SELF ASSESSMENT ANSWERS

Skeletal dysplasia with unusual visceral manifestations

Q1: What is the diagnosis?

The diagnosis is pycnodysostosis, which is a rare form of skeletal dysplasia characterised by moderate and generalised osteosclerosis. The diagnosis is based on clinical features and radiological findings. The cardinal features are short stature, large open fontanelles (the fontanelles may remain open even in adulthood), an obtuse mandibular angle, dysplastic clavicles, and hypoplastic/aplastic distal phalanges. Radiography of the bones show generalised and uniform hyperdensity and marked obliteration of the medullary cavity.

Q2: What is the most important differential diagnosis?

The most important differential diagnosis is osteopetrosis tarda, which is also called Albers-Schonberg disease. This disorder is characterised by severe generalised osteosclerosis, anaemia due to bone marrow failure, and hepatosplenomegaly due to extramedullary erythropoiesis. Neurological deficits like deafness, blindness, and cranial nerve palsies are common due to bony sclerosis. Radiography of the bones shows no medullary cavity. But short stature, open fontanelles, clavicular dysplasia, and distal phalangeal hypoplasia/aplasia are not seen in osteopetrosis tarda.

Q3: What complications can be anticipated in this case?

In most cases of pycnodysostosis there is adequate bone marrow function with no anaemia or hepatosplenomegaly. The life span is normal. But this case has atypical features that are usually seen in osteopetrosis tarda. These atypical features—namely, anaemia, splenohepatomegaly, and papilloedema—will require close clinical monitoring. The anticipated complications are bone marrow failure, hypersplenism, and optic atrophy. Also other neurological deficits due to ongoing bony sclerosis like deafness and cranial nerve palsies are to be watched for. Lastly, the child may develop transverse bone fractures and obstructive sleep apnoea, which are known complications in a typical case of pycnodysostosis.

Discussion

Pycnodysostosis was first described by Maroteaux and Lamy in 1962. The word pycnodysostosis is of Greek origin ("pycnos" means dense or thick, "dys" means defective and "ostosis" means bone).[1] The inheritance of pycnodysostosis is believed to be autosomal recessive. The diagnosis rests on clinical and radiological features.[2–4] The exact incidence of pycnodysostosis is not known. Until 1988, 78 cases had been reported.[5] The reported male to female occurrence is 1:1.

The characteristic features of this rare syndrome include short stature, a large head with open fontanelles (often remaining open in adulthood), separated sutures, an obtuse or absent mandibular angle, under developed facial bones, dysplastic clavicles, and hypoplasia or aplasia of distal phalanges.[2 3] The osteolysis of distal phalanges may progressively become more severe. The teeth are malformed, hypoplastic, malpositioned, and prone to caries. Deciduous teeth may persist into adulthood giving rise to a double row of teeth. Trunk deformities like kyphosis, scoliosis, and a narrow chest may be seen. There is a tendency for multiple transverse fractures with minimal trauma in the long bones of lower limbs, metatarsals, clavicles, and mandible. These fractures can occur at any age, are usually self limited, but may lead to deformities. Other features include bilateral proptosis, a long uvula, obstructive sleep apnoea, and a blue sclera. Most cases have a normal intelligence.[2 3] The most consistent radiological feature is moderate generalised osteosclerosis. The osteosclerosis in long bones is most prominent proximally.[2]

A close differential diagnosis of pycnodysostosis is osteopetrosis tarda (Albers-Schonberg disease) or the benign dominant variety of osteopetrosis, but there are distinct differentiating features. Osteopetrosis tarda occurs in 1:100 000 live births; the reported male: female ratio is 1:1.[6] In osteopetrosis tarda, the inheritance is autosomal dominant in most cases and autosomal recessive in a few; also stunted growth and open fontanelles, clavicular dysplasia, and distal phalangeal hypoplasia are not seen.[4] Osteopetrosis tarda is characterised by progressive obliteration of the bone marrow due to formation of new bone, as there is failure of osteoclasts to resorb bone matrix. Progressive anaemia due to bone marrow failure and splenohepatomegaly due to extramedullary erythropoeisis are common findings. Hypersplenism may ensue, leading to pancytopenia.[7] Leucoerythroblastosis is found with crowding of cells out of the marrow prematurely (myelophthisis). Deafness, blindness, and neurological deficits due to bony sclerosis are common.[7] There is hypotubulation of the ends of shafts of bones with alternating lines of increased and decreased bone density; a finding never found in pycnodysostosis.

It was earlier believed that pycnodysostosis is not associated with anaemia and splenohepatomegaly.[2] However a few cases of pycnodysostosis with visceral and haematological manifestations have been described.[4 5 8–10]

The child reported here had classical clinical and radiological findings of pycnodysostosis along with atypical features like splenohepatomegaly, anaemia, and thrombocytopenia. These atypical features are common in osteopetrosis tarda. The boy also had bilateral papilloedema, which has not been reported earlier in association with pycnodysostosis. Thus our case is a link between pycnodysostosis and osteopetrosis tarda indicating that these two disorders are related to each other in a manner more complex than the morphological similarity of increased bone density. Our case is an example of phenotypic heterogeneity in metabolic diseases.

The atypical features in our case warrant follow up for bone marrow failure, hypersplenism, and decreased visual acuity.

Final diagnosis

Pycnodysostosis with splenohepatomegaly, myelophthisic anaemia, and papilloedema.

References

1 **Maroteaux P**, Lamy M. Deux observations d'une affection osseuese condensante: la pycnodysostose. *Archives Francaises de Pediatrie* 1962;**19**:267–74.
2 **Elmore SM**. Pycnodysostosis. A review. *J Bone Joint Surg Am* 1967;**49**:153–61.
3 **Jones KL**. *Smith's recognizable patterns of human malformation*. 5th Ed. Philadelphia: WB Saunders, 1997.
4 **Kozlowski K**, Yu JS. Pycnodysostosis. A variant form with visceral manifestations. *Arch Dis Child* 1972;**47**:804–7.
5 **Kumar R**, Misra PK, Singhal R. An unusual case of pycnodysostosis. *Arch Dis Child* 1988;**63**:558–9.
6 **Cervenka J**, Rimoin DL, Hollister DW. Osteopetrosis, benign dominant. In: Buyse ML, ed. *Birth defects encyclopedia*. Massachusetts: Blackwell Scientific Publications, 1990: 1331–2.
7 **Alter BL**, Young NS. The bone marrow failure syndromes. In: Nathan DG, Orkin SH, eds. *Nathan and Oski's hematology of infancy and childhood*. Philadelphia: WB Saunders, 1998: 310–11.
8 **Shah KN**, Bajaj RT. Pycnodysostosis—case reports of two patients. *Indian Pediatr* 1979;**16**:187–90.
9 **Cetinkaya F**, Aydin M, Selouk M. Pycnodysostosis with anemia. *Indian J Pediatr* 1993;**60**:696–8.
10 **Santhanakrishnan BR**, Panneerselvam S, Ramesh S, *et al*. Pycnodysostosis with visceral manifestation and rickets. *Clin Pediatr (Phila)* 1986;**25**:416–18.

Learning points

- Pycnodysostosis is a rare genetic disorder of the skeletal system characterised by generalised osteosclerosis. The common clinical features are short stature, open cranial fontanelles, an obtuse mandibular angle, dysplastic clavicles, and short stubby hands and feet.
- Osteopetrosis tarda (Albers-Schonberg disease) is another rare genetic disorder characterised by osteosclerosis. Anaemia, splenohepatomegaly, and neurological deficits like deafness and cranial nerve palsies are common findings.
- Pycnodysostosis can rarely have visceral manifestations like anaemia, splenohepatomegaly, and neurological deficits like papilloedema.
- Pycnodysostosis and osteopetrosis tarda are linked to each other in a manner more complex than the morphological similarity of increased bone density.

Complications associated with influenza infection

Q1: What do the chest radiograph (fig 1B) and computed tomogram of the thorax (fig 1C; see p 100) show and how would the clinical and radiological findings be best treated?

The chest radiograph on admission (fig 1A) showed right middle lobe consolidation. The second chest radiograph taken six days later (fig 1B) shows that bilateral cavitating masses have developed. These were confirmed by computed tomography to be multiple lung abscesses (fig 1C), the largest of which was 10 × 8 cm in the left lower lobe.

Lung abscesses are areas of suppuration and necrosis with subsequent cavity formation. An air-fluid level is seen radiologically. They can occur in previously normal lung.

They are often found after aspiration pneumonia or bronchial obstruction, due to either a foreign body or malignant lesion, but can occur in cases of primary pulmonary infection with *Klebsiella pneumoniae* or *Nocardia asteroides*, in cases of septicaemia with *Streptococcus milleri*, or as staphylococcal metastases in cases of *Staphylococcus aureus* septicaemia.

It is unusual for *S pneumoniae* pulmonary infection to cause a primary lung abscess. More commonly it causes an empyema, which is pus within the pleural cavity requiring drainage.

Lung abscesses should be initially treated conservatively with antibiotics and intensive chest physiotherapy to facilitate drainage.[1] As more than 90% of lung abscesses will be caused at least in part by anaerobic bacteria, antibiotic treatment should include metronidazole, as well as aerobic organism cover, such as a penicillin or cephalosporin.

Antibiotics should be given to all patients, whatever the causative organism. This treatment should be initially intravenous, until the temperature settles and the patient clinically begins to improve. This will usually take about four to eight days. Antibiotics are then given orally for a further six to eight weeks, until the chest radiograph has cleared completely, or abnormalities become small and stable.[2]

Lung abscesses should not be treated surgically initially, unless there are complications with massive haemoptysis, empyema, or bronchopulmonary fistula. Ten per cent of patients are found to be unresponsive to medical therapy and may require surgical drainage of the abscess.

Failure of medical treatment is associated with large cavities of greater than 6 cm, abscesses associated with an obstructing lesion, recurrent aspiration pneumonia, development of an empyema, or prolonged symptom complex before presentation.

Lung abscesses are associated with a 15% to 20% mortality rate. The prognosis of patients with lung abscesses often depends on their underlying condition. Debilitated or immunocompromised patients have a worse prognosis, as do those with larger abscesses, in a right lower lobe location, infected by *P aeruginosa*, *S aureus*, or *K pneumoniae*.[3]

Primary lung abscesses often become colonised by *P aeruginosa.* This is found in the oropharynx of debilitated patients, where it is a commensal organism, often along with *Proteus* species and *K pneumoniae*. They require combination antibiotics along with treatment of the underlying condition.

This man's chest radiograph returned to normal after one month with medical treatment alone.

Q2: Is the high influenza A titre relevant to this case?

It is well documented that influenza A infection can predispose an individual to subsequent respiratory tract infection, which often results in pneumonia.[4] This may be caused by the influenza virus itself or by secondary infection due to *Streptococcus pneumoniae*, *S aureus*, or *Haemophilus influenzae*. All can cause considerable mortality and morbidity, even in the young and previously healthy.

Q3: What is the cause of his acute renal failure?

He had acute tubular necrosis causing his acute renal failure. This was due to the haemodynamic disturbance caused by septicaemia. This man became dialysis independent almost one month after his original presentation.

Q4: What is the cause of his abnormal liver function tests?

In cases of *S pneumoniae* pulmonary infections, there may be associated jaundice around day 4 to 5. The exact cause of this is unknown, but it is often associated with right lower lobe consolidation. It is unusual for bilirubin to rise above 100 µmol/l and the other liver function tests are usually normal.[5]

Final diagnosis

Influenza with secondary *S pneumoniae* pneumonia and acute renal failure.

References

1 **Neild JE**, Ekykn SJ, Phillips I. Lung abscess and empyema. *Q J Med* 1985;**57**:875–82.
2 **Baum S**, Crapo JD, Celli B, *et al*. Lung abscesses. *Textbook of pulmonary disease*. 6th Ed. Philadelphia: Lippincott-Raven, 1998: 651–2.
3 **Hirshberg B**, Sklair-Levi M, Nir-Paz R, *et al*. Factors predicting the mortality of patients with lung abscesses. *Chest* 1999;**115**:746–50.
4 **Macfarlane JT**, Colville A, Guion A, *et al*. Prospective study of aetiology and outcome of adult lower respiratory tract infections in the community. *Lancet* 1993;**341**:511–4.
5 **Macfarlane JT**. Acute lower respiratory tract infections. *Oxford textbook of medicine*. 3rd Ed. Oxford: Oxford University Press, 1994: 2696.

An atypical case of periodic paralysis

Q1: What is the diagnosis?

Episodic weakness beginning after age 25 is almost never due to primary periodic paralysis.[1] Furthermore, the absence of a similar family history raises a strong suspicion of a secondary disorder rather than the primary form.[2] Tachycardia and a wide pulse pressure in a nervous individual are suggestive of thyrotoxicosis, which can precipitate hypokalaemia and periodic paralysis by enhancing Na^+K^+-ATPase activity. The most likely diagnosis, therefore, is hypokalaemic periodic paralysis secondary to thyrotoxicosis.

Q2: How did we confirm it?

Thyroid function tests confirmed the thyrotoxicosis: triiodothyronine 6 nmol/l (1.1–2.9 nmol/l), thyroxine 240 nmol/l (64–154 nmol/l), and thyroid stimulating hormone 0.03 mU/l (0.4–5 mU/l). On careful examination, a barely visible goitre was detected and an ultrasound study established its multinodular nature.

Q3: How should the patient be managed?

Treatment is that of thyrotoxicosis. The attacks cease when the euthyroid state is restored.

Discussion

Thyrotoxic periodic paralysis is six times more common in males than in females. It is usually seen in orientals, especially between the ages of 20 and 39 years.[2] Occasionally, it is the presenting symptom of thyrotoxicosis.[3] Episodes of muscle weakness can be precipitated in susceptible thyrotoxic patients by the ingestion of ethanol or carbohydrate, and by strenuous physical exercise in hot humid weather. Despite these precipitating factors, the episodes occur erratically in most patients.[4] This condition can occur in patients with thyrotoxicosis of any cause, and the thyrotoxicosis may be clinically mild. The episodes of muscle weakness are invariably associated with a decrease in serum potassium concentration, although it may not always be subnormal. Hypokalaemia alone is not the only cause because potassium levels sufficient to provoke paralysis in a thyrotoxic patient has no effect when the same patient is euthyroid. The exact cause of susceptibility of some thyrotoxic patients to periodic paralysis is not known.[4] Whatever the mechanism, the attacks cease in all the patients when the euthyroid state is restored.[2] Therefore, it is important that clinicians consider the diagnosis of thyrotoxicosis in any patient with atypical hypokalaemic periodic paralysis.

Learning points

- Episodic weakness beginning after age 25 is almost never due to primary periodic paralysis.
- Periodic paralysis can occur in patients with thyrotoxicosis of any cause, and the thyrotoxicosis may be clinically mild.
- In all the patients the attacks cease when the euthyroid state is restored.

Final diagnosis

Hypokalaemic periodic paralysis secondary to thyrotoxicosis.

References

1 **Mendell JR**, Griggs RC, Ptacek LJ. Diseases of muscle. In: Fauci AS, Braunwald E, Isselbacher KJ, *et al*, eds. *Harrison's principles of internal medicine*. 14th Ed. New York: McGraw-Hill, 1998: 2473–85.
2 **Moxley III RT**. Metabolic and endocrine myopathies. In: Walton J, Karpati G, Hilton-Jones D, eds. *Disorders of voluntary muscle*. 6th Ed. New York: Churchill Livingstone, 1994: 647–716.
3 **Boyages SC**. The neuromuscular system and brain in thyrotoxicosis. In: Braverman LE, Utiger RD, eds. *Werner and Ingbar's the thyroid—a fundamental and clinical text*. 8th Ed. Philadelphia: Lippincott Williams and Wilkins, 2000: 631–3.
4 **Scheinman SJ**, Moses AM. The kidneys and electrolyte metabolism in thyrotoxicosis. In: Braverman LE, Utiger RD, eds. *Werner and Ingbar's the thyroid—a fundamental and clinical text*. 8th Ed. Philadelphia: Lippincott Williams and Wilkins, 2000: 617–21.

Swollen and stiff shoulder

Q1: What are the pathological changes seen in the radiograph (see p 101)?

The radiograph shows destruction of proximal humerus and glenoid with joint effusion and no periosteal reaction. Neuropathic joint is one of the conditions in which such radiographic appearances are seen (box 1).

Q2: What are the pathological changes seen in the MRI scan (see p 101)?

The MRI scan shows Arnold-Chiari malformation with the herniation of cerebellum and

Box 1: Differential diagnosis

- Neuropathic joint (Charcot's joint).
- Tuberculous arthritis.
- Septic arthritis.
- Primary and metastatic tumour.
- Gorham's disease (vanishing bone disease).

Box 2: Causes of neuropathic joints

1. Neural abnormality
- Tabes dorsalis.
- Syringomyelia.
- Meningocele.
- Spinal cord trauma.
- Multiple sclerosis.
- Paraplegia.
- Arachnoiditis.
- Adhesive arachnoiditis.
- Arnold-Chiari malformation.
- Charcot-Marie-Tooth disease.
- Alcoholic neuropathy.
- Leprosy.
- Myelopathy of pernicious anaemia.
- Congenital insensitivity to pain.
- Familial amyloid neuropathy.
- Non-familial amyloid neuropathy in dialysis patients.
- Familial dysautonomia.

2. Endocrine pathology
- Diabetes mellitus.
- Acromegaly.

3. Infections
- Leprosy.
- Yaws.

4. Drugs
- Thalidomide.
- Intra-articular steroids.

5. Others
- Calcium pyrophosphate dihydrate crystal deposition.
- Amyloidosis associated with Waldenstorm's macroglobinuria.
- Chronic haemodialysis.
- Juvenile rheumatoid arthritis.
- Scleroderma (with cervical osteolysis).

medulla in the cervical canal region. A combination of central nervous pathology with bone destruction is consistent with neuropathic joint (Charcot's joint).

Discussion

Charcot's joint or neuropathic joint has been described as a disorganised and relatively painless joint. There are a number of causes of this condition (box 2) but no consensus regarding the pathogenesis. The neurotraumatic theory suggests that the changes result from repeated mechanical trauma to a joint that is insensitive to pain. The neurovascular theory proposes that the changes result from a neurally initiated vascular reflex that leads to hyperaemia and active bone resorption by osteoclasts.[1] Forty years back, 90% of neuropathic arthropathies were related to tabes dorsalis, the remainder being distributed among the other disease entities. With the control of syphilis, diabetes mellitus and syringomyelia now account for a substantially larger proportion of Charcot's joints.[2] Different aetiologies have predisposition to affect different joints in the body (box 3). Presently it is most commonly seen in the midfoot and forefoot of diabetic patients.

Pain is most often the presenting feature, though it is not commensurate with the severity of the joint destruction. Some patients have no pain in the affected joints. Pain often increases with spontaneous fractures and dislocations. The joint is distended due to the effusion and synovitis. It is not inflammatory in nature, though in calcium pyrophosphate dihydrate crystal deposition disease it can be inflammatory. It may even be bloody or xanthochromic in nature at times.[3]

Box 3: Joints frequently involved in different conditions

1. Diabetes mellitus
- Tarsal and metatarsal joints.
- Ankle joint.

2. Tabes dorsalis
- Knee.
- Hip.
- Spine.

3. Syringomyelia
- Shoulder.
- Elbow.
- Cervical spine.

4. Calcium pyrophosphate dihydrate crystal deposition
- Knee.
- Hip.

Radiographs show changes similar to those of osteoarthritis in the initial stages. But later on there is subluxation, fragmentation, and proliferation of bone with lot of debris in the joint. The bone destruction and joint disorganisation seen in radiographs should be distinguished from other causes of osteolysis (box 1). Bone scan shows increased uptake even in early disease. Pathological changes are similar to those of osteoarthritis but there is active pannus formation in Charcot's joints. Often the infection in these joints is difficult to diagnose. Delay in diagnosis of neuropathic joint is fairly common.[4]

Neuropathic shoulder is relatively a rare disorder and Arnold-Chiari malformation is an exceptionally rare cause of Charcot's joint. This is probably the fourth case of Charcot's shoulder due to Arnold-Chiari malformation.[2]

Treatment requires the management of the underlying condition if possible and the control of infection of the joint if present. Patient education has a major role in the management. They have to be taught regarding the use of protective footwear, braces, a cane, and immobilisation. Arthrodesis can be performed for unstable joints, though it is difficult and requires resection of great amount of bone. Total joint replacement is also not recommended because of lack of capsuloligamentous support, though they have been performed in hip and knee with success in 3–7 years follow up.[5]

Final diagnosis

Charcot's arthropathy of shoulder due to Arnold-Chiari malformation.

References

1 **Brower AC**, Allman RM. Pathogenesis of neuropathic joint: neurotraumatic vs neurovascular. *Radiology* 1981;**139**:349–54.
2 **Davis PR**, Ko KR, Sachdev VP. Charcot shoulder as the initial symptom in Arnold-Chiari malformation with hydromyelia: a case report. *Mt Sinai J Med* 1988;**5**:406–8.
3 **Ellman MH**. Neuropathic joint disease. In: McCarty DJ, Koopman WJ, ed. *Arthritis and allied conditions. A textbook of rheumatology*. Vol 2. 12th Ed. Philadelphia: Lea and Febiger, 1993: 1407–25.
4 **Hatiz N**, Karr TK, Wirth MA, *et al*. Neuropathic arthropathy of shoulder. *J Bone Joint Surg [Am]* 1998;**80A**:1314–19.
5 **Soudry M**, Binazzi R, Johanson NA, *et al*. Total knee arthroplasty in Charcot and Charcot like joints. *Clin Orthop* 1986;**208**:199–204.

A woman with dysphagia and Raynaud's phenomenon

Q1: Comment on the appearance of her tongue (fig 1) face (figs 3 and 4), and hands (fig 5) (see p 102–103)

Figure 1 reveals florid telangiectasias affecting the buccal mucosa and tongue. Figures 3 and 4 reveals facial telangiectasias and perioral radial furrowing. Figure 5 shows taught shiny skin and acrocyanosis of the digits.

Q2: Comment on the appearance of her barium swallow (fig 2) and suggest a unifying diagnosis

The barium swallow (see p 102) shows moderate oesophageal dilatation with no evidence of active peristalsis, suggesting a motility disorder. The underlying diagnosis is CREST syndrome (see discussion below).

Q3: Examination of her left elbow revealed a hard nodule over the extensor aspect. What does the radiograph (fig 6) show?

The radiograph of the elbow (see p 103) illustrates extensive subcutaneous calcification.

Discussion

Scleroderma is a generic term describing a group of related connective tissue diseases characterised by the development of skin/organ fibrosis, Raynaud's phenomenon, and specific autoantibodies in sera. A working classification normally divides these diseases into systemic and localised cutaneous forms.

Localised cutaneous forms include morphoea, linear scleroderma, and en coup de sabre (linear sclerotic lesion often affecting the scalp).

Systemic forms include two main disease patterns. First, limited cutaneous systemic sclerosis where skin sclerosis is restricted to the extremities and face; CREST (**C**alcinosis, **R**aynaud's phenomenon, o**E**sophageal dysmotility, **S**clerodactly, and **T**elangiectasia) syndrome is a subset of this group. Although limited forms have prominent vascular instability characterised by severe Raynaud's phenomenon and pulmonary hypertension, internal organ fibrosis is uncommon compared with the diffuse disease pattern group and this is reflected in an overall 10 year survival of around 75%. Patients in this group often have a long history (up to 15 years) of Raynaud's phenomenon before the development of sclerodactly, facial disfigurement, etc.

The second disease pattern is the diffuse cutaneous systemic sclerosis group; this group represents the most serious form of the condition. These patients typically have a very short history of Raynaud's phenomenon before constitutional symptoms, skin oedema (then sclerosis), and internal organ involvement become apparent. The latter may manifest in the respiratory system (pulmonary fibrosis), genitourinary system (hypertensive renal crisis), cardiovascular system (conduction defects, restrictive cardiomyopathy), or gastrointestinal tract (malabsorption, bacterial overgrowth).

An interesting clinical problem which can often present to the practising physician or general practitioner alike is that of a young

Box 1: Primary idiopathic Raynaud's compared with secondary (underlying connective tissue disorder) Raynaud's

Primary idiopathic Raynaud's
- Onset at puberty.
- <5 attacks a day.
- No ischaemic injury to digits.
- No abnormal capilloroscopy.
- No autoantibodies in serum.

Secondary (underlying connective tissue disorder) Raynaud's
- Onset >25 years.
- 5–10 attacks a day.
- Ischaemic injury to digits.
- Abnormal nailfold capilloroscopy.
- Autoantibodies present in serum.

woman (of about 20 years) presenting with Raynaud-like symptoms. Is it an idiopathic isolated pathology with a benign course (Raynaud's disease) or is it the forerunner of a potentially life threatening underlying connective tissue disorder (Raynaud's phenomenon)? Although no specific test can provide the answer, by searching for specific features in the history, on examination and at the laboratory, one can often reassure the patient or alternatively arrange long term outpatient follow up (see box 1).

It is worthwhile elaborating on the gastrointestinal manifestations of the scleroderma cohort of patients, especially in view of the presentation of the case described above. Oesophageal dysmotility is by far the commonest manifestation in the gut and presents clinically with heartburn, dysphagia, and odynophagia. Later manifestations include bleeding, stricture, Barrett's oesophagus, and finally adenocarcinoma of the distal oesophagus. At a histological level, distal oesophageal biopsies reveal smooth muscle atrophy coupled with submucosal fibrosis. Endoscopy with biopsy, barium studies, and manometry all have a place in the diagnostic process. Management may be medical (proton pump inhibitors) or surgical (fundoplication).

Small and large bowel involvement is also seen and again is a result of muscle atrophy and fibrosis causing dysmotility, stasis and bacterial overgrowth. Patients complain of colic, bloating, diarrhoea, and even steatorrhoea with small intestinal disease. Breath tests and duodenal aspirates at endoscopy help to identify bacterial overgrowth which may be amenable to oral broad spectrum antimicrobial therapy. Colonic disease is rarely clinically significant and predominantly causes constipation.

It is worth noting that primary biliary cirrhosis (PBC) is a recognised association of scleroderma. Thus patients should have at least annual liver function tests performed at the clinic. Management of PBC in this situation is as for patients without non-scleroderma.

Investigations in a patient with a likely scleroderma subtype should include nailfold capilloroscopy, serology +/- skin biopsy (note that the latter test is not necessary for diagnosis in the majority).

Serological testing in systemic sclerosis is an evolving field. The majority of patients (90%) are antinuclear antigen positive. Three main serological subsets can be identified within the scleroderma population.

(1) Anticentromere antibody positive (36% overall):

Box 2: Complications and treatment for systemic sclerosis

- **Raynaud's phenomenon:** Socks and gloves, avoid smoking, calcium blockers, intermittent iloprost infusions, digital sympathectomy.
- **Gastro-oesophageal reflux:** Proton pump inhibitor.
- **Small bowel bacterial overgrowth:** Rotating courses of oral antibiotics.
- **Hypertensive renal crisis:** Angiotensin converting enzyme inhibitor.
- **Fibrosing alveolitis:** Prednisolone +/- azathioprine.
- **Pulmonary hypertension:** Calcium blockers, iloprost infusions, long term oxygen, oral anticoagulation.
- **Cardiac arrhythmias:** Antiarrhythmics, pacemaker insertion.

- Patients typically have the best prognosis of the three groups.
- Patients usually present in limited cutaneous systemic sclerosis (including CREST).
- Thought to confer "protection" from internal organ fibrosis, for example, renal disease.
- Associated with pulmonary hypertension.

(2) Antitopoisomerase (Scl-70) positive (40% overall):
- Associated with diffuse cutaneous systemic sclerosis.
- Highest risk of developing fibrosing alveolitis.

(3) Anti-RNA polymerase I or III positive (20% overall):
- Associated with diffuse cutaneous systemic sclerosis.
- Patients tend to have the most severe scleroderma and renal involvement

Other staging investigations will depend on the clinical features present. For example, pulmonary function testing, high resolution computed tomography of chest and echocardiography for those complaining of breathlessness (?pulmonary fibrosis, ?pulmonary hypertension).

There is no curative treatment for systemic sclerosis but the majority of patients can be helped with an organ based approach to the complications which arise (see box 2).

No drug has been shown to halt the progression of systemic sclerosis in a sufficiently large and powerful prospective randomised controlled clinical trial. Ascertaining improvement or deterioration in scleroderma is difficult. Moreover, the disease is variable in severity and rate of progression. Also, spontaneous improvement may occur after several years, especially involving the skin. Thus trials are difficult to design and interpret in the context of systemic sclerosis. Suggested treatments to halt the fibrotic process include D-penicillamine and gamma interferon, but efficacy remains to be proven in a randomised trial setting. In addition, it may not be justifiable to use treatments with potentially serious side effects in some scleroderma subsets with good prognoses (for example, limited cutaneous disease) especially given the lack of proved efficacy.

Final diagnosis
CREST syndrome.

References
1 **Denton CP**, Black CM. Scleroderma and related disorders: therapeutic aspects. *Baillieres Clin Rheumatol* 2000;**14**:17–35.
2 **Harvey GR**, McHugh NJ. Serologic abnormalities in systemic sclerosis. *Curr Opin Rheumatol* 1999;**11**:495–502.
3 **Abu-Shakra M**, Lee P. Mortality in systemic sclerosis: a comparison with the general population. *J Rheumatol* 1995;**22**:2100–2.

An unusual case of chronic renal failure

Q1: What does the MRI scan show (see p 104)?
The MRI scan of the brain shows generalised cerebral and cerebellar atrophy. There is a quite extensive abnormal high signal on the T2-weighted images and fluid attenuated inversion recovery (FLAIR) sequence in both the cerebellar hemispheres, pons, and in the cerebral white matter involving both periventricular and subcortical areas. These appearances are not specific but are likely to be due to widespread ischaemic changes.

Q2: What is shown in fig 3 (see p 104)?
Angiokeratomas. These are vascular lesions of the skin, which usually appear at puberty, increase, with age, and are mainly confined to the bathing trunk area. These occur as a result of ectatic dilatation of the blood vessels weakened by endothelial deposition of ceramide.

Q3: What is the diagnosis?
Fabry's disease.

Q4: What do you expect to see in the electron microscopic examination of the kidney?
Multilamellar bodies (zebra bodies).

Q5: What investigation will you do to confirm the diagnosis?
The α-galactosidase levels should be measured as they are diagnostic. In our patient the α-galactosidase levels were undetectable.

Discussion
Fabry's disease is a rare (1:40 000) X linked recessive disorder in which partial or total deficiency of lysosomal α-galactosidase results in the progressive accumulation of glycolipids in various tissues including the kidneys. The single most debilitating symptom of Fabry's disease is the pain. The painful crises most often begin in childhood and consists of agonising burning pain initially in the palms and soles which often radiates to the proximal extremities and other parts of the body. Cardiac manifestations include anginal chest pain, myocardial ischaemia, and infarction, congestive cardiac failure, and cardiac enlargement. The electrocardiogram may show left ventricular hypertrophy, ST segment changes, and T wave inversion. Short PR intervals have been reported.[1] Cerebrovascular manifestations result primarily from multifocal small vessel involvement and may include personality changes, psychotic behaviour, thrombosis, seizures, aphasia, hemiplegia, etc.[2] Progressive glycosphingolipid deposition in the kidney results in proteinuria and other signs of renal impairment with gradual deterioration of renal function and development

of azotaemia in middle age. Ocular involvement is most prominent in the cornea (opacities), lens (cataract), conjunctiva, and retina (vascular lesions). Other clinical features include lymphoedema, episodic diarrhoea, avascular necrosis of the head of femur, delayed puberty, fine facial and body hair, dyspnoea, and wheezing respiration.[3] Treatment of patients with regard to cardiac, pulmonary, and central nervous system manifestations remain non-specific and symptomatic. Since renal insufficiency is the most frequent late complication in patients with this disease, chronic haemodialysis and/or renal transplantation have become life saving. At present the most practical and effective therapy is preventive screening of all suspect heterozygotes, genetic counselling, and prenatal diagnostic studies should be made available to all at risk families. Enzyme replacement has been shown to be beneficial over short term in small studies. With recent developments in molecular genetics it is possible to produce the human recombinant enzyme α-galactosidase. In addition the results of a trial of gene therapy in a Fabry's disease gene knocked out mouse appear promising.[4]

Final diagnosis

Fabry's disease.

References

1 **Pochis WT**, Litzow JT, King BG, *et al.* Electrophysiologic findings in Fabry's disease with a short PR interval. *Am J Cardiol* 1994;**74**:203–4.
2 **Utsumi K**, Yamamoto N, Kase R, *et al.* High incidence of thrombosis in Fabry's disease. *Intern Med* 1997;**36**:327–9.
3 **Brown LK**, Miller A, Bhuptani A, *et al.* Pulmonary involement in Fabry's disease. *Am J Respir Crit Care Med* 1997;**155**:1004–10.
4 **Ziegler RJ**, Yew NS, Li C, *et al.* Correction of enzymatic and lysosomal storage defects in Fabry mice by adenovirus-mediated gene transfer. *Hum Gene Ther* 1999;**10**:1667–82.

A case of cough and dysphagia

Q1: What abnormalities are seen on the computed tomogram (fig 1; see p 104) and on views of the right main bronchus at bronchoscopy (fig 2; see p 105)?

The computed tomogram shows the presence of a large fistula between the right main bronchus and oesophagus, with resultant areas of shadowing seen in both lungs due to aspiration. At bronchoscopy, the oesophagus containing the nasogastric tube can be visualised through the fistula.

Q2: What is the most likely cause of these appearances?

The most likely cause of these appearances is a malignant broncho-oesophageal fistula. Oesophageal biopsies confirmed adenocarcinoma.

Q3: What other conditions may cause similar appearances?

Non-malignant causes of oesophago-respiratory fistula include congenital lesions, infection, and trauma.

Q4: What treatment options are available?

Possible treatment modalities include:

- Insertion of oesophageal stent.
- Oesophageal bypass.
- Oesophageal exclusion.
- Chemo/radiotherapy.
- Supportive therapy.

Discussion

Malignant oesophago-respiratory fistula is estimated to develop in 4.5% and 0.3% of all primary oesophageal and bronchial carcinomas respectively.[1] It is associated with a dismal prognosis, with a median survival for untreated cases of between one to six weeks. Typical features include cough, which is worse on swallowing (Ono's sign), aspiration, fever, dysphagia, and pneumonia. Appropriate investigations include bronchoscopy, oesophagoscopy and contrast radiography, although all may be misleadingly normal. Initial management is primarily aimed at reducing pulmonary contamination from the fistula, and should be started as soon as possible after diagnosis, as delay is associated with exponential increase in early mortality. Immediate treatment includes keeping the patient nil by mouth, and providing general supportive therapy, including broad spectrum antibiotics where appropriate. Insertion of an oesophageal stent, which occludes the opening of the fistula, is generally effective in preventing pulmonary aspiration, but may be complicated by bleeding, migration, oesophageal obstruction, and perforation.[2] Surgical techniques, including oesophageal exclusion or by-pass, are associated with high operative mortality, but result in effective symptom palliation in survivors.

Congenital oesophago-respiratory fistulae generally present in early childhood, although are occasionally not diagnosed until adult life.[3] Other reported causes of fistula include tuberculosis,[4] and herpes virus infection, chest trauma, and pressure necrosis from tracheal cuff after prolonged ventilation. Surgical repair is generally required for non-malignant oesophago-respiratory fistulae, but lesions may be amenable to less invasive techniques, including closure with fibrin glue applied via the bronchoscope.

Final diagnosis

Oesophageal carcinoma resulting in broncho-oesophageal fistula and bronchopneumonia.

References

1 **Burt M**, Diehl W, Martini N, *et al.* Malignant esophagorespiratory fistula: management options and survival. *Ann Thorac Surg* 1991;**52**:1222–9.
2 **Merandi SF**, Quinn SF, Clark RA. Complications of esophageal prostheses: roentgenologic manifestations. *South Med J* 1989;**82**:1365–9.
3 **Danton MH**, McMahon J, McGuigan J, *et al.* Congenital oesophageal respiratory tract fistula presenting in adult life. *Eur Respir J* 1993;**6**:1412–4.
4 **Macchiarini P**, Delamare N, Beuzeboc P, *et al.* Tracheoesophageal fistula caused by mycobacterial tuberculosis adenopathy. *Ann Thorac Surg* 1993;**55**:1561–3.

An elderly lady with collapse

Q1: What are the findings in figs 1 an 2 (see p 105)?

Figure 1 shows right sided partial ptosis and a divergent squint due to pupil sparing third nerve (oculomotor) palsy—that is, there is no pupil asymmetry. In fig 2, the patient was asked to raise both arms and it shows weakness of the left arm in comparison with the right arm. Indeed the patient had left hemiparesis. The right arm, however, is not fully raised probably due to a degree of proximal weakness. Figure 2 also shows a feeding pump next to the patient and a feeding tube looped over the back of her chair leading to her percutaneous endoscopic gastrostomy (PEG).

Q2: What is the diagnosis?

Crossed hemiplegia due to a vascular lesion affecting the right mid-brain involving the right third nerve and the corticospinal tract at the level of the cerebral peduncles.

Computed tomography of the brain did not reveal any evidence of bleed, but a low density area in the left occipital lobe. The left hemiplegia gradually improved but dysphagia persisted requiring insertion of a PEG for feeding. Eventually the patient was discharged to a residential home. Six months after the onset, she remains with a residual hemiparesis, partial third nerve palsy, and PEG feeding.

Discussion

Clinical features of the third, fourth, and sixth cranial nerve palsies

The third nerve supplies all the extraocular muscles of the eye except the lateral rectus muscle which is supplied by the sixth (abducent) nerve, and the superior oblique muscle being innervated by the fourth (trochlear nerve) nerve. The features of complete third nerve palsy include ptosis, divergent squint, diplopia, fixed dilatation of the pupil, and paralysis of accommodation.[1] Patients with third nerve palsy are often relatively asymptomatic because of the ptosis, but on raising the eyelid, they would have diplopia in all directions except on lateral gaze to the side of the lesion.

However when the fourth nerve palsy develops, it often leads to a very subtle diplopia that is worse when the head is tilted down and away such as when descending the stairs. This abnormality results because of a failure of extorsion leading to an unopposed pull of the inferior rectus which raises the eye. Consequently patients slightly tilt the head and in children this sometimes may be felt to mimic a torticollis.

The sixth nerve palsy causes medial (convergent) squint with failure of abduction.[2] Patients with sixth nerve palsy often complain of more diplopia than in those with third nerve palsy because they have no ptosis to mask the false image. In fact patients with sixth nerve palsy voluntarily close their affected eye, and the diplopia persists in all directions.

The third nerve nucleus and its relations

The third nerve nucleus in the mid-brain has two components: the third nerve motor nucleus and the Edinger-Westphal.[2] The third nerve has such a long vertical extent that damage at various points can often lead to incomplete lesions. The third nerve motor nucleus is situated in the lower mid-brain and gives rise to the motor fibres supplying the extraocular muscles as mentioned earlier.[2] The Edinger-Westphal nucleus is situated adjacent to the third nerve motor nucleus, and receives fibres from the periaqueductal grey matter involved in the consensual light reflex as well as information from the adjacent third nerve nucleus mass which is activated when the medial rectus muscle is activated in accommodation. The Edinger-Westphal nucleus gives rise to the preganglionic parasympathetic fibres.

The third nerve emerges from the mid-brain between the cerebral peduncles where the corticospinal tracts are carried, and at this point it

Box 1: Learning points

- The third nerve nucleus has two components in the mid-brain: the Edinger-Westphal nucleus and the motor oculomotor nucleus.
- The Edinger-Westphal nucleus is situated in the upper mid-brain and gives rise to the preganglionic parasympathetic neurones responsible for the pupilloconstrictor fibres.
- The motor third nucleus is situated in the lower mid-brain and gives rise to the motor fibres supplying the extraocular muscles.
- The pupilloconstrictor fibres and those innervating the levator palpebrae superioris lie superficially in the trunk of the nerve.

lies between the posterior cerebral artery and superior cerebellar artery and then it runs parallel to the posterior communicating artery until it reaches the cavernous sinus. After entering the orbit through the superior orbital fissure, the third nerve divides into an upper and lower branch. The upper branch supplies the levator palpebrae superioris and superior rectus muscles. The lower branch supplies three muscles: the medial rectus, the inferior rectus, and the inferior oblique muscle.[1]

The nerve to the inferior oblique muscle conveys the preganglionic parasympathetic fibres to the ciliary ganglion from which the post-ganglionic parasympathetic fibres arise to supply the ciliary muscle and the muscles of the iris (pupilloconstrictor fibres). After the ciliary ganglion, the parasympathetic fibres subdivide into 8–10 ciliary nerves supplying the pupilloconstrictor muscles.

The pupilloconstrictor fibres and those innervating the levator palpebrae lie in a superficial and dorsal position on the nerve relaying in the ciliary ganglion which is in the posterior orbit. Because of this anatomical characteristic, a fixed dilated pupil is often the first sign of third nerve (oculomotor) compression and ptosis the second, before the external ophthalmoplegia develops.[3]

The particular anatomical features of the third nuclei, and the nerve trunk described earlier, allows selective damage to the motor nucleus or the fibres in the nerve trunk to present as pupil sparing third nerve palsy, with or without features of long tract signs. For example, the corticospinal fibres descend into the mid-brain where they rotate into the medial part of the of the cerebral peduncles with the fibres supplying the leg lying laterally and those supplying the arm medially. The corticospinal fibres are then spread out by numerous transverse pontine fibres coming together in the lower third of the pons as a preliminary to their decussation in the medullary pyramid. As they decussate, the arm fibres lie medially and cross the mid line above the leg fibres assuming a medial position in the corticospinal tract on the opposite side of the cord.

The sudden occurrence of the pupil sparing third nerve palsy on the right side and hemiplegia on the left side indicate a mid-brain vascular lesion for the clinical manifestations of the patient. Pupil sparing third nerve palsy could occur both intra-axially (within the mid-brain) or extra-axially, that is, in the nerve trunk. Pupil sparing third palsy is a recognised complication in some patients with

Box 2: Pupil sparing third palsy may occur in:

- Diabetes mellitus.
- Ischaemic damage to the nerve.
- Ischaemic mid-brain lesions involving the lower mid-brain.

diabetes mellitus, and in ischaemic damage of the nerve.[4] Selective intra-axial lesions of the third nerve with or without pupillary involvement have been observed.[5] In the latter report, lesions of the mid-brain sparing the upper part where the Edinger-Westphal nucleus is placed, the pupils were not affected whereas lesions involving both upper and lower parts of the mid-brain were associated with pupillary dilatation. Earlier reports have also demonstrated vascular causes of intra-axial pupil sparing third palsy due to mid-brain haemorrhage and infarction.[6 7] The classical description of the Weber's syndrome includes ipsilateral third nerve palsy with mydriasis and crossed hemiplegia.[8] However, the patient described here is similar to classical Weber's syndrome but the pupils were spared.

Final diagnosis

Crossed hemiplegia due to a vascular lesion affecting the right mid-brain involving the right third nerve and the corticospinal tract.

References

1 **Walton J**. The cranial nerves and special senses. *Brain's diseases of the nervous system*. 9th Ed. Oxford: Oxford University Press, 1985: 83–134.
2 **Crossman AR**, Neary D. Cranial nerves and cranial nerve nuclei. *Neuroanatomy*. 1st Ed. Edinburgh: Churchill Livingstone, 2000: 71–84.
3 **Sunderland S**. Neurovascular relations and anomalies at the base of the brain. *J Neurol Neurosurg Psychiatry* 1948;**11**:243.
4 **Nadeau SE**, Trobe JD. Pupil sparing in oculomotor palsy: a brief review. *Ann Neurol* 1983;**13**:143–8.
5 **Saeki N**, Murai N, Sunami K. Mid-brain tegmental lesions affecting or sparing the pupillary fibres. *J Neurol Neurosurg Psychiatry* 1996;**61**:401–2.
6 **Fleet WS**, Rapcsak SZ, Huntley WW, *et al*. Pupil-sparing oculomotor palsy from midbrain hemorrhage. *Ann Ophthalmol* 1988;**20**:345–6.
7 **Breen LA**, Hopf HC, Farris BK, *et al*. Pupil-sparing oculomotor palsy due to midbrain infarction. *Arch Neurol* 1991;**48**:105–6.
8 **Silverman IE**, Liu GT, Volpe NJ, *et al*. The crossed paralyses. The original brain-stem syndromes of Millard-Gubler, Foville, Weber and Raymond-Cestan. *Arch Neurol* 1995;**52**:635–8.

A developing visual field defect

Q1: What is the visual field defect (fig 1; see p 106)?

Left temporal hemifield defect.

Q2: What is the neuroanatomical correlate of this clinical finding?

Non-congruent (heteronymous) hemianopic defects usually suggest a lesion in the chiasmal region. A unilateral temporal hemifield defect, as seen here, suggests a prechiasmal lesion, situated at the point where the optic nerve joins the chiasm (the anterior angle of the chiasm).

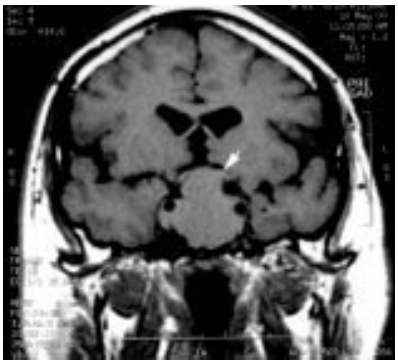

Figure 1 Coronal section of a T1-weighted MRI scan, showing a large pituitary tumour, selectively compressing the left optic nerve as it enters the optic chiasm (arrow).

At this point, fibres from the nasal and temporal sides of the retina are separated within the optic nerve and so may be selectively affected by pathological processes. The nasal fibres, which lie closer to the midline, are more vulnerable to compression by enlargement of the pituitary gland, causing an ipsilateral temporal field defect. This phenomenon, which is of great value in topographical diagnosis, was first pointed out by Traquair and hence this visual field defect is known as the junctional scotoma of Traquair.[1 2] In some instances, the defect may be confined to the paracentral region alone.[3] The earliest detectable sign of visual field defects of chiasmatic origin is desaturation of the red colour of a pin as it is moved from the nasal into the temporal field (temporal desaturation).

Q3: What further investigations should be performed?

The structure and function of the pituitary gland may be assessed by imaging (preferably with magnetic resonance imaging, MRI) and specific blood tests respectively. MRI of the pituitary region (fig 1 above) showed a large mass lesion arising from the pituitary fossa, the bony walls of which showed some erosion, and extending above the sella turcica to the right of the midline. Coronal sections showed that the tumour selectively compressed the left optic nerve just at its point of entry into the chiasm (fig 1 above, arrow). The lesion showed marked enhancement with intravenous contrast (gadolinium).

Tests of pituitary function revealed a greatly increased prolactin level (>160 000 mIU/l), indicating that the lesion was a giant prolactinoma. Retrospectively, it was noted that the patient had been increasingly lethargic and sleepy, with reduced energy and facial hair, but there was no history of galactorrhoea. He was treated with the long acting dopamine agonist cabergoline (0.5 mg/week), and followed up in the pituitary clinic with monitoring of visual fields, prolactin levels, and tumour size. After six months his visual symptoms had resolved, prolactin level had fallen, and there was considerable shrinkage of the tumour on repeat MRI.

Discussion

Although bitemporal hemianopia is the commonest visual field defect detected in patients with pituitary adenoma, the junctional scotoma of Traquair has been found in 1%–10% of cases in large series (which predate computed tomography and MRI).[4 5] This visual field defect may also occur

occasionally in the context of other pathologies, such as meningioma, aneurysm, and craniopharyngioma.[6]

Traquair also described another type of junctional scotoma,[2] which, although it produces a quite different clinical picture, may be a possible source of confusion with the aforementioned type. Involvement of the crossing and ventral nasal retinal fibres as they loop anteriorly into the contralateral optic nerve (Wilbrand's knee) produces a contralateral upper temporal scotoma, along with a visual field defect (central scotoma) in the ipsilateral eye; because the latter dominates the clinical picture, the former is easily missed. This "junctional scotoma", so called to differentiate it from the junctional scotoma of Traquair, is usually due to intrinsic optic nerve pathology, but it has also been reported in association with a pituitary adenoma.[7]

Final diagnosis

Giant pituitary prolactinoma causing junctional scotoma of Traquair.

Learning points

- There are two types of junctional scotoma, both of clinicoanatomical localising value.
- The junctional scotoma of Traquair is an ipsilateral temporal field defect with midline hemianopic character, resulting from involvement of crossing nasal fibres at the anterior angle of the chiasm.
- The junctional scotoma is an easily overlooked contralateral superior temporal scotoma associated with ipsilateral optic neuropathy, resulting from lesions of the optic nerve just anterior to the chiasm which damage the crossing ventral nasal fibres looping into the optic nerve (Wilbrand's knee).
- Large pituitary tumours may be associated with subtle neuro-ophthalmological signs, emphasising the importance of careful clinical examination of the visual fields.

References

1 **Traquair HM**. Bitemporal hemianopia: the later stages and the special features of the scotoma. With an examination of current theories of the mechanism of production of the field defects. *Br J Ophthalmol* 1917;**1**:216–39.
2 **Traquair HM**. *An introduction to clinical perimetry*. 6th Ed. London: Kimpton, 1949.
3 **Mojon DS**, Odel JG, Rios RJ, *et al*. Pituitary adenoma revealed by paracentral junctional scotoma of Traquair. *Ophthalmologica* 1997;**211**:104–8.
4 **Lyle TK**, Clover P. Ocular symptoms and signs in pituitary tumours. *Proc R Soc Med* 1961:**54**:611–9.
5 **Elkington SG**. Pituitary adenoma, preoperative symptomatology in a series of 260 patients. *Br J Ophthalmol* 1968;**52**:322–8.
6 **Bird A**. Field loss due to lesions at the anterior angle of the chiasm. *Proc R Soc Med* 1972;**65**:519–20.
7 **Candiloros H**, Saudax E, George JL, *et al*. Adénome hypophysaire révélé par un syndrome de Traquair. *Ann Endocrinol (Paris)* 1992;**53**:236–40.