with symptoms, thyroid-stimulating hormone, free thyroid hormone measurements and antibody results. In this patient, treatment followed the biochemical diagnosis of hypothyroidism rather than the Graves-like vascular pattern, and both thyroid function and vascularity improved at follow-up.

Conclusion

Marked thyroid hypervascularity does not by itself establish a diagnosis of Graves disease. In this patient, a "thyroid inferno" appearance coexisted with a strongly hypothyroid biochemical profile and high anti-TPO antibodies. Clinical and biochemical correlation prevented the vascular imaging pattern from overriding the primary diagnosis, and levothyroxine treatment was followed by biochemical and sonographic improvement.

Learning points

- Interpret thyroid Doppler vascularity together with the biochemical thyroid profile rather than in isolation.
- A Graves-like "thyroid inferno" appearance may create diagnostic confusion when TSH and free thyroid hormone results indicate hypothyroidism.
- Strongly positive anti-TPO antibodies supported autoimmune thyroid disease in the case.
- Follow-up after levothyroxine showed normalisation of the thyroid profile and resolution of the reported hypervascularity.

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CASE REPORT 19

Pheochromocytoma with Bilateral Adrenal Lesions and Suspected von Hippel-Lindau Syndrome

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Abstract

A 26-year-old woman presented with right upper quadrant pain, episodic headaches, sweating, dizziness and hypertension. Markedly elevated plasma metanephrines and normetanephrines, bilateral adrenal lesions and spinal MRI abnormalities suspicious for haemangioblastomas raised concern for von Hippel-Lindau (VHL) syndrome. Following alpha-blockade and subsequent beta-blockade, laparoscopic right adrenalectomy was performed in January 2025. Histopathology confirmed pheochromocytoma. Genetic testing remained pending because of resource constraints. Follow-up was planned for the residual left adrenal lesion, spinal abnormalities and blood pressure. The case illustrates the importance of syndromic evaluation in young patients with pheochromocytoma.

Keywords: pheochromocytoma; von Hippel-Lindau syndrome; bilateral adrenal lesions; haemangioblastoma; hereditary tumour syndrome

Introduction

Pheochromocytoma in a young adult, particularly with bilateral adrenal lesions and a suggestive family history, warrants assessment for an inherited tumour syndrome. This report describes a histologically confirmed right adrenal pheochromocytoma in a patient with clinical features suspicious for VHL syndrome; molecular confirmation was not available.

Case presentation

A 26-year-old unmarried female student presented with right upper quadrant pain for one month and intermittent headaches, sweating and dizziness. Hypertension had been detected during evaluation in China, where nifedipine 30 mg once daily was started. Menstrual cycles were regular. She reported no hirsutism, weight change, diarrhoea, nausea, jaundice, wheeze or cough, and had no significant past medical history.

Family history included diabetes and reported brain and renal cysts in siblings, with possible haemangioblastoma and concern for VHL syndrome. These diagnoses were not genetically confirmed in the supplied record. An uncle had died following a cardiac event at 55 years.

She appeared well. Blood pressure was 149/87 mmHg, pulse 76 beats/min, weight 46 kg and height 153 cm. There was no significant postural fall in blood pressure.

Investigations

Plasma metanephrines were 302.24 against a reference range of 0-90, and normetanephrines were 1971.6 against 0-190. The corresponding assay units were not provided. Other reported laboratory findings are summarised below; units and reference ranges are retained only where supplied.

Investigation	Reported result	Reference range or note
Haemoglobin / white cell count / platelets	12.0 / 8.5 / 413	Units not supplied

Investigation	Reported result	Reference range or note
Creatinine	0.5	Unit not supplied
Sodium / potassium / bicarbonate	139 / 4.1 / 22.3	Units not supplied
Fasting / random glucose	116 / 152	Units not supplied
Prothrombin time	13	9.3-12.8; unit not supplied
APTT	43.4	22.9-34.5; unit not supplied
Cortisol	1.01 micrograms/dL	Sampling time and test context not supplied
Magnesium	1.4	Unit not supplied
Calcium	8.4	8.6-10.2; unit not supplied
PTH / vitamin D / phosphate	102.9 / 5.4 / 3.4	Units not supplied
Aldosterone / renin	18.40 / 150.9	Units and sampling conditions not supplied
DHEA	188	160-449; unit not supplied
Plasma metanephrines	302.24	0-90; unit not supplied
Plasma normetanephrines	1971.6	0-190; unit not supplied
17-hydroxyprogesterone	0.35	Unit not supplied

Initial CT described a well-defined nodular soft-tissue lesion, the largest dimension being 45 × 26 mm, without renal abnormalities. Dedicated adrenal CT subsequently showed a right adrenal mass measuring 3.6 × 2.3 × 3.5 cm, with unenhanced attenuation of 33 HU, absolute washout of 82% and relative washout of 66%. A left adrenal nodule measured 1.3 × 0.9 × 0.4 cm, with unenhanced attenuation of 32 HU, absolute washout of 78% and relative washout of 67%.

Brain MRI showed no abnormality. Spinal MRI was reported to show diffuse signal abnormalities with lesions suspicious for haemangioblastomas at C2-C3 and C6-C7. Ophthalmological assessment identified no retinal haemangioblastoma. Neurosurgical review recommended surveillance.

Diagnosis

The working diagnosis was pheochromocytoma with suspected VHL syndrome. Histology confirmed the right adrenal pheochromocytoma, but the left adrenal lesion and spinal abnormalities were not histologically characterised. VHL genetic testing had not been performed.

Management and follow-up

Doxazosin was started at 2 mg twice daily and increased to 4 mg twice daily when home blood pressure remained approximately 140/90 mmHg. Persistent readings around 150/90 mmHg led to further escalation, recorded as 6-4-4 mg across the day. Metoprolol 50 mg twice daily was subsequently added for heart rates of 100-110 beats/min. These are the documented case doses, rather than a general dosing protocol.

Following surgical assessment, laparoscopic right adrenalectomy was performed in the first week of January 2025. The adrenal gland measured 3.8 × 3.2 × 2.8 cm and contained a well-circumscribed haemorrhagic lesion measuring 2.5 × 2.2 cm, located 0.4 cm from the inked resection margin. Microscopy demonstrated nests of polygonal to epithelioid cells within a vascular stroma, granular basophilic to amphophilic cytoplasm and nuclei with speckled chromatin. Mitotic activity was up to 1-2 per 10 high-power fields; necrosis was absent.

Immunohistochemical marker	Result
Synaptophysin / chromogranin	Positive in tumour cells
CK AE1/AE3 / inhibin / Melan-A	Negative in tumour cells
S100	Focal positivity around tumour cells
Ki-67	Up to 2%

The diagnosis was right adrenal pheochromocytoma, 2.5 × 2.2 cm. The supplied PASS assessment reported no periadrenal adipose, capsular or vascular invasion; no atypical mitoses, necrosis, cellular spindling, cellular monotony, marked nuclear pleomorphism, diffuse growth, high cellularity or hyperchromasia; and no mitotic count above three per 10 high-power fields. A formal numerical PASS was not stated.

The postoperative plan included home blood pressure monitoring, repeat plasma metanephrines and normetanephrines, and repeat spinal MRI and adrenal CT in 6-12 months. Doxazosin was reduced to 2 mg at bedtime, while metoprolol 50 mg twice daily was continued. Genetic testing was deferred because of resource constraints. Postoperative biochemical results and longer-term outcomes were not available.

Discussion

VHL is an autosomal dominant tumour predisposition syndrome caused by pathogenic germline variants in the VHL gene. Associated lesions include central nervous system and retinal haemangioblastomas, clear-cell renal cell carcinoma, pheochromocytoma, pancreatic cysts and neuroendocrine tumours, endolymphatic sac tumours and papillary cystadenomas. The combination of a young age, bilateral adrenal lesions, suspicious spinal lesions and a suggestive family history makes VHL a clinically important consideration in this patient [1].

Pheochromocytoma-associated VHL is conventionally grouped as type 2: type 2A has lower renal cell carcinoma risk, type 2B higher renal cell carcinoma risk and type 2C predominantly pheochromocytoma. Type 1 carries relatively low pheochromocytoma risk; type 1B is associated with deletions that may include BRK1 and lower renal carcinoma risk. These classifications describe familial phenotypes and cannot be assigned confidently from this unconfirmed case [1].

The presence of favourable histological findings does not remove the need for ongoing surveillance. In this patient, postoperative reassessment is also needed to determine biochemical response and the significance of the contralateral adrenal lesion. The original 6-12-month imaging plan addresses known abnormalities; broader VHL surveillance should be coordinated across endocrinology, genetics, ophthalmology, neurosurgery and radiology if the syndrome is established or remains strongly suspected [2].

Surveillance considerations

The age-based schedule below summarises the surveillance framework supplied with the case. It describes general VHL surveillance rather than completed investigations in this patient; established lesions may require more frequent review [2].

Age or domain	Surveillance framework
From infancy	Retinal examination every 6-12 months; annual clinical assessment from age 1 and blood pressure/pulse from age 2
From age 5	Annual plasma free or 24-hour urinary fractionated metanephrines
From age 11	Brain and whole-spine MRI approximately every 2 years; audiological assessment approximately every 2 years

Age or domain	Surveillance framework
From age 15	Abdominal MRI approximately every 2 years; dedicated internal auditory canal imaging during adolescence to assess for endolymphatic sac tumours
Known lesions	Individualised follow-up based on lesion site, size, symptoms and specialist assessment

Conclusion

A young woman with confirmed pheochromocytoma, bilateral adrenal lesions and suspected spinal haemangioblastomas requires syndromic evaluation and coordinated follow-up. The available evidence raises strong suspicion of VHL, but genetic confirmation and further characterisation of the associated lesions remain outstanding.

Learning points

- Young age and bilateral adrenal lesions should prompt assessment for a hereditary pheochromocytoma syndrome.
- Distinguish a confirmed tumour diagnosis from a suspected inherited syndrome.
- Postoperative biochemical assessment and surveillance of residual lesions remain essential.

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CASE REPORT 20

Resistance to Thyroid Hormone Beta with a Shared Heterozygous THRB Variant in a Child and Her Mother

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Abstract

An eight-year-old girl presented with weight loss, palpitations, goitre, hair loss and attention difficulties. Repeated testing showed elevated free thyroid hormones with non-suppressed TSH. Initial treatment for presumed Graves disease produced no clinical improvement. Pituitary MRI showed no lesion. Whole-exome sequencing reportedly identified the same heterozygous THRB variant in the child and her mother, supporting resistance to thyroid hormone beta (RTH β). The case illustrates the diagnostic value of persistent biochemical discordance and family evaluation. The exact variant, maternal phenotype and subsequent clinical outcome were not provided.

Keywords: resistance to thyroid hormone beta; THRB; discordant thyroid function tests; goitre; familial endocrine disorder

Introduction

Persistently raised FT4 and FT3 with non-suppressed TSH require reassessment before treatment as conventional primary hyperthyroidism. RTH β , assay interference and TSH-secreting pituitary tumours are important diagnostic considerations [1,2].

Case presentation

An eight-year-old girl presented with a three- to four-year history of weight loss, palpitations, anterior neck swelling, hair loss and attention difficulties. She had no significant past medical history. Her grandmother had undergone thyroidectomy, although the indication was not reported. Examination showed tachycardia at 110 beats/min, a low BMI and diffuse goitre without ophthalmopathy. Exact anthropometric measurements were unavailable.

The initial impression was hyperthyroidism, and she was treated for presumed Graves disease without clinical improvement. Drug details and treatment duration were not supplied.

Investigations

Date	TSH	FT3	FT4
February 2024	Normal	High	High
May 2024	Normal	High	High
June-August 2024	Fluctuating	High	High
January 2025	Non-suppressed	Not reported	High

Numerical values, assay units and reference ranges were not available. Thyroid ultrasonography showed an enlarged vascular gland, and scintigraphy described a hyperfunctioning thyroid. Pituitary MRI was normal. Whole-exome sequencing reportedly identified a shared autosomal dominant

heterozygous THRB variant in the patient and her mother. The variant designation and formal laboratory classification were not provided.

Diagnosis

The reported molecular finding, family concordance and biochemical pattern supported RTH β , also known as Refetoff syndrome. A normal pituitary MRI reduced suspicion of a visible TSH-secreting lesion but did not, by itself, exclude a small TSH-secreting tumour.

Management and follow-up

After diagnostic reassessment, the supplied case discussion favoured conservative management with regular clinical and biochemical monitoring rather than continued treatment directed at Graves disease. The final medication regimen, maternal assessment, growth trajectory and subsequent outcome were not reported.

Discussion

RTH β causes reduced responsiveness to thyroid hormone, often producing raised circulating thyroid hormones with normal or mildly raised TSH. Tissue responses vary, so goitre, tachycardia and attention difficulties may coexist with otherwise compensated thyroid status. The shared familial variant offers a unifying explanation for the biochemical findings, although its exact pathogenic classification must be reviewed [1].

The diagnostic process should first consider assay interference, medication effects and altered thyroid hormone binding. Differentiating RTH β from a TSH-secreting tumour may require genetic analysis, biochemical markers, dynamic testing and imaging together. THRB-directed testing can confirm the diagnosis when an appropriate pathogenic variant is identified; whole-exome sequencing is not mandatory for every patient with this pattern [1,2].

Treatment is individualised to clinically important symptoms and associated thyroid disease. Lowering thyroid hormone concentrations solely to normalise laboratory values can be inappropriate in compensated RTH β . The original report mentioned anti-thyroglobulin antibody positivity without providing a result; this was not included as a documented patient finding. Autoimmune thyroid disease, if suspected, requires separate assessment [1].

Conclusion

Repeated elevation of FT4 and FT3 with non-suppressed TSH should prompt investigation for RTH β and other causes of discordant thyroid testing. In this child, reported identification of the same THRB variant in her mother supported a familial disorder and redirected management. Confirmation of the precise variant and longitudinal follow-up would strengthen the report.

Learning points

- Non-suppressed TSH is a key clue when thyroid hormone concentrations are persistently high.
- A normal pituitary MRI is not sufficient to exclude a TSH-secreting tumour.
- Family assessment and appropriate molecular testing can prevent unnecessary antithyroid treatment.

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CASE REPORT 21

Androgen-Secreting Adrenocortical Carcinoma Presenting as Longstanding Hirsutism and Secondary Amenorrhoea

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Abstract

A 37-year-old woman with longstanding hirsutism and oligomenorrhoea, previously treated as polycystic ovary syndrome, presented with seven months of secondary amenorrhoea and a palpable left abdominal mass. Testosterone was 604 ng/dL and DHEA-S exceeded 1000 micrograms/dL. Imaging demonstrated an 85 × 52 mm left adrenal lesion with bilateral pulmonary nodules interpreted as metastases. Left adrenalectomy and renal vein thrombectomy were performed, and histopathology confirmed conventional adrenocortical carcinoma. Mitotane was initiated postoperatively. The case highlights the importance of reassessing severe hyperandrogenism despite a longstanding PCOS label. Detailed pathological staging and postoperative response were not available.

Keywords: adrenocortical carcinoma; androgen-secreting adrenal tumour; hirsutism; amenorrhoea; PCOS mimic; mitotane

Introduction

Androgen-secreting adrenal tumours are uncommon and may initially resemble polycystic ovary syndrome. This report describes histologically confirmed adrenocortical carcinoma with predominant androgen excess and radiologically suspected pulmonary metastases.

Case presentation

A 37-year-old unmarried woman with no known comorbidities reported excessive facial hair since 2012 and secondary amenorrhoea for seven months, with a last menstrual period in July 2025. Menarche had occurred at 13 years, followed by initially regular cycles. From 2012, cycles occurred approximately every 60 days. Hirsutism involved the upper lip, chin and beard area. She reported no acne or weight gain. She had previously been managed as PCOS and had received metformin for four years. Her sister had breast carcinoma.

Blood pressure was 120/64 mmHg, pulse 87 beats/min and respiratory rate 19 breaths/min; she was afebrile. Weight was 47 kg, height 155 cm and BMI 19.6 kg/m². Examination revealed hirsutism in a male-pattern beard distribution and a tender palpable mass in the left lumbar region. Other signs of virilisation were not documented.

Investigations

Investigation	Result	Supplied reference range
DHEA-S	>1000 micrograms/dL	60.9-337 micrograms/dL
17-hydroxyprogesterone	20.93 ng/mL	Not supplied
Cortisol	9.58 micrograms/dL	Not supplied
Sex hormone-binding globulin	20.40 nmol/L	32.4-128 nmol/L
Free androgen index	102.7%	0.3-5.62%
Testosterone	604.0 ng/dL	Not supplied

The supplied report described cortisol, aldosterone and metanephrines as normal. Aldosterone and metanephrine values, cortisol sampling time and formal cortisol suppression testing were not provided. Accordingly, the report supports predominant androgen secretion without independently establishing the absence of cortisol co-secretion.

MRI of the abdomen and pelvis showed an encapsulated left adrenal lesion measuring 85 × 52 mm and multiple bilateral pulmonary nodules. PET/CT described a left suprarenal neoplastic mass with bilateral lung nodules interpreted as metastatic. Histological confirmation of the lung lesions was not supplied.

Diagnosis

Histologically confirmed conventional adrenocortical carcinoma with predominant androgen excess and radiologically suspected pulmonary metastases. The original submission described the phenotype as a pure androgen-secreting adrenal tumour; the available hormonal documentation is insufficient to independently confirm that designation.

Management and follow-up

Left adrenalectomy was performed. Renal vein thrombosis was identified intraoperatively and managed by thrombectomy. The supplied record did not distinguish bland thrombosis from tumour thrombus. Histopathology confirmed conventional adrenocortical carcinoma; tumour weight, Weiss score, Ki-67 index, margin status and vascular invasion assessment were not provided.

Postoperatively, aspirin 75 mg once daily was prescribed. Mitotane was started at 500 mg twice daily for one week and then increased to 1000 mg twice daily. This reproduces the documented regimen; mitotane concentrations, hormone replacement requirements, chemotherapy decisions, postoperative androgen values and clinical response were not available.

Discussion

Pure androgen-secreting adrenal tumours are rare, and both benign and malignant lesions are reported. Hirsutism and menstrual disturbance are common presentations. Published cases of malignant tumours tend to have larger lesions, but tumour size or androgen concentration alone cannot establish histology [1]. This patient had a large adrenal mass and subsequently confirmed carcinoma; her prolonged symptom history should not be interpreted as proof that malignancy had been present since 2012.

The major diagnostic lesson is the need to revisit an established PCOS label when the biochemical severity or examination findings are atypical. Testosterone of 604 ng/dL, DHEA-S above 1000 micrograms/dL and a palpable mass warranted evaluation for an androgen-secreting neoplasm. Raised 17-hydroxyprogesterone is not, in isolation, sufficient to diagnose congenital adrenal hyperplasia; steroid precursor secretion may accompany an adrenal tumour [2]. The supplied data do not establish the contribution of any earlier ovarian disorder.

A single cortisol measurement does not fully characterise autonomous cortisol secretion. Detailed hormonal assessment is therefore important before classifying the tumour as purely androgen-secreting. Likewise, a reported encapsulated appearance on imaging does not establish benignity. Here, histopathology confirmed carcinoma, while pulmonary findings were interpreted radiologically as metastatic. Renal vein thrombosis was treated surgically, but its pathological nature remained unspecified.

Expert multidisciplinary review is central to ACC care. Guidelines recommend adrenal-focused imaging, complete hormonal assessment and expert pathology review with proliferation and prognostic indices. For this patient, the missing margin status, Ki-67 and metastatic confirmation limit independent staging and assessment of the rationale for the postoperative strategy [2]. Her sister's breast cancer supports documenting a detailed family history, but does not alone establish a hereditary cancer syndrome.

Mitotane requires specialist monitoring of blood concentrations, toxicity and adrenal function. Hormonal markers that were elevated at diagnosis can also assist follow-up alongside imaging [2]. The record documents initiation and dose escalation of mitotane, but not monitoring results or response; these remain important elements for the authors to report when available.

Conclusion

Severe hyperandrogenism and a palpable mass require renewed investigation even when hirsutism and menstrual disturbance have previously been attributed to PCOS. In this patient, imaging and adrenal histopathology established androgen-secreting ACC. Complete pathological documentation, characterisation of metastatic disease and longitudinal biochemical and oncological follow-up are needed to define the subsequent course.

Learning points

- Reassess PCOS when androgen excess is marked or an abdominal mass is present.
- A long symptom history and encapsulated imaging appearance do not establish benignity.
- Separate histologically confirmed ACC from radiologically suspected metastatic disease.
- Mitotane treatment and follow-up require coordinated endocrine and oncology care.

References

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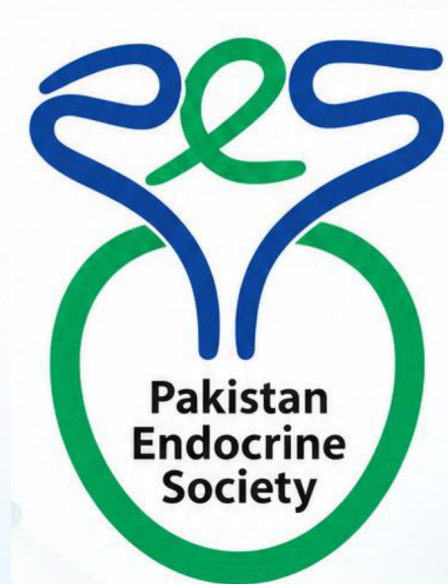


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