

## SELF ASSESSMENT ANSWERS

### Congenital renal anomaly in a patient with situs inversus

#### Q1: Name the congenital renal anomaly identified in fig 1 (see p 355)

Horseshoe kidney. The lower poles of the kidney being displaced towards the midline, joined by either functioning renal tissue or a fibrous band.

#### Q2: What is the incidence and sex ratio of this anomaly?

Incidence is one in 400. It is more commonly found in males at a ratio of 2:1.

#### Q3: What complications occur with this condition?

Thirty percent of cases are asymptomatic and are identified incidentally. Stasis of urine due to the malrotation of the kidneys, and impaired ureteric drainage result in infection and stone formation.

#### Q4: Name three other genitourinary anomalies that can be associated with this condition

These are: (1) hypospadias; (2) undescended testis; (3) ureteral duplication. Vaginal septation and bicornuate uterus can also be associated with this condition.

#### Discussion

Horseshoe kidney was first recognised during a necropsy by DeCarpi in 1521, but Botallo in 1564 provided the first description and illustration of a horseshoe kidney.<sup>1</sup> Horseshoe kidneys are believed to result from the median fusion of metanephric tissue due to mechanical forces. However studies have suggested that abnormal fusion of tissue associated with the parenchymatous isthmus of horseshoe kidney is the result of a teratogenic event involving the abnormal migration of posterior nephrogenic cells.

In most cases the kidneys are linked at the lower poles by a parenchymatous or fibrous isthmus that crosses the midline of the body. In general isthmus lies anterior to aorta and vena cava. Because kidneys fail to rotate, the calyces point posteriorly. The ureter inserts higher on the renal pelvis and lies laterally and crosses over and anterior to isthmus. The blood supply can be quite variable.<sup>1</sup>

The horseshoe kidney is frequently found in other congenital anomalies, some of which are incompatible with long term survival. Most common congenital anomalies involved include skeletal, cardiovascular, and central nervous systems. There is increased occurrence of other genitourinary anomalies. Females with Turner's syndrome have a high incidence of horseshoe kidney. Horseshoe kidney with situs inversus is a rare and interesting association.<sup>2</sup>

One third of all patients remain asymptomatic. Others present with vague abdominal pain resulting from hydronephrosis, infection, or calculus formation. Horseshoe kidney is associated with an increased relative risk of Wilms' tumour, transitional cell carcinoma, and renal carcinoid.<sup>3</sup>

Ultrasound or an excretory urogram readily makes the diagnosis. Ultrasound diagnosis depends on the demonstration of an isthmus or band of renal tissue across the midline. In a

number of cases the band of renal tissue may evade ultrasonic detection.<sup>4</sup> Computed tomography may be necessary to confirm the diagnosis.

Intervention is required because of obstruction or calculi. The combination of horseshoe kidney with an aortic aneurysm presents a diagnostic and therapeutic challenge to the vascular surgeon.<sup>5</sup>

#### Final diagnosis

Horseshoe kidney with situs inversus.

#### References

- 1 **Bauer SB**, Perlmutter AD, Retik AB. Anomalies of the upper urinary tract. *Campbell's urology*. 6th Ed. Philadelphia: WB Saunders, 1992: 1376–81.
- 2 **Matsushita K**, Veda S, Kegami K. Horseshoe kidney in a patient with situs inversus totalis. *J Urol* 1982;**128**:604–5.
- 3 **Krishnan B**, Troung LD, Saleh G, et al. Horseshoe kidney is associated with an increases relative risk of primary renal carcinoid tumor. *J Urol* 1997;**157**:2059–66.
- 4 **Banerjee B**, Brett I. Ultrasound diagnosis of horseshoe kidney. *Br J Radiol* 1991;**64**:898–900.
- 5 **Stroosma OB**, Kooftstra G, Schurink GWH. Management of aortic aneurysm in the presence of a horseshoe kidney. *Br J Surg* 2001;**88**:500–9.

### A man with numbness and limb weakness

#### Q1: What is the diagnosis?

The diagnosis is spinal (cervical) intramedullary cysticercosis. The MRI scan (fig 1; see p 355) shows a cyst located in the intramedullary region. Cervical laminectomy with removal of the cyst was done. Histopathology examination (fig 2; see p 355) proved the lesion to be a cysticercus cyst with scolex (larval cyst).

#### Q2: What are the treatment options?

The treatment of spinal intramedullary cysticercosis could be surgical, medical (that is, cysticidal therapy) or both, based on location and stage of the cyst as also on the experience of the physician. Surgical treatment includes laminectomy with removal of the cyst. Cysticidal drugs given are albendazole in a dose of 15 mg/kg body weight for 14–30 days or praziquantel 50 mg/kg body weight for 15 days along with steroids to reduce the perilesional oedema and to prevent neurological deterioration during the course of cysticidal drugs. Administration of cysticidal drugs before or after surgery is a point of personal preference for the individual doctor as no systematic evaluation has been possible due to the rarity of the disease.

#### Discussion

Intramedullary cysticercosis is a rare manifestation of neurocysticercosis,<sup>1</sup> and fewer than 50 cases have been reported. The cysts are commonly located in spinal subarachnoid space and rarely at intramedullary locations. The majority of reported cases have cysts in the dorsal cord, which is in accordance with the regional blood flow to the spinal cord. In 90% of reported cases of intramedullary cysticercosis due to neurocysticercosis the patients were between 20 and 45 years of age. The duration of symptoms varied from a week

to 10 years. The mode of spread of intramedullary cysticercosis is either haematogenous or ventriculoependymal.<sup>2</sup> MRI studies help in diagnosing and correctly correlating the pathological diagnosis of neurocysticercosis (including intramedullary cysticercosis).<sup>3</sup>

Treatment modalities like drug therapy (cysticidal drug)/surgery, or both, can be planned according to the pathological stage and location of the cyst as seen on MRI. Since the cysticidal drugs albendazole and praziquantel were shown to be effective in parenchymal brain cysticercosis, these drugs have been considered potentially useful in patients with intramedullary cysticercosis. Successful management of intramedullary cysticercosis by cysticidal drugs alone has also been reported in the literature.<sup>4</sup>

In the present case when the diagnosis of intramedullary cysticercosis was established on MRI, surgery was undertaken due to its location in cervical segment, and this was followed by albendazole therapy (15 mg/kg × 28 days). The patient showed complete neurological improvement with resolution of the intramedullary lesion.

It is concluded that with present generation MRI and also successful surgical/drug management, the outcome of intramedullary cysticercosis is not as dismal as was reported earlier, and patients with paraplegia also have a favourable outcome.

#### Final diagnosis

Spinal (cervical) intramedullary cysticercosis.

#### References

- 1 **Corral I**, Quereda C, Moreno A, et al. Intramedullary cysticercosis cured with drug treatment. A case report. *Spine* 1996;**21**:2284–7.
- 2 **Mathuriya SN**, Khosla VK, Vasishtha RK, et al. Intramedullary cysticercosis: MRI diagnosis. *Neurology India* 2001;**49**:72–4.
- 3 **Mohanty A**, Venkatrama SK, Das S, et al. Spinal intramedullary cysticercosis. *Neurosurgery* 1997;**40**:82–7.
- 4 **Sotelo J**, Guerrero V, Rubio F. Neurocysticercosis. A new classification based on active and inactive forms—a study of 753 cases. *Arch Intern Med* 1985;**145**:442–5.

### An interesting case of hemiparesis

#### Q1: What is the differential diagnosis in this patient?

The differential diagnosis of HIV patients presenting with focal neurological deficits should include disorders such as toxoplasmosis, primary central nervous system lymphoma, cerebral Chagas' disease, progressive multifocal leucoencephalopathy (PML), central nervous system tuberculosis, and cryptococcosis.<sup>1</sup>

#### Q2: What are the computed tomography and MRI findings?

Computed tomography of the head (fig 1; see p 356) shows well defined hypodense areas in the white matter in bilateral posterior parietal regions and in the right temporoparieto-frontal region without areas of enhancement or mass effect. Figure 2A (see p 356) shows the gadolinium enhanced T1 sagittal MRI of the brain showing non-enhancing white matter changes. Figure 2B (see p 356) shows the T2 weighted coronal MRI showing white matter changes without mass effect. The findings of non-enhancing white matter lesions with typical increased T2 and decreased T1 signals on MRI head are highly suggestive of PML.<sup>2</sup>

**Q3: How is the diagnosis confirmed?**

Though the definitive diagnosis of PML depends on identification of characteristic neuropathological abnormalities on brain biopsy, it is not necessary to confirm the diagnosis.<sup>3</sup> Neuroimaging is most helpful in diagnosis with typical computed tomography and MRI findings as described above, MRI being more sensitive than computed tomography. Recently polymerase chain reaction amplification of JC virus DNA from the cerebrospinal fluid has become the favoured diagnostic modality to confirm the diagnosis.<sup>4</sup>

**Discussion**

The neurological infections commonly presenting in HIV<sup>1</sup> are toxoplasmosis, cryptococcal meningitis, PML, while the less common ones are central nervous system tuberculosis, syphilis, cytomegalovirus, HTLV, acanthamoeba, or naegleria. Among the neoplasms, primary central nervous system lymphoma is the more common entity in HIV positive individuals.

Toxoplasmosis is one of the most common secondary central nervous system infections in AIDS presenting late at CD4+ counts <200/μl. The most common clinical presentation is fever, headache, with focal neurological deficits. The diagnosis is suspected on finding multiple ring enhancing lesions on MRI head and positive serology for *Toxoplasma gondii*. Definite diagnosis is by brain biopsy. Trypanosomiasis or Chagas' disease may present in HIV patients as acute meningoencephalitis with fever, vomiting, seizures, and focal neurological signs. Lesions appear on MRI as single or multiple hypodense ring enhancing lesions mainly in the subcortical areas. Cryptococcal meningitis is one of the leading neurological complications in HIV patients and generally occurs in patients with CD4+ T cell counts <100/μl. The diagnosis is confirmed by identifying organisms in the cerebrospinal fluid on India ink examination or by detection of cryptococcal antigen. Central nervous system tuberculosis in the form of tubercular meningitis or tuberculomas is common in HIV patients and may present with focal deficits. Computed tomography findings show prominent leptomeningeal and basal cistern enhancement or rim enhancing granulomas. Cerebrospinal fluid analysis often helps in establishing the diagnosis.

PML, caused by JC virus, a human papilloma virus, is an important neurological manifestation in patients with AIDS. It is a subacute demyelinating disease of the central nervous system and is caused by reactivation of the latent JC virus in presence of underlying immunosuppression. Since the onset of AIDS epidemic, HIV infection has become, by far, the most common risk factor for the disease and currently more than 60% cases of PML occur in patients with AIDS. It commonly occurs in the setting of advanced immunosuppression and only infrequently heralds AIDS.<sup>5-7</sup> However in this patient, PML was the initial and the only manifestation of AIDS.

Patients most often present with visual deficits, motor weakness, or other focal neurological deficits with or without changes in sensorium. Neuroimaging is most helpful in diagnosis with MRI typically revealing multiple non-enhancing white matter lesions, predominantly in the occipitoparietal areas. Yan Geisen *et al* have laid down diagnostic criteria on the basis of epidemiological, neuroradiological, and cerebrospinal fluid parameters

to make the clinical diagnosis of PML.<sup>3</sup> Recently polymerase chain reaction amplification of JC virus DNA from the cerebrospinal fluid has become the favoured diagnostic modality to confirm the diagnosis.<sup>4</sup>

Currently, outlook for patients with PML is poor and there is no effective treatment. Few authors have reported promising results with HAART treatment.<sup>8,9</sup> Recently treatment with cidofovir has been tried in such patients with varying results.<sup>10</sup> Mean survival time after diagnosis is about six months.

**Final diagnosis**

Progressive multifocal leucoencephalopathy in AIDS.

**References**

- 1 Mamidi A, DeSimone JA, Pomerantz RJ. Central nervous system infections in individuals with HIV-1 infection. *J Neuroviral* 2002;**8**:158-67.
- 2 Wilson BG. CT assessment of CNS complications of AIDS. *Radiol Technol* 2002;**73**:424-37.
- 3 Yan Geisen HT, Neuen Jacob E, Dorriea K. Diagnostic criteria and clinical procedures in HIV-1 associated progressive multifocal leucoencephalopathy. *J Neurol Sci* 1997;**147**:63-72.
- 4 Antinori A, Ammassari A, De Luca A, *et al*. Diagnosis of AIDS-related focal brain lesions: a decision-making analysis based on clinical and neuroradiologic characteristics combined with polymerase chain reaction assays in CSF. *Neurology* 1997;**48**:687-94.
- 5 Clavo Sanchez A, Garcia-Gil D, Sasian Martinez S, *et al*. Progressive multifocal leucoencephalopathy in acquired immunodeficiency. *Rev Clin Esp* 1994;**194**:13-6.
- 6 Sanchez Herrero J, Lopez Facal S, Arnal Monreal F, *et al*. Progressive multifocal leucoencephalopathy as the initial manifestation of acquired immunodeficiency syndrome. *Med Clin (Barc)* 1988;**90**:416-8.
- 7 Berger JR, Kaszovitz B, Post MJ, *et al*. Progressive multifocal leucoencephalopathy associated with human immunodeficiency virus infection. A review of the literature with a report of sixteen cases. *Ann Intern Med* 1987;**107**:78-87.
- 8 Simpson D. HIV rounds at Cornell: selected neurologic complications of HIV disease. *AIDS Patient Care STDS* 1998;**12**:209-15.
- 9 Clifford DB, Yiannoutsos C, Glicksman M, *et al*. HAART improves prognosis in HIV-associated progressive multifocal leucoencephalopathy. *Neurology* 1999;**52**:623-5.
- 10 Wilcox RD. Cidofovir: progress in the treatment of progressive multifocal encephalopathy (PML)? *HIV Clin* 2002;**14**:1-2.

**A misdiagnosed potentially dangerous shoulder injury****Q1: What is the diagnosis?**

The patient has sustained a posterior fracture dislocation of the left sternoclavicular joint with compression of the upper mediastinal structures, including the oesophagus. The fracture dislocation can be visualised on the computed tomogram (fig 1; see p 357) where the difference between the left and right sternoclavicular joints can be clearly seen. It is also possible the patient suffered from a transient brachial plexus palsy after injury.

**Q2: What do the angiograms demonstrate?**

Arteriography when performed with the limb in the resting position (fig 2; see p 357) demonstrates a patent subclavian artery but with

the limb in the abducted positions (fig 3; see p XXX) virtual occlusion of the subclavian artery can be seen. Venography demonstrated similar positional compression of the subclavian vein. The vascular compression accounts for the limb colour changes and lack of pulses during abduction and for the symptoms when working overhead.

**Q3: How should injury have been managed upon initial presentation?**

This patient presented after a fall onto his shoulder with pain and swelling in his neck and left medial end of clavicle, symptoms and signs of neurovascular compromise of his left upper limb, and asymmetry between the medial end of his clavicles. This history strongly suggests posterior sternoclavicular joint dislocation with mediastinal structure compromise, but this diagnosis was not made post-injury as the plain radiographs appeared normal. This injury is often not demonstrated by plain radiographs and therefore computed tomography should have been performed at initial presentation, and would have demonstrated the injury. The fracture dislocation should then have been reduced, thereby resolving symptoms both from the dislocation and from compression of nearby structures. It is important not to miss posterior sternoclavicular joint dislocations as injury to the upper mediastinal structures can cause serious complications including death.

**Q4: What are the management options nine years after injury?**

The options available to the patient are to live with his disability or to undergo surgery to prevent the medial clavicle compressing mediastinal structures.

The patient chose to proceed to surgery due to the severity of his symptoms. At operation a fracture dislocation of the clavicle 1 cm from the medial end was noted and as reconstruction of the fracture-dislocation was not possible the medial 2 cm of the clavicle was resected subperiosteally leaving the costoclavicular ligament intact. At review six weeks postoperatively symptoms had resolved, the medial clavicle was stable and he had returned to work. At six and 12 months postoperatively the patient felt that both his upper limbs were normal and on examination his shoulders and upper limbs were functionally normal with full power, normal range of joint movements and normal pulses in all limb positions.

**Discussion**

Posterior sternoclavicular dislocation is a rare injury.<sup>1</sup> It is nearly always a result of trauma and is rare after the age of 25 years.<sup>2</sup> It can result in significant morbidity or death due to the proximity of the superior mediastinal contents, which may be compressed or injured by the medial end of the clavicle.<sup>3</sup>

Early diagnosis can often be difficult due to extensive local swelling and bruising,<sup>4</sup> difficulties in assessment using plain radiographs,<sup>5</sup> and as this injury is rare it is often overlooked. Computed tomography is the best method of demonstrating the anatomy of the sternoclavicular joint and its surroundings structures.<sup>5</sup> In most cases the dislocation can be reduced by closed methods within 48 hours of injury and after 48 hours open reduction is more likely to be required.<sup>2</sup> It is therefore important to maintain a high level of suspicion of this injury as early diagnosis improves the success of closed treatment and reduces complications. Our patient's injury was missed due to poor

awareness and inadequate imaging after the injury. At presentation nine years later, the diagnosis was confirmed using computed tomography and angiography.

Our patient suffered from dysphagia due to compression of the oesophagus, which is the most common mediastinal symptom from posterior sternoclavicular joint dislocation.<sup>4</sup> The positional vascular symptoms experienced by our patient are rare.<sup>6</sup>

Due to the length of time that had elapsed since the fracture, scarring between the medial end of clavicle and the great vessels was anticipated and therefore the operation was performed jointly by orthopaedic and vascular surgeons. Fortunately, the medial end of clavicle was mobilised easily, without damage to the great vessels.

There is conflicting advice from previous authors regarding the surgical approach for chronic posterior sternoclavicular dislocation. Rockwood *et al* recommend resection of the medial clavicle and retention of the costoclavicular ligament for support.<sup>7</sup> Other authors suggest that reconstruction of the joint provides better results.<sup>8,9</sup> In this patient reconstruction would not have produced normal joint function due to the degree of joint damage and thus resection was performed.

Medical practitioners should maintain a high index of suspicion of posterior sternoclavicular joint dislocation in patients complaining of pain near the joint after direct or indirect trauma to the neck or shoulder as this injury is easily missed. Also radiographs should not be relied upon to exclude sternoclavicular dislocation and further imaging, usually a computed tomogram, is indicated.

#### Final diagnosis

Posterior fracture dislocation of the left sternoclavicular joint with compression of the upper mediastinal structures.

#### References

- 1 Nettles JL, Linscheid RL. Sternoclavicular dislocations. *J Trauma* 1968;**8**:158.
- 2 Buckerfield CT, Castle ME. Acute traumatic retrosternal dislocation of the clavicle. *J Bone Joint Surg Am* 1984;**66**:379–85.
- 3 Stankler L. Posterior dislocation of the clavicle: a report of two cases. *Br J Surg* 1962;**50**:164–8.
- 4 Gangahar DM, Flogaites T. Retrosternal Dislocation of the clavicle producing thoracic outlet syndrome. *J Trauma* 1978;**18**:369–72.
- 5 Cope R. Dislocations of the sternoclavicular joint. *Skeletal Radiol* 1992;**22**:233–8.
- 6 Noda M, Shiraiishi H, Mizuno K. Chronic posterior sternoclavicular dislocation causing compression of a subclavian artery. *J Shoulder Elbow Surg* 1997;**6**:564–9.
- 7 Rockwood CA, Groh GI, Wirth MA, *et al*. Resection arthroplasty of the sternoclavicular joint. *J Bone Joint Surg Am* 1997;**79**:387–93.
- 8 Booth CM, Roper BA. Chronic dislocation of the sternoclavicular joint. *Clin Orthop* 1979;**140**:17–20.
- 9 Eskola A, Vainionpaa S, Vastamaki M, *et al*. Operation for old sternoclavicular dislocation. *J Bone Joint Surg Br* 1989;**71**:63–5.

## A child with growth failure

### Q1: What are the radiological and biochemical features and the diagnosis of this case?

The computed tomogram shows extensive cerebral calcification (fig 1; see p 358), and the radiograph shows the dense osteosclerosis (fig 2; see p 358) that is characteristic of osteopetrosis. Biochemical investigations show hypokalaemia, hyperchloraemia, low bicarbonate levels, and a low arterial pH in

association with a high urinary pH, indicating distal renal tubular acidosis. The diagnosis is carbonic anhydrase II (CA II) deficiency syndrome, which is characterised by the triad of osteopetrosis, intracranial calcification, and renal tubular acidosis.<sup>1</sup> Intracranial calcification and renal tubular acidosis distinguish CA II deficiency from classical varieties of osteopetrosis. Also, severe anaemia, a common finding in classical osteopetrosis, is absent or very mild in CA II deficiency.<sup>1</sup>

CA II deficiency is a rare autosomal recessive disorder attributed to mutations of the CA II isoenzyme gene (chromosome 8).<sup>1,2</sup> CA II is the most catalytically active as well as the most widely distributed isoenzyme of the CA series. CA II is important for acid-base regulation as well as bone resorption.<sup>3</sup> The latter function is mediated by its effects on osteoclast function: it enables H<sup>+</sup> pump activity, which helps the osteoclast in secreting acid that helps to dissolve bone mineral as well as digest bone matrix. Therefore, in CA II deficiency, bone resorption is markedly affected, leading to osteopetrosis. The raised serum acid phosphatase levels are attributed to defective osteoclast activity. A similar deficiency in acid excretion by the kidney may explain renal tubular acidosis. The reason for cerebral calcification is presently unclear. Children usually present with mental subnormality, short stature, and involvement of lower cranial nerves (due to sclerosis of skull base). As this is an inherited condition, family members also need to be investigated if molecular studies are readily available.

### Q2: What are the radiological features of this disorder?

Skeletal radiography in CA II deficiency reveals findings indistinguishable from classical osteopetrosis—that is, a generalised increase in bone density; hence the term “marble bone disease”. Skull radiographs typically show a thick dense cranium with basal osteosclerosis and under-pneumatisation of the paranasal and mastoid sinuses. Another well described radiological feature of osteopetrosis is the appearance of alternating dense and lucent bands in the long bones and skull, which occurs due to a fluctuating skeletal growth.<sup>1</sup> However, in CA II deficiency, osteosclerosis can spontaneously diminish. Cerebral calcification involving the cortex and the basal ganglia on computed tomography may appear at about 2–5 years of age.<sup>1</sup>

#### Learning points

- CA II deficiency is an atypical variant of classical osteopetrosis and is characterised by renal tubular acidosis and cerebral calcification.
- Radiological features of osteopetrosis include uniformly dense, sclerotic bones; alternating dark and lucent bands have also been described.
- Children with CA II deficiency syndrome present with growth failure, asymptomatic cerebral calcification, and osteopetrosis.
- The disorder is compatible with long life.
- Bone marrow transplantation may improve osteopetrosis, but does not reverse acidosis; hence alkali supplementation is required.

### Q3: What are the treatment options and prognosis of this disorder?

Bicarbonate supplementation is the mainstay of treatment, but the long term outcome of therapy is not known. Bone marrow transplantation may improve the skeletal disorder,<sup>4</sup> but not the renal defect.<sup>1</sup> A low calcium, high phosphate diet may be useful in this disorder. CA II deficiency is reportedly compatible with long life.

#### Final diagnosis

Carbonic anhydrase II deficiency syndrome.

#### References

- 1 White MP. Skeletal disorders characterized by osteosclerosis and hyperostosis. In: Avioli LV, Krane SM, eds. *Metabolic bone disease and clinically related disorders*. 3rd Ed. San Diego: Academic Press, 1998: 697–738.
- 2 Felix R, Hofstetter W, Cecchini MG. Recent developments in the understanding of the pathophysiology of osteopetrosis. *Eur J Endocrinol* 1996;**134**:143–56.
- 3 Blair HC, Schlesinger PH, Ross FP, *et al*. Recent advances toward understanding osteoclast physiology. *Clin Orthop* 1993;**294**:7–22.
- 4 McMahon C, Will A, Hu P, Shah GN, *et al*. Bone marrow transplantation corrects osteopetrosis in the carbonic anhydrase II deficiency syndrome. *Blood* 2001;**97**:1947–50.

## Multiorgan involvement in thalassaemia major

### Q1: What are the findings on the MRI images?

MRI scans of the sella (fig 1 in questions; see p 358) show markedly decreased signal intensity in the anterior lobe of the pituitary gland in all the sequences, though best seen on gradient echo images. Hypointense signal is also seen in bilateral basal ganglia.

### Q2: What is the diagnosis?

The diagnosis is secondary (erythropoietic) haemochromatosis with hypogonadotropic hypogonadism developing in a patient with  $\beta$ -thalassaemia major.

The child had been diagnosed as having thalassaemia major at the age of 5 months and had received numerous blood transfusions since. She had also been treated with desferrioxamine B. Her serum ferritin level was 8672  $\mu$ g/L, luteinising hormone was zero, and follicle stimulating hormone level was 0.20 U/L.

MRI of the abdomen and chest (fig 1, next page), done at the same sitting, demonstrates low signal intensity, equal to that of background, in liver, spleen, pancreas and myocardium, indicating iron deposition in these organs also.

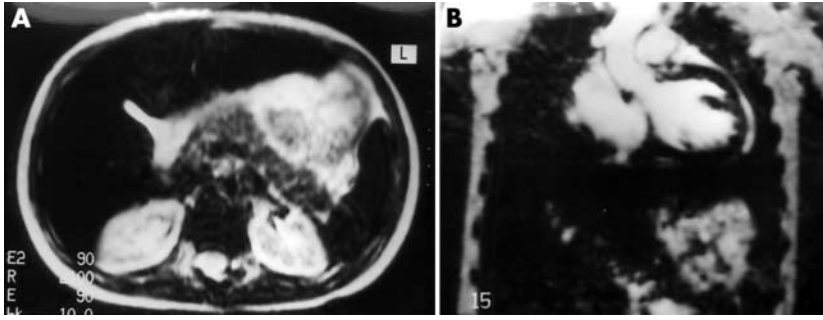
#### Discussion

Haemochromatosis refers to a group of disorders in which there is a progressive increase in total body iron stores with deposition of iron in the liver, heart, pancreas, and other organs.<sup>1</sup>

Two generalised categories of iron deposition in iron overload have been described:

(1) Parenchymal cell iron deposition (see box 1)—this is seen in idiopathic (primary haemochromatosis), secondary to anaemia and ineffective erythropoiesis, intravascular haemolysis, cirrhosis, after portocaval anastomoses, and secondary to high intake.

(2) Reticuloendothelial cell iron deposition (see box 2)—this is seen most commonly in



**Figure 1** (A) Coronal gradient echo image at the level of the heart shows hypointense signal in the myocardium indicating iron deposition and (B) axial gradient echo MRI scan through the upper abdomen showing hypointense signal in the liver, spleen, and the pancreas.

#### Box 1: Parenchymal cell iron deposition

- Idiopathic (primary haemochromatosis), secondary to ineffective erythropoiesis, intravascular haemolysis, etc.
- Organs involved: liver (hepatocytes), pancreas (acinar cells), heart, endocrine glands (anterior pituitary etc).
- May lead to cellular damage and organ dysfunction.

patients who have received multiple transfusions and also in patients with rhabdomyolysis.

Parenchymal cell iron deposition occurs primarily in liver (hepatocytes), pancreas (acinar cells), heart, and other endocrine glands (anterior lobe of pituitary gland). The spleen is usually spared. However, there have been few reports of low signal intensity in the spleen without any history of blood transfusion, the cause of which is unknown.<sup>2</sup> Parenchymal cell iron deposition leads to cellular damage and organ dysfunction unless treated.

In transfusional iron overload, haemosiderin is deposited in the reticuloendothelial system, such as the Kupffer cells of the liver and the reticuloendothelial cells of the spleen and bone marrow. This iron is derived from the extravascular haemolysis of intact red blood cells by the reticuloendothelial cells, which occurs during the metabolism of senescent native and transfused erythrocytes. The pancreas is spared because it is not a reticuloendothelial organ. However, pancreatic iron deposition in transfusional iron overload may result from massive transfusion

#### Box 2: Reticuloendothelial cell iron deposition

- Secondary to multiple transfusions, in patients with rhabdomyolysis.
- Organs involved: liver (Kupffer cells), spleen (reticuloendothelial cells), bone marrow, lymph nodes.
- No significant organ dysfunction.

beyond the iron storage capacity of the reticuloendothelial cell system (10 g), which is the amount of iron in 40 units of blood.<sup>3</sup> Reticuloendothelial iron deposition does not produce any significant organ dysfunction.

Thalassaemia major, characterised by ineffective erythropoiesis and hypercellular bone marrow, results in secondary erythropoietic haemochromatosis. These patients also absorb iron inappropriately and can develop severe parenchymal cell overload. Also, iron accumulation of the reticuloendothelial system may develop due to repeated transfusions for the anaemia, accounting for the decreased splenic signal intensity. Thus, this group of patients share MRI features of both reticuloendothelial and parenchymal cell iron overload, as seen in our case.

Excess iron deposition in the anterior pituitary leads to degranulation of theadenohypophysis and decreased hormone storage with ensuing hypogonadism due to pituitary hyporesponsiveness to gonadotrophin releasing hormone.<sup>4</sup> Iron deposition in the posterior lobe and diabetes insipidus usually do not occur.

Cardiac iron deposition occurs in the ventricular myocardium before atrial myocar-

dium. Furthermore, cardiac iron deposition is exclusively sarcoplasmic and not interstitial; therefore, wall thickness in haemochromatosis is usually normal.<sup>5</sup>

At MRI, the marked signal intensity reduction is due to decreased T2 relaxation time and magnetic field inhomogeneities created by the excess intracellular iron.

Ferritin and haemosiderin, being paramagnetic substances, cause a proton relaxation effect on neighbouring hydrogen nuclei; T1 and T2 relaxation time decreases. Since both T1 and T2 are shortened, intensity may either increase or decrease depending on which relaxation effect, T1 or T2, dominates. For relatively low concentration of iron, as seen in organs like muscle and kidney which do not accumulate iron in high concentration, T1 is considerably shortened and T2 values only slightly shortened leading to increased signal intensity of these tissues. With increasing concentrations of iron, as in liver etc, T2 shortening becomes dominant leading to decreased signal intensity in these organs.<sup>6</sup>

GRE T2\*-weighted sequence is regarded as the most sensitive technique for the detection of parenchymal iron deposition. This is likely due to the lack of a 180° refocusing pulse that partially recovers signal loss from the field in homogeneity in spin echo imaging.<sup>4</sup>

#### Final diagnosis

Secondary (erythropoietic) haemochromatosis with hypogonadotropic hypogonadism in a patient with  $\beta$ -thalassaemia major.

#### References

- 1 Powell LW, Bassett ML, Halliday JW. Hemochromatosis: 1980 update. *Gastroenterology* 1980;**78**:374–81.
- 2 Seigelman ES, Mitchell DG, Rubin R, et al. Parenchymal versus reticuloendothelial iron overload in the liver: distinction with MR imaging. *Radiology* 1991;**179**:361–6.
- 3 Yoon DY, Choi BI, Han JK, et al. MR findings of secondary hemochromatosis: transfusional vs erythropoietic. *J Comput Assist Tomogr* 1994;**18**:416–19.
- 4 Sparacia G, Iaia A, Banco A, et al. Transfusional hemochromatosis: quantitative relation of MR imaging pituitary signal intensity reduction to hypogonadotropic hypogonadism. *Radiology* 2000;**215**:818–23.
- 5 Blankenberg F, Eisenberg S, Scheinman MN, et al. Use of cine gradient echo (GRE) MR in the imaging of cardiac hemochromatosis. *J Comput Assist Tomogr* 1994;**18**:136–8.
- 6 Brasch RC, Wesbey GE, Gooding CA, et al. Magnetic resonance imaging of transfusional hemosiderosis complicating thalassaemia major. *Radiology* 1984;**150**:767–71.