

Figure 2 Axial T1-weighted MRI of the neck with contrast enhancement

Questions

- 1 What do the MR images show?
- 2 What are the possible diagnoses?
- 3 What further investigations are required to confirm the diagnosis?

Answers

QUESTION 1

Sagittal T1-weighted MRI scans of the neck (figure 1) show extradural compression of the cervical cord from the level of the second (C2) to sixth (C6) cervical vertebrae. The axial images show that the dura at these levels is markedly thickened (particularly at the left posterolateral aspect of the cord) and enhances after gadolinium injection (figure 2). The C4, C5 and C6 vertebral bodies show low signal intensity on the sagittal MRI (figure 1A) that enhances with gadolinium (figure 1B); patchy enhancement is also evident within the cord. The discs appear intact and there was no vertebral collapse. The MRI findings confirm involvement of the vertebral bodies, dural and spinal cord extending from the C2 to C6 vertebrae level.

QUESTION 2

The possible diagnoses for the neurological lesions include tuberculosis or lymphoma. The radiological findings are not compatible with an abscess or haematoma. The patient's unexplained fever, night sweats and weight loss are consistent with the constitutional symptoms of tuberculosis or non-Hodgkin's lymphomas (NHL). In developing countries tuberculosis of the central nervous system (CNS) is the most common type of subacute CNS infection and is a disease of younger age group, usually childhood. The meninges, brain, or spinal cord may all be affected, either individually or in various combinations. The spine is involved in less than 1% of patients with only 10% affecting the cervical segments and there is often

Learning points

- the absence of pancytopenia or leucoerythroblastic change does not exclude significant bone marrow infiltration
- bone marrow examination remains an important diagnostic tool when the diagnosis of lymphoma is clinically suspected
- NHL patients with CNS disease at presentation often have marrow involvement and typically have aggressive histology
- NHL in children often grows rapidly, therefore metastatic disease at the time of first presentation is common
- in NHL, the spleen may be clinically and radiologically normal in the presence of widespread disease
- hospitalisation more than a week after the development of tetraparesis with sphincter dysfunction invariably results in permanent neurological sequelae
- rapidly evolving tetraparesis or paraparesis represents a neurological emergency; early treatment is critical to restore full neurological function

destruction of the intervening disc spaces. Spinal cord and meningeal involvement are relatively common neurological complications of NHL with spinal cord segments C5 to T8 being most commonly affected.

QUESTION 3

The main investigations will include a detailed work-up for tuberculosis and lymphoma. The Mantoux test was non-reactive and sputum and urine examinations were negative for acid-fast bacilli. Cerebrospinal fluid analysis was unremarkable. CT of the abdomen showed numerous hypodense lesions in the liver, pancreas and kidneys. The bowel wall appeared thickened and there were masses in the para-aortic region (figure 3). The spleen was not enlarged and was free of lesion. CT of the brain and thorax were normal. Biopsy for histological diagnosis is essential in this case. The histology of the lesions in the liver, para-aortic masses and the bone marrow aspirate (figure 4) was consistent with Burkitt's lymphoma and negative for tuberculosis. HIV antibodies were negative. Serology, culture and molecular studies to detect concomitant tuberculous infection were negative.

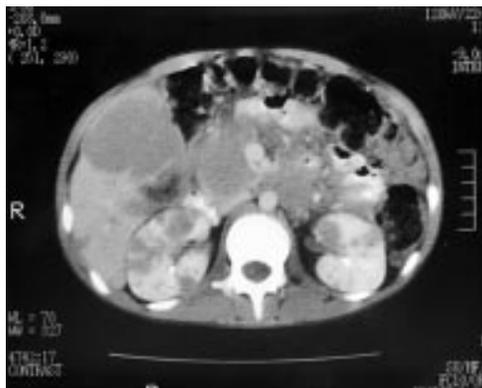


Figure 3 CT of the abdomen

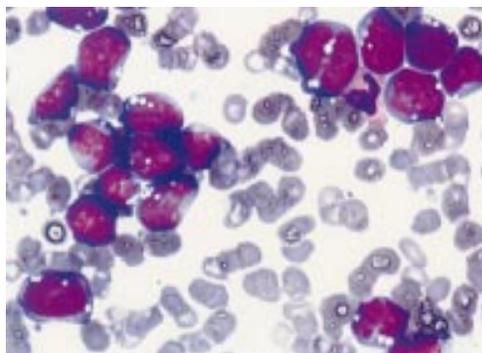


Figure 4 Aspirate of the bone marrow shows that abnormal mononuclear cells heavily infiltrate the marrow. The cells are large and uniform in appearance with strongly basophilic vacuolated cytoplasm and cleft or folded nuclei. The immunophenotyping studies were positive for B cell. (May-Grunwald-Giemsa, orig $\times 400$)

Discussion

CNS lymphoma can be primary or secondary. Secondary CNS involvement has been reported in 5–12% of patients with NHL and in up to 30% of those with high-grade NHL.¹ The histological type of NHL is the most significant risk factor for secondary CNS involvement. The highest incidence is observed in patients with lymphoblastic or sporadic Burkitt's lymphoma.² Other factors that may increase the risk of CNS involvement are the presence of an underlying immune deficiency, age below 40 years, and other extranodal sites (especially bone marrow, bone or testis).² Lymphoma can cause neurologic symptoms in various ways. It

can infiltrate the meninges or brain parenchyma and metastasize to bone or infiltrate the epidural space via the intervertebral foramina to cause neurologic dysfunction by compressing adjacent CNS structures. Direct CNS invasion by lymphoma is associated with short survival despite intensive therapy.³ Neurologic dysfunction may develop as a result of infections that occur secondary to immunosuppression, or paraneoplastic syndromes.

Burkitt's lymphoma is an aggressive, rapidly dividing B-cell lymphoma most commonly seen in children. The staging evaluation should be considered a medical emergency, and the patient should receive chemotherapy within 48 to 72 hours after establishing the diagnosis. In the majority of patients, the peripheral blood shows no abnormality. Even when the bone marrow is heavily infiltrated, circulating lymphoma cells are present in less than half of the patients. Among patients with Burkitt's lymphoma,⁴ CNS disease at the time of

diagnosis is associated with the greatest risk of treatment failure. The clinical condition at the onset of treatment is the most important prognostic indicator. The likelihood that decompressive surgery and radiation for spinal metastasis will restore neurological function is minimized if the patients had total weakness of more than 12 hours duration, sphincter loss of more than 24 hours duration, major sensory loss, and uncontrolled metastatic disease elsewhere.⁵

Our patient underwent a laminectomy and received intensive chemotherapy with no improvement in the neurological status. Two weeks after initiation of chemotherapy, he died of neutropenic sepsis.

Final diagnosis

Stage IV Burkitt's lymphoma.

Keywords: tetraparesis; Burkitt's lymphoma

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Hyperthyroidism in an elderly patient

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A 72-year-old woman presented with a 3-day history of increasing breathlessness on effort, orthopnoea, and nocturnal dyspnoea in the absence of chest pain or haemoptysis. She was a life-long smoker of 10 cigarettes per day but her medical history was otherwise without note and she was not taking any regular medication. On examination she was thin, neither anaemic nor clubbed and was clinically euthyroid. The pulse was 150 beats/min, blood pressure 130/90 mmHg. There were signs of biventricular failure with a raised venous pressure, bilateral ankle oedema, bibasal crackles and a left pleural effusion. A 3/6 pan systolic murmur was audible at the cardiac apex with radiation to the left axilla. Routine blood tests, including thyroid function tests, were normal apart from a mild derangement in liver function tests consistent with hepatic congestion. An electrocardiogram revealed atrial flutter with a 2 : 1 AV block and a chest X-ray was consistent with cardiac failure. A subsequent echocardiogram confirmed a dilated cardiomyopathy, severe mitral regurgitation, secondary tricuspid regurgitation and a globally reduced cardiac output. A small pericardial effusion was also noted.

The patient was treated along standard lines with diuretics and an angiotensin-converting enzyme (ACE) inhibitor, and in view of the dilated cardiomyopathy was anticoagulated with warfarin. She was digitalised but the ventricular rate was inadequately controlled with digoxin and amiodarone was introduced. She remained well until she sustained a fall and was admitted to hospital 6 months later. At that time she was clinically euthyroid but routine thyroid function testing revealed a suppressed thyroid-stimulating hormone (TSH) < 0.1 mU/l (normal range 0.35-3.3 mU/l), and a raised thyroxine (T4) of 31 pmol/l (10-25). The auto-antibody profile was negative and a thyroid uptake scan showed reduced uptake at 4.4% (0-35).

Questions

- 1 What is the probable diagnosis?
- 2 How can the condition be treated?

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Answers

QUESTION 1

The probable diagnosis is amiodarone-induced hyperthyroidism.

QUESTION 2

The medical treatment is with carbimazole, and, if clinically indicated, with beta-blockers. In some cases, surgical intervention with total or sub-total thyroidectomy may be preferred.

Discussion

Amiodarone is a Class III anti-arrhythmic agent which is used in the treatment of serious ventricular arrhythmias, paroxysmal supraventricular arrhythmias, atrial flutter and fibrillation. In addition, it may reduce complex ventricular arrhythmias and mortality following acute myocardial infarction and may improve survival in patients with advanced cardiac failure. Amiodarone has a number of well known side-effects (box 1) and can interfere with thyroid function as in this case.

Amiodarone is an iodine-rich benzofuran derivative and 37% of the drug is organic iodine. A maintenance dose of 200–600 mg/day results in a daily intake of organic iodide of between 75 to 225 mg, at least 10% of which is deiodinated to yield free iodine.¹ Since the normal daily requirement of iodine is 0.2–0.8 mg/day,² treatment of any patient with amiodarone results in a massive expansion of the iodide pool which consequently affects thyroid physiology in a variety of ways. Peripheral deiodination of T4 to triiodothyronine (T3) is reduced by enzyme inhibition,³ with a resultant increase in both serum T4 and reverse T3 and a decrease in the serum T3, analogous to a sick euthyroid state. Peripheral uptake of both T4 and T3 is also directly inhibited by amiodarone. Consequently there is a temporary rise in TSH levels which typically return to normal within 3 months. These are expected findings and do not equate with a hyperthyroid state.

The incidence of amiodarone-induced thyroid dysfunction is estimated to be between 2–24%.⁴ Thyrotoxicosis is prevalent in areas with low iodine intake, while hypothyroidism is found typically in areas with a high iodine intake. Thus, amiodarone-induced thyrotoxicosis results from over-production of thyroid hormone induced by iodine. Other mechanisms have been proposed with regard to the pathogenesis of this condition and include a direct cytotoxic effect of amiodarone on the thyroid follicles resulting in destructive changes and an outpouring of iodothyronines. The typical biochemical findings are, therefore, a low TSH, and a high free T4 and free T3.

Although the clinical features may present in a classical fashion with unexplained weight loss, muscle weakness, goitre, and tremor, the features may equally be muted and present in less obvious guises such as increased frequency

Side-effects of amiodarone

- hyper-/hypothyroidism
- photosensitivity
- corneal microdeposits
- pulmonary toxicity
- hepatotoxicity
- peripheral neuropathy
- drug interactions

Box 1

of angina or an unexplained tachyarrhythmia. Thyrotoxicosis can occur throughout the period during which a patient is receiving amiodarone and may be induced even after the cessation of therapy, since the drug has a long half-life.

The treatment of amiodarone-induced hyperthyroidism involves several issues. Consideration should always be given to the option of stopping the drug itself. Clearly this is a clinical decision based on the original indication for the treatment and the merits, or otherwise, of stopping treatment. It is important to be aware, however, that even if treatment is discontinued thyrotoxicosis can take up to 8 months to subside.

The medical treatment of amiodarone-induced hyperthyroidism typically involves carbimazole and beta-blockers. Some sources claim that the use of potassium perchlorate to obtain a prompt release of intrathyroidal iodine, in concert with antithyroid drugs, can achieve a euthyroid state within 90 days.⁵

Controlling amiodarone-induced thyrotoxicosis with medical treatment takes several weeks to be effective and side-effects of drug therapy have to be screened for. In addition, many patients with this condition will have amiodarone discontinued. If this is not an option, or indeed if faster control of the thyrotoxic state is required, surgical intervention with total or sub-total thyroidectomy may be favoured.

Radioactive iodine would not be beneficial since the uptake of radioactive iodine is suppressed by the high iodide concentration resulting from amiodarone therapy.

In summary, treatment with amiodarone can affect thyroid function in a variety of ways. In up to a quarter of patients, clinically relevant thyroid dysfunction results. Therapeutic options include cessation of amiodarone therapy, surgical intervention, if rapid control is required of a thyrotoxic state, or medical treatment. Radioiodine treatment is not an option in amiodarone-induced thyrotoxicosis.

Final diagnosis

Amiodarone-induced thyrotoxicosis.

Keywords: thyrotoxicosis; amiodarone; adverse drug reaction; iodine metabolism

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A case of intestinal obstruction

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A 66-year-old woman was referred with a 2-month history of increasing abdominal pains which were central, colicky and associated with abdominal distension. Her symptoms were worse after food. Over this period she had also developed loose stools 2-3 times per day. She denied weight loss. Medical history included psoriasis complicated by a small joint arthropathy. There had been no previous abdominal surgery and she was taking prescribed slow-release diclofenac and sulphasalazine. On examination she was anaemic with a psoriatic rash on her elbows and shins. The distal interphalangeal joints were deformed. The abdomen was distended, more so on the right, but there were no palpable masses or organomegaly. Bowel sounds were normal. Investigations revealed an iron deficiency anaemia (haemoglobin 8.6 g/dl) and low serum albumin (29 g/dl). Other tests of liver function were normal as were inflammatory markers. An upper gastrointestinal endoscopy and duodenal biopsies were normal. A colonoscopy was performed and three strictures were found in the transverse colon, the most proximal of which could not be passed (figure).

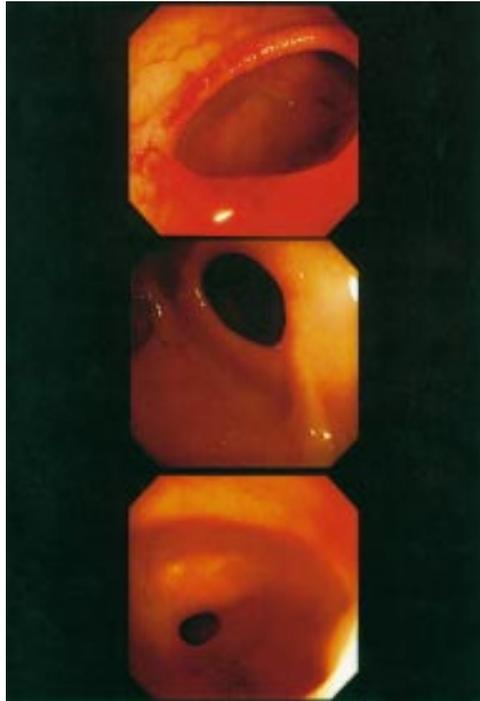


Figure Colonoscopic appearances of the ascending colon.

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Questions

- 1 What do the pictures taken at colonoscopy show?
- 2 What is the likely aetiology of such lesions?
- 3 What gastrointestinal diseases are associated with psoriasis?

Answers

QUESTION 1

The figures show smooth diaphragm-like strictures with linear ulceration of the inner rim.

QUESTION 2

These lesions are characteristically associated with non-steroidal anti-inflammatory drugs (NSAIDs).

QUESTION 3

Patients with Crohn's disease, and their first degree relatives, are more likely to develop psoriasis suggesting a genetic link. HLA B13, Bw58, Cw6 and DR7 are over-represented in both psoriasis and Crohn's disease. To a lesser extent, ulcerative colitis is associated with psoriasis.

Discussion

NSAIDs are a well known cause of intestinal ulceration, inflammation and haemorrhage. The commonest clinical side-effects occur in the stomach and duodenum but, in post-mortem studies, damage is most frequently observed in the small bowel.¹ NSAID enteropathy is usually asymptomatic but may result in hypoalbuminaemia and iron deficiency anaemia, which can be severe and refractory to oral supplementation. Rarely, such small bowel ulcers may heal by fibrosis with expansion of the submucosa myocytes resulting in thin diaphragm-like strictures. Such strictures pre-

dominate in the small bowel, but have been reported in the right colon in association with slow-release NSAID formulations.^{2,3} These observations, and the similarity between NSAID and potassium-induced strictures, suggest a local effect. However, there have been reports of diaphragms complicating rectal indomethacin in the absence of oral preparations.⁴ In such cases mucosal injury may be mediated via the systemic effects of NSAIDs on prostaglandin synthesis which results in increased mucosal permeability and translocation of luminal contents. The consequent inflammation is compounded by impaired repair mechanisms.

Clinical presentation of NSAID enteropathy varies from vague abdominal pains to symptoms of subacute obstruction as mucosal inflammation and ulceration repair with stricture formation.⁵ In the absence of symptomatic strictures, NSAID enteropathy has successfully been treated with metronidazole, sulphasalazine, 5-aminosalicylates and misoprostol. Symptomatic strictures require surgical resection. In this case symptoms resolved entirely on a low residue diet and cessation of diclofenac (sulphasalazine was continued).

Final diagnosis

NSAID-induced strictures in the transverse colon.

Keywords: non-steroidal anti-inflammatory drugs; intestinal obstruction; adverse drug reaction

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Isosexual precocity: uncommon presentation of a common disorder

A Bhansali, A Kashyap, S Lodha, N Kotwal, B Ganapathi, B R Mittal, R J Dash

A 7-year-old girl presented with bilateral symmetrical enlargement of breasts of one year duration and one episode of vaginal bleed in August 1996. She did not have history of seizure disorder, meningitic or encephalitic illness, head injury or administration of oestrogen-containing preparations. She was an active child and had good scholastic performance.

On examination, her height was 108 cm (< 3rd centile), weight 21 kg (10–25th centile) and bone age was 3 years. Her pubertal status (Tanner) was B₃A₁P₁ (figure 1). She had no goitre and her deep tendon reflexes showed delayed relaxation.



Questions

- 1 What is the diagnosis?
- 2 What investigations would you perform next?
- 3 How would you treat this case?

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Figure 1 Photograph showing short child with premature breast enlargement (reproduced with the parents' permission)

Answers

QUESTION 1

The diagnosis is juvenile hypothyroidism presenting with isosexual precocious puberty.

QUESTION 2

Serum thyroxine (T_4), thyroid-stimulating hormone (TSH), prolactin and thyroid scan are required to establish the diagnosis. Her serum T_4 was 10 ng/ml (normal 60–120 ng/ml), TSH 50 μ U/ml (0.5–5 μ U/ml), prolactin 20 ng/ml (6–25 ng/ml) and ^{99m}Tc thyroid scan revealed a lingual thyroid (figure 2). As a lingual thyroid is smaller in mass, it fails to compensate for the increasing need of a growing child and results in hypothyroidism.



Figure 2 ^{99m}Tc thyroid scan showing tracer uptake in lingual region only

QUESTION 3

After confirmation of diagnosis she was put on thyroxine replacement therapy in gradually increasing doses (25–100 μ g). She had ‘catch up’ growth, regression of breasts and no recurrence of menses in 18 months of follow-up with normalisation of serum TSH (0.25 μ U/ml).

Discussion

Isosexual precocity is a rare monosymptomatic manifestation of juvenile hypothyroidism and other presenting features are summarised in box 1.¹ This was first described by Van Wyk-Grumbach in a series of three cases who presented with premature thelarche, galactorrhoea and menarche.² In this disorder the pubertal events are associated with decelerated growth and retarded bone age. The exact cause of precocity in hypothyroidism is not clear.

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Monosymptomatic presentations of juvenile hypothyroidism

- short stature
- delayed puberty
- poor scholastic performance
- puberty menorrhagia
- isosexual precocity (Van Wyk-Grumbach syndrome)

Box 1

Learning points

- isosexual precocity is a monosymptomatic but rare presentation of juvenile hypothyroidism
- isosexual precocity with short stature and retarded bone age is a strong pointer towards diagnosis of thyroprivic hypothyroidism
- thyroxine therapy leads to complete arrest and regression of disorder

Box 2

Postulated mechanisms are ‘specificity spill-over’ which means positive feed-back effect of low serum thyroxine on pituitary gonadotropins as they are also glycoprotein hormones like TSH.² Hyperprolactinaemia,³ reduced gonadotropin clearance and decreased dopaminergic and opioid tone at the hypothalamo-pituitary axis⁴ are other plausible explanations. Elevated serum gonadotropins and oestradiol levels sometimes confuse the picture with gonadotropin-dependent precocious puberty (GDPP). However, this can be differentiated by the gonadotropin response to leutinising hormone releasing hormone (LHRH) which is present in GDPP but not in hypothyroidism-associated precocity.⁵ Our patient had normal prolactin (20 ng/ml) and elevated gonadotropins (leutinising hormone 6.5 IU/l, follicle-stimulating hormone 12.5 IU/l) and oestradiol (163 pmol/l) levels, however, her gonadotropin response to LHRH was prepubertal.

Thyroxine replacement therapy in optimal doses results in ‘catch up’ growth and complete arrest and regression of pubertal events.⁶

Final diagnosis

Juvenile thyroprivic hypothyroidism presenting as isosexual precocious puberty (Van Wyk-Grumbach syndrome).

Keywords: precocious puberty; juvenile hypothyroidism; lingual thyroid

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Calf hypertrophy following paralytic poliomyelitis

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A 41-year-old man developed an acute illness at the age of 9 months during which, following a viral illness with headache, he developed severe weakness and wasting of the limbs of the left side. After several months he began to recover, such that he was able to walk at the age of 2 years and later was able to run, although he was never very good at sports. He had stable function until the age of 18 when he began to notice greater than usual difficulty lifting heavy objects. By the age of 25 he was noticing progressive difficulty walking due to weakness of both legs, and he noticed that the right calf had become larger. The symptoms became more noticeable over the course of the next 10 years and ultimately both upper as well as both lower limbs had become noticeably weaker.

On examination there was wasting of the muscles of upper and lower limbs on the left, and massively hypertrophied gastrocnemius, soleus and tensor fascia late on the right. The calf circumference on the right exceeded that on the left by 10 cm (figure 1). The right shoulder girdle, triceps, thenar eminence and small muscles of the hand were wasted and there was winging of both scapulae. The right quadriceps was also wasted. The wasted muscles were also weak but the hypertrophied right ankle plantar flexors had normal power. The tendon reflexes were absent in the lower limbs and present in the upper limbs, although the right triceps was reduced. The remainder of the examination was normal.



Figure 1 The patient's legs, showing massive enlargement of the right calf and wasting on the left

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Questions

- 1 What is that nature of the acute illness in infancy?
- 2 What is the nature of the subsequent deterioration?
- 3 What investigations should be performed?
- 4 What is the differential diagnosis of the cause of the progressive calf hypertrophy?

Answers

QUESTION 1

An acute paralytic illness which follows symptoms of a viral infection with or without signs of meningitis is typical of poliomyelitis. Usually caused by one of the three polio viruses, it may also occur following vaccination and following infections with other enteroviruses.¹ Other disorders which would cause a similar syndrome but with upper motor neurone signs would include acute vascular lesions, meningoencephalitis and acute disseminated encephalomyelitis.

QUESTION 2

A progressive functional deterioration many years after paralytic poliomyelitis is well known, although its pathogenesis is not fully understood.² It is a diagnosis of exclusion; a careful search for alternative causes, for example, orthopaedic deformities such as osteoarthritis or worsening scoliosis, superimposed neurological disorders such as entrapment neuropathies or coincidental muscle disease or neuropathy, and general medical causes such as respiratory complications and endocrinopathies.³

QUESTION 3

Investigations revealed normal blood count and erythrocyte sedimentation rate and normal biochemistry apart from a raised creatine kinase at 330 IU/l (normal range 60–120 IU/l), which is commonly seen in cases of ongoing denervation. Electromyography showed evidence of denervation in the right APB and FDI with polyphasic motor units and complex repetitive discharges, no spontaneous activity in the left calf and large polyphasic units in the right calf consistent with chronic partial denervation. Motor and sensory conduction velocities were normal. A lumbar myelogram was normal. Magnetic resonance imaging (MRI) scan of the calves is shown in figure 2.

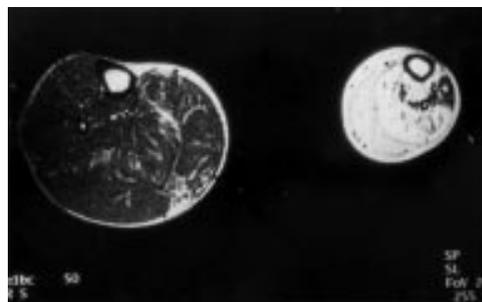


Figure 2 Axial T₁ weighted MRI scan (TR 588 ms, TE 15 ms) of the calves, showing gross muscle atrophy and replacement by adipose tissue on the left, and hypertrophy of the muscles on the right, with only minor adipose tissue deposition

QUESTION 4

The differential diagnosis of the progressive calf hypertrophy is given in the box.

Causes of calf muscle hypertrophy

Chronic partial denervation

- radiculopathy
- peripheral neuropathy
- hereditary motor and sensory neuropathy
- spinal muscular atrophy
- following paralytic poliomyelitis

Neuromyotonia and myokymia

- Isaac's syndrome
- generalised myokymia
- neurotonia
- continuous muscle fibre activity due to: chronic inflammatory demyelinating polyradiculopathy, Guillain Barre syndrome, myasthenia gravis, thymoma, thyrotoxicosis, thyroiditis

Muscular dystrophies

Myositis

Infiltration

- tumours
- amyloidosis
- cysticercosis

Discussion

Calf enlargement may occur due to muscle infection such as in cysticercosis,⁴ infiltration by tumour or amyloidosis⁵ or by inflammation, as in myositis.⁶ It is well known that it may occur in muscular dystrophies, particularly Duchenne and Becker types. True muscle hypertrophy has been shown to arise in a variety of neuromuscular disorders such as radiculopathy,^{7–10} peripheral neuropathy,^{12–14} spinal muscular atrophy^{15–17} and also in disorders of continuous muscle activity such as myotonia congenita, dystonia and Isaac's syndrome.^{18, 19} In these circumstances muscle biopsy has shown that there is hypertrophy and hyperplasia of both group I and group II muscle fibres.^{8, 10, 20, 21} There is both experimental and clinical evidence that group II fibre hypertrophy occurs in response to an increase in muscular work load,²² whilst group I fibre hypertrophy is thought to occur only when there is chronic partial denervation. Hence, following paralytic poliomyelitis in which there is chronic partial denervation with re-innervation, there may be group I fibre hypertrophy of muscles which are partially denervated due to muscle stretch and group II fibre hypertrophy in fibres with normal innervation which are exposed to greater work loads imposed by atrophy of other denervated fibres.

Three previous reports of patients with calf muscle enlargement following paralytic poliomyelitis have been described^{21, 23, 24}; this was attributed to deposition of adipose tissue without muscle hypertrophy in two cases. In this case we have provided MRI evidence that whilst fat infiltration of the denervated muscle had occurred, hypertrophy of residual muscle had taken place in the stronger leg, and this is likely to have caused the calf enlargement.

It would also appear that degenerative disease of the knee on the weaker side plays an important role, particularly *genu recurvatum*.

Progressive joint deformity has recently been implicated in the pathogenesis of late functional deterioration following previous paralytic poliomyelitis.³ This probably results in a greater than normal stress placed on the gastrocnemius on the other side in order that the patient may continue to walk, with the result that it hypertrophies.

Final diagnosis

Progressive functional deterioration after paralytic poliomyelitis.

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Keywords: poliomyelitis; late functional deterioration

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A healthy patient who suddenly developed a foot-drop

Gus Plaut

A 76-year-old man had taken up gardening. A few days after a particularly tiring day he suddenly developed a right-sided foot-drop. There were no other muscle weaknesses. He had not used chemical garden sprays. His medical history included treatment for asthma with inhaled steroids and a successful resection of the colon for carcinoma.

He was suspected to have a metastatic tumour in the upper sacral or lower lumbar region, affecting the sciatic nerve, and was referred to the local oncology clinic. X-Rays and an abdominal computed tomography scan showed no abnormality, apart from minor osteo-arthritis of the vertebral column.

Questions

- 1 What further investigations would you advise?
- 2 What is the likely diagnosis?
- 3 What treatment is indicated and what is the prognosis?

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Answers

QUESTION 1

A detailed history and physical examination should have preceded the request for investigations. The patient had knocked the lateral side of his knee while carrying a heavy rolled-up garden hose. No bruise developed at any time, and the discomfort from the injury subsided within 24 hours. Apart from the loss of dorsiflexion at the ankle, eversion of the foot and extension of the toes were reduced. There was an anaesthetic area on the dorsum of the foot. No other neurological signs were present.

QUESTION 2

The patient had injured the peroneal nerve (synonym: lateral popliteal nerve) at the point where it curves round the neck of the fibula. The sciatic nerve divides into medial and lateral popliteal nerves in the lower thigh. The lateral division or peroneal nerve then curves round the neck of the fibula, where it is only covered by subcutaneous tissue and skin. It is easily palpable at this site. Further down it innervates the tibialis anterior muscle, the peroneal muscles and the long extensors of the toes. It supplies the skin of the dorsum of the foot. The peroneal nerve was compressed at the neck of the fibula.

QUESTION 3

Nerve stimulation studies may be performed to ascertain whether the nerve is completely divided. If it is not divided, recovery usually is complete in 4–6 months, as occurred in this patient.

¹ Wechselberger G, Schoeller T, Bauer T, Otto A, Rainer C. Increased peroneal nerve injuries caused by ski edges. *Lancet* 1999;**353**:753–4.

Discussion

A recent letter in *The Lancet*¹ describes injuries to the peroneal nerve at the neck of the fibula due to ski injuries. The authors state “This type of peroneal injury has rarely been reported and its cause is widely ignored ...” Many of their patients did not recover completely, even with immediate microsurgical repair. They advocate prevention with protective pads on the lateral aspect of the ski pants.

A series of 302 patients with peroneal nerve lesions seen in 30 years at the Department of Neurosurgery in Louisiana, USA, includes injuries to this nerve by sharp lacerations, gunshot wounds and tumours.² If the nerve is divided they advise surgical repair or nerve graft. If spontaneous recovery of a compressed nerve has not occurred in about 6 months, neurolysis is advised. In their series 45% of patients made an acceptable recovery.

Final diagnosis

Compression of the peroneal nerve at the neck of the fibula.

Keywords: peroneal nerve; peripheral nerve injuries; fibula

² Kim HD, Kline DG. Management and results of peroneal nerve lesions. *Neurosurgery* 1996;**39**:312–20.

An unusual cause of bowel obstruction

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A 73-year-old woman presented with a 24-hour history of colicky abdominal pain, abdominal distension and vomiting. Medical history revealed that her bowels were opening normally and there was no history of recent change in bowel habit or weight loss. She was hypertensive and had not undergone previous abdominal surgery. The patient had previously been investigated for rectal haemorrhage when a barium enema was performed (figure 1). Examination of her abdomen revealed distension with no scars or external herniae. On auscultation tinkling bowel sounds were heard. No peritonism was present and digital rectal examination was normal. Plain abdominal radiograph was obtained (figure 2). The patient underwent an exploratory laparotomy, following which she made uneventful recovery. A post-operative small bowel enema confirmed the diagnosis (figure 3).



Figure 1 Barium enema



Figure 2 Plain abdominal X-ray



Figure 3 Small bowel enema

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Questions

- 1 What is the diagnosis?
- 2 What are the differential causes of this condition?
- 3 What are the surgical options at laparotomy?

Answers

QUESTION 1

Mechanical small bowel obstruction.

QUESTION 2

Small bowel obstruction may be divided into luminal, intrinsic or extrinsic (box 1). Adhesions, herniae and intra-abdominal neoplasms account for 95% of cases with all other conditions being relatively rare. At laparotomy the patient was found to have an enterolith impacted in the ileum with proximal small bowel distension and distal collapse. Multiple jejunal diverticulae were noted, commencing at the ligament of Treitz and extending distally for 45 cm. The enterolith had migrated from a diverticulum into the small bowel lumen and impacted distally causing a bolus obstruction. Extensive diverticular disease of the large bowel was also noted and the rest of the laparotomy was normal.

Causes of small bowel obstruction

Luminal

- foreign bodies
- faeco- and enteroliths
- gallstones
- bezoars
- parasites
- polypoidal tumours

Intrinsic

- atresia
- tumours
- strictures (including tuberculosis, Crohn's)

Extrinsic

- adhesions
- herniae
- volvulus
- intussusception
- bands
- inflammatory masses
- neoplastic masses

Box 1

QUESTION 3

Small bowel obstruction due to an enterolith may be relieved either by enterotomy or by simply crushing the enterolith digitally and milking the fragments into the caecum (as was done in this case). In rare cases of small bowel diverticular disease, where intussusception, haemorrhage or perforation are present, the diseased segment should be resected and primary anastomosis performed. It may, however, be necessary to exteriorise the bowel if gross contamination or infection is present.

Obstruction caused by band adhesion or volvulus can frequently be relieved by the division of the band without resection. However,

Learning points

- causes of small bowel obstruction may be categorised into luminal, intrinsic and extrinsic
- most jejunal diverticula are asymptomatic (60%). When present, symptoms include abdominal discomfort, flatulence, borborygmi, malabsorption, pseudo-obstruction, stasis or 'blind loop' syndrome
- surgical intervention may be necessary for intestinal obstruction, perforation, haemorrhage and neoplastic growth
- obstruction may arise from enterolith formation, volvulus, intussusception, and adhesion bands

Box 2

where the bowel is ischaemic or gangrenous, resection with primary anastomosis should be performed.

Discussion

Jejunal diverticula are usually acquired, multiple, and located on the mesenteric border of the small bowel where the vessels penetrate the muscle. Incidence at autopsy is 0.7%,¹ but this is probably an underestimate as the radiological detection rate is up to 2.3%.² Aetiology is unclear but formation may be from disordered small bowel function and structure, leading to abnormal intestinal motility.³ Synchronous colonic diverticulosis is present in 30–61% of patients.⁴

Asymptomatic jejunal diverticula discovered incidentally should be left alone. About 40% of patients with small bowel diverticula are symptomatic.³ These include abdominal discomfort, flatulence, borborygmi, malabsorption, pseudo-obstruction, stasis and 'blind loop' syndrome. In 10% of patients surgical intervention is necessary. Reasons include intestinal obstruction, haemorrhage and perforation. Neoplastic growth may also occur and include fibroma, lipoma, carcinoma and sarcoma formation.²

Intestinal obstruction may arise from enterolith formation, intussusception or volvulus.^{1 6 7} In the latter situation the diverticulum acts as a pivot, especially where previous diverticulitis results in adhesive band formation. Such adhesions may also cause obstruction by direct kinking of the bowel or by trapping another loop of bowel underneath.

Final diagnosis

Mechanical small bowel obstruction secondary to an enterolith arising from jejunal diverticulum.

Keywords: jejunal diverticulum; enterolith; bowel obstruction

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Adverse drug reaction

Disseminated intravascular coagulation and vasculitis during propylthiouracil therapy

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The use of antithyroid drugs in the early 1940s revolutionised the management of hyperthyroidism. Since their introduction, a variety of adverse reactions, including haematological, dermatological, and rheumatological effects, have been associated with these drugs. The incidence of these side-effects is similar to many other commonly used drugs, ie, 1–5%.¹ The most common side-effects include skin rash, fever, arthralgias/arthritis and neutropenia while lupus-like reaction, vasculitis, hepatitis, agranulocytosis and thrombocytopenia are uncommon.² Disseminated intravascular coagulation (DIC) is a rare adverse effect of propylthiouracil therapy.³ Herein we report a case of DIC and vasculitis following a short course of propylthiouracil therapy.

Case report

A 42-year-old African-American woman with Grave's disease, diagnosed 20 years earlier, had received propylthiouracil (100 mg tid) for the past 2 weeks because of recent exacerbation of symptoms. She was admitted to the hospital because of sudden onset of palpable purpuric rash, which started on the face and later spread to her trunk and extremities.

Laboratory test results on admission disclosed the following data: haemoglobin 12.2 g/dl, haematocrit 37.8, white blood cells $15.5 \times 10^9/l$, platelets $49 \times 10^9/l$, erythrocyte sedimentation rate 23 mm/h, free thyroxine 3.7 ng/dl (normal 0.71–1.85); and thyroid-stimulating hormone <0.03 mIU/ml. Tests for erythrocytes were normal. Tests for coagulation studies revealed prothrombin time 14.3 s (10.6–13.4); activated partial prothrombin time 28.0 s (18–38); D-dimer test positive; fibrinogen degradation products positive; fibrinogen level 344 mg/dl (152–392). Serum complement studies showed C_3 133 mg/dl (88–200), C_4 12 mg/dl (16–47) and CH_{50} 126 U/ml (100–300 CH_{50}). Serum haptoglobin level was normal.

Urinalysis showed trace protein and moderate blood in the urine. Antinuclear, anti-DNA single stranded, anti-DNA double stranded, antihistone, antithyroglobulin and antineu-

trophil cytoplasmic antibody (ANCA) titres were normal. Blood cultures were negative and chest X-ray was normal. Bone marrow aspiration showed myelosuppression with no evidence of leukaemia. Skin biopsy showed acute vasculitis involving small and medium-sized vessels with fibrin thrombi. No immunohistochemical testing was done. The skin of the left cheek revealed focal superficial epidermal and dermal haemorrhagic necrosis with marked acute inflammation and pustule formation.

The patient was admitted to the hospital and treated with intravenous methylprednisolone 125 mg every 8 hours. Propylthiouracil was discontinued. She responded to intravenous methylprednisolone and the purpuric rash gradually disappeared. Subsequently steroids were tapered over next 2 weeks. The haematological abnormalities returned to normal.

Discussion

The most frequent adverse effects related to propylthiouracil and methimazole, the two most commonly used thionamides, are haematological. Transient leucopenia, perhaps the most common side-effect, has been reported in 12% of adults and up to 25% of children,⁴ while cutaneous adverse reactions occur in 3–5% of adults and up to 18% of children.^{4,5} Generalised maculopapular and papular purpuric eruptions are perhaps the most common thionamide-induced cutaneous reactions, but rarely bullous haemorrhagic, generalised vesicular and necrotic ulcerative forms have been described.⁵ Propylthiouracil induces a clinically distinctive cutaneous eruption consisting of symmetrical, tender, palpable purpuric lesions, often in a livedoid pattern and curiously involves the ear lobes and malar areas.^{5–9} Cutaneous vasculitis is usually seen early in the course of propylthiouracil therapy, but has also been observed after long-term treatment. Its exact incidence is not known. Vasculitic involvement of skin is far more common than other organs. Cases of nephritis, myositis, and cavitary pulmonary infiltrates have been reported.^{6,7}

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The exact pathogenesis of propylthiouracil-induced vasculitis is not known. It has been suggested that circulating immune complexes may play a role, as immunoglobulin and complements have been found in the glomeruli and in the walls of dermal vessels using immunofluorescence.⁶ In our patient, low C₃ serum level suggests the possibility of involvement of immune complex mechanism. The detection of ANCA in association with vasculitis suggests other possible pathogenic mechanisms.⁹ No dose-dependent or age preference factor has been noted.^{4,9}

In addition to leucopenia and agranulocytosis, the other reported haematological abnormalities associated with propylthiouracil therapy include anaemia, thrombocytopenia and polyclonal hypergammaglobulinaemia.² There has been only one reported case of DIC, which occurred in a paediatric patient.³ Our case report is the first case of DIC secondary to propylthiouracil in an adult patient to be reported to the US Food and Drug Administration (FDA). Since our report, FDA have received a second adverse event report of DIC following propylthiouracil in a female patient. In our patient a diagnosis of DIC was suggested by the histological examination of purpuric skin lesion which showed fibrin thrombi in small blood vessels, a finding more

Learning points

- propylthiouracil therapy is associated with a clinically distinctive vasculitic cutaneous rash
- propylthiouracil should be considered in the differential diagnosis of drug-induced DIC and vasculitis
- corticosteroid use, in addition to the discontinuation of propylthiouracil, helps to resolve the symptoms

appropriate for DIC than for primary vasculitis, in addition to low platelet count and abnormal coagulation profiles.

The outcome of propylthiouracil-associated adverse effects is mostly favourable, as exemplified in our patient. However, fatal cases of peri-arteritis and vasculitis have been described in the literature.¹⁰ Most adverse effects usually reverse with discontinuation of the drug.⁸ Steroids, and in some cases, non-steroidal anti-inflammatory drugs have been used successfully to alleviate the symptoms.^{5,6,8} Our patient responded to both discontinuation of propylthiouracil and intravenous steroid.

Keywords: propylthiouracil; vasculitis; disseminated intravascular coagulation; adverse drug reaction

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