Short reports

The hibernating heart: reversible left ventricular dysfunction in chronic heart failure

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Summary

A patient with severe heart failure secondary to coronary heart disease is presented. Following investigation he was thought to have significant areas of myocardial hibernation and was therefore treated with coronary revascularisation, with major clinical benefit.

Keywords: heart failure; myocardial hibernation

Chronic heart failure is an increasing public health problem and coronary heart disease is the single commonest cause. The prognosis,

even with optimal medical therapy, is poor. However, reversible ventricular dysfunction is becoming increasingly recognised as a cause of heart failure and may be amenable to myocardial revascularisation in selected patients.

Case history

A 57-year-old man was referred for further investigation of his ischaemic heart disease. Angina had first been diagnosed in 1990 and he had suffered an antero-septal Q-wave myocardial infarction in 1993. There was a history of type 2 diabetes, hypertension, hyper-

Figure Rest thallium single photon emission computed tomography image. Immediate images are in the first rows, with the corresponding 4-hour-delayed images in the second rows for each projection

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cholesterolæmia and peripheral vascular disease. On review in November 1994 he had not experienced angina for 9 months but had NYHA Class III dyspnoea and fatigue with frequent episodes of paroxysmal nocturnal dyspnoea, despite treatment with frusemide, enalapril, gliclazide and simvastatin. On physical examination, a third heart sound gallop was noted, along with bilateral basal lung crackles.

At cardiac catheterisation the left ventricle was dilated with globally poor wall motion. The left ventricular ejection fraction was only 9% (normal 59–75%). Left ventricular end-diastolic pressure was 34 mmHg (normal 6–12 mmHg). There were tight proximal stenoses in the right coronary artery with complete proximal occlusions of the left anterior descending and left circumflex coronary arteries. A diagnosis of severe three-vessel coronary disease with severe left ventricular impairment and grade III heart failure was made.

In view of the poor prognosis, it was felt that surgical therapy should be considered. His comorbid conditions of diabetes, hypertension, and peripheral vascular disease were thought to make cardiac transplantation a less favourable option; however his coronary disease was anatomically suitable for revascularisation if there were a realistic prospect of benefit and survival. Therefore, a thallium perfusion study was performed, with 74MBq of thallium-201 injected at rest with immediate and 4-hour-delayed imaging. This showed considerable lung activity with a severe perfusion defect at the cardiac apex and reduced activity in the remaining segments. After 4 hours, improvement was noted throughout the heart, though incomplete at the apex (figure). The study was interpreted as showing evidence of extensive myocardial viability despite the poor left ventricular function. Therefore, coronary artery bypass grafting was performed in June 1995. The immediate postoperative course was uncomplicated, without the requirement for prolonged intensive care or haemodynamic support. However, he did suffer a minor pulmonary embolus some 27 days after surgery.

At review four months after surgery he was noted to be in NYHA Class I with a normal physical examination. Radionuclide ventriculography showed a left ventricular ejection fraction of 32% (normal >45%).

Discussion

The term 'myocardial hibernation' was first coined by Rahimtoola when commenting on the results of the large randomised trials of coronary artery surgery.¹ He envisaged a state of chronic coronary hypoperfusion, insufficient to cause necrosis but leading to a prolonged reduction in myocardial contractility; this could occur even in the absence of limiting angina. He proposed that this state was revers-

Learning points

- myocardial dysfunction due to coronary artery disease can be reversible if the muscle is 'hibernating'
- even patients with previous myocardial infarctions and severe heart failure can have significant areas of viable myocardium on investigation
- such patients can improve markedly after successful revascularisation
- accurate non-invasive methods to detect areas of viability exist and are clinically validated

ible if the coronary blood supply could be improved. Subsequent authors have termed the hibernating heart the 'smart heart'.² Such reversible left ventricular dysfunction has been shown to occur in several stages of coronary heart disease, including chronic heart failure.³ In most patients with coronary heart disease, any associated left ventricular dysfunction is likely to be the result of various factors; reversible ones such as 'hibernation' and myocardial 'stunning' (persistent but slowly reversible dysfunction due to *transient* episodes of ischaemia) and irreversible factors such as pre-existing myocardial necrosis.

The accurate detection of regions of myocardial hibernation is vital if such patients, often with poor left ventricular function, are to be offered coronary revascularisation with a reasonable expectation of benefit. Various methods have been described; the main methods currently in use involve either the assessment of inotropic reserve with dobutamine echocardiography or the demonstration of cellular integrity with radionuclides. The so-called 'gold standard' for assessment is positron emission tomography, looking for metabolic activity in dysfunctional and hypoperfused areas; pooled data indicates a sensitivity of 88% with a specificity of 73%.⁴ Low-dose dobutamine echocardiography has reported sensitivities of 71–97%, with generally higher specificities. Of the radioisotope methods described, those using thallium-201 are the most widely available and offer acceptable predictive accuracy if appropriate protocols are used.⁴ If thallium-201 is used as the radionuclide it is important to realise that conventional stress-imaging protocols will seriously underestimate the extent of viable myocardium; protocols utilising rest imaging are more appropriate.⁵

Heart failure due to coronary heart disease continues to carry a grim prognosis, even with optimal medical therapy. In carefully selected patients myocardial revascularisation can improve symptomatic status; evidence is also beginning to emerge that it can improve prognosis in those patients with truly reversible contractile dysfunction.⁶

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Clearance of acanthosis nigricans associated with the HAIR-AN syndrome after partial pancreatectomy: an 11-year follow-up

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Summary

We describe a woman with the syndrome characterised by hyperandrogenism, insulin resistance and acanthosis nigricans (the HAIR-AN syndrome), and an associated insulinoma (islet B-cell tumour), whose signs and symptoms cleared after partial pancreatectomy.

Keywords: acanthosis nigricans; insulinoma; HAIR-AN syndrome; hyperinsulinaemia

In 1986, an obese 16-year-old white woman presented with drowsiness, lethargy, and headaches of one year's duration. She had had a mumps-like illness with parotid gland enlargement, amenorrhoea for 3 months (having previously had regular periods), and often felt thirsty. Her weight had increased by 13 kg to 122 kg (height 1.75 m). She had facial acne, sweaty palms, multiple abdominal striae, hirsutism on the arms and legs, a deep voice, and clitoromegaly. The neck, abdomen and axillae showed acanthosis nigricans (figure 1).¹ Her blood pressure was 160/100 mmHg with a regular pulse of 100 beats/min. Neurological examination was normal. Her haemoglobin was 17.0 g/dl and erythrocyte sedimentation rate was 52 mm in the first hour. A prolonged glucose tolerance test showed hypoglycaemia with a hyperinsulinaemic state. Other endocrine tests showed follicle-stimulating hormone (FSH) 33 IU/l (normal), luteinising hormone (LH) 25 IU/l (normal), LH:FSH ratio < 3 (>3 suggests polycystic ovarian disease), plasma testosterone 3.2, 7.1 and 9.3 nmol/l at monthly intervals (normal 0.2–3.0: slightly increased, consistent with obesity), and androstenedione 15 nmol/l (normal <10.2: not high enough to suggest an androgen-secreting tumour). Pelvic ultrasound scan was normal. Serum prolactin, triiodothyronine, thyroxine, thyroid-stimulating hormone, and thyroid-releasing hormone were normal. Urinary free cortisol was 355 nmol/24 h (normal), plasma cortisol 236 nmol/l at 09.00 am (normal) and 584 nmol/l at midnight (normal <150). Adrenocorticotropin was <10 ng/l (normal).

A diagnosis of HAIR-AN syndrome, characterised by hyperandrogenism, insulin resistance and acanthosis nigricans, was made and she was treated with dietary restriction to 800 kcal daily, and oral diazoxide, cyproterone acetate and ethinyloestradiol. In 1987, a diagnosis of insulinoma (islet cell hyperplasia) was made after extremely high serum levels of C-peptide were recorded: 3645 pmol/l basal (normal <1324), increasing to 11 590 pmol/l at 2 hours on a prolonged glucose tolerance test; serum insulin was 697 pmol/l and 2426 pmol/l, respectively (normal <50). The patient was insulin-resistant, but anti-insulin receptor antibodies were not detected. A distal hemipancreatectomy with splenectomy was performed in 1988, and her hypoglycaemia ceased. In 1989, she developed torsion of the left ovary, treated by salpingo-oophorectomy. Perioperative findings excluded polycystic ovaries. In 1990, after recurrent pulmonary emboli, warfarin was commenced.

Figure 1 Acanthosis nigricans of the left axilla in 1986

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Figure 2 The left axilla in 1997; acanthosis nigricans has virtually cleared

In 1995, her usually high requirement for insulin (typically 146 IU daily) dropped dramatically to 30 IU daily, and she experienced occasional hypoglycaemic episodes. A recurrence of the insulinoma could not be established, even though the C-peptide level was elevated at 2085 pmol/l. A short period without insulin, with dietary restriction only, resulted in recurrent hyperglycaemia and insulin was reinstated, the current dose being 20 IU bid.

In 1989, 3 years after her initial presentation and one year after hemipancreatectomy, the signs of virilism had regressed. She was not hirsute, the clitoral enlargement had regressed and her periods was normal. In 1997, 11 years after initial presentation, the acanthosis nigricans had virtually cleared (figure 2).

Summary points

- insulin may act as a growth factor to the skin leading to acanthosis nigricans when there is hyperinsulinaemia
- acanthosis nigricans may remit if high insulin levels, insulin resistance and insulin-binding defect are effectively treated

Discussion

Acanthosis nigricans has been associated with obesity, often with insulin resistance.¹ The resistance to insulin may result in hyperinsulinaemia and a down-regulation of insulin receptors to prevent hypoglycaemia.² Large amounts of unbound insulin are free to bind to insulin-like growth factor 1 (IGF-1) receptors.³ The binding of insulin to IGF-receptors on keratinocytes or fibroblasts leads to proliferation of the epidermis.³ This is clinically manifest as acanthosis nigricans, a cutaneous marker for tissue resistance to insulin with insulinaemia.¹⁻³ IGF receptors are also present in the ovarian stroma and, when bound by insulin, increased androgen production occurs, causing hirsutism and virilism.⁴

Only 1–3% of women with hyperandrogenism have been reported to show insulin resistance and acanthosis nigricans.⁵ This syndrome is probably underdiagnosed, as hyperandrogenetic women are not regularly screened for insulin resistance and acanthosis nigricans.¹ Our case shows that acanthosis nigricans and signs of virilism can remit if insulin levels, insulin resistance, and the insulin-binding defect are effectively treated. Spontaneous remission of the HAIR-AN syndrome has rarely been observed, although occasionally acanthosis nigricans associated with obesity can remit with weight reduction.¹

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Conjunctival MALT lymphoma: an unusual cause of red eye

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Summary

We describe a patient presenting with a red eye who was found to have conjunctival non-Hodgkin's lymphoma of the mucosa-associated lymphoid tissue (MALT) type.

Keywords: conjunctiva; lymphoma; MALT; red eye

A 79-year-old man presented with a 3-week history of a painless, red left eye. There was no discharge and minimal irritation. The vision in his left eye had deteriorated over several months secondary to cataract. His ophthalmic history included right cataract surgery one year previously. There was no relevant medical history.

On examination, right visual acuity was 6/9 and left was 6/18. He was found to have an infected left eye with an enlarged left caruncle and a fleshy 'salmon-pink' swelling that extended into the inferior forniceal conjunctiva (figure 1). The remainder of the ocular examination revealed a left cataract but no other abnormalities. There was no preauricular or submandibular lymphadenopathy and general examination confirmed localised disease. A biopsy of the inferior conjunctiva was performed.

Orbital computed tomography (CT) scans showed a soft tissue swelling anterior to the left globe. Conjunctival biopsy revealed a lymphoid infiltrate of the connective tissue and epithelium (figure 2). Immunostaining showed predominantly B cells with small numbers of T cells. This was consistent with a diagnosis of low grade non-Hodgkin's lymphoma of the MALT type (mucosa-associated lymphoid tissue). Blood tests including bone profile, serum immunoglobulins, marrow biopsy and

Figure 2 Biopsy specimen showing conjunctival epithelium and underlying stroma infiltrated by small lymphoid cells. Haematoxylin & eosin; orig magnification x 100

CT scans of head, neck, chest, abdomen and pelvis confirmed that the disease was localised.

He was referred to the radiotherapists for treatment. He was reviewed in the eye clinic 3 months later and found to have new conjunctival lesions in the right eye. A second biopsy of the right inferior forniceal conjunctiva showed a focal infiltrate of B and T cells with lymphoepithelial lesions consistent with the working diagnosis.

In view of the multifocal nature of his disease chemotherapy was commenced with oral chlorambucil. After six courses his lesions improved and the conjunctival infection resolved. He remains under regular review.

Discussion

In the early 1980s the term MALT was coined in order to describe a characteristic arrangement of lymphoid tissue found in certain mucosal surfaces.¹ Mucosa-associated lymphoid tissue is now recognised as giving rise to a specific form of tumour with distinct features, distinguishing MALT lymphoma from other forms of primary, non-Hodgkin's, extranodal lymphoma.^{2,3}

The commonest site of MALT in humans is the gastrointestinal tract, specifically stomach, terminal ileum and appendix.² It has also been described in the bronchus, salivary, thyroid and thymus glands. It was described in the conjunctiva in 1980 by Knowles and Jakobiec.³ Lymphoid tumours of the conjunctiva can pose problems in diagnosis since there is considerable overlap between benign and malignant lesions. Under normal circumstances the conjunctiva contains small numbers of

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Figure 1 Photograph of the left eye showing a fleshy, 'salmon-pink' lesion arising from the caruncle

MALT: characteristic histological features

- submucosal B cell follicles
- mantle zone of small lymphocytes
- region of B cells extending from mantle to overlying epithelium with centrocytic appearance
- lympho-epithelial lesions: extension of B cells into overlying epithelium

Box 1

lymphocytes together with a few mast cells and Langerhans' cells. This conjunctival-associated lymphoid tissue is associated with the production of local immune responses.^{4 5}

The majority of lymphoid tumours at this site are low grade B cell neoplasms.⁴ They are composed mainly of small lymphocytes with occasional larger blasts. Some tumours have a plasmacytoid morphology and pure plasma cell neoplasms are found rarely. High-grade B cell lymphomas are usually of the lymphoblastic type.⁶ Conjunctival lymphoma may be limited to this site or it may be associated with systemic disease. The characteristic histological features of MALT are listed in box 1.^{7 8}

The behaviour of MALT is different from other B cell extranodal non-Hodgkin's lymphoma.^{6 9} It is less aggressive and tends to

Summary points

- in cases of 'red eye' a careful examination of all ocular structures should be made
- the differential diagnosis of red eye includes conjunctival lymphoma
- a low threshold for biopsying suspicious lesions is required
- MALT are not aggressive, respond well to radiotherapy, and carry a good prognosis

Box 2

remain localised to mucosal surfaces. It also has a better prognosis.

Conjunctival MALT usually presents with mild symptoms of redness, irritation and photophobia.⁷ Examination findings are of orange-pink, salmon-pink or pale masses in the upper or lower fornices and are often bilateral. In all known cases no recurrence or dissemination after treatment has been described.⁷ The mainstay of treatment is local radiotherapy.¹⁰ However, chemotherapy is an alternative when radiation is inappropriate.

This case illustrates an unusual cause of unilateral red eye and highlights the importance of careful ocular examination and the value of a histological diagnosis.

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Acute lymphoblastic leukaemia presenting with arthritis in an adult patient

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Summary

The earliest manifestations of leukaemia often include rheumatic signs and symptoms. Arthritis is a well recognised complication of leukaemia in children, but acute and chronic leukaemia may also cause arthritis in adults. Leukaemic arthritis may occur at any time during the course of leukaemia and may be the presenting manifestation. It should therefore be considered in the differential diagnosis of both childhood and adult rheumatic disease. We present an adult patient presenting with arthritis due to acute leukaemia.

Keywords: arthritis; leukaemia; synovial fluid analysis

Figure 1 Ankle radiographs showing soft tissue swelling and joint effusion

A significant number of patients with leukaemia have bone or joint symptoms as a part of their disease.¹ However, arthritis as an initial manifestation of leukaemia is extremely rare.² Leukaemic arthritis (LA) may be defined as joint pain and swelling in association with peripheral blood or bone marrow leukaemia after other causes of arthritis have been excluded.³ Early in the course of the disease there may be difficulty in arriving at the correct diagnosis when studies of peripheral blood are not diagnostic.

We report an adult patient presenting with arthritis whose peripheral smear was normal. However, examination of synovial fluid and bone marrow revealed LA and acute lymphoblastic leukaemia (ALL).

Case report

A 22-year-old man was referred to our hospital with complaints of pain and swelling of his ankles for the last 3 months. On initial evaluation, he was conscious and fully oriented. Body temperature, blood pressure, pulse rate were 38.3°C, 130/80 mmHg, and 86 beats/min, respectively. On physical examination there was diffuse swelling and tenderness with erythema and discharge in both ankles. Other physical findings were within the normal range. Haematological studies revealed a haemoglobin level of 9.6 g/dl, leukocytes $10.3 \times 10^9/l$ (55% neutrophils, 22% lymphocytes, 19% monocytes, 4% eosinophils), platelets $310 \times 10^9/l$, with an erythrocyte sedimentation rate of 103 mm/h. Blood biochemical values were normal. Serum uric acid was 5.4 mg/dl (normal range 3.5–8.5 mg/dl). Antinuclear antibody, rheuma-

toid factor, and serological tests for hepatitis B were negative. Anti-DNA and serum complement level were within normal limits. Radiographs of the ankles showed soft tissue swelling and joint effusion (figure 1). The synovial fluid could not be aspirated during the first arthroscopy. The patient was prescribed indomethacin and colchicum for the pain, but during the following 2 weeks there was no benefit and the patient's symptoms increased, with complaints of pain and swelling of knees. Arthroscopy was repeated and cytologic examination revealed immature blastic cells (figure 2). Flow cytometric analysis of synovial fluid revealed CD19 58%, CD20 70%, and HLA-DR 91%. A bone marrow aspiration and biopsy was performed. Infiltration of leukaemic cells was seen on bone marrow aspiration (figure 3), and a diagnosis of ALL (L2, B-cell origin) was made. Mitoxantrone, vincristine and prednisolone were

Figure 2 Synovial fluid examination revealing immature blast cells

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Figure 3 Bone marrow aspiration showing infiltration by leukaemic cells (large, nonuniform sizes with irregular nuclear shape)

started immediately. However, his overall condition deteriorated and he died of neutropenia and sepsis on the seventh day of chemotherapy.

Discussion

The leukaemias are a heterogenous group of neoplasms arising from the malignant transformation of haematopoietic cells. Leukaemic cells proliferate primarily in the bone marrow and lymphoid tissues where they interfere with normal haematopoiesis and immunity. Leukaemias are classified according to the cell types primarily involved (myeloid or lymphoid) and as acute or chronic based upon the natural history of the disease. Acute leukaemia can be identified and classified on the basis of morphology, immunologic phenotype, and cytochemistry (table). It is critical to distinguish ALL from acute myeloid leukaemia (AML) since these two diseases differ considerably in their clinical behaviour, prognosis, and response to therapy.⁴

In addition to suppressing normal marrow function, leukaemic cells can infiltrate normal organs. In general, this occurs more commonly in ALL than AML.⁴ LA, an uncommon complication of acute leukaemias, develops due to infiltration of synovial membrane by leukaemic cells. Childhood leukaemias (especially ALL) are complicated by arthritis more frequently than adult leukaemias. It has been

Summary points

- leukaemia must be remembered in the differential diagnosis of arthritis of unknown aetiology which is resistant to palliative therapy
- cytologic examination of synovial fluid and bone marrow examination can confirm the diagnosis in such patients

reported that LA occurs in 12% of cases of childhood leukaemia,⁵ but leukaemia presenting with arthritis in an adult patient has been reported only in occasional case reports.⁶

Arthritis can occur at any time during the course of leukaemia and may rarely be the initial manifestation of the disease.⁷ Proposed pathogenic mechanisms for arthritis in leukaemia include infiltration of leukaemic cells into synovial tissue, haemorrhage into the joint from thrombocytopenia, synovial reaction to periosteal or capsular infiltration, and immune-complex-induced synovitis. However, synovial infiltration appears to be the predominant mechanism.⁷⁻⁸ In acute leukaemias, arthritis usually presents early in the course of disease, whereas in chronic leukaemias it presents later and more symmetrically. Large joints, most commonly the knees, are usually affected, although involvement of the ankle, wrist, elbow, shoulder, and hip have been described.⁷⁻⁹

Involved joints are usually warm, swollen, and tender on palpation. Effusions, if present, are small; most swelling is due to synovial hypertrophy. Fever may accompany joint swelling.⁷⁻⁹ The diagnosis of LA may be difficult as it can mimic other rheumatic diseases, especially juvenile arthritis.¹⁰ In some cases of LA, the peripheral blood smear and complete blood count show nonspecific findings such as anaemia or mild leukocytosis, and bone marrow aspirate or biopsy is necessary to make the diagnosis. One method of diagnosing LA is direct pathological demonstration of synovial membrane infiltration by leukaemic cells. Leukaemic blasts may be present in specimens of synovial fluid, as in our patient.

In conclusion, arthritis is a well recognised complication of leukaemia in children, but acute and chronic leukaemia may also cause arthritis in adults. LA may present before, after, or at the same time as the underlying disease. Because the leukaemia may not be obvious, another cause of the arthritis may be considered. As early diagnosis is one of the most important prognostic factors in leukaemia, this possibility must be remembered in the differential diagnosis of arthritis of unknown aetiology which is also resistant to palliative therapies. In such patients, cytologic examination of synovial fluid and bone marrow examination can be important diagnostic procedures.

Table Classification of acute leukaemias

FAB subtype	Morphology variant	% cases
AML		
M0	minimally differentiated leukaemia	2-3
M1	myeloblastic leukaemia without maturation	20
M2	myeloblastic leukaemia with maturation	25-30
M3	hypergranular promyelocytic leukaemia	8-15
M4	myelomonocytic leukaemia	20-25
M5	monocytic leukaemia	20-25
M6	erythroleukaemia (Di Guglielmo's disease)	5
M7	megakaryoblastic leukaemia	1-2
ALL		
L1	small; uniform (pre-B cell, T cell)	75
L2	large; nonuniform (pre-B cell, T cell)	20
L3	large; uniform; vacuola (B cell, Burkitt's)	5

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Calcium phosphate stones during long-term acetazolamide treatment for epilepsy

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Summary

We report a case of recurrent renal calculi containing calcium phosphate associated with long-term acetazolamide treatment for epilepsy. Unfortunately, the cause of stone formation was not recognised for many years, by which time irreversible renal damage had occurred.

Keywords: calcium phosphate renal calculi; renal failure; acetazolamide; adverse drug reaction

Patients with recurrent renal calculi may experience serious morbidity. It is important that such patients are adequately assessed in an attempt to identify an underlying cause. This is especially important if preliminary investigations produce unusual results.

Stones composed predominantly of calcium phosphate are uncommon; they accounted for 9.3% of 41 000 stones of renal origin in 11 series from five countries.¹ The majority of patients who form calcium phosphate stones have renal tubular acidosis.²

We report a patient with recurrent calcium-phosphate-containing renal calculi in whom the cause of stone formation was not recognised for a considerable time, despite regular specialist urological review.

Case report

A 32-year-old man was admitted for percutaneous nephrolithotomy (PCNL). He had required four previous PCNLs and numerous extracorporeal shock wave lithotripsy treatments and ureteroscopies since first passing a stone 11 years previously. Stone analysis performed seven years previously had shown calcium phosphate, but this had not been investigated further. The kidneys, initially anatomically normal, were now both scarred, with a small, poorly functioning left kidney (figure 1) and recurrent staghorn on the right (figure 2). Serum creatinine had been abnormal on occasions, probably reflecting episodes of partial obstruction.

Figure 1 DMSA scan showing markedly reduced uptake and scarring on the left

Figure 2 Plain abdominal radiograph showing large staghorn calculus on the right

He had been treated for epilepsy since the age of 11, initially with conventional anticonvulsants and then with the addition of acetazolamide for recurrent seizures. Current medication was acetazolamide 500 mg bid and carbamazepine 600 mg mane, 400 mg nocte.

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Repeat stone analysis on this occasion confirmed pure calcium phosphate. Urine pH was 6.0 with a concurrent venous bicarbonate of 22 mmol/l; serum creatinine and calcium were normal; 24-h urinary calcium excretion was 7.5 mmol and 24-h urinary citrate excretion was low at 72 μ mol/day using an enzymatic assay (hypocitratemia normally being defined as < 1.76 mmol/day).

Discussion

The carbonic anhydrase inhibitor acetazolamide is used in the treatment of glaucoma and, less commonly, in refractory childhood epilepsy.³ It has been known for many years to cause renal calculi,⁴ which are frequently calcium phosphate,⁵ and is used to induce stone formation in experimental animals. The mechanisms include induction of partial renal tubular acidosis with resultant hypercalciuria and hypocitratemia,^{6,7} both recognised risk factors for stone formation.^{8,9} Ordinarily, urinary citrate forms a soluble complex with calcium,

Summary points

- it is important to be aware of and exclude reversible causes of renal calculi
- the presence of calcium phosphate renal calculi should alert the clinician to the possibility of an unusual underlying cause
- acetazolamide causes renal tubular acidosis which can result in calcium phosphate calculi

thereby reducing available ionised calcium, which could otherwise precipitate as an insoluble salt. Hypocitratemia and alkaline urine increase calcium phosphate supersaturation.¹⁰

Calcium phosphate stones are uncommon; renal tubular acidosis is a recognised risk factor for this type of stone.² The occurrence of such stones, therefore, merits early investigation. There is a high probability that this patient's recurrent calcium phosphate nephrolithiasis was caused by acetazolamide. Earlier recognition of this might have enabled irreversible renal damage to be avoided.

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