SELF ASSESSMENT QUESTIONS

A 60 year old woman with axillary mass

Answers on p 515.

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A 60 year old women, a resident of Delhi, presented to the medical outdoor department of Lady Hardinge Medical College with complaints of recurrent fever accompanied by chills, rigor, headache, and malaise. She had no complaints suggestive of respiratory or urinary tract involvement. She had been treated with antimalarials (chloroquine and sulfadoxine-pyrimethamine), however, she continued to be febrile. Subsequently, the patient reported a painful lump in the right axilla accompanied by pain in the right upper limb. There was no history of nipple discharge or breast lump, local injury to the limb, insect bite, haemoptysis, or chest pain, loss of weight, bleeding diathesis, any skin rash, and urinary or bowel complaints. Past and family history were non-contributory.

Physical examination revealed a conscious middle aged women, with normal pulse rate (80 beats/min) and blood pressure (140/80 mm Hg). Respiratory rate was 26 breaths/min and her body temperature was 39°C. She was anaemic; however, there was no jaundice, cyanosis, clubbing, and oedema. Bilateral axillary lymph nodes were enlarged, measuring 2 × 2 cm, firm, tender, and mobile. There was no lymph node enlargement elsewhere on the body. There was a tender, reddish streak on the medial aspect of right arm. Examination of breast and other systems was normal. With provisional diagnoses of streptococcal lymphangitis, tubercular lymphadenitis, secondaries from internal malignancy and primary lymphoma, the patient was subject to further investigations.

Investigations revealed a haemoglobin of 128 g/l, total lymphocyte count of 7800/mm³, erythrocyte sedimentation rate of 30 mm/hour with eosinophilia (22% with an absolute count of 900/mm³). Peripheral smear revealed no haemoparasites. All other investigations including chest radiography, a sonographic study of the abdomen, Mantoux test, and urinary and blood cultures were normal. Serum IgE concentrations were not measured as the investigation was not available to us when the patient presented. The results of a fine needle aspiration from one of the right axillary lymph nodes are shown in fig 1. Aspiration from the left axillary nodes revealed only non-specific lymphadenitis.

Figure 1 Results of fine needle aspiration from right axillary lymph node.

Questions

- (1) What is the diagnosis?
- (2) How will you treat this patient?
- (3) What is Weingarten's syndrome?

Renal colic in a young woman

N Sarath Krishna, J Sinclair

Answers on p 516.

A 37 year old woman presented to our accident and emergency department with a history of pain in her right loin. There was no radiation of pain to her groin. She had no dysuria, urinary frequency, or vaginal discharge and was afebrile. On examination she had right loin tenderness. She was treated with analgesics which relieved her pain. Her urine analysis was positive for blood. A mid-stream specimen of urine showed no growth of organisms. Full blood count, electrolytes, urea, and creatinine

Figure 1 Plain film of IVU.

Figure 2 Cystogram phase of IVU.

were all within normal limits. A plain film and cystogram phase of an intravenous urogram (IVU) are shown in figs 1 and 2 respectively.

Questions

- (1) What are the findings on the plain and cystogram films of the IVU?
- (2) What are the types of ureteroceles and how does an ureterocele present?
- (3) How do you manage this condition?

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An unusual cause of watery diarrhoea

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Answers on p 517.

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A 40 year old housewife was referred with a nine month history of intermittent watery diarrhoea and intermittent abdominal pain. The diarrhoea occurred four to five times a day and there was no blood or mucus in the stools. Her only past medical history consisted of heartburn which was treated with ranitidine 150 mg twice a day by her general practitioner. She did not smoke and only drank occasionally. Physical examination revealed a 5 cm enlarged non-tender liver. Stool cultures revealed no growth. She underwent upper gastrointestinal endos-

copy which revealed grade II oesophagitis and diffuse duodenitis and a small bowel series showed fine ileal ulceration. Colonoscopy was normal. Computed tomography of the abdomen showed multiple lesions throughout the right and the left liver highly suspicious of metastatic disease.

Questions

- (1) What is the diagnosis?
- (2) How would you confirm this?
- (3) What are the treatment options?

A patient presenting with hoarseness

Kim-Hatt Lim, Chong-Kin Liam, Catherine Mee-Ming Wong

Answers on p 518.

A non-smoking 34 year old man was seen for hoarseness of voice and non-productive cough of three months' duration. Apart from mild weight loss he was otherwise well. He had no significant past medical illness.

Findings of physical examination were unremarkable except for the hoarseness. Laryngoscopy revealed paralysis of the left vocal cord with no intrinsic lesion of the larynx. Neurological and lung examinations showed no abnormal finding.

Figure 2 Computed tomogram of thorax.

Figure 1 Chest radiograph, posteroanterior view.

Laboratory investigations revealed a haemoglobin of 135 g/l, total white cell count of $7.5 \times 10^9/l$ with 64% neutrophils, 24% lymphocytes, 9% monocytes, and 3% eosinophils. The erythrocyte sedimentation rate was 15 mm/hour. His serum protein concentration was 78 g/l, albumin 33 g/l, alkaline phosphatase 203 IU/l, aspartate aminotransferase 33 IU/l, alanine aminotransferase 52 IU/l, and calcium 2.38 mmol/l. Twenty four hour urine calcium was raised at 9.3 mmol/24 hours (normal range 2.2–7.5). His renal function was normal. Chest radiography (fig 1) and computed tomography of the thorax (fig 2) were performed. The Mantoux test (10 tuberculin units) produced a negative response on two occasions.

Questions

- (1) What does the computed tomogram of the thorax show?
- (2) What is the most probable diagnosis?
- (3) Describe the three mechanisms causing hoarseness in this condition?

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Young male with headache, blindness, and hypogonadism

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Answers on p 519.

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A 20 year old man presented with a history of diffuse, moderately severe headache of six years' duration. He had noticed gradual onset, slowly progressive diminution of vision in both eyes, and poorly developed secondary sexual characters of the same duration. On clinical examination his height was 152 cm, upper segment to lower segment ratio of 0.82 (mean 0.92 in white adults, 0.85 in black adults), arm span 162 cm (normal <5 cm more than height), there were no pubic, axillary, or secondary sexual facial hair. His testicular volume was 3 ml (normal adult 12–25 ml), stretched penile length 4 cm [mean in Asians 10.6 cm]. His bone age by the Tanner-

Whitehouse 2 method was 18 years. His visual acuity was reduced to perception of light in both eyes; fundoscopy revealed bilateral optic atrophy. Clinically he was euthyroid and eucortisolic. Other general and systemic examinations were normal. The skull radiograph lateral view taken earlier was reviewed (fig 1). Luteinising hormone concentration was 1 IU/l (normal range 1.3–13 IU/l), testosterone 3 nmol/l (10–35 nmol/l), prolactin 100 µg/l (2–15 µg/l), thyroxine 140 nmol/l (64–154 nmol/l), cortisol at 8am 600 nmol/l (140–690 nmol/l) and at 4pm 300 nmol/l (80–330 nmol/l), simultaneous plasma and urine osmolality were 287 mmol/kg serum water (285–295 mmol/kg serum water) and 800 mmol/kg respectively. The urine volume was 2000 ml/day and specific gravity 1.020. Serum sodium, potassium, and blood glucose (fasting and postprandial) concentrations were normal. He could not afford tests for growth hormone.

Questions

- (1) What are the abnormalities shown in the skull radiograph?
- (2) What is the diagnosis?
- (3) What are the various clinical presentations of this condition?

Figure 1 Radiograph of the skull.

Right shoulder pain in a body builder

Answers on p 521.

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A 23 year old body builder presented with a two year history of pain and stiffness in his right shoulder. There was no history of trauma to the shoulder either at work or during his weight training. On examination there was point tenderness of the right acromioclavicular joint and restriction in the terminal range of shoulder abduction. Laboratory investigations were nor-mal. A plain anteroposterior radiograph of the right shoulder joint was taken (fig 1).

Questions

- (1) Identify the pertinent findings on radiography.
- (2) What is the clinical diagnosis? What could be the cause?
- (3) What would be your line of management for this patient? Rationalise your answer.

Figure 1 Anteroposterior radiograph of the right shoulder.

Unexpected elevation of parathyroid hormone in an asymptomatic patient with multiple endocrine neoplasia syndrome type 2A

Answers on p 522.

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Two years ago, a 19 year old man underwent total thyroidectomy because of medullary thyroid carcinoma in association with the multiple endocrine neoplasia syndrome type 2A. At the same time as total thyroidectomy, total parathyroidectomy and heterotopic autotransplantation of parathyroid tissue to the right forearm was performed. Postoperative course and follow up over two years was uneventful; this included repeated biochemical testing (including parathyroid hormone level, calcitonin, and urinary catecholamines). The patient did not complain of any symptoms on the occasion of the last routine check up, but laboratory investigations revealed the results shown in table 1.

Table 1 Results of investigations

	Result	Normal	Interpretation
Calcium (mmol/l)	2.3	2.1–2.6	Normal
Phosphate (mmol/l)	1.2	0.6–1.3	Normal
Creatinine (μmol/l)	85	70–105	Normal
Albumin (g/l)	46	43–58	Normal
Parathyroid hormone (ng/l)	337	12–72	↑↑

Questions

- (1) What is the differential diagnosis?
- (2) What is your assessment?

SELF ASSESSMENT ANSWERS

A 60 year old woman with axillary mass

Q1: What is the diagnosis?

The slide (fig 1, see p 510) shows a microfilaria of *Wuchereria bancrofti* present within the lymph node, which was subjected to fine needle aspiration cytology. The microfilariae (embryos) usually found in the blood of the infected patient are sheathed, transparent bodies measuring about 290 µm in length and 6–7 µm in breadth. The microfilariae are surrounded by a hyaline sheath and have a central column of nuclei. The nuclei do not extend up to the tail in *W bancrofti* and serve as a distinguishing feature of the species. Hence the diagnosis is filarial lymphadenitis.

Q2: How will you treat this patient?

The treatment of lymphatic filariasis is currently limited to diethylcarbamazine administered in a daily dose of 6 mg/kg given in either single or three divided doses for 2–3 weeks. The drug exerts no direct lethal action on the microfilariae but modifies them so that they are engulfed by the phagocytes of the endothelial system and thereby removed from circulation. Ivermectin, a drug effective in the treatment of onchocerciasis has been used for lymphatic filariasis. However, currently available evidence is against its use in lymphatic filariasis, where the treatment of choice continues to be diethylcarbamazine. Treatment of chronic lymphatic obstruction is difficult. Elevation of the affected limb, use of elastic stockings, and local foot care are advisable and may be of help. Surgical decompression with nodovenous shunts may provide relief to severely affected limbs. Filarial hydrocele should be drained or managed surgically. Our patient was treated with diethylcarbamazine given in a dose of 100 mg three times a day for three weeks. Her lymphadenopathy and fever subsided within one week of treatment. The patient is currently on follow up and continues to be symptom free.

Q3: What is Weingarten's syndrome?

Weingarten's syndrome or tropical pulmonary eosinophilia is a condition characterised by cough, lassitude, dyspnoea on exertion and asthmatic attacks especially at night, occasionally with haemoptysis. The most striking feature is severe peripheral eosinophilia, which may rise to values as high as 60%. Chest radiography shows disseminated pulmonary mottling in about 20% cases. Lung function tests show a restrictive abnormality in 70% and an obstructive one in 30% of patients. One form presents as axillary lymphadenopathy. Total serum IgE concentrations and antifilarial antibody titres are characteristically raised. Diethylcarbamazine is used in a daily dose of 4–6 mg/kg for 14 days. Relapse may occur in up to 25% of patient and requires retreatment.

Learning points

- Filariasis, an endemic disease of the tropics can cause fever, lymphadenitis, funiculitis, epididymitis, orchitis, or abscesses.
- Chronic obstructive filariasis may manifest as lymphadenopathy, lymph varices, lymph scrotum, hydrocele, chyluria, chylocele, and elephantiasis.
- Tropical pulmonary eosinophilia may manifest as cough, dyspnoea and asthmatic attacks. Hypereosinophilia is striking and IgE concentrations are characteristically raised.
- Treatment is with diethylcarbamazine in 6 mg/kg/day in three divided doses.

Discussion

Filariasis is a morbid condition produced by a nematode (filariae). The adults of both sexes live in the lymphatics, skin, connective tissues or serous membranes, producing live embryos (microfilariae) which find their way into the blood stream and skin where they are capable of living. In the endemic areas, people become infected early in life and develop microfilaraemia. The disease may result in early filariasis or chronic obstructive filariasis. Early filariasis may manifest as filarial fever, filarial lymphadenitis and lymphangitis, filarial funiculitis and epididymitis, filarial orchitis or abscesses. Chronic obstructive filariasis may manifest as lymph gland enlargement, thickened lymphatic trunks, lymph scrotum, hydrocele, chyluria and lymphuria, chylocele, chylous ascites, or chylous diarrhoea. Gradually, chronic filariasis may lead to lymphoedema and the dramatic elephantiasis. Rarely, there may be filarial arthritis, ocular filariasis presenting as unilateral proptosis. Raised intracranial tension¹ and psychoneurotic disturbances have been seen. Unusually, haemorrhagic pericardial effusion² and glomerulonephritis³ have been described. Our patient manifested the disease as lymphadenitis and lymphangitis of the axillary lymph nodes. Filariasis is an unusual cause of axillary lymphadenopathy, more so, manifesting *only* as axillary lymphadenopathy. Our patient was started on diethylcarbamazine and her fever and lymph nodes subsided within a week of starting treatment.

Final diagnosis

Axillary lymphadenitis: filarial.

1 Das GC, Sen SB. Chylous arthritis. *BMJ* 1968;ii:27–9.

2 Reddy GS, Balasundaram S. Filarial pleural effusion. *J Assoc Physicians India* 1975;23:349–51.

3 Au ACS, Denham DA, Draper CC, *et al*. The pathology of glomerulonephritis in feline filariasis. *Trans R. Soc Trop Med Hyg* 1980; 74: 674–5.

Renal colic in a young woman

Q1: What are the findings on the plain and cystogram films of the IVU?

In the plain film (fig 1, see p 511) a small radio-opaque shadow (calculus) is seen in the area of the bladder to the right of the midline. On the cystogram film a typical cobra head appearance characteristic of a ureterocele is seen. The wall of the ureterocele is radiolucent whereas the contrast present within the ureterocele and in the bladder is radio-opaque. This gives the typical cobra head appearance of the ureterocele. The diagnosis in this case is an intravesical stenotic ureterocele containing a calculus.

Q2: What are the types of ureteroceles and how does an ureterocele present?

A ureterocele is a cystic dilatation of the terminal ureter and is a developmental abnormality. They are broadly classified into two categories: 1, intravesical and 2, ectopic. An ureterocele is termed ectopic if any portion of the ureterocele extends to the bladder neck or the urethra. Ureteroceles are classified further according to the number of systems (single or duplex) and the type of orifice (for example, stenotic, sphincteric, sphincterostenotic). This classification was established by the American Academy of Pediatrics and is most frequently used today. Clinical presentation varies considerably (see box 1). Patients commonly present with infection but calculi can develop secondary to urinary stasis and are often seen in the distal ureter.

Q3: How do you manage this condition?

In our case the ureterocele was intravesical, single with a stenotic orifice and there was a calculus in it. An endoscopic transurethral incision of ureterocele with a Collin's knife and extraction of the calculus was performed under general anaesthesia.

Discussion

The term ureterocele is used to describe the cystic dilatation of the terminal portion of the ureter. It may be either intravesical or ectopic. Ureterocele has been attributed to incomplete dissolution of the Chwalle's membrane which divides the early ureteric bud from the urogenital sinus.¹ The cystic dilation forms between the superficial and deep muscle layers of the trigone.

Box 1: Clinical presentation of a ureterocele

- Urinary tract infection.
- Ureteric colic due to a calculus.
- Bladder outflow obstruction.
- Urinary incontinence.
- Mass prolapsing through female urethra.
- Haematuria.
- Palpable abdominal mass may be detectable in some children (hydronephrotic kidney).

Learning points

- Ureterocele is a cystic dilatation of lower end of ureter (congenital abnormality).
- Intravesical ureteroceles are generally associated with single ureters, whereas ectopic ureteroceles most often are associated with the upper pole moiety of duplex ureters.
- Seven times more common in girls. 10% of cases are bilateral. Ectopic ureteroceles are four times more common.
- Commonest presentation is urinary tract infection.
- Excretory urography is usually diagnostic.
- Transurethral endoscopic incision of ureterocele is the treatment of choice for symptomatic intravesical ureterocele.
- Prenatal diagnosis of the ureterocele with ultrasound scan enables neonatal transurethral incision of ureterocele which effectively decompresses the ureterocele with preservation of renal parenchyma.

Ureteroceles of a single ureter are characteristically of the intravesical type and are less prone to severe obstruction and dysplasia. Ectopic ureteroceles are most commonly encountered in paediatrics and usually develop with ureteral duplication and are often responsible for serious complications.² Stasis of urine in this obstructed system can lead not only to urinary tract infection but also to calculus formation. Some children may present with a palpable mass in their abdomen, which is a hydronephrotic kidney. An ectopic ureterocele can prolapse out of the urethra and present as a vaginal mass. This is termed a prolapsing ureterocele. A large ureterocele can obstruct the bladder neck or even the contralateral ureteric orifice causing hydronephrosis. Ectopic ureteroceles can cause urinary incontinence by interfering with the normal sphincteric function at or distal to the bladder neck. Excretory urography often demonstrates the characteristic cobra head (or spring onion) deformity—an area of increased density similar to the head of a cobra with a halo or a less dense shadow around it. At cystoscopy the ureterocele usually expands rhythmically with each peristaltic wave that fills it and then shrinks as a thin jet of urine drains through the thin orifice. Treatment of ureterocele must be individualised. Single system ureteroceles are more amenable to endoscopic incision³ and are less likely to exhibit postoperative reflux. Treatment of ectopic ureterocele associated with an upper pole moiety of a duplex system is more complicated. In most instances the upper pole moiety of the duplex system is obstructed, hydronephrotic and contributes little to overall renal function. This involves upper pole nephrectomy and partial ureterectomy.⁴ Less commonly, when significant upper pole function is present a ureteropyelostomy is advocated. This

should decompress the ureterocele, with return of the trigone to a more normal configuration and resolution of ipsilateral lower pole reflux. However if the patient has high grade reflux into the ipsilateral lower pole ureter, a combination of ureterocele excision with or without nephroureterectomy, and lower pole ureteral reimplantation (common sheath) may be necessary. Separation of the duplicated ureters during intravesical dissection should be discouraged because it can lead to sacrifice of the common blood supply running longitudinally in between the ureters, hence the need for common sheath reimplantation of the ureters. With the advent of frequent prenatal ultrasonography early diagnosis of ureteroceles is possible. Treatment of ureterocele in the neonatal period by endoscopic incision enables effective decompression of the ureterocele, preservation of renal function in the neonate and reduces the risk of severe infection in the neonate.⁵

Final diagnosis

Intravesical stenotic ureterocele containing a calculus.

- 1 Chwalle R. The process of formation of cystic dilatations of the vesical end of the ureter and of diverticula at the ureteral ostium. *Urol Cutan Rev* 1927;31:499.
- 2 Rickwood AM, Reiner I, Jones M, *et al*. Current management of duplex system of ureteroceles. *Br J Urol* 1992;70:196.
- 3 Rich MA, Keating MA, Snyder HM III, *et al*. Low transurethral incision of single system intravesical ureteroceles in children. *J Urol* 1990;144:120.
- 4 Reitelman C, Perlmuter AD. Management of obstructing ectopic ureteroceles. *Urol Clin North Am* 1990;17:317.
- 5 Pfister C, Ravasse P, Barret E, *et al*. *J Urol* 1998;159:1006-9.

An unusual cause of watery diarrhoea

Q1: What is the diagnosis?

The diagnosis is metastatic Zollinger-Ellison syndrome.

Q2: How would you confirm this?

Gastrinoma should be confirmed by measurement of the fasting gastrin concentration. Proton pump inhibitors should be stopped for one week and histamine-2-receptor antagonists for 48 hours before measurement of the gastrin concentration as they can contribute to hypergastrinaemia. If the gastrin is raised it should then be repeated with simultaneous measurement of the gastric fluid pH. If the pH is >2.5 hypergastrinaemia may be due to gastric acid hyposecretion such as in cases of pernicious anaemia and *Helicobacter pylori* infection, or secondary to the use of acid suppressing drugs. A raised serum gastrin of >1000 ng/l in association with a gastric pH of <2.5 is diagnostic of gastrinoma. In cases where the serum gastrin is only moderately raised at <1000 ng/l a secretin provocation test should be performed. A paradoxical rise in the serum gastrin of 200 ng/l after administration of secretin confirms the diagnosis.

In this case the serum gastrin concentration was 1452 ng/l and metastatic gastrinoma was confirmed on liver biopsy.

Q3: What are the treatment options?

The aims of treatment are twofold. Initially the gastric acid hypersecretion needs to be controlled, which can now be done successfully in virtually all cases with the use of proton pump inhibitors. Gastric acid secretion should be reduced to <5 mmol/hour which often requires high doses. Treatment of the gastrinoma itself is based on the site of the primary tumour, the presence and extent of metastatic disease, and whether the tumour is part of the multiple endocrine neoplasia (MEN) type I syndrome. This requires accurate imaging to determine the appropriate treatment. Somatostatin receptor scintigraphy should be performed in all newly diagnosed cases to assess the extent of the disease. In the absence of metastatic disease stringent attempts should be made to resect the primary tumour. Metastatic disease needs to be treated in accordance with the position and extent of the metastases, along with the rate of growth of the tumour.

Discussion

The clinical syndrome of peptic ulceration and hypergastrinaemia in the presence of a non- β islet cell pancreatic tumour was first described by Zollinger and Ellison in their landmark paper published in 1955.¹ After this, the treatment of choice was total gastrectomy which decreased the mortality from peptic ulceration. However the introduction of potent inhibitors of gastric acid secretion over the last 20 years has changed the natural history of the disease. Increasingly metastatic disease, and in particular the extent of liver involvement, is determining life expectancy as the complications related to gastric ulceration diminish.² This change in the natural history of gastrinomas has shifted the emphasis in treatment towards earlier diagnosis, more accurate tumour localisation, and more active treatment of metastatic disease.

In most reported series there is a delay in the diagnosis of gastrinoma of three to six years from the onset of symptoms. This may be due to the majority of cases presenting with a solitary peptic ulcer rather than the classical situation of multiple ulcers in unusual sites.³ Furthermore in up to 30% of cases the sole presenting feature is oesophageal reflux or persistent secretory diarrhoea. Thus a high index of suspicion is necessary, especially in cases of peptic ulceration that are *H pylori* negative where there is no history of non-steroidal anti-inflammatory drug use, or if the symptoms are resistant to usual measures. As 60%–90% of cases are malignant earlier diagnosis and surgical treatment at a premetastatic stage should increase survival.

The decision as to appropriate treatment depends on accurate knowledge of the site of the primary tumour and the presence and extent of metastatic disease. The advent of somatostatin receptor scintigraphy has improved the detection of these tumours, which are often difficult to image with conventional means. Recent studies have shown it to alter management in up to 47% of cases initially imaged with a combination of ultrasound, computed tomography, and magnetic

Learning points

- The natural history of Zollinger-Ellison syndrome is changing.
- Earlier diagnosis through increased awareness may lead to improved survival.
- Somatostatin receptor scintigraphy is the imaging modality of choice in all patients with Zollinger-Ellison syndrome.
- Surgical resection should be attempted if possible.
- At present there is no definitive treatment for metastatic disease, although a variety of therapeutic interventions are undergoing trials.
- Orthotopic liver transplantation should be considered in carefully selected patients with advanced metastatic disease confined to the liver.

When to consider Zollinger-Ellison syndrome

- Peptic ulceration in atypical sites.
- Peptic ulceration in *H. pylori* negative patients with no history of non-steroidal anti-inflammatory drug use.
- Combination of peptic ulceration and diarrhoea.
- Peptic ulceration resistant to medical therapy.
- Persistent secretory diarrhoea.
- Severe oesophageal reflux or oesophageal strictures.
- Patients with a strong familial history of peptic ulceration.

resonance imaging.⁴ It is now advocated that somatostatin receptor scintigraphy should replace conventional radiology as the initial imaging study in all cases of gastrinoma.⁵

The treatment of patients with gastrinomas is dependent on the position and potential for surgical resection of the primary tumour, the presence or absence of metastatic disease, and whether the gastrinoma is part of the MEN type I syndrome.

Patients without metastatic disease or MEN type I who undergo curative resection of the primary tumour have a very good long term prognosis. Therefore patients without evidence of liver or distant metastases on imaging should undergo routine surgical exploration, including a thorough search of the duodenum, with a view to complete surgical excision.

The treatment of patients with metastatic disease without MEN type I is more complicated. At present there is no consensus as to the best treatment despite many papers advocating a multitude of modalities including chemotherapy, chemoembolisation, hepatic cryosurgery, laparoscopic thermal ablation, extensive hepatic resection, and liver transplantation. At

present only hepatic resection of isolated metastases where the primary can also be removed has been shown to improve five year survival.⁶ However due to the diffuse nature of the tumour hepatic resection is normally only possible in a limited number of cases. In the remainder, if there is no extrahepatic disease, orthotopic liver transplantation should be considered as recent studies have now indicated that in highly selected patients, liver transplantation can yield long term survival.⁷

Finally, the 25% of patients whose gastrinoma is part of the MEN type I syndrome need to be approached differently. These cases normally have multiple tumours and as yet surgery has not been shown to offer a survival benefit over medical treatment and as such, cannot be recommended. Acid suppression remains the mainstay of treatment.

In summary, earlier diagnosis through increased awareness, improved detection of metastatic disease, and the aggressive treatment of patients with metastatic disease may improve patient survival. Surgical intervention is the only present treatment that results in a cure and should be undertaken where possible. The optimal medical treatment for patients who do not undergo curative surgery remains to be established. In the future improved tumour localisation with somatostatin receptor scintigraphy may lead to more appropriate treatment and therefore improve patient survival.

In this case, the patient underwent orthotopic liver transplantation and enjoyed three and a half years of good quality life before dying of recurrent disease.

Final diagnosis

Metastatic Zollinger-Ellison syndrome.

- 1 Zollinger RM, Ellison EH. Primary peptic ulceration of the jejunum associated with islet cell tumours of the pancreas. *Ann Surg* 1955;142:709–28.
- 2 Yu F, Venzon DJ, Serrano J, *et al*. Prospective study of the clinical course, prognostic factors, causes of death, and survival in patients with long-standing Zollinger-Ellison syndrome. *J Clin Oncol* 1999;17:615–30.
- 3 Jensen RT. Gastrinoma. *Baillieres Clin Gastroenterol* 1996;10: 603–43.
- 4 Termanini B, Gibril F, Reynolds JC, *et al*. Value of somatostatin receptor scintigraphy: a prospective study in gastrinoma of its effect on clinical management. *Gastroenterology* 1997;112:335–47.
- 5 Proye C, Malvaux P, Pattou F, *et al*. Noninvasive imaging of insulinomas and gastrinomas with endoscopic ultrasonography and somatostatin receptor scintigraphy. *Surgery* 1998; 124:1134–43.
- 6 Jensen RT. Gastrin-producing tumours. *Cancer Treat Res* 1997;89:293–334.
- 7 Dousset B, Houssin D, Soubrane O, *et al*. Metastatic endocrine tumours: is there a place for liver transplantation? *Liver Transpl Surg* 1995;1:111–17.

A patient presenting with hoarseness

Q1: What does the computed tomogram of the thorax show?

The computed tomogram (see p 512) demonstrated enlarged mediastinal and bilateral hilar lymph nodes.

Q2: What is the most probable diagnosis?

The clinical and radiographic features are consistent with the diagnosis of sarcoidosis. The cause of hoarseness is due to left vocal cord

palsy as a result of compression of the left recurrent laryngeal nerve by enlarged mediastinal lymph nodes. Other differential diagnoses to be considered are lymphoma and tuberculosis.

For this patient a mediastinal lymph node biopsy was performed by mediastinostomy. This revealed numerous granulomas consisting of epithelioid cells and lymphocytes. Foci of caseation necrosis were present. Stains for acid-fast bacilli and fungi were negative.

Q3: Describe the three mechanisms causing hoarseness in this condition

Compression of the left recurrent laryngeal nerve by enlarged mediastinal lymph nodes is not the only mechanism of hoarseness in sarcoidosis. Hoarseness in sarcoidosis may also be due to granulomatous infiltration of the larynx, which is identified in about 5% of patients.¹ Sarcoid cranial polyneuropathy involving the vagus nerve may also lead to dysphonia. This situation is often associated with other neurological lesions, in particular facial nerve palsy.

Discussion

The left recurrent laryngeal nerve originates from the vagus nerve and progresses below the aortic arch, then ascends to the vocal cord. In the thorax the left recurrent laryngeal nerve travels in close proximity to the aorta, left atrium, trachea, left main bronchus, oesophagus, and the mediastinal lymph nodes. Diseases affecting any of these structures may lead to nerve palsy and subsequent left vocal cord paralysis. Unilateral vocal cord palsy usually presents with hoarse voice due to inadequate compensation by the contralateral vocal cord.

Vocal cord paralysis is an unusual complication of sarcoidosis. There have been few reports of sarcoidosis with mediastinal lymphadenopathy compressing on left recurrent laryngeal nerve leading to left vocal cord palsy and hoarseness of voice.¹⁻⁴

Conventional chest radiography reveals evidence of intrathoracic lymph node enlargement in 75% to 85% of patients with sarcoidosis.⁵ It is usually localised to the hilar, tracheobronchial, and paratracheal groups and typically is bilateral and symmetrical. The aortopulmonary lymph nodes are involved in 75% of 62 patients with sarcoidosis and intrathoracic lymphadenopathy in one review.⁶ In this patient, computed tomography demonstrated intrathoracic lymphadenopathy involving all the mentioned groups of lymph nodes.

The pathological hallmark of sarcoidosis is the granuloma. The majority of granulomas are non-caseating. However, as in this patient, some granulomas contain foci of caseation, the presence of which does not exclude the diagnosis.⁷ Such caseation typically occurs in the central portion of the granuloma and appears as amorphous eosinophilic material often associated with degenerated, hyperchromatic nuclei. In a review of 100 patients with hepatic sarcoidosis,⁸ granulomas with central caseation were noted in 1% of the cases.

Learning points

- Hoarseness can be a presenting complaint in sarcoidosis which may be the result of left vocal cord palsy due to compression of the left recurrent laryngeal nerve by enlarged mediastinal lymph nodes.
- Pathological finding of granulomas with central caseation does not exclude the diagnosis of sarcoidosis.

This patient was treated with corticosteroid. His symptoms improved rapidly with resolution of his hoarseness and dry cough. The 24 hour urine calcium concentration fell to normal at 5.8 mmol/24 hours. Resolution of the left vocal cord paralysis was confirmed by a repeat laryngoscopy two months later. A repeat computed tomogram of the thorax eight months later revealed marked regression of the mediastinal lymphadenopathy.

Final diagnosis

Sarcoidosis with left vocal cord paralysis due to compression of left recurrent laryngeal nerve by enlarged mediastinal lymph nodes.

- 1 El-Kassimi FA, Ashour M, Vijayaraghavan R. Sarcoidosis presenting as recurrent left laryngeal nerve palsy. *Thorax* 1990;45:565-6.
- 2 Chijimatsu Y, Tajima J, Washizaki M, et al. Hoarseness as an initial manifestation of sarcoidosis. *Chest* 1980;78:779-81.
- 3 Swinburn CR, Pozniak AL, Davies DG, et al. Left recurrent laryngeal nerve palsy as the presenting feature of sarcoidosis. *Sarcoidosis* 1986;3:67-8.
- 4 Tobias JK, Santiago SM, Williams AJ. Sarcoidosis as a cause of left recurrent laryngeal nerve palsy. *Arch Otolaryngol Head Neck Surg* 1990;116:971-2.
- 5 Kirks DR, McCormick VD, Greenspan RH. Pulmonary sarcoidosis. Roentgenologic analysis of 150 patients. *AJR Am J Roentgenol* 1973;117:777-86.
- 6 Bein ME, Putman CE, McLoud TC, et al. A reevaluation of intrathoracic lymphadenopathies in sarcoidosis. *AJR Am J Roentgenol* 1978;131:409-15.
- 7 Mitchell KN, Scadding JG, Heard BE, et al. Sarcoidosis: histopathological definition and clinical diagnosis. *J Clin Pathol* 1977;30:395-8.
- 8 Devaney K, Goodman ZD, Epstein MS, et al. Hepatic sarcoidosis. Clinicopathologic features in 100 patients. *Am J Surg Pathol* 1993;17:1272-80.

Young male with headache, blindness, and hypogonadism

Q1: What are the abnormalities shown in skull radiograph (see p 513)?

The skull radiograph shows sutural diastases, beaten silver appearance, enlarged sella with sellar destruction, and suprasellar flocculonodular calcification.

The lesions producing suprasellar calcification are as shown in box 1.

Q2: What is the diagnosis?

The diagnosis is hypogonadotropic hypogonadism, secondary to a structural lesion of hypothalamus. The structural lesions of the hypothalamus can interfere with the normal pattern of gonadotrophin releasing hormone synthesis, secretion, or stimulation of gonadotropes. In view of features of raised intracranial tension, bilateral optic atrophy, hypogonadotropic hypogonadism, childhood onset, and

Box 1: Suprasellar calcification: differential diagnosis

- Craniopharyngioma
- Pituitary adenoma
- Hypothalamic germinomas
- Meningioma
- Dermoid tumours
- Epidermoid
- Aneurysm of internal carotid artery
- Tuberculoma
- Sarcoid granuloma
- Oligodendroglioma

presence of suprasellar calcification most likely structural lesion is craniopharyngioma. Other structural lesions of the hypothalamic-pituitary axis producing hypogonadotrophic hypogonadism are depicted in box 2.

Q3: What are the various clinical presentations of this condition?

The clinical presentations of craniopharyngioma are as shown in box 3.

Discussion

Craniopharyngiomas constitute 3%–5% of all intracranial neoplasms. Most of these are suprasellar, but about 15% are intrasellar. Rarely they may be found in the nasopharynx or the third ventricle. The peak incidence of craniopharyngiomas is between ages of 6 and 14 years. Although craniopharyngiomas are usually manifested in childhood, 45% of patients are over age 20, and 20% are over age 40 at the time of diagnosis.

Craniopharyngiomas arise from remnants of Rathke's pouch, which is the diverticulum of the roof of the embryonic oral cavity that normally gives rise to anterior pituitary. It is a congenital malformation present at birth and gradually grows over ensuing years. The tumour arises from rests of squamous cells at the junction of the adenohypophysis and neurohypophysis. It is usually well encapsulated and composed of cystic and solid components. It does not undergo malignant degeneration.

Box 2: Structural lesions of the hypothalamic-pituitary axis producing hypogonadotrophic hypogonadism¹*Tumours*

- Pituitary adenomas
- Craniopharyngiomas
- Germinomas, gliomas, meningiomas

Infiltrative disorders

- Sarcoidosis
- Haemochromatosis
- Histiocytosis X

*Head trauma**Radiation therapy***Box 3: Clinical presentations of craniopharyngioma²***Children*

- Hypopituitarism (growth hormone, thyroid stimulating hormone, corticotrophin, gonadotrophin deficiency)
- Increased intracranial pressure due to hydrocephalus (80%)
- Loss of vision and field defects (60%)
- Short stature (7%–40%) and retarded bone age
- Delayed sexual development (20%)
- Diabetes insipidus

Adults

- Visual complaints (80%)
- Papilloedema (15%)
- Headaches (40%)
- Mental deterioration or personality changes (26%)
- Hypogonadism (35%)
- Hyperprolactinaemia (33%–50%), usually <150 µg/l
- Intellectual deterioration and dementia (30%)
- Diabetes insipidus (15%)
- Weight gain (15%)
- Panhypopituitarism (7%)
- Aseptic meningitis, inflammatory hypophysitis

It forms a cyst as it enlarges, which contains degenerated cells and may calcify. The calcifications may be microscopic or gross. The cysts may be multiloculated. The degenerative changes are associated with the deposition of cholesterol crystals that confer an oily appearance to the cyst fluid. This dark brown, oily fluid ranges from a "machinery oil" or "crank-case oil" to a shimmering cholesterol laden liquid. The presence of immunoreactive human chorionic gonadotrophin has been reported in cyst fluid of this neoplasm.³ There are two histological patterns of craniopharyngioma, adamantinomatous and papillary. The first is composed of lace-like strands of stellate epithelial cells with a basal pallisade enclosing many cystic spaces. The masses of eosinophilic, necrotic, keratinised cells that accumulate within the epithelium often become heavily calcified and may dominate the histology of a small biopsy. The less common papillary craniopharyngiomas usually occur in adults and are formed by mature squamous epithelial cells encasing a fibrovascular core.⁴ This type does not calcify and only rarely invades the sella. The tumour cells are keratin immunoreactive, do not contain secretory granules on electron microscopy, and have characteristic bundles of tonofilaments and desmosomes. The tumour cells contain oestrogen receptor

Box 4: Radiological features of craniopharyngioma²*Plain skull radiograph*

- Enlargement or distortion of sella.
- Suprasellar calcification: flocculent, granular, nodular, or curvilinear (80%–90% children, 50% adults).

Computed tomogram

- Cystic component with ring or nodular calcification (most children and 80% adults).
- Computed tomogram can reveal calcification not visible on a plain radiograph.

Magnetic resonance imaging scan

- Findings variable: some cysts resemble cerebrospinal (CSF), others less intense than CSF on T1 images but brighter than CSF on T2 images, some mimic subacute haemorrhage.
- Varying signal intensities of mixed cystic and solid components (80%).
- Areas of homogenous T1 hyperintensities and enhancement of solid and cystic components.
- Calcification not usually visible on magnetic resonance imaging unless present in very large amounts.

mRNA.⁵ The plain skull radiograph, computed tomogram, and magnetic resonance imaging scan features of craniopharyngioma are shown in box 4.

Magnetic resonance imaging with contrast is the most sensitive diagnostic technique, allowing identification of cystic and solid components and delineation of the anatomic relationships necessary for a rational operative approach.⁶

The treatment is generally unsatisfactory. Complete surgical removal is often attempted but the recurrence rate is high. Tumours less than 3 cm in diameter have a better prognosis.² The combination of limited tumour removal, and radiation therapy of large craniopharyngiomas leads to at least as satisfactory neurological prognosis and better cognitive and endocrinological outcome than attempts at complete surgical extirpation.⁷ The postoperative sequelae (more frequently seen with radical removal) are as in box 5.

Follow up

The patient's magnetic resonance imaging scan showed a suprasellar tumour 6 cm² in size with solid and cystic components, consistent with craniopharyngioma. A partial removal of the tumour revealed a craniopharyngioma of adamantinomatous pattern on histopathological examination. There was rapid relief in symptom of headache. The visual acuity has improved to perception of hand movements at a distance of 1 m in both eyes after four weeks.

Box 5: Postoperative sequelae in craniopharyngioma⁸

- Hypopituitarism
- Obesity and postoperative hyperphagia
- Aberrant sleep pattern
- Diabetes insipidus
- Normal linear growth without growth hormone (the growth without growth hormone syndrome)

The patient is undergoing radiotherapy and is being followed up in endocrinology and neurosurgery clinics.

Final diagnosis

Craniopharyngioma presenting with hypogonadotrophic hypogonadism.

- 1 Hayes FJ, Seminara SB, Crowley WF. Hypogonadotropic hypogonadism. *Endocrinol Metab Clin North Am* 1998;27:739–63.
- 2 Miller BMK, Daniels GH. Neuroendocrine regulation and diseases of the anterior pituitary and hypothalamus. In: Fauci AS, Braunwald E, Isselbacher KJ, et al, eds. *Harrison's principles of internal medicine*. New York: McGraw-Hill. 1998; 1972–99.
- 3 Harris PE, Perry L, Chard T, et al. Immunoreactive human chorionic gonadotropin from the cyst fluid and CSF of patients with craniopharyngioma. *Clin Endocrinol (Oxf)* 1988;29:503–8.
- 4 Sartoretti-Schefer S, Wichmann W, Aguzzi A, et al. MR differentiation of adamantinous and squamous papillary craniopharyngioma. *Am J Neuroradiol* 1997;18:77–87.
- 5 Thapar K, Stefanescu L, Kovacs K, et al. Estrogen receptor gene expression in craniopharyngioma: an in situ hybridization study. *Neurosurgery* 1994;35:1012–17.
- 6 Chakeres DW, Curtin A, Ford G. Magnetic resonance imaging of pituitary and parasellar abnormalities. *Radiol Clin North Am* 1989;27:265–81.
- 7 Paja M, Lucas T, Garcia-Uria J, et al. Hypothalamic-pituitary dysfunction in patients with craniopharyngioma. *Clin Endocrinol (Oxf)* 1995;42:467–73.
- 8 Curtis J, Daneman D, Hoffman HJ, et al. The endocrine outcome after surgical removal of craniopharyngioma. *Pediatr Neurosurg* 1994;21(suppl 1):24–7.

Right shoulder pain in a body builder**Q1: Identify the pertinent findings on radiography**

The radiograph (see p 514) of the right shoulder joint shows bone resorption and subchondral cysts on either side of the acromioclavicular joint.

Q2: What is the clinical diagnosis? What could be the cause?

The clinical diagnosis is atraumatic osteolysis of the distal end of the clavicle. Though the exact aetiology is unknown, it is likely to be a repetitive stress loading induced osteolysis of the distal clavicle, and typically occurs in body builders, weight lifters, and rugby players.^{1 2}

Q3: What would be your line of management for this patient? Rationalise your answer

The condition is generally self limiting and responds to rest and analgesics with the majority showing osseous restoration of the clavicle in six to 12 months.³ Local steroid injections have not proved beneficial unlike in other shoulder pathologies.⁴ Cases not responding

conservative measures benefit from surgical excision of the distal end of the clavicle.⁵

Final diagnosis

Stress induced osteolysis of the right distal clavicle.

- 1 Matthew LS, Simonson BG, Wolock BS. Osteolysis of the distal clavicle in a female body builder. *Am J Sports Med* 1993;21:150–2.
- 2 Scavenius M, Inversen BF. Non-traumatic clavicular osteolysis in weight lifters. *Am J Sports Med* 1992;20:463–7.
- 3 Kaplan PA, Resnick D. Stress-induced osteolysis of the clavicle. *Radiology* 1986;158:139–40.
- 4 Cahill BR. Osteolysis of the distal part of the clavicle in male athletes. *J Bone Joint Surg Am* 1982;64:1053–8.
- 5 Petersson CJ. Resection of the lateral end of the clavicle. *Acta Orthop Scand* 1983;54:1904.

Unexpected elevation of parathyroid hormone in an asymptomatic patient with multiple endocrine neoplasia syndrome type 2A

Q1: What is the differential diagnosis?

Laboratory errors must be considered, especially because clinical and laboratory findings are not obviously compatible. Site localisation of a blood sample may determine the parathyroid hormone concentration in patients who have undergone autotransplantation of parathyroid tissue to the forearm. Otherwise, potential differential diagnosis of the normocalcaemic hyperparathyroidism such as pseudohypoparathyroidism and secondary

Table 1 Results of investigations

	Result	Normal	Interpretation
Parathyroid hormone (left arm) (ng/l)	14.7	12–72	Normal
Parathyroid hormone (right arm) (ng/l)	337	12–72	↑↑

hyperparathyroidism is unlikely in this patient because of known normal biochemical tests taken previously. Primary hyperparathyroidism of transplanted parathyroid tissue seems to be unlikely because of normocalcaemia and normophosphataemia.

Q2: What is your assessment?

The site from which the blood sample was taken should be verified first. The blood sample in the described patient was obtained from the right arm, where parathyroid tissue was implanted two years before. A blood sample obtained from the left arm, revealed the laboratory results shown in table 1 above.

Discussion

The increase in the parathyroid hormone concentration in the described patient was caused by taking a blood sample from the arm on which autotransplantation of parathyroid tissue was performed two years before. To prevent unnecessary diagnostic procedures, blood sampling of patients who have undergone transplantation of parathyroid tissue to the forearm should be performed as a matter of routine on the unoperated arm.

Otherwise, the function of transplanted parathyroid glands (that is, in transitory hypoparathyroidism directly after transplantation) can be determined, when the blood sample is taken proximal of the transplanted parathyroid tissue. Moreover, through compression of blood flow for a few minutes proximal of transplanted parathyroid gland, parathyroid hormone secreted of transplanted tissue is not measured when the blood sample is taken from the opposite arm (circulating half life of parathyroid hormone: 2–4 minutes). This can be helpful in the evaluation of persistent hyperparathyroidism postoperatively to prove biochemically an additional parathyroid hormone source (that is, an ectopic parathyroid gland).

Learning points

- Site localisation of the taken blood sample in patients who have undergone autotransplantation of parathyroid tissue to the forearm, may influence the parathyroid hormone concentration. This can be used to determine the biochemical function of transplanted tissue or to prove additional parathyroid tissue (that is, ectopic parathyroid tissue) postoperatively.
- Blood samples from patients who have undergone autotransplantation of parathyroid tissue to their forearm should be routinely taken from their unoperated arm.