Pulmonary nodules and splinter haemorrhages

Q1: What is the main differential diagnosis of this patient’s pulmonary nodules?

Multiple pulmonary nodules may have varied causes (box 1), however, they strongly suggest metastatic tumour and this diagnosis, together with fungal or tuberculous granulomas, accounts for well over 95% of the cases. Many types of tumours may disseminate causing pulmonary nodules but some of the more frequently encountered include breast, urogenital, testicular, and thyroid cancers as well as choriocarcinoma, melanoma, and osteosarcoma. Considerably less common in this presentation are primary pulmonary lymphoma, bronchoalveolar carcinoma, and Kaposi’s sarcoma. However, the absence of a detectable primary tumour on clinical evaluation decreases the likelihood ratio of this diagnosis. The adrenal mass is unlikely to be a primary cancer since these tumours are rare (only 4% of all single adrenal masses) and usually large in size (only 4/130 adrenal cancers were <3 cm). The characteristics of the pulmonary nodules (large, variable in size, and non-calcified) all indicate that this is not a granulomatous disease, and moreover the patient is not immunocompromised and has no history of being in an endemic area. The patient’s systemic symptoms and acute phase response are consistent with both diagnostic possibilities as well as with less common alternatives of septic pulmonary emboli or vasculitis. The first could be due to right sided infective endocarditis on the tricuspid valve, although the patient (who used drugs 17 years before) vehemently denied current intravenous drug abuse. Pulmonary vasculitis could perhaps be linked to the patient’s recent history of upper respiratory symptoms and to his eye involvement. Drenching night sweats, sometimes a valuable clue, can however occur in many of the suspected conditions (box 2) and do not seem to be helpful here. The mild eosinophilia observed is rarely encountered in infections (other than parasitic infestations) but may occur in patients with malignant disease (lymphomas or solid tumours, especially with metastases or necrosis) as well as in the context of autoimmune disorders such as vasculitides or in sarcoidosis. Therefore it was not really helpful here.

Q2: How does the appearance of the skin signs affect the diagnosis?

Splinter haemorrhages are commonly due to minor trauma to the nails and are often considered clinically unhelpful. This is not the case when a patient with undiagnosed systemic illness develops new splinter haemorrhages. Although omitted from many textbooks, such an appearance suggests an association with several systemic conditions including small arteriolar vessels such as the primary antiphospholipid antibody syndrome, systemic vasculitis, and cholesterol crystal emboli. They can also occur in about 1:6 patients with infective endocarditis. However, the absence of a murmur or a predisposing condition, the negative blood cultures, and the normal echocardiography make infective endocarditis unlikely in this patient, as does the

Box 1: Multiple pulmonary nodules*: main differential diagnosis

- Malignancy, mostly metastatic.
- Granulomatous disease (histoplasmosis, cryptococcosis, etc, tuberculosis, sarcoidosis).
- Pulmonary infarcts (especially septic) or abscesses.
- Pneumococcosis.
- Wegener’s granulomatosis.
- Rheumatoid arthritis.
- Rare causes such as pulmonary amyloidosis, arteriovenous malformations, etc.

*Cavitation may occur in most nodules mainly indicating an active disease process.

Box 2: Drenching night sweats: main differential diagnosis

- Protracted viral infection (for example herpesvirus, HIV).
- Granulomatous disease (for example tuberculosis, sarcoidosis, brucellosis, fungal infection).
- Infective endocarditis.
- Hepatic abscess.
- Malignancy, especially haematological (for example lymphoproliferative disease, leukaemia, myelodysplastic syndrome; also metastatic carcinoma or sarcoma).
- Vasculitis (for example temporal arteritis, polyarteritis).

Box 3: Palpable purpura*: main differential diagnosis

- Mixed cryoglobulinaemia.
- Infection associated (for example upper respiratory tract infection).
- Drug associated (for example antibiotics).
- Malignancy associated, mostly haematological.
- Autoimmunity associated in the context of known rheumatoid arthritis, systemic lupus erythematosus, etc and in the context of active systemic vasculitis.
- Idiopathic.

*Some cases of septicaemia, endocarditis, cholesterol, or myxoma emboli and the antiphospholipid antibody syndrome may mimic palpable purpura and should be considered and excluded.
near normal temperature. Cancer and granulomatous disease do not cause splinter haemorrhages. Thus, their appearance places a systemic vasculitis at the top of the differential diagnosis. The development of palpable purpura confirms this diagnosis and even narrows it further. Palpable purpura is caused by skin infiltration by small vessel vasculitis. Once the probability of an infection is lessened by the negative evaluation and cryoglobulinaemia is excluded by the normal rheumatoid factor and complement, the lack of drug exposure or previous autoimmune disease leaves vasculitis of malignancy or systemic vasculitis as the main differential diagnosis (box 3). Malignancy associated cutaneous vasculitis is not only uncommon (less than 10% of all cases), but almost always limited to haematological malignancies, which are not likely here.

Thus, again, cutaneous vasculitis as part of a systemic vasculitis syndrome is suggested. This is encountered mainly in polyarteritis and overlap syndromes (up to 33% on presentation) which do not cause pulmonary nodules, and in Wegener's granulomatosis (up to 10% on presentation).

Q3: How would you proceed with the diagnosis?

To confirm a postulated diagnosis of Wegener’s granulomatosis and rule out diagnostic alternatives, an urgent testing of the patient’s serum for antineutrophil cytoplasmic antibodies (ANCA) is indicated, as well as a percutaneous computed tomography guided biopsy of a pulmonary nodule.

Progress

Within 24 hours of the appearance of splinter haemorrhages and palpable purpura, the patient had undergone a computed tomography guided biopsy of a large superficial pulmonary nodule and the results of a test for ANCA were obtained. The latter was positive for c-ANCA by indirect immunofluorescence assay (score + 4) and anti-PR-3 by enzyme linked immunosorbent assay (ELISA; over 10 times the cut off point in normals). The biopsy demonstrated small vessel necrotising vasculitis with prominent giant cells, granulomas, and eosinophils. Skin biopsy showed leucocytoclastic vasculitis. Upper respiratory tract involvement was confirmed by the appearance of aphthous ulcers in the soft palate and tonsillar exudate. Sinus examination and computed tomography were normal. The patient was immediately started on intravenous hydrocortisone, which was later switched to oral prednisone at 1 mg/kg with the addition of methotrexate 15 mg/week. Oral bisphosphonates, calcium, vitamin D, and folic acid were prescribed to decrease adverse drug reactions due to the corticosteroids and methotrexate, respectively. The patient, who by then was bedridden and severely ill, responded dramatically. He became ambulatory and felt much better within 48 hours and could be discharged soon after. His chest x ray was much improved on last follow up.

Discussion

Wegener’s granulomatosis is an uncommon necrotising vasculitis distinguished by its predilection to affect small vessels of the upper respiratory tract, pulmonary parenchyma, and kidneys. Our patient exhibits two distinct histopathological patterns of Wegener’s granulomatosis: microvasculitis or capillaritis is the infiltration and destruction of capillaries, venules, and arterioles by neutrophils. This is seen in the patient’s skin involvement but did not occur in the kidney, which is affected in only about 20% of patients at presentation. The second pattern, granulomatous vasculitis, involving small/medium sized arteries and veins with prominent multinucleated giant cells, was revealed in the lung biopsy. Pulmonary involvement on presentation was reported in almost 50% of the patients and may be asymptomatic in 1:3. Multiple or solitary nodules with or without cavitation, are the most frequent manifestations. Nasal, sinus, tracheal, or ear symptoms are present on diagnosis in about 75% of the patients but are often considered trivial at first, as in our patient who had a blocked nose, mild epistaxis, pain upon swallowing and ear pain attributed to upper respiratory infection. However, these complaints are often accompanied by systemic symptoms such as fatigue, arthralgia/myalgia (67%), fever (23%), and weight loss (15%) which should alert the clinician to their true meaning. On retrospective, our patient’s eye involvement (15% on presentation) was also a clue, but the appearance of striking skin signs (13% initially) was almost diagnostic in this context. Palpable purpura (most commonly), but also skin ulcers, vesicles, papules, and subcutaneous nodules have all been seen in Wegener’s granulomatosis. However, we have not encountered a previous mention of splinter haemorrhages in this disease. ANCA is a sensitive and highly specific test for active Wegener’s granulomatosis (91% and 98%, respectively). The likelihood ratio of a positive test result was 33 and of a negative test result was 0.3. As in our patient, the antigenic specificity of ANCA in most patients with Wegener’s granulomatosis is antiproteinase 3, whereas most patients with other forms of small vessel vasculitis such as microscopic polyangitis or Churg-Strauss syndrome, have perinuclear ANCA antineutrophil cytoplasmic antibodies. Combined corticosteroids and low dose daily cyclophosphamide treatment have dramatically improved the survival of patients with Wegener’s granulomatosis whose mean survival is otherwise five months. Extended follow up of patients treated with this regimen indicate, however, that relapses are common and that treatment related adverse drug reactions, in particular an increase in malignancies, is also a significant problem. Thus, in patients like ours, who do not have a life threatening disease, substituting cyclophosphamide for methotrexate and later adding co-trimoxazole for the prevention of relapses, might prove worthwhile.
Learning points

- Cholesterol embolisation is a clinical condition occurring after cardiac catheterisation.
- Livedo reticularis is the most common skin manifestation followed by gangrene, cyanosis, and ulceration.
- Eosinophilia, eosinophiluria, raised sedimentation rate, and decreased complement levels may support its diagnosis. The final diagnosis is only established with biopsy.
- It should always be considered in an elderly patient with cutaneous lesions and acute renal failure after an invasive procedure.

Final diagnosis

Cholesterol crystal embolisation.

The authors would like to thank the staff of the library and the research and development department, King George Hospital.

Breathlessness after percutaneous biliary drainage

Q1: What is the most likely cause of her jaundice and why was this suspected clinically?
Bile duct obstruction by a pancreatic tumour is suggested from the history of painless progressive jaundice associated with weight loss. Furthermore in the presence of jaundice and a palpable gallbladder, Courvoisier’s law* states that the diagnosis is unlikely to be due to cholelithiasis because previous cholecystitis would have caused fibrosis and shrinkage of the gallbladder (the only exception being the presence of simultaneous stones in both the common bile duct and cystic duct). A tumour of the pancreatic head was confirmed on abdominal computed tomography.

Q2: What complication of PTC has occurred?
The thoracic radiograph (see p 787) showed the presence of fluid in the right pleural cavity. The pleural aspirate was bile stained suggesting an iatrogenic biliary pleural fistula; this is a rare complication of PTC. It results from the inadvertent passage of the cholangiography needle through the costodiaphragmatic recess of the pleural cavity and into the liver thus creating an abnormal communication between the two. The pleural cavity provides a low pressure, low impedance reservoir for the drainage of bile from the high pressure obstructed biliary tree.

Q3: What is the treatment of this complication?
In the absence of distal biliary obstruction, spontaneous closure of the fistula may be achieved with several weeks of percutaneous biliary drainage. Octreotide, a somatostatin analogue that suppresses gastrointestinal secretion by inhibiting the release of pancreatic and gastrointestinal hormones, may be given as an adjunct to reduce biliary output. However, early active intervention has been suggested for this complication if the biliary tree remains obstructed and may involve:

- Surgery with the aim of relieving the bile duct obstruction. This may require a biliary enteric anastomosis, excision of the fistulous tract, repair of the diaphragmatic defect, and drainage of the subphrenic space. In a series of 15 patients treated surgically, all had resolution of symptoms with no postoperative mortality.
- Combined endoscopic percutaneous techniques to decompress the common bile duct and the re-establishment of normal bile flow either by biliary stent placement, sphincterotomy, or balloon dilatation thus allowing the biliary pleural fistula to heal spontaneously. All reported cases have been successfully treated by these techniques but due to the rarity of the condition, there has been no large series comparing outcome with surgery. Management should also include parental nutrition, correction of electrolyte abnormalities with particular attention to possible hyponatraemia due to the loss of the sodium in the bile, chest physiotherapy, and treatment of sepsis with intravenous antibiotics.

Discussion
PTC provides direct access to the proximal bile tree when ERCP has failed. In this case, PTC was performed to relieve biliary pressure resulting from an obstructed stent. In experienced hands PTC is relatively safe since dilated ducts are easily punctured percutaneously, enabling excellent visualisation of the upper biliary tree. However, complications occur in up to 69% of patients, with cholangitis occurring in 47%, haemobilia in 7%, and biliary pleural fistula in 2.5%.

A biliary pleural fistula may be a congenital abnormality or it may be secondary to thoracoabdominal trauma, suppurative complications of biliary tract obstruction, or parasitic liver infections. Diagnosis is confirmed either by aspiration of bile from the pleural space or cholangiography demonstrating the fistulous tract. Biliary pleural fistulas are usually associated with a high morbidity and mortality because of the risk of biliary mediastinitis and sepsis, from which this patient subsequently succumbed. Early diagnosis with prompt correction of the biliary obstruction is therefore required for the management of this rare complication.

Final diagnosis
Biliary pleural fistula.

Episodic weakness in a young woman

Q1: What is the metabolic abnormality?
Hypokalaemic metabolic alkalosis.

Q2: What are the differential diagnoses?
Barter’s syndrome; Gitelman’s syndrome; diuretic use; vomiting.

In this case, the history, the normal blood pressure, the presence of alkalosis, the presence of hypokalaemia between attacks, and a high

* Ludwig Georg Courvoisier (1843–1918) Professor of Surgery, Basle, Switzerland.
hour urine potassium excretion limits the possible diagnoses. These include Bartter's syndrome, Gitelman's syndrome, diuretic use, and vomiting. Figure 1 illustrates how we excluded the other possible diagnoses. Hypokalaemic periodic paralysis is characterised by recurrent attacks of paralysis and hypokalaemia with normal serum potassium concentration between attacks.

Q3: What investigations will help distinguish between the possible diagnoses?
Twenty four hour urinary chloride and calcium; serum magnesium; urine diuretic screen. Her urinary chloride was 142 mmol/24 hours and urinary calcium was 0.4 mmol/24 hours. Her serum magnesium was 0.5 mmol/l (0.7–1.0). A diuretic screen was negative.

Q4: What is the likely diagnosis?
Gitelman’s syndrome.

The high urinary chloride excludes vomiting as a potential cause. Vomiting results in hypochloreaemia as a result of loss of hydrochloric acid in gastric fluid. In this setting the combination of hypochloreaemia and hypovolaemia result in appropriate chloride retention by the kidneys, as a result urine chloride will be low. The urinary chloride concentration can be misleading in patients taking diuretics, if the diuretic effect has worn off the concentration will be low, if the diuretic is still acting the urine chloride concentration will be high.

The high urinary chloride concentration suggests continued diuretic ingestion, Bartter’s syndrome, or Gitelman’s syndrome. The low urinary calcium excludes the diagnosis of Bartter’s syndrome and loop diuretic use. The combination of the low urine calcium and low serum magnesium makes the diagnosis of Gitelman’s syndrome or thiazide diuretic use more likely. Gitelman’s syndrome can often be diagnosed only after repeated urine samples for diuretic use.

It is important to remember that there are no “fixed normal” values for urine electrolytes, the kidney varies the rate of excretion to match dietary intake.

Discussion
Hypokalaemia is a common clinical problem. It is often serious and can be life threatening, with cardiac arrhythmias and paralysis as the most serious complications. Potassium enters the body in the diet, or in the form of an oral or intravenous drug; 98% of the total body potassium is intracellular. It is excreted by the kidneys with only small amounts lost via the intestine and skin.

Hypokalaemia, therefore, can only be caused by decreased intake, movement into cells, or...
increased loss of potassium. Decreased oral intake is an unusual cause of hypokalaemia, reduced intake is more often seen in hospital with incorrect intravenous replacement of potassium in patients who are taking nil by mouth. Movement of potassium into the cells can be the result of alkalosis, treatment of pernicious anaemia and other conditions with rapid turnover of cells, barium toxicity, and hypokalaemic periodic paralysis. The causes of potassium loss are highlighted in fig 1. Taking a careful history will often reveal the diagnosis. If the diagnosis is still in doubt, measurement of blood pressure, acid-base status, and urinary potassium are invaluable.

The normal renal response to hypokalaemia is to retain potassium. A high urinary potassium in the presence of hypokalaemia suggests the kidneys are the problem. If in doubt as to whether the cause is renal or extrarenal, measurement of the transtubular potassium gradient (TTKG) can help.1 The TTKG is a semiquantitative index of the activity of potassium secretion from the distal convoluted tubule and the cortical collecting duct.

The TTKG is defined as:

$$\text{TTKG} = \frac{\text{potassium}_{\text{urine}}/\text{urine}_{\text{osm}}/\text{plasma}_{\text{osm}}}{\text{potassium}_{\text{serum}}}$$

In the presence of hypokalaemia a TTKG <2 suggests extrarenal loss, whereas a TTKG >2 suggest a renal cause.

**Gitelman’s syndrome and Bartter’s syndrome**

Gitelman’s syndrome and Bartter’s syndrome are usually autosomal recessive diseases. Both are caused by defects in renal tubular function.2 3 The tubular defects are similar to those caused by thiazide and loop diuretics respectively. Both syndromes cause hypokalaemia, metabolic alkalosis, hyper-reninaemia, and hyperaldosteronism. The differences are highlighted in table 1.4 In Bartter’s syndrome, proton secretion from the distal convoluted tubule and the cortical collecting duct.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Bartter’s syndrome and Gitelman’s syndrome: distinguishing features between the two conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Early in life</td>
</tr>
<tr>
<td>Urinary calcium</td>
<td>High</td>
</tr>
<tr>
<td>Serum magnesium</td>
<td>Generally normal</td>
</tr>
<tr>
<td>Site of tubular defect</td>
<td>Ascending limb of the loop of Henle</td>
</tr>
<tr>
<td>Tubular defect</td>
<td>Loop diuretic sensitive sodium-potassium-chloride cotransporter</td>
</tr>
<tr>
<td>Concentrating ability</td>
<td>Impaired</td>
</tr>
<tr>
<td>Renal excretion of prostaglandins</td>
<td>Increased</td>
</tr>
<tr>
<td>Bartter’s syndrome</td>
<td>Late childhood/adulthood</td>
</tr>
<tr>
<td>Gitelman’s syndrome</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Low/normal</td>
</tr>
<tr>
<td></td>
<td>Distal tubule</td>
</tr>
<tr>
<td></td>
<td>Thiazide sensitive sodium-chloride cotransporter</td>
</tr>
<tr>
<td></td>
<td>Maintained</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
</tr>
</tbody>
</table>


From cutaneous ulceration to chronic diarrhoea

**Q1: What is the skin lesion shown in fig 1 (see p 788)?** Pyoderma gangrenosum.

**Q2: What is the gastrointestinal diagnosis?** Crohn’s disease.

**Q3: What other skin lesions are associated with this disease?** Erythema nodosum is the commonest dermatological manifestation of Crohn’s disease. Sweet’s syndrome (acute pyrexial neutrophilic dermatosis) is a rare complication and may
represent a form of pyoderma gangrenosum. Psoriasis is also over-represented in Crohn’s patients.

Discussion
Pyoderma gangrenosum is a rare condition characterised by the development of painful erythematous nodules with central blue discoloration that rapidly enlarge and develop central ulceration. These ulcers typically have thickened, purple edges which may become irregular and undermined. Extensive lesions can develop at any site but there is a predilection for areas of previous minor trauma (pathergy), the calves, thighs, buttocks, and face. There are no pathognomonic histological changes but areas of ulceration are typically associated with a neutrophil-rich infiltrate of the dermis and a lymphocytic or leucocytoclastic vasculitis. Venous thrombosis with secondary infarction and haemorrhage is common.

Pyoderma gangrenosum occurs in isolation in 45% of cases where it tends to have a female preponderance. However, in the majority of cases there is an association with either an inflammatory, haematological, or neoplastic process (box 1). Although its pathogenesis remains unclear a defective immune response seems likely based on its associations, the reported abnormalities in the type 4 contact hypersensitivity, the presence of a vasculitis on biopsy and its response to immunosuppressants. Indeed, it has been suggested that the immune complex mediated vasculitis is of primary pathological importance.

Pyoderma gangrenosum occurs in about 2% of cases of inflammatory bowel disease (IBD) and is more likely to complicate ulcerative colitis than Crohn’s disease. It has generally been reported that pyoderma gangrenosum reflects the activity of the underlying IBD, but there is increasing evidence that this is not the case; skin lesions occur when the disease is in remission and resection of the inflamed bowel may not alter pyoderma gangrenosum activity.

Pyoderma gangrenosum may therefore be an associated disease rather than a complication of IBD. This is supported by our observation of pyoderma gangrenosum presenting two years before the clinical development of Crohn’s disease in this case.

Pyoderma gangrenosum associated with neoplastic or inflammatory conditions usually responds to treatment aimed at the underlying disease. In idiopathic pyoderma gangrenosum there are no published randomised controlled trials so treatment remains empirical. High dose systemic steroids are generally used but may be required for long periods for complete healing and are not always effective. Concomitant immunosuppressive therapy with azathioprine or cyclosporin may be effective in some cases and there are several positive reports on alternatives therapies including salazopyrine, clofazimine, hyperbaric oxygen, and heparin.

In all cases underlying infections should be excluded. Local treatments are generally aimed at keeping the ulcers clean, although topical therapies including steroids, cyclosporin, and sodium cromoglycate have been suggested.

Peristomal pyoderma gangrenosum is an uncommon complication of surgically treated IBD and is particularly difficult to manage as surgical debridement and stoma revision are universally unsuccessful. In such cases meticulous wound care and prolonged medical therapy with immunosuppressants are the treatments of choice.

Final diagnosis
Pyoderma gangrenosum and Crohn’s disease.

Multiple small opacities of metallic density in the lung

Q1: What is the likely diagnosis?
This is a case of metallic mercury embolism, after intravenous self administration of metallic mercury by the patient, who is a chemist, with suicidal intent.

Q2: What is the differential diagnosis?
In most reported cases, the presence of metallic mercury in the tissues was demonstrated by radiography, the metal being either at the site of introduction or in the form of emboli in the lung. The chest radiographs of patients with pulmonary mercury emboli are striking and reveal numerous abnormal metallic densities scattered throughout both lungs, mostly in the periphery. However HRCT findings have been described only in a few cases. HRCT of the thorax in this patient revealed multiple hyperdense foci clustered in the periphery of both lungs, more so in the lower zones; similar hyperdensities were also seen in the right ventricular apex. The diagnosis of mercury emboli is suggested by the density, size, and characteristic spherical shape of the mercury droplets. Pulmonary emboli occurring after lymphangiography or hysterosalpingography exhibit a diffuse haziness and are less dense. The presence of a spurted barium or bronchography contrast media may be diagnosed by their more linear nature, by review of previous radiographs, and by clinical history. Distinguishing between pulmonary emboli and aspired intrabronchial mercury may be the most difficult. The presence of intraintestinal mercury suggests mercury aspiration. Identification of associated intracardiac mercury and mercury in the abdominal vessels and subcutaneous tissue of the extremities would indicate a diagnosis of mercury embolisation.

Discussion
Mercury embolisation of the lungs is rarely reported. Pulmonary embolisation may be
accidental or intentional—accidently from injury from a broken thermometer or from venous blood sampling with mercury sealed syringe, and intentionally from injection by drug abusers “for kicks”, or with suicidal intent. This patient tried to commit suicide by injecting metallic mercury (2.5 ml) from a broken thermometer, five days before admission. The metal reaches the right ventricle and is disseminated throughout the pulmonary tree. Roentgenographically, the appearance is distinctive because of the very high density of mercury, in the form of bilateral spherules or tinctive because of the very high density of metallic mercury. 5 Multiple metallic densities in the lungs suggest mercury emboli as well as aspiration. Radiographic examination of possible injection sites and detailed history and evaluation of the chest, abdomen, and extremities can provide important evidence of intravenous administration. The presence of mercury in the right ventricle strongly suggests intravenous embolisation. Metallic mercury causes local chronic inflammation, however mercurialism—the clinical syndrome associated with mercury salt intoxication—has not been reported commonly with elemental mercury injection hence treatment with chelating agents such as dimercaprol (British antilewisite) and penicillamine is usually not warranted, as in this patient. Metallic mercury in the tissues is thought to undergo slow biological oxidation and may remain unchanged on chest radiography up to one year after injection, disappearing gradually.

Final diagnosis
Metabolic mercury pulmonary embolism.

Q2: Give possible differential diagnoses of an abduction deficit

An abduction deficit can be caused by muscle disorders, neuromuscular junction, cranial nerves, and brainstem lesions (box 1). Although the diagnosis of sixth nerve palsy is often made without the consideration of other causes, abduction paresis less commonly arises from myasthenia gravis, Duane’s syndrome, convergence spasm, congenital esotropia, and INO. The absence of esotropia when the eyes are fixated in the primary position makes the diagnosis of sixth nerve palsy unlikely. In Duane’s syndrome, there is usually globe retraction and palpebral fissure narrowing on attempted adduction. Convergence spasm is characterised by intermittent and usually painless convergence and miosis. In INO, nystagmus is often seen in the abducting eye, possibly as a result of altered inhibitory input to the lateral rectus muscle. INO can be categorised into posterior and classic INO. The latter condition is characterised by an addition deficit with intact abduction. Myasthenia gravis may present as an isolated abduction deficit. The key to the neuromuscular nature of an abduction deficit is ptosis and an end-of-day fatigability. A tension test should be undertaken if there is any suggestion of myasthenia gravis.

Box 1: Causes of abduction deficit
- Muscle: myopathy and restrictive syndromes.
- Neuromuscular junction: myasthenia gravis.
- Cranial nerves: sixth nerve palsy.
- Brainstem: internuclear ophthalmoplegia, Duane’s syndrome.
- Other causes: convergence spasm, congenital esotropia.

Q3: How would you manage a patient with an abduction deficit?

Based on the information above, it is obvious that the evaluation of a patient with abduction deficit demands a thorough description of the ocular movement and function to determine the diagnosis. Once the mechanism of an abduction deficit has been established, a complete neurological evaluation should be meticulously carried out to search for evidence of an intracranial lesion. In children and adolescents, central nervous system infection, brain tumour, and head injury account for the majority of abduction disorders. Therefore, these patients should have a full clinical examination, and be investigated and treated appropriately.

Discussion
Horizontal gaze is mediated by the neurons in the region of the para-abducens nuclear group via the medial longitudinal fasciculus. The presence of lateral gaze palsy without cranial nerve, muscular, and neuromuscular involvement should indicate involvement of the brainstem internuclear pathways leading to INO.

Unusual cause of an abduction deficit in a 14 year old girl

Q1: What is the most likely diagnosis?
The most likely diagnosis is internuclear ophthalmoplegia (INO) of abduction or so-called posterior INO. In this case, the presence of cerebellar signs, neuroradiological findings, and cerebrospinal abnormalities with a history of transient upper respiratory tract infection suggests a diagnosis of acute encephalitis.
The description of INO of abduction goes back to Lutz in 1923, though we have found no report of it in childhood. This patient’s illness fulfilled the criteria for this condition in that she had an impaired abduction of the left eye and abduction nystagmus of the contralateral eye. In this case, insufficient vestibulocular reflex and slow saccades in the paretic eye suggest a lesion of the paraabducens region. In addition, MRI revealed multiple lesions located in the lower pons at the level of the paramedian pontine reticular formation and abducens nucleus. In all levels of pontine lesions some degree of cerebellar involvement will usually be found. In this patient, cerebellar dysfunction was evident with ataxic gait, dysmetria, and slurred speech.

Conclusive laboratory diagnosis of the cause of infective encephalitis can be very difficult. In this patient, the clinical course, biochemical, neuroradiological, and electroencephalography findings with a history of transient upper respiratory tract infection suggested the diagnosis of acute encephalitis. However, serological evidence of common infective agents was absent.

Although, the pathogenesis of INO of abduction remains uncertain, we suggest that in our patient an immune mechanism due to a transient inflammatory process led to a lesion and dysfunction of the para-abducens region in the pons. In conclusion, with knowledge of the neurophysiology of the ocular movements, a careful evaluation of each patient with an abduction deficit should alert the examiner to the appropriate diagnostic work-up.

Final diagnosis

Internuclear ophthalmoplegia of abduction.


An unusual cause of acute bacterial meningitis

Q1: What is the lesion shown on the magnetic resonance imaging scan (see p 791)?
The scan shows a large pituitary tumour (>10 mm diameter: macroadenoma) extending laterally into the cavernous sinus.

Q2: How does this usually present?
Clinical presentation varies according to the age and sex of the patient and with size of the tumour. In the majority of premenopausal women, the lesion is usually a microadenoma and presents with menstrual abnormalities, infertility, or galactorrhoea. In postmenopausal women and men, pituitary tumours are mostly slow growing lesions that present neurologically with headache or visual field defects; classically bitemporal hemianopia due to compression of the optic chiasm. In men there may be signs of partial or complete hypogonadism. These macroadenomas may enlarge and become locally invasive with extrasellar extension into the cavernous sinus resulting in ophthalmoplegia. A large tumour may compress normal pituitary tissue and cause disturbance in the secretion of other pituitary hormones.1

Giant macroadenomas (several cm in diameter) are rare, usually show evidence of extrasellar extension on computed tomography, and are difficult to treat.

Q3: How may this condition present with meningitis?

Pituitary tumours may present with meningeal irritation in a number of ways. Pituitary infarction or haemorrhage (apoplexy) is characterised by sudden onset drowsiness, headache, diplopia, and meningism. Rarely, it may be the presenting feature of an underlying asymptomatic tumour, or the complication of a known lesion. These symptoms usually merit lumbar puncture, to exclude the clinical suspicion of infection, and can reveal a sterile and often lymphocytic response.2–4

It is rare that bacterial meningitis is the presenting condition in a patient with an underlying pituitary adenoma. Bacterial infection, however, may rarely complicate and follow pituitary microsurgery.5 For lesions invading or eroding into surrounding areas such as the sphenoid sinus, the resulting skull base defect and CSF leak can act as an entry portal for organisms such as Streptococcus pneumoniae predisposing to meningitis.4–6 Two published reports of fatal bacterial meningitis, one with S pneumoniae, were discovered to have an underlying invading pituitary tumour at postmortem examination.6–8

Q4: What is the treatment of the underlying lesion?

Dopamine agonist drugs such as bromocriptine usually lower prolactin concentrations, reduce tumour size, and reduce the degree of complications. Most patients require long term treatment and withdrawal may result in tumour expansion and rising prolactin concentrations. In giant macroadenomas, bromocriptine therapy alone is often inadequate and surgical intervention may be required.4 Treatment with bromocriptine, resulting in tumour regression, can be complicated by the appearance of skull base defects causing CSF rhinorrhoea and even pneumocephalus.6–11 Occasionally, extensive CSF rhinorrhoea has required lumbarperitoneal shunting or surgical repair.

Our patient was started on depot testosterone injections and bromocriptine therapy and transsphenoidal resection of the lesion was performed. He remains well with normal biochemistry values.
Q5: What are the causes of hyperprolactinaemia?

The causes of hyperprolactinaemia are:

1. **Hypothalamic diseases**
   - Tumour: metastasis, craniopharyngioma, glioma.
   - Infiltration: sarcoidosis, tuberculosis, granuloma.
   - Cranial irradiation.
   - Pseudotumour cerebri.

2. **Pituitary diseases**
   - Tumours: prolactinoma, adenoma, meningioma, metastases.
   - Acromegaly.
   - Cushing’s disease.
   - Infiltration: sarcoidosis, tuberculosis.

3. **Drugs**
   - Dopamine antagonists: chlorpromazine, metoclopramide.
   - Cimetidine.
   - Opiates.
   - Oestrogens.
   - Antihypertensives: verapamil, methyldopa.

4. **Metabolic**
   - Hypothyroidism.
   - Chronic renal failure.
   - Liver cirrhosis.

5. **Stress**

Final diagnosis

Macroprolactinoma with extrasellar extension.

Episodic weakness in a young woman

Postgrad Med J 2001 77: 792
doi: 10.1136/pmj.77.914.792c

Updated information and services can be found at:
http://pmj.bmj.com/content/77/914/792.4

These include:

References
This article cites 4 articles, 0 of which you can access for free at:
http://pmj.bmj.com/content/77/914/792.4#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/