

## Self-assessment questions

### An unusual shoulder injury

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A 23-year-old man was riding his motor bike on a wet country road. Negotiating a sharp curve the bike slipped and he landed on his outstretched left hand while the bike toppled over him, trapping the left leg underneath. On examination there was an obvious deformity of his left leg with swelling and bruising over the left shoulder along with some friction burns. Radiographs revealed a closed, displaced fracture of the tibia and fibula (figure 1). Anteroposterior, lateral and transthoracic views of the shoulder joint were read as normal in the casualty department (figure 2). A diagnosis of soft tissue injury to the shoulder was made. The patient was given a broad arm sling and was admitted for an intramedullary nailing of the tibia. On orthopaedic review in the morning the patient complained of progressive swelling and pain in his left shoulder. The limb was held close to the body with the elbow flexed. Attempts to move the shoulder generated severe pain and no active or passive external rotation was possible. The patient was taken to theatre for intramedullary nailing prior to which, under general anaesthesia, an axillary view of his left shoulder was obtained using the image intensifier (figure 3).



**Figure 1** Radiograph of the fractured tibia and fibula



**Figure 2** Anteroposterior radiograph of the left shoulder

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Accepted 26 January 1999



**Figure 3** Axillary view of the shoulder under image intensifier

### Questions

- 1 What is the diagnosis and what are the pathomechanics of the injury?
- 2 How would you treat the problem?

## Answers

### QUESTION 1

This is a posterior fracture dislocation of the anatomical head of the humerus. Electrical or neurological seizures, fall on an outstretched limb, or a blow to the anterior shoulder in trauma or sports, are events exerting large posterior forces on the shoulder joint. The continuing muscular contraction of deltoid and the subscapularis may then force the anterior portion of the humeral head onto the posterior rim of the glenoid, leading to a shearing of the anatomical head. The characteristic finding is the inability to externally rotate the shoulder. An anteroposterior and an axillary view in the scapular plane will confirm the diagnosis. On close inspection, figure 2 shows a faint fracture line across the humeral head while in figure 3 the anatomical head is separated from proximal humerus and completely displaced posterior to the glenoid.

### QUESTION 2

No attempt should be made to reduce these fracture dislocations in the casualty department. Under general anaesthesia an attempt should be made to reduce the fracture manually. If unsuccessful after the first attempt, closed manipulation must be abandoned and the fracture should be exposed using an anterior deltopectoral approach. Shoulder hemi-arthroplasty has been used frequently in the past to replace the damaged head. However, it is now established that anatomical reduction of the fracture using cancellous, cannulated or Herbert screws will allow the head fragment to unite and regain its vascularity by 'creeping substitution' with minimal incidence of avascular necrosis.

## Discussion

The majority of the daily workload in an accident and emergency department comprises musculoskeletal injuries. Rushed examination, work overload, and inadequate consideration of differential diagnosis for routine injuries have led to cases of missed diagnosis.

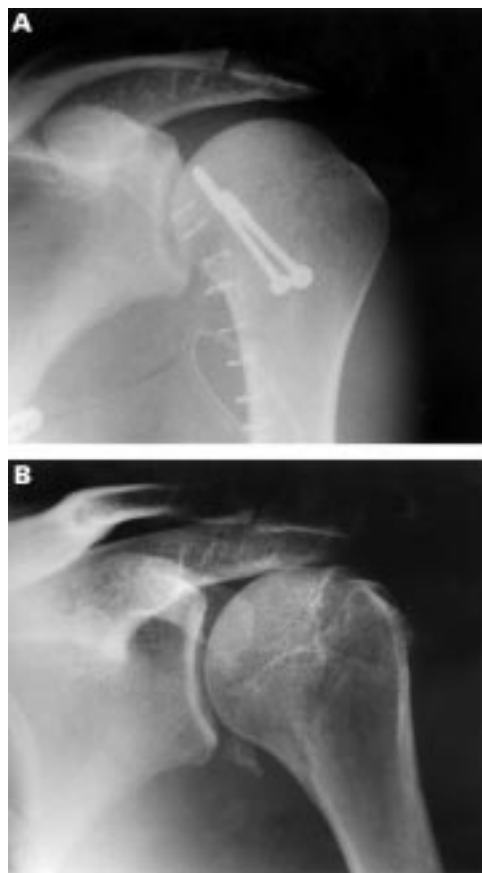
Posterior shoulder dislocation is a rare injury and represents 1–4% of shoulder dislocations. A fracture associated with a posterior shoulder dislocation is even more uncommon, accounting for less than 1% of all reported cases.<sup>1</sup> Because of its rarity and deceptive clinicoradiological features, it has been called a 'diagnostic trap' for the unsuspecting. It is estimated that approximately 60% of posterior fracture dislocations are missed by the initial examining clinicians.<sup>2</sup> Most of these fracture dislocations are three- or four-part, involving the surgical neck, head and the two tuberosities. Isolated fracture dislocation of the anatomical head of humerus is a rare injury, and only a few case reports are available in the literature.<sup>2–4</sup>

The vascular supply of the humeral head is mainly through the ascending branch of the anterior circumflex humeral artery, called the 'arcuate artery', and partly through the posterior circumflex humeral artery which enters the

humeral metaphysis just below the level of the anatomic neck. Other smaller contributions arise from capsular and muscular attachments. They form a rich anastomotic network supplying the articular surface. Fractures through the anatomical neck carry the highest risk of damage to the vascular supply of the head, leading to avascular necrosis. In most cases all vessels are disrupted and soft tissue attachments torn. Avascular necrosis has been reported in 75% of patients treated with internal fixation or closed manipulation.<sup>2</sup> To overcome this complication, which leads to bony collapse and arthritic changes in the shoulder joint, a prosthetic replacement of the fractured head has been suggested. However this seems a radical procedure, especially in young patients, as the reported functional results have been variable. Tanner and Cofield<sup>5</sup> could not obtain more than 100° abduction in the majority of their patients, while Neer found satisfactory to excellent results in 39 of his 43 patients.<sup>6</sup> Due to recent refinements in techniques of open reduction, encouraging results have been achieved following internal fixation of the separated head. All patients with a posterior fracture dislocation of the anatomical head treated with screw fixation have reported excellent results.<sup>2–4</sup> However, these results could only be achieved in those patients who were promptly diagnosed and operated upon immediately.

At operation, we found complete separation of the anatomical head from its capsular attachments. This was reduced anatomically and fixed using two cancellous lag screws (figure 4A). The fracture united radiologically at 3 months and 5 months later the screws were removed (figure 4B). The head, which lost all of its blood supply, was revascularised by intraosseous vascular growth across the fracture site extending to the articular surface, a process called 'creeping substitution'.<sup>4</sup> It shows no signs of avascular necrosis. On last review at 1 year since surgery the patient has made a full functional recovery and remains asymptomatic.

Several valuable points can help to reduce the chance of missing a posterior fracture dislocation. A thorough history and clinical examination should arouse suspicion. The majority of these injuries result from road traffic accidents involving a motorbike. Flattening of the anterior contour of the shoulder with posterior prominence, inability to rotate the shoulder externally, and prominence of coracoid process are the classic clinical features. All patients with glenohumeral trauma should have a 'shoulder trauma series'.<sup>2</sup> This consists of three views, anteroposterior, lateral and axillary. These radiographs are taken in reference to the plane of the scapula (30–40° anterior tilt in the coronal plane) and not the plane of the body, as the glenohumeral joint may not be adequately visualised on ordinary exposures leading to diagnostic errors. The anteroposterior view is taken at right angles to the plane of the scapula while the lateral view is taken in the plane of the scapula. Both views improve the chance of diagnosing these fracture dislocations.



**Figure 4** (A) Immediate post-operative film, (B) after removal of screws 8 months post-operatively

tions by 50%. An additional axillary view confirms the diagnosis. If doubt persists, clinical observation and comparative radiographs of the uninjured side should be used to help in the diagnosis. Computed tomography and magnetic resonance imaging are invaluable where such facilities exist.

This case is interesting since very few case reports of fracture dislocation of the anatomic head of humerus have been reported in the literature, especially with full functional recovery after open reduction and internal fixation. This result may be related to early detection and prompt intervention. It also re-emphasizes the point that these injuries can easily be missed in a busy accident and emergency department unless thorough clinical examination and proper films are obtained.

#### Final diagnosis

Posterior fracture dislocation of the anatomical head of humerus.

**Keywords:** shoulder dislocation; humerus; fracture

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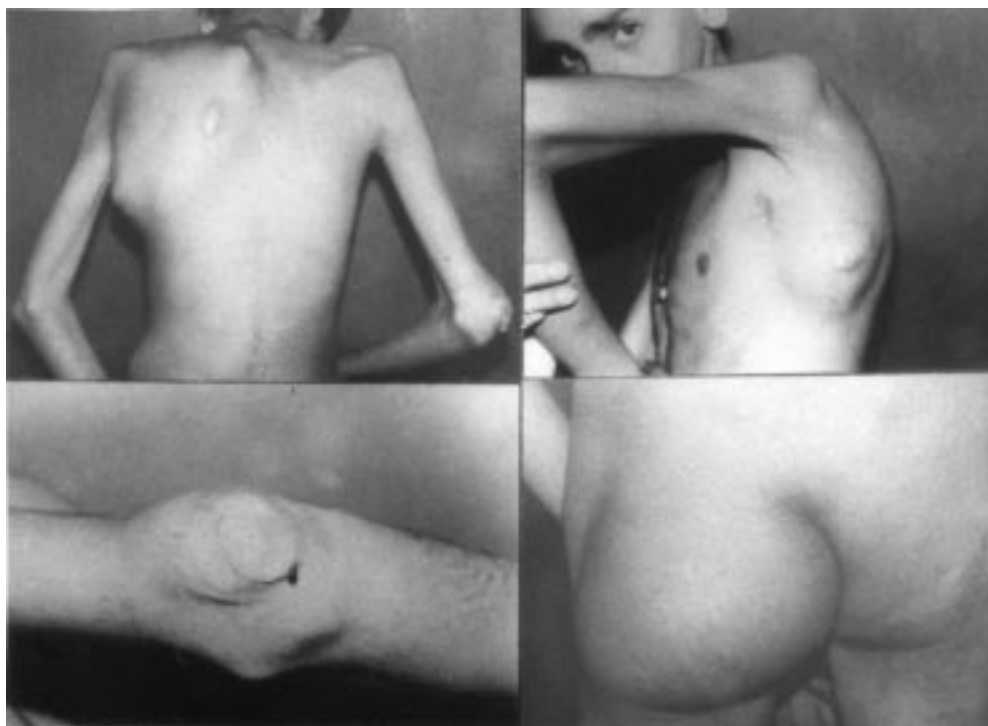
## Peri-articular 'hard tumours' in soft tissues

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A 17-year-old man presented with painless, progressively increasing, non-simultaneous, peri-articular swellings evolving for the last 7 years. He had undergone repeated drainage of white chalky material and received adequate antitubercular therapy without any relief. He subsequently developed multiple non-healing sinuses. There was no history of colicky pain, graveluria, dyspnoea, excessive intake of antacids and vitamin D preparations, trauma or family history of similar disorder. Examination revealed pallor, axillary and inguinal lymphadenopathy and multiple, soft-to-firm, non-tender swellings of varying sizes (2–5 × 3–8 cm) with non-healing sinuses at left shoulder, both hips and right elbow (figure 1). The mobility of the left shoulder and right elbow joints was markedly restricted. The rest of the examination was normal.

On investigation he had a haemoglobin of 9.2 g/dl and total leucocyte count of  $10 \times 10^9/l$  with 90% polymorphs. Biochemistry on normal diet schedule revealed serum sodium of 132 mmol/l, potassium 3.8 mmol/l, fasting glucose 6 mmol/l, urea 4.9 mmol/l, creatinine 53  $\mu\text{mol/l}$ , calcium 2 mmol/l (normal 2–2.6) corrected for albumin, inorganic phosphorous 2.23 mmol/l (1–1.4), ionised calcium 1.1 mmol/l (1–1.4), alkaline phosphatase 49.7 U/l and intact parathormone (PTH) 5 pg/ml (12–72). Arterial blood gas analysis was normal. His 24 hour urinary calcium was 300 mg (100–400), phosphate 275 mg (600–1200), creatinine clearance 97.2 ml/min, tubular reabsorption of phosphate 97% (85–90%) and TmP/GFR 2.9 mmol/l (0.82–1.45).

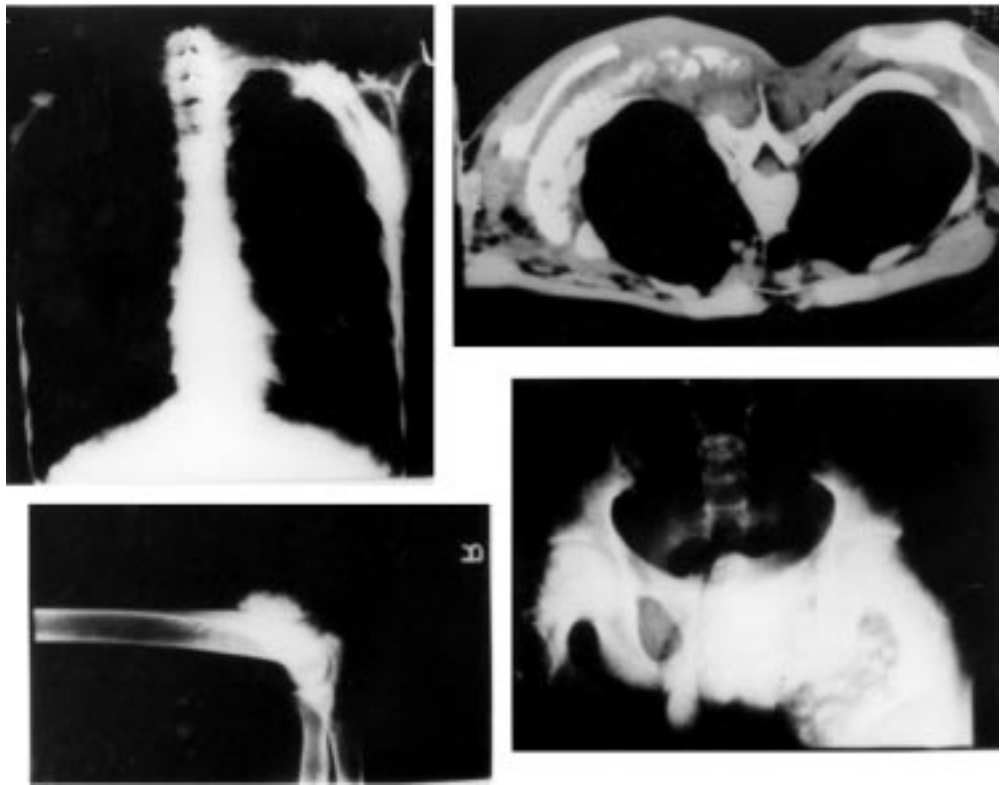
His radiological survey, including computed tomography (CT) scan, is shown in figure 2. Extensive soft tissue calcification in the regions shown in figure 2 was confirmed by  $^{99\text{m}}\text{Tc-MDP}$  bone scan. Aspirated fluid from the soft tissue was rich in calcium, phosphate, and proteins.



**Figure 1** The patient (reproduced with his permission)

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**Figure 2** Corresponding CT scans

### Questions

- 1 What is your diagnosis?
- 2 What are other disorders that mimic this condition?
- 3 What are the management strategies?



## Answers

### QUESTION 1

Peri-articular swellings with sinuses and soft tissue calcification as shown in figures 1 and 2, normocalcaemia, hyperphosphataemia with supranormal TmP/GFR and otherwise normal renal functions, suggest a diagnosis of hyperphosphataemic tumoral calcinosis.<sup>1,2</sup>

### QUESTION 2

Other disorders associated with peri-articular soft tissue calcification are milk alkali syndrome, sarcoidosis, vitamin D intoxication, systemic sclerosis/CREST syndrome and chronic renal failure. Hypercalcaemia predominates in all except the last two disorders.

### QUESTION 3

Treatment with phosphate-binding antacids along with dietary restriction of calcium and phosphate has been helpful.<sup>3</sup> Surgical resection of soft tissue calcified masses is indicated when these cause discomfort, interfere with function, or become cosmetically unacceptable. Recurrences are rare after complete surgical resection. Preliminary studies have shown the efficacy of calcitonin therapy since this hormone increases renal phosphate wasting.<sup>4</sup>

## Discussion

Tumoral calcinosis is a disorder with autosomal recessive or an autosomal dominant inheritance with variable clinical expressivity.<sup>2,5</sup> It is characterised by peri-articular soft tissue cystic and solid tumorous calcium deposits in association with hyperphosphataemia, and elevated serum calcitriol levels but normocalcaemia and normal renal functions.<sup>1,2</sup> However, hyperphosphataemia is not consistently present and may be documented in only one third of patients.<sup>1</sup>

Hyperphosphataemic patients are more frequently black individuals of either sex with a positive family history and manifest disease with multiple lesions before 20 years of age.<sup>1</sup> Common sites of these soft tissue tumours, in order of frequency, are around the hip, elbow and shoulder joints. These tumours are usually painless, firm-to-hard, lobulated, firmly attached to the deep fascia and occasionally infiltrating into the muscle and tendons.<sup>1</sup> Sometimes the lesions cause ulceration of the overlying skin with formation of a sinus that drains chalky material. Other manifestations include anaemia, low-grade fever, splenomegaly and regional lymphadenopathy.<sup>3</sup> Our patient had extensive soft tissue involvement around the hip, shoulder and elbow joints with infiltration into the trapezius and serratus anterior muscles, multiple sinuses and regional lymphadenopathy.

Hyperphosphataemia and supranormal TmP/GFR are present in one third of patients

## Learning points: tumoral calcinosis

- clinical: soft tissue, peri-articular tumorous swellings.
- biochemical: hyperphosphataemia, supranormal TmP/GFR, normocalcaemia and normal renal function
- radiology: soft tissue peri-articular calcification
- treatment: phosphate- and calcium-restricted diet; phosphate-binding antacids; surgical excision

while serum calcium; alkaline phosphatase and renal functions are normal.<sup>2</sup> Serum calcitriol is elevated in most patients while serum parathormone levels are low or normal.<sup>2</sup> However, affected subjects are in positive calcium and phosphate balance. Irregular, densely calcified lobules with occasional fluid levels confined to the soft tissues are hallmarks of tumoral calcinosis on radiology.<sup>1</sup> The cystic character of the lesion and its lack of contact to the bone can be confirmed by non-contrast CT or bone scan as shown in our case. Interestingly, vascular or visceral calcification does not occur. A dental abnormality consisting of short bulbous root and calcific deposits obliterating the pulp chamber, characteristic of hyperphosphataemic tumoral calcinosis,<sup>5</sup> was also present in our case. Histopathology reveals multiloculated cysts filled with calcareous material with foreign body giant cells in thick fibrous walls.

The pathogenetic abnormalities in tumoral calcinosis are increased renal reclamation and enhanced intestinal absorption of phosphate. It is attributed to elevated renal phosphate reabsorption threshold, enhancement of other phosphate transport systems independent of PTH, and increased calcitriol synthesis due to abnormal regulation of renal  $1\alpha$ -hydroxylase activity.<sup>1,2</sup> Increased dietary calcium absorption by calcitriol in turn suppresses PTH.<sup>2</sup> Normal serum calcium in these patients is a consequence of precipitation of calcium phosphate salts in the soft tissues.<sup>1</sup> Repeated local trauma resulting in tissue damage with fat necrosis may be a predisposing factor in normophosphataemic patients.<sup>6</sup>

Our patient received a phosphate- and calcium-restricted diet and 20 ml of aluminium hydroxide gel with each meal. The calcareous tissue at the elbow and hips was excised which resulted in healing of the sinuses and restoration of the joint mobility.

## Final diagnosis

Hyperphosphataemic tumoral calcinosis.

**Keywords:** tumoral calcinosis; peri-articular calcification; hyperphosphataemia

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## Fever of unknown origin

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A 68-year-old man presented with a history of low-grade, continuous fever and malaise for 3 years. There was no associated history of cough, breathlessness, palpitations, headache, vomiting, joint pains, rash, urinary or bowel disturbances. The patient had been investigated on many occasions in the past for the fever. The investigations, including haemoglobin, blood counts, peripheral smear examination, kidney and liver functions tests, chest X-ray and ultrasonography of the abdomen, were all normal. The only abnormality detected was a persistently elevated erythrocyte sedimentation rate (ESR) of between 65 and 130 mm in the first hour. The patient had received several courses of antibiotics and was currently receiving antitubercular drugs prescribed empirically by a practitioner.

Examination revealed a conscious, febrile male with pulse 100 beats/min regular, and blood pressure 130/70 mmHg. The respiratory, cardiovascular, abdominal and neurological examination was unremarkable. The laboratory investigations of the patient are summarised in the table. A magnetic resonance imaging (MRI) scan of the thorax is shown in the figure.

**Table** Laboratory investigations

Investigations	Observed value (normal range)
Haemoglobin (g/l)	110 (120-140)
Total leucocyte count ( $\times 10^9/l$ )	8.4
ESR (mm 1st hour)	66 (0-20)
Fasting blood sugar (mmol/l)	5.0 (4.2-6.4)
Blood urea nitrogen (mmol/l)	5.3 (3.6-7.1)
Serum creatinine ( $\mu\text{mol/l}$ )	100 (<133)
Alanine transaminase (IU/l)	24 (0-30)
Aspartate transaminase (IU/l)	23 (0-30)
Alkaline phosphatase (IU/l)	100 (<200)
Total proteins (g/l)	70 (60-80)
Serum protein electrophoresis	increase in the gamma globulin fraction
ANA, RA, VDRL and Elisa for HIV 1 and 2	were all negative
Urine examination, chest X-ray, ECG, and ultrasound abdomen	were all normal



**Figure** MRI of the thorax

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Accepted 14 January 1999

### Questions

- 1 What is your provisional diagnosis?
- 2 How would you investigate the patient further?
- 3 Describe the MRI findings.
- 4 What is your final diagnosis?



## Answers

### QUESTION 1

Fever of unknown origin (FUO). By definition,<sup>1</sup> FUO consists of:

- fever higher than 38.3°C (101°F) on several occasions
- a duration of more than three weeks, and
- failure to reach a diagnosis after 1 week of in-patient investigations.

FUO is one of the most frequently encountered clinical situations. Keen observation, patience and a diligent diagnostic work-up are mandatory for evaluating the cause of FUO. The major causes of FUO are listed in box 1. Of these, infections are still the leading cause, followed by neoplasms. With increasing duration of fever, the likelihood of an infectious aetiology diminishes and the other causes become more important.

#### Causes of FUO

- infections: bacterial, mycobacterial, fungal, rickettsial, viral, parasitic, etc
- neoplasms: benign and malignant
- collagen vascular disorders
- granulomatous diseases
- inherited and metabolic diseases
- miscellaneous causes, eg, drug fever, haematomas, aortic dissection, etc

#### Box 1

### QUESTION 2

Since the initial evaluation for the cause of fever was non-contributory, the further diagnostic work-up should include bone marrow aspiration/biopsy, liver biopsy, echocardiography and computed tomography or MRI of the chest and abdomen. Most causes of FUO can be detected after this screening. In our patient, the bone marrow aspiration revealed a normoblastic marrow with a myeloid to erythroid ratio 2:1. There was an increase in the plasma cells to 10–15% and megakaryopoiesis was normal.

### QUESTION 3

The MRI scan of the thorax reveals a 5.2 × 3.6 cm mass arising from the interatrial septum on the left side in the region of the fossa ovalis and extending to the left ventricle, suggestive of a left atrial mass (? myxoma)

### QUESTION 4

The patient successfully underwent tumour excision by a biatrial approach under cardiopulmonary bypass and histopathology confirmed the diagnosis of an atrial myxoma.

## Discussion

Primary cardiac tumours are rare and are observed in 0.0017% to 0.28% of all autopsies.<sup>2</sup> Atrial myxomas constitute 50–90% of these<sup>3–4</sup> and 75% of the atrial myxomas have

a left atrial origin. The tumours are considered to be benign by most, and recent evidence suggests that they may originate from the endocardial sensory nerve tissue.<sup>5</sup>

Atrial myxomas remain asymptomatic for varying periods before they manifest with classic features (box 2). Most tumours present with dyspnoea, chest pain, and fatigue; a third heart sound, tumour plop and a diastolic murmur are prominent auscultatory findings.<sup>4</sup> Constitutional symptoms occur frequently, although it is rare for a cardiac myxoma to present as FUO alone, without any symptoms or signs referable to the cardiovascular system, as in this case. In two large series of 366 patients with FUO, an atrial myxoma was detected in only two patients.<sup>6–7</sup> Many associated conditions coexist with atrial myxomas, especially with the familial types (box 3).<sup>8</sup>

#### Atrial myxomas: clinical presentations

- obstructive: features of mitral valvular obstruction simulating mitral stenosis
- embolic to: cerebrovascular circulation leading to neurologic syndromes; coronary vessels leading to myocardial infarction; other rare sites, eg, peripheral circulation
- constitutional symptoms: fever, weight loss, anorexia, arthralgias, anaemia; raised ESR, leucocytosis
- combinations of the above

#### Box 2

#### Associations of familial atrial myxomas

- skin manifestations: naevi, lentigenes, cutaneous myxomas
- myxoid mammary fibroadenomas
- hyperadrenalism and Cushing's syndrome
- haemolytic anaemia
- testicular (Sertoli cell) tumours
- thrombocytopenia
- acromegaly

#### Box 3

#### Learning points

- atrial myxomas may rarely present as isolated FUO
- all patients with FUO of a long duration should be screened by echocardiography for an underlying atrial myxoma

#### Box 4

Anaemia, leucocytosis and a raised ESR are usual, and cardiomegaly may be evident on a chest X-ray in some patients. Echocardiography is mandatory for the diagnosis of atrial myxomas and the transoesophageal route is superior to the transthoracic route

in the identification of atrial masses.<sup>9</sup> Recently, MRI has been shown to delineate the nature and extent of cardiac myxomas very well.<sup>10</sup>

Surgical excision is advisable for all atrial myxomas, even asymptomatic ones, as embolisation may have drastic results, and can even lead to sudden cardiac death. Recurrence of atrial myxomas after an initial excision is well known and is thought to represent an

incomplete resection. The present case was unusual in that the atrial myxoma produced nosymptoms and signs other than a prolonged fever.

### Final diagnosis

Left atrial myxoma.

**Keywords:** atrial mass; myxoma; fever of unknown origin

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## A young woman with fever of unknown origin

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A 33-year-old woman presented with a 2-month history of moderate-grade fever associated with chills, headache and diminished appetite. She had lost 8 kg since the onset of illness. Clinically, she had fever (temperature 38.5° C), but the rest of the general physical and systemic examinations were normal.

Investigations revealed an erythrocyte sedimentation rate (ESR) of 80 mm after 1 h. Routine haemogram, blood smear for malarial parasite, urine microscopic examination, urine culture, blood culture, chest X-ray and ultrasounds of abdomen and pelvis were noncontributory. Mantoux test was negative. She was initially treated empirically for malaria with chloroquine and subsequently with ciprofloxacin for enteric fever with no response. On repeated clinical examinations she was detected to have small, diffuse, nontender thyromegaly. A 131-radioiodine scan revealed markedly low uptake of tracer. Radioactive iodine uptake (RAIU) was negligible at 24 h. Serum tri-iodothyronine (T<sub>3</sub>) was 180 ng/dl (normal 60–181), serum thyroxine (T<sub>4</sub>) 10 µg/dl (normal 4.5–10.9) and thyroid-stimulating hormone (TSH) 0.4 µU/ml (normal 0.5–5.0).

### Questions

- What is the diagnosis?
- Name two characteristic laboratory findings of this condition?

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Accepted 14 January 1999

## Answers

### QUESTION 1

Diagnosis in this case is subacute or De Quervain's thyroiditis, painless variant, presenting as fever of unknown origin.

### QUESTION 2

A high ESR and suppressed radioactive iodine uptake are characteristic laboratory findings in this condition.

## Discussion

Subacute or De Quervain's thyroiditis is an uncommon but well documented cause of fever of unknown origin.<sup>1</sup> Symptoms of thyroiditis usually follow upper respiratory tract infection. In addition to general symptoms of infection, a characteristic feature is gradual appearance of pain in the region of the thyroid gland. Pain may be referred to the lower jaw, ear or occiput. In some patients, typical features are absent and they have prolonged fever, significant weight loss and no local symptoms. The clinical course may simulate a chronic systemic infection or malignancy.<sup>2</sup> Systemic symptoms and fever may persist for weeks or months before diagnosis is clinched. Acute onset with severe pain over the thyroid is uncommon. A few patients have symptoms of thyrotoxicosis.<sup>3</sup> Clinical findings include exquisite tenderness and nodularity of the thyroid gland.<sup>4</sup> Aetiologically, mumps, coxsackie virus, echovirus and adenoviruses have been implicated.<sup>5</sup> Histopathologically, the lesions are patchy in distribution. Affected follicles show infiltration with mononuclear cells and disruption of epithelium, partial or complete loss of colloid, fragmentation and duplication of the basement membrane. Colloidophagy and multinucleate giant cells surrounding colloid are characteristic features. Primary events are destruction of follicular epithelium and loss of follicular integrity.

Preformed hormones are released leading to elevated  $T_3$ ,  $T_4$ , suppressed TSH and clinical features of thyrotoxicosis. Low TSH is a conse-

## Learning points

- subacute thyroiditis is an uncommon but important cause of fever of unknown origin
- high ESR and low RAIU are characteristic features of this condition
- painless variant may simulate systemic or malignant disease, without signs or symptoms directly related to thyroid
- NSAIDs and steroids are the mainstay of treatment
- disease usually subsides within few months with complete recovery of thyroid function

quence of raised thyroid. Later, serum  $T_4$  and  $T_3$  levels come down, sometimes into the hypothyroid range as hormone stores are depleted, with a rise in TSH levels.  $T_4$  and  $T_3$  concentrations rise as hormone secretion resumes and TSH concentration decreases to normal. Ultimately, as the disease subsides, thyroid function returns to normal. Cytokine interleukin-6 has been implicated in thyroid destruction.

Treatment is with aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) to control symptoms. In severe cases glucocorticoids (20–40 mg prednisolone daily) alleviate the symptoms. Steroid therapy is continued to maintain the patient in a symptom-free state. Steroids are tapered gradually once RAIU and serum  $T_4$  return to normal.<sup>6</sup> Transient thyrotoxicosis is controlled by beta-blockers.

In this patient, in addition to the above investigation results, fine needle aspiration biopsy revealed subacute thyroiditis. She was treated with prednisolone 40 mg/day. She became asymptomatic after 3 weeks. Steroids were tapered off over the next 8 weeks by which time RAIU and  $T_4$  had returned to normal.

## Final diagnosis

Subacute or De Quervain's thyroiditis.

**Keywords:** fever of unknown origin; thyroiditis

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## Intracerebral haemorrhage in previously healthy young adults

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A 31-year-old right-handed man was admitted to hospital with vomiting, severe headaches, photophobia and weakness of the left arm and leg. There was no medical or family history of note. He smoked about 20 cigarettes a day. On examination, he was drowsy but rousable to a Glasgow Coma Scale of 15/15. There was mild neck stiffness but Kernig's sign was negative. His oral body temperature on admission was 35.7°C. The radial pulse was 70 beats/min, regular and of good volume. Blood pressure was 125/60 mmHg. Examination of the nervous system confirmed severe flaccid left hemiparesis (muscle power MRC 3/5 and 0/5 in the lower and upper limbs, respectively). There was also a left upper motor neurone facial weakness. Tendon reflexes were brisk on the left side and the left plantar response was extensor. There were no sensory signs, visual field defects or dyspraxia. Language function appeared intact. Formal psychological assessment confirmed a significant deterioration in cognitive function, especially in performance items. Attention, concentration, and delayed recall were particularly severely affected. The rest of the neurological and general physical examination was unremarkable.

Haemoglobin was 14.1 g/dl and the total white blood count was  $12.8 \times 10^9/l$  with 93% neutrophils. Platelet count was normal. Liver function tests and urea and electrolytes were also normal on admission. An electrocardiogram was normal. A computed tomography (CT) brain scan with contrast enhancement confirmed the presence of a large right frontal lobe haemorrhage approximately 6 cm in diameter with some mass effect. Blood was also present in the right Sylvian fissure.

The patient's headaches, photophobia and vomiting resolved in 2–3 days and his neurological signs also improved quickly. Two weeks after his stroke he had fully recovered muscle power and function of the left arm and leg. However, there was mild but progressive deterioration in his liver function. On the fourth day of admission his  $\gamma$ -glutamyl transpeptidase and aspartate transaminase were 377 and 105 IU/l, respectively. One week later his  $\gamma$ -glutamyl transpeptidase was 609 IU/l and aspartate transaminase was 152 IU/l. Other liver enzymes and serum bilirubin remained within the normal limits. A urine test suggested the cause of the intracerebral bleed. Six weeks after the stroke all liver enzymes were within the normal limits.

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Accepted 26 January 1999

### Questions

- 1 What urine test suggested the cause of the patient's intracerebral bleed?
- 2 What other investigation would you ask for?
- 3 What are the possible mechanisms of intracerebral haemorrhage in this patient?
- 4 How would you explain the abnormalities of liver function?

## Answers

### QUESTION 1

Urine amphetamine levels. Amphetamines are excreted in the urine unchanged. The rate of excretion is dependent on the urine pH. Approximately 70% of the ingested dose is excreted in 16 hours if the urine is acidic but less than 5% if the urine is alkaline.

Amphetamines (eg, Speed) and their ring-substituted derivatives, 3,4-methylenedioxyethyl amphetamine (Ecstasy, Adam, etc) and methylenedioxyethyl amphetamine (Eve) are widely used, especially by young adults, for their mood-elevating effect and their tendency to enhance sociability. An anonymous survey of the attitudes of college students towards the recreational use of amphetamines has shown that 39% of the students in a university campus had taken the drug at least once.<sup>1</sup> However, despite this widespread use, mortality and severe morbidity due to these drugs is rare. Most patients die from heat stroke, rhabdomyolysis, disseminated intravascular coagulation, renal and liver failure.<sup>2</sup> Stroke has been reported only in a small number of cases. Nevertheless, amphetamines seem to be a leading cause of stroke in this patient population. In a review of 72 young patients (aged 15–45 years) who presented with non-traumatic intracerebral haemorrhage, amphetamines were found to be the cause of the stroke in five cases.<sup>3</sup>

### QUESTION 2

Magnetic resonance angiography. This is a powerful non-invasive method for the diagnosis of intracerebral vascular malformations. Cases

of ruptured congenital berry aneurysms following the ingestion of amphetamine derivatives (presumably due to the severe increase in blood pressure) have been reported.<sup>4</sup>

### QUESTION 3

The mechanism of the intracerebral haemorrhage cannot be established from the available clinical data. The patient had a normal blood pressure when first seen but it is possible that a brief sudden surge in arterial blood pressure at the peak of amphetamine blood concentration had caused the haemorrhage. This transient sympathomimetic effect of amphetamines has been documented in both experimental animals<sup>5</sup> and in man.<sup>6</sup> Intracerebral haemorrhage may also result from vasculitis in some amphetamine users.<sup>4</sup> However, vasculitis is unlikely to have had an aetiological role in this case because of the short period between the ingestion of the drug and the stroke onset.

### QUESTION 4

Liver damage may result from an idiosyncratic reaction to amphetamines. This suggests the need for regular monitoring of these patients in the first few days after amphetamine consumption.

### Final diagnosis

Intracerebral haemorrhage, possibly related to amphetamine use.

**Keywords:** brain haemorrhage; amphetamines

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## Hyperkalaemia following blood transfusion

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A 35-year-old man weighing 63 kg was presented for elective repair of an atherosclerotic thoraco-abdominal aortic aneurysm. He was a known hypertensive on oral nifedipine 20 mg 12 hourly and propranolol 20 mg 8 hourly. He had no known allergies. Routine biochemistry ( $\text{Na}^+$  135 mmol/l,  $\text{K}^+$  3.6 mmol/l, urea 5.1 mmol/l, creatinine 56  $\mu\text{mol/l}$ ) and haematological investigations were within normal limits. Echocardiography suggested normal left ventricular function and the electrocardiogram (ECG) was normal. An aortogram demonstrated a fusiform aneurysm extending from the descending thoracic aorta (distal to the left subclavian artery) to just distal to the renal arteries.

After anaesthetising the patient, the aneurysm was exposed using a thoraco-abdominal incision. Mannitol 0.5 g/kg and heparin 1 mg/kg were given before aortic cross-clamping. No temporary arterial shunts were used during the aortic cross-clamping and the total cross-clamped time was 65 min. On declamping, the patient developed severe hypotension (a systolic pressure of 40 mmHg), which was treated with rapid transfusion of 1 litre of crystalloids, 1 litre of colloids, 4 units of warmed CPD-A (citrate-phosphate-dextrose-adenine) stored whole blood and 10 ml of 10% calcium gluconate. Despite this, the hypotension persisted; therefore the aorta was re-clamped (supra-coeliac) to maintain the blood pressure and coronary perfusion. This was immediately followed by bradycardia, widening of QRS complexes and ventricular fibrillation (VF). The VF did not respond to two internal DC shocks of 20 J each and one DC shock of 30 J. Internal cardiac massage was started; the heart was found to be very flabby. Intravenous lignocaine (2 mg/kg) and additional doses of calcium gluconate (10 ml of 10%) and 7.5% sodium bicarbonate 100 ml produced no improvement. In view of the VF resistant to DC shock and a 'flabby' heart, hyperkalaemia was suspected. Blood transfusion was discontinued, even though the haemoglobin was 7 g/dl and the hypovolaemia was treated by infusing crystalloid and colloid solutions only. The patient's blood was analysed for serum potassium, which was 7.0 mmol/l. The blood used for transfusion was noted to be 16 days old and biochemical analysis of the unwarmed bag blood showed a pH= 6.803, standard bicarbonate content 7.8 mmol/l, base deficit 20.1 mmol and potassium 16.6 mmol/l.

The hyperkalaemia was treated with 100 ml of 50% dextrose and 20 units of actrapid insulin infused over 15 min along with frusemide 100 mg. Following this the heart recovered its tone and reverted to sinus rhythm with a systolic blood pressure of 80 mmHg. Dopamine 10  $\mu\text{g/kg/min}$  was started to augment the blood pressure with successful declamping of the aorta. At this stage the serum potassium was found to be 5.5 mmol/l, falling to 3.3 mmol/l one hour later. Subsequently only fresh blood was given. Unfortunately, the patient died of multiple organ failure 3 days after the operation in the intensive care unit.

### Questions

- 1 What are the causes of hyperkalaemia during surgery?
- 2 What are the causes of hyperkalaemia during blood transfusion?

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## Answers

### QUESTION 1

The various causes of hyperkalaemia during surgery are listed in box 1.

#### Causes of hyperkalaemia during surgery

*Shift of potassium from tissues/cells due to:*

- drugs: eg, suxamethonium
- acidosis
- tissue damage: muscle injury (crush/ischaemic injury); haemolysis; internal bleeding; catabolic states; malignant hyperpyrexia
- blood transfusion
- impaired excretion: acute renal failure

### Box 1

### QUESTION 2

Following massive blood transfusion of stored blood, complications such as hyperkalaemia and citrate toxicity are well recognised but fortunately very rare. Normally, plasma contains 4–5 mmol/l of potassium whereas red blood cells contain 100–105 mmol/l. During storage there is a slow, but constant leakage of potassium from the cells into surrounding plasma as a result of sodium/potassium ATPase pump failure. The plasma level of potassium may increase by 0.5–1 mmol/l per day of refrigerator storage.<sup>1</sup> Accordingly, the total amount of extracellular potassium in a unit of whole blood stored for 35 days is about 8.2 mmol and that of red cell concentrate is 5.5 mmol.<sup>2</sup> On collection into a blood bag containing CPD or CPDA-1 solution (pH 5.5), the pH of blood decreases to approximately 7.0. The pH continues to decline further and may be as low as 6.6 after 21–35 days of storage. This is not only due to citrate in the anticoagulant, but also due to the metabolic processes in the red blood cells, resulting in accumulation of fixed acids and CO<sub>2</sub>.<sup>3</sup> The potassium level of the recipient is determined by the factors summarised in box 2.

#### Potassium levels in transfusion recipients are determined by

- amount of extracellular potassium in the blood infused
- pre-existing level of potassium in the recipient
- rate of transfusion of blood
- renal excretion of potassium
- acidaemia/acidosis

### Box 2

## Discussion

Circulatory collapse on declamping the aorta is a frequent occurrence during aortic surgery.

The commonest cause as confirmed by two-dimensional transoesophageal echocardiography is severe hypovolaemia.<sup>4</sup> If hypotension persists despite volume resuscitation for more than 4 min, re-clamping of the aorta below the renal arteries is recommended.<sup>4</sup>

In the present case, after unsuccessful volume resuscitation, the aorta was partially re-clamped (supra-coeliac) to increase the proximal arterial pressure and to maintain coronary perfusion. In the presence of a supra-coeliac aortic cross-clamp the coronary blood flow is increased by 43–46%.<sup>5</sup> As the aorta was still partially clamped, the major quantity of citrated, hyperkalaemic, acidotic blood might have circulated in the upper part of the body, including the coronary arteries, producing widened QRS complexes, ventricular fibrillation and a 'flabby' heart. The impact of transfusion of stored blood on the potassium and acid-base status of the recipient is complex. It depends upon the rate of transfusion, the rate of citrate metabolism and the changing state of peripheral perfusion of the recipient.<sup>6,7</sup> Although we did not measure plasma citrate concentration in our patient, citrate toxicity cannot be excluded, as massive blood transfusion can result in a plasma concentration of 2–4 mmol/l leading to myocardial depression and hypotension.<sup>8</sup>

The other possible cause of ventricular fibrillation is coronary ischaemia, which cannot be excluded, though there were no ST segment and T-wave changes in the ECG leads monitored prior to the events described.

The homeostatic disturbances which follow transfusion therapy are related to both the quality and quantity of blood infused. Weisel and co-workers have suggested that massive transfusion of blood with a low 2,3-diphosphoglycerate concentration may impair myocardial performance.<sup>9</sup> Blood also contains important free radical scavenging systems, and with storage a decline in red cell<sup>10</sup> as well as plasma<sup>11</sup> antioxidant activity has been reported. As associated coronary artery disease has been reported in patients with aortic aneurysm,<sup>12</sup> the use of fresher blood could be considered when such patients require massive transfusion. Although we did not use cell saver, it has an important role in minimising homologous blood transfusion in major surgeries.

In conclusion, potassium toxicity and citrate intoxication need to be considered during resuscitation of an acutely injured patient in the accident & emergency department or a patient bleeding in the operating theatre after aortic surgery. We believe that fresher blood may be beneficial in preventing these complications.

## Final diagnosis

Hyperkalaemia following rapid blood transfusion during thoraco-abdominal aortic reconstructive surgery.

**Keywords:** aortic surgery; blood transfusion; hyperkalaemia; citrate toxicity

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## A wheezy man with a bony abnormality

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A 56-year-old man presented to the chest clinic with worsening wheeze. His general practitioner had diagnosed asthma 3 years previously. At the time of presentation, he was taking inhaled terbutaline as required and budesonide 400 µg bid. Prednisolone 15 mg daily had been added following a recent exacerbation. He had been unable to work for 6 months owing to frequent attacks of asthma. He had stopped smoking 4 years previously but before this had had a 20 pack year history. On examination there was mild bilateral wheeze. Pulmonary function tests showed an obstructive pattern without significant reversibility. Chest X-ray showed hypertransradiancy of the left lung with normal appearance of the left pulmonary artery (figure 1). A computed tomography (CT) scan was performed (figure 2).



**Figure 1** X-ray of the chest showing hypertransradiancy of the left lung



**Figure 2** CT scan of the thorax at the level of the left main bronchus

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### Questions

- 1 What does the CT scan show?
- 2 How would you further investigate and manage this patient?

## Answers

### QUESTION 1

The thoracic CT scan shows a densely calcified lesion within the proximal part of the left main bronchus.

### QUESTION 2

The next investigation was flexible bronchoscopy which confirmed the presence of an inflamed, non-segmental lesion in the left main bronchus. Biopsy of the lesion showed granulation tissue with areas of calcification. At rigid bronchoscopy, two small pieces of bone were removed. At this point, the patient recalled choking on a chicken bone at around the same time that asthma had been diagnosed.

### Outcome

The patient's symptoms subsequently improved and X-ray changes resolved. Bronchodilators and anti-inflammatory medications have been discontinued, lung function tests are normal, and the patient has returned to work.

### Discussion

The diagnosis of foreign body aspiration is often overlooked in adults, especially when, as

in this case, the clinical syndrome is suggestive of another, more common condition. The history of choking on a bone was only elicited after the bone had been retrieved and was shown to the patient. Previous reports suggest that 25% of adults with foreign body aspiration never recall the actual event.<sup>1</sup> Whilst the anatomy of the bronchial tree favours aspiration to the right, it is not unusual for a foreign body to lodge in the left side,<sup>1-4</sup> as in this case. In our patient there were no factors, such as trauma, sedation, or neurological deficit, which would have predisposed to aspiration.

Removal of the foreign body at rigid bronchoscopy is the preferred treatment, although some advocate the use of the flexible bronchoscope<sup>1</sup> and, in extreme cases, thoracotomy is necessary. It is important to have a high index of suspicion in considering the diagnosis of foreign body aspiration, so that prolonged morbidity and ineffective treatment are avoided.

### Final diagnosis

Foreign body aspiration with chronic bronchial inflammation.

**Keywords:** asthma; foreign body aspiration

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## Electrocardiographic abnormalities in an elderly woman

P R T Atkinson, G B Turner, N A Herity

An elderly woman was admitted as an emergency from home. Figure 1 shows an electrocardiogram (ECG) taken at the time of admission.

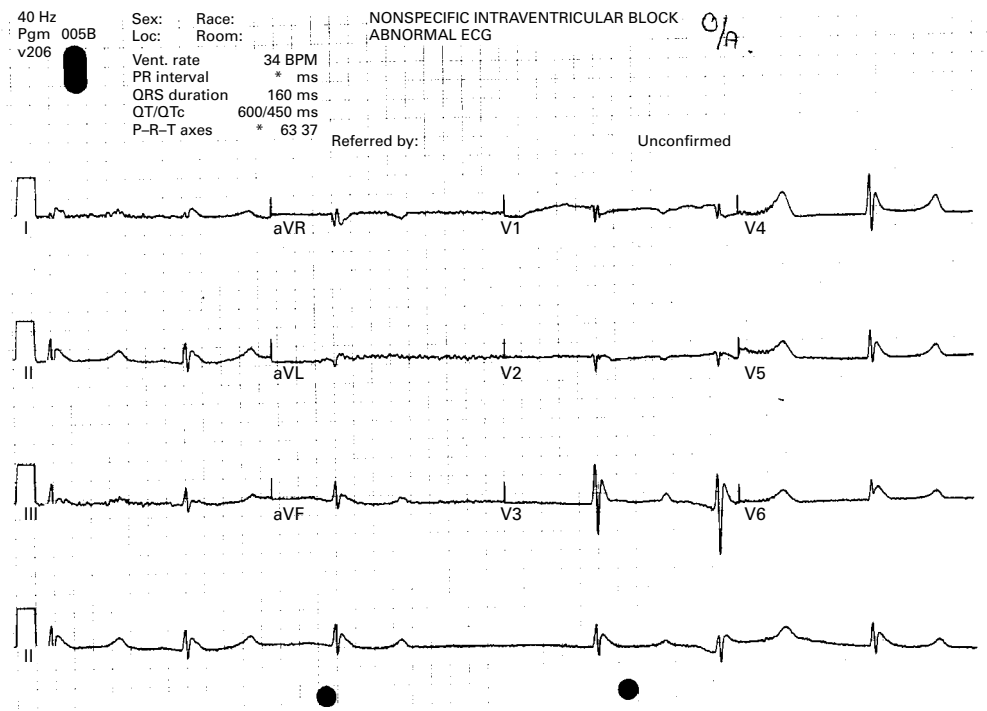


Figure 1 Admission ECG

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### Questions

- 1 What electrocardiographic abnormalities are seen in figure 1?
- 2 What is the diagnosis?

## Answers

### QUESTION 1

Junctional (J) waves, prolongation of the QT interval, bradycardia, atrial fibrillation, and shivering artefact.

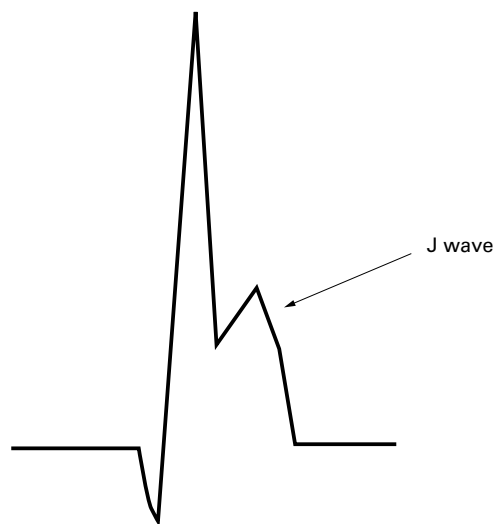
### QUESTION 2

Hypothermia.

## Discussion

Junctional waves, hump-like deflections at the junction of the QRS complex and ST segment are seen best in the unipolar chest leads (V2-V6).<sup>1</sup> These deflections (also known as Osborn waves) may appear in hypercalcaemia and in patients predisposed to early repolarisation.<sup>2</sup> Possible mechanisms include altered myocardial repolarisation and depolarisation rates during cooling<sup>1,3</sup> or altered epicardial action potential morphology resulting in a voltage gradient across the ventricular wall.<sup>2</sup> The amplitude of J waves increases with the severity of hypothermia and they are consistently seen below 25°C. Their prognostic significance is uncertain.

Prolongation of the QT interval may persist beyond rewarming, as repolarisation recovers more slowly than depolarisation. Bradycardia is common below 33°C. Prior to reaching this temperature the patient is often tachycardic due to homeostatic mechanisms including shivering and sympathetic activation. At lower temperatures tremor may not be obvious but electrocardiographic shivering artefact is usual, as seen here. Other electrocardiographic abnormalities include QRS widening, ST segment depression, T wave abnormalities, atrioventricular block, and arrhythmias, of which atrial fibrillation is the commonest.<sup>3</sup>



**Figure 2** Illustration of the J wave

These electrocardiographic abnormalities disappear with rewarming (figure 2). In this patient atrial fibrillation was longstanding and she was on no anti-arrhythmic medication. On rewarming her ventricular rate rose to 80–100 beats/min.

## Final diagnosis

Hypothermia.

**Keywords:** hypothermia; electrocardiogram; junctional waves; QT prolongation

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## A yellow patient with hepatomegaly

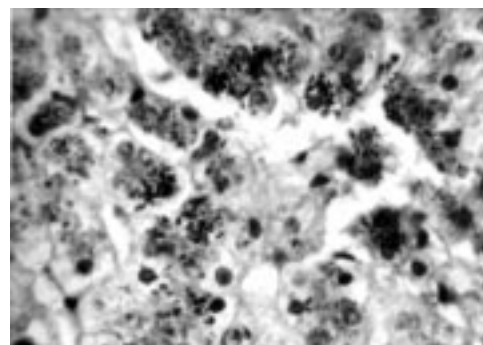
O P Mishra, Mohan Kumar, V K Dixit, V K Shukla

A 17-year-old woman, born to non-consanguineous parents, presented with 5-year history of persistent yellow discoloration of eyes and urine without any history of nausea, vomiting, pruritus, white faeces, features of hepatocellular failure and blood transfusion. On examination, she had jaundice and hepatomegaly (2 cm), soft in consistency, non-tender with smooth surface. Examination of other systems were non-contributory. At the age of 16 years, she had had an episode of acute cholecystitis and ultrasonography of the hepatobiliary system revealed cholelithiasis (figure 1) with normal hepatic echotexture, biliary system, and hepatic and common bile ducts (CBD). Other investigations revealed haemoglobin 12 g/dl, total leucocyte count  $7.6 \times 10^9/l$ , neutrophils 64%, lymphocytes 31%, eosinophils 5%, platelets  $250 \times 10^9/l$ , conjugated hyperbilirubinaemia and normal levels of serum proteins, transaminases, alkaline phosphatase and prothrombin time (table). Oral cholecystography and BSP excretion tests were not performed. The patient was managed conservatively but jaundice persisted and after 3 months she had another attack of cholecystitis. Repeat ultrasonograph showed persistence of gall stones with dilatation of upper part of the CBD. Cholecystectomy with exploration of CBD was performed. Per-operative findings demonstrated that the gall bladder was full of multiple stones but no stones were found in the CBD. Histopathology showed chronic cholecystitis with lithiasis. Liver biopsy revealed gross blackish discoloration of tissue. Microscopically, lobular architecture was preserved and hepatocytes in the pericanalicular regions were studded with blackish-brown pigment in the cytoplasm (figure 2). Some of the Kupffer cells showed similar pigment deposition. The T-tube cholangiogram done on the tenth post-operative day was normal and she made an uneventful recovery. Liver function tests 4 weeks after surgery were similar to those performed pre-operatively.

The younger sister of the patient, aged 12 years, was also found to have jaundice, hepatomegaly (2 cm), soft in consistency, non-tender with smooth surface. Her liver function tests were similar to those of the patient. Ultrasonography of her hepatobiliary system was normal, and liver biopsy was not performed. There was no jaundice in the parents and liver function tests were normal.



**Figure 1** Ultrasonograph demonstrating stones in the gallbladder



**Figure 2** Microphotograph showing black pigment deposition in liver parenchymal cells, concentrated in centrilobular area (H&E stain  $\times 500$ )

**Table** Laboratory findings

Tests	Patient	Sister
Total bilirubin ( $\mu\text{mol/l}$ )	95.7	94.0
Conjugated bilirubin ( $\mu\text{mol/l}$ )	78.6	71.8
Serum protein (g/dl)	7.4	6.5
Albumin:globulin ratio	4.2:3.2	4.0:2.5
Alanine transaminase (IU/l)	40	29
Aspartate transaminase (IU/l)	35	19
Alkaline phosphatase (IU/l), normal range 37–147 IU/l	93	103
Prothrombin time (s), control value 16 s	18	17
Australia antigen (HbsAg)	negative	negative

### Questions

- 1 What is the diagnosis and what disorders are associated with this syndrome?
- 2 What is the cause of cholelithiasis in this disease?

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## Answers

### QUESTION 1

The patient suffers from Dubin-Johnson syndrome with cholelithiasis. Certain rare associations have been observed with this disorder (box). An isolated deficiency of coagulation factor VII has been reported in a significant proportion of patients in Israel.<sup>1</sup> There was also a mild decrease in level of factor II and diminished prothrombin activity (< 70%) in 60% of patients. This is not due to impaired liver function as there is no hepatocellular necrosis. However, the two defects have been found to segregate independently in family studies. Another association is cholelithiasis, which was reported for the first time by Estrada-Rodriguez *et al.*<sup>2</sup>

### QUESTION 2

Non-visualisation of gall bladder on oral cholecystography is found in this disorder and it is due to impaired biliary secretion of cholecystographic contrast medium. The cause of cholelithiasis is difficult to explain. It could be just an association with the disease.

### Discussion

The presence of jaundice, hepatomegaly, positive family history, and conjugated hyperbilirubinaemia with normal levels of transaminases and alkaline phosphatase suggested the diagnosis of Dubin-Johnson syndrome in our case. Histopathological examination of liver tissue confirmed the diagnosis. The disorder is

### Associations with Dubin-Johnson syndrome

- coagulation factor VII deficiency
- mild decrease in level of factor II
- decreased prothrombin activity (< 70%)
- cholelithiasis

transmitted as an autosomal recessive trait and the majority of patients are asymptomatic except for chronic or recurrent jaundice of fluctuating intensity.<sup>3</sup> The cholelithiasis in the present case may be just an association or the result of the original disease process where the primary defect is impaired biliary canalicular transport of organic anions and conjugated bilirubin due to an abnormality in the membrane carrier system.<sup>4</sup> Since, this benign disorder has a good prognosis with normal life expectancy, no specific therapy is required, except to treat problems like cholelithiasis. However, patients should be warned about the aggravating effect of drugs such as oestrogen-containing preparations, erythromycin, azithromycin, cloxacillin, ceftriaxone, etc, and pregnancy, on the intensity of the jaundice.

### Final diagnosis

Dubin-Johnson syndrome with cholelithiasis.

**Keywords:** Dubin-Johnson syndrome; cholelithiasis

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