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*Self-assessment questions***Refractory thrombocytopenia, recurrent abortions and inferior vena cava thrombosis**

Atul Kakar, Ved Prakash

A 23-year-old woman was admitted in January 1983 with complaints of purpuric spots all over her body for 4 days prior to admission. She had been married for 3 years, had undergone three spontaneous abortions (one first trimester and two second trimester), and had one live birth. On examination, she had no splenomegaly. Investigations revealed a haemoglobin of 11.2 g/dl, total leukocyte count $4 \times 10^9/l$ (polymorphs 64%, lymphocytes 36%), erythrocyte sedimentation rate 12 mm in first hour, platelets $40 \times 10^9/l$. Blood film showed isolated thrombocytopenia. Renal function, liver function tests, chest X-ray and ultrasound of the abdomen were normal. Bone marrow aspiration showed increased megakaryocytes while other cell lines were normal. Antinuclear antibody (ANA) and dsDNA were negative. A platelet antibody test was not available. The patient had isolated thrombocytopenia without any systemic illness. A diagnosis of idiopathic thrombocytopenic purpura (ITP) was considered. The patient was started on 60 mg prednisolone per day. The platelet count had risen to $70 \times 10^9/l$ by the 10th day and she was discharged.

In March 1983, she was re-admitted with falling platelet counts, mucosal and gingival bleeding, and epistaxis. The platelet count was $15 \times 10^9/l$. The dose of oral steroid was increased and platelet concentrate was transfused. The platelet count did not increase and the patient developed menorrhagia and haematuria while still in the hospital. She was referred to a surgeon and, in view of the refractory thrombocytopenia, a splenectomy was performed. Postoperatively, her platelet count increased transiently for 1-2 days and then stabilised at $15-20 \times 10^9/l$. She was put on danazol and cyclophosphamide after a period of 12 days postoperatively. Platelets were monitored and there was gradual but definite improvement. Six months after surgery, the platelet count was $150 \times 10^9/l$ and the medicines were tapered gradually.

Between January 1984 and September 1997, she did not return for follow-up. She had eight more spontaneous abortions, six of which were in the second trimester. The cause of this was investigated. Gynaecological examination and her husband's semen analysis were normal. Abdominal ultrasound was also normal and TORCH test was negative. Her platelet count, bleeding time and clotting time were normal.

In October 1997, the patient was re-admitted with complaints of gradually increasing abdominal distension and low-grade fever. She was febrile with no pallor or lymphadenopathy. Her abdomen was distended, the umbilicus was stretched transversely and there were no dilated veins over the abdomen or back. The liver was palpable and non-tender with evidence of free fluid in the abdomen. Investigations showed normal complete blood counts including platelet count, renal and liver function tests; urine examination revealed trace proteins and chest X-ray was normal. An ascitic tap showed 150 cells, 90% lymphocytes, and was transudative in nature. Contrast abdominal computed tomography (CT) scan (figure 1) showed gross ascites; the liver was enlarged and there was inferior vena cava (IVC) thrombosis. There were prominent retroperitoneal collateral vascular channels. On magnetic resonance angiography (MRA) (figure 2) the IVC was well visualised from its formation at the L5 level up to the L2 vertebral level. There was no

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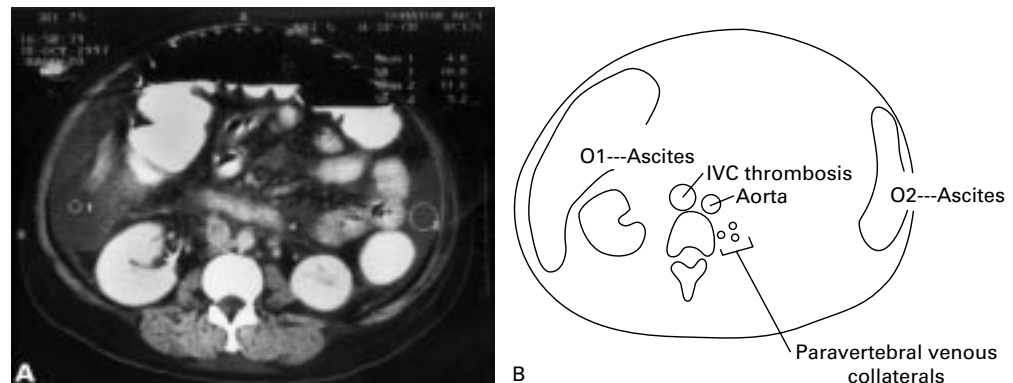


Figure 1 Contrast CT scan of abdomen showing hepatomegaly, ascites and inferior vena cava thrombosis (seen as hypodense eccentric filling defect)

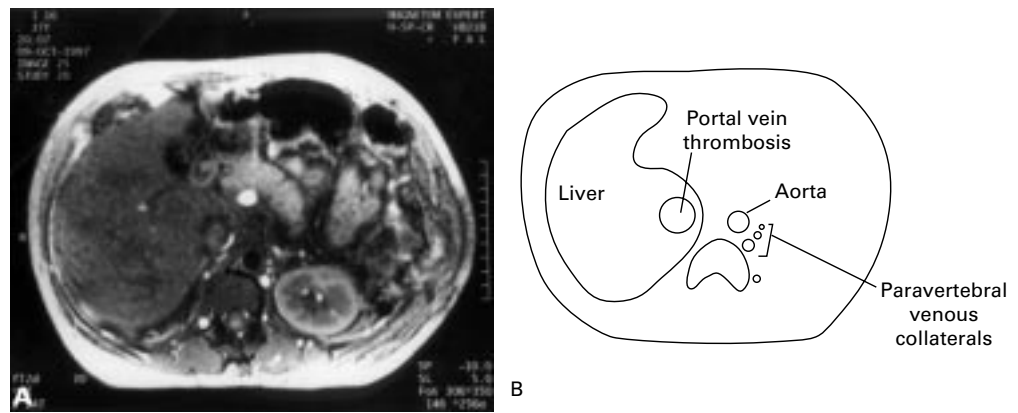


Figure 2 MRA, flash 2-D sequence, showing dark signal flow void in aorta, heterogenous slightly hyperintense signals in the intrahepatic part of the IVC due to thrombus formation. Intense bright signals are seen in portal vein and prominent paraspinal

evidence of flow intensity noted above L2 level. The flow in the inferior vena cava appeared slow and contained a central area of thrombus formation. The findings were suggestive of IVC thrombosis with collateral formation.

The patient's blood was screened for a hypercoagulable state. The activated partial thromboplastin time was 54 s (control 23 s), lupus anticoagulant was 55.8 s (control 37 s), anticardiolipin antibody IgG 64.413 g/l (normally less than 10). The levels of protein C, S, antithrombin and fibrinogen were normal. ANA and dsDNA were both positive. Echocardiography showed pericardial effusion and 24-h urinary proteinuria was 1.2 g.

Questions

- 1 What was the cause of the initial episode of severe thrombocytopenia?
- 2 What is the diagnosis?

Answers

QUESTION 1

This patient had isolated thrombocytopenia with no systemic involvement. She was diagnosed as a case of ITP. Both ANA and dsDNA were negative initially.

QUESTION 2

This patient had IVC thrombosis due to antiphospholipid syndrome (APS), as both lupus anticoagulant and IgG anticardiolipin antibodies were positive. She had underlying evidence of systemic lupus erythematosus (SLE) as she had pericardial effusion, significant proteinuria, and both ANA and dsDNA were ultimately positive.

Outcome

The patient was diagnosed as having IVC thrombosis due to APS with SLE. She was started on deltaparin 5000 units bid, with prednisolone 40 mg/day, low-dose aspirin, and diuretics. On this treatment ascites decreased and she improved symptomatically. She was discharged on request on the 18th day of treatment on deltaparin and steroids. She discontinued the treatment on her own in the next 10 days and died 6 weeks later, probably due to pulmonary embolism.

Discussion

The triad of thrombosis (arterial and venous), foetal loss and thrombocytopenia constitutes APS. Our patient had historically all components of this syndrome but the initial event of thrombocytopenia was probably due to ITP and not to APS. An antiplatelet antibody test, if available, would have supported the diagnosis. Thrombocytopenia may be the first manifestation of SLE but when it was present in our patient, there were no systemic manifestations of SLE and both ANA and dsDNA were negative. The differentiating features between thrombocytopenia in a patient with APS and due to ITP are shown in the table. In APS associated with SLE thrombocytopenia is usually mild and seldom requires treatment.¹ However, our patient presented with severe thrombocytopenia which had a stormy course. Another differentiating feature is that splenectomy is not the long-term solution for thrombocytopenia in case of APS.² Our patient had two rare coexisting diseases. The presence of these diseases simply reflect an underlying autoimmune disease. About 30% of patients

with ITP may have elevated IgG antiphospholipid antibodies at the time of diagnosis.³ Coexistent APS would increase the risk of thrombosis following splenectomy as was seen in our patient. Such patients should be given prophylactic anticoagulants.⁴

The term refractory ITP is applied to cases that do not respond to standard doses of steroid and splenectomy and require some other form of therapy to raise their platelet count.⁵ Therapy for such patients is divided into four levels, depending on the severity of side-effects (box 1).

The treatment of acute thrombotic attack is not different from thrombosis elsewhere. Low molecular weight heparin is preferred because of a more predictable response and less incidence of thrombocytopenia. After an acute event of thrombosis, high-intensity warfarin has to be given on a long-term basis.²

It has been suggested recently that testing of lupus anticoagulant and antiphospholipid antibodies may be unnecessary for the diagnosis of ITP (box 2).⁶ We would conclude by

Therapy used for refractory ITP

Level 1: prednisolone, dexamethasone, vincristine, danazole, colchicine, dapsone
 Level 2: staphylococcal A-immunoadsorption, cyclophosphamide, azathioprine
 Level 3: high-dose cyclophosphamide, if unsuccessful then combination chemotherapy
 Level 4: interferon, gammaglobulin, vinblastine, cyclosporine

Box 1

Diagnosis of ITP

- exclusion of other causes of thrombocytopenia (eg, HIV infection, SLE, lymphoproliferative disorders, myelodysplasia, drug induced, thyroid dysfunction)
- isolated thrombocytopenia with normal red cell and white cell counts and morphology
- peripheral smear showing thrombocytopenia, platelet size normal or larger than normal but giant platelets absent
- thrombocytopenia with isolated abnormality, eg, positive ANA, APS antibodies but no clinical evidence of SLE are suggestive of ITP

Box 2

Table Thrombocytopenia in ITP and APS

	ITP	APS
Incidence of thrombocytopenia	All patients	20–25% patients
Risk of thrombosis	None	Yes
Severity	Mild to severe	Usually mild
Clinical features	Petechiae, mucosal bleeds, menorrhagia	Seldomly occur due to thrombocytopenia
Antibodies directed against	Glycoprotein IIB & IIIA or to IB-IX complex	Exposed phospholipid on platelet membrane & internal platelet antigen
Collagen markers	Negative	Positive, except in primary type
Bone marrow	Normal or increased megakaryocytes & precursors	Normal marrow

recommending these tests to be done in all patients with ITP at the time of diagnosis and particularly before pregnancy or any surgical procedure.

Final diagnosis

Refractory idiopathic thrombocytopenic purpura with inferior vena cava thrombosis due to

antiphospholipid syndrome and systemic lupus erythematosus.

Keywords: idiopathic thrombocytopenic purpura; antiphospholipid syndrome; systemic lupus erythematosus; inferior vena cava thrombosis

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Abdominal pain in a patient using warfarin

Javier Jimenez

A 32 year-old man presented with complaints of nose bleeding and mild postprandial abdominal pain for 3 days. The patient had prior history of rheumatic heart disease. Four weeks prior to the onset of symptoms the patient had undergone a double mechanical valve replacement using a number 21 Masters St Jude valve in the aortic position and a number 29 Masters St Jude valve in the mitral position. He was started on warfarin at that time. A few days prior to admission, the patient developed an upper respiratory infection and was placed on a 4-day course of azithromycin. Physical examination was unremarkable. Rectal examination revealed no gross blood, however occult blood test was positive. At the time of this visit the haemoglobin was 14 g/dl and the International Normalised Ratio (INR) was 12. In view of these results the patient was given 5 mg of vitamin K orally and sent home with close follow-up. The following day the patient was admitted to hospital with persistent abdominal pain and nausea. A repeat INR showed a level of 5. A plain abdominal X-ray was obtained, but revealed no abnormality. A few hours after admission the abdominal symptoms worsened and an abdominal computed tomography (CT) scan was ordered (figure).

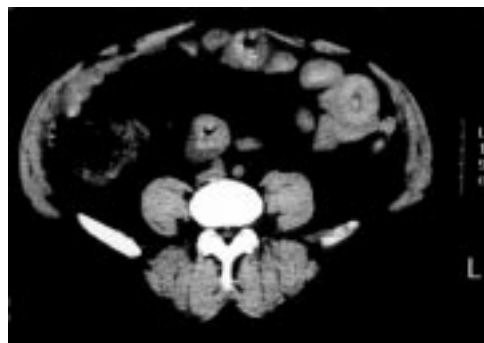


Figure Abdominal non-contrast CT scan

Questions

- 1 Comment on the history and CT scan.
- 2 How would you treat this patient?

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Answers

QUESTION 1

Oral anticoagulation is commonly used for multiple medical conditions; however, on occasions, the appropriate anticoagulation range is difficult to maintain due to patient non-compliance and/or drug interactions. Over-anticoagulation can be associated with severe bleeding complications. The abdominal non-contrast CT shows small bowel segments with areas of hyperattenuation and thickened walls. These findings, in the setting of the clinical presentation described before, are very suggestive of an intramural haematoma.

QUESTION 2

Conservative management with nasogastric suction and total parenteral nutrition can achieve resolution of obstructive symptoms. Reversal of warfarin effects is achieved acutely with vitamin K (10–15 mg intravenously or intramuscularly). Whole blood or fresh frozen plasma can be used to control bleeding by replacing clotting factors. Surgery should be reserved for active bleeding, presence of pneumoperitoneum, patients whose symptoms progress to an acute abdomen, or those in whom intestinal obstruction does not resolve.^{1 2}

Discussion

Coumadin drug interactions are common and may affect anticoagulation levels very rapidly. Bleeding complications of over-anticoagulation may present in unusual ways. There have been several reports describing small bowel haematomas as a complication of oral anticoagulation. The incidence of intramural haematoma of the small bowel in the setting of anticoagulation is relatively rare. Bettler *et al* reported an incidence of 1 in 2500 patients.³ Common medications that may increase warfarin effect are cimetidine, clofibrate, alcohol, non-

Learning points

- interactions with warfarin are common, namely antibiotics, alcohol, non-steroidal anti-inflammatory drugs and cimetidine
- spontaneous intramural bowel haematoma is a possible complication in patients receiving warfarin therapy
- diagnosis of intramural bowel haematoma is best performed by non-contrast abdominal CT
- intramural bowel haematoma can be treated in a conservative manner unless symptoms progress to an acute abdomen

steroidal anti-inflammatory drugs and most antibiotics, namely ciprofloxacin, erythromycin, fluconazole, ketoconazole, metronidazole and sulfonamides.

The initial symptom of patients presenting with this complication is usually abdominal pain. Associated symptoms are nausea and vomiting. Occasionally there may also be gastrointestinal bleeding. Symptoms may progress to an acute abdomen if complete intestinal obstruction and bowel ischaemia develops.⁴

Noninvasive diagnosis can be performed in most cases with non-contrast abdominal CT.⁵ Common findings are hyperattenuation of the involved bowel segments, with thickened bowel walls and dilated segments. Other diagnostic tools that may be used with less accuracy are abdominal X-ray films with and without contrast, and abdominal ultrasound.^{6 7}

Final diagnosis

Intramural haematoma of the small bowel in the setting of warfarin anticoagulation.

Keywords: bowel haematoma; anticoagulation; warfarin

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A rare complication of dental abscesses

A Doss, P N Taylor, P F Down

A 27-year-old cannabis smoker was admitted with a 3-week history of gradually worsening occipital headache. He had been pyrexial one week earlier, and had been put on an oral course of amoxycillin by his general practitioner. He had a history of recurrent dental abscesses and childhood asthma. He was not an intravenous drug abuser.

On examination he was well with a temperature 37.5°C, pulse rate 80 beats/min, blood pressure 130/80 mmHg. He had bilateral papilloedema, sustained ankle clonus, and brisk knee and ankle jerks. Examination was otherwise unremarkable. Full blood count, apart from a mean corpuscular volume of 101 fl, was normal. Liver function tests, urea, electrolytes, clotting, thrombophilia screen, auto-immune profile, erythrocyte sedimentation rate, serum electrophoresis and blood cultures were unremarkable. Visual field testing showed slightly enlarged blind spots in both eyes. An urgent brain computed tomography (CT) scan was performed within (figure 1).

Two days following admission he developed pain and swelling of the right lower jaw and was referred to the maxillofacial surgeons who diagnosed dental abscesses. He went on to have incision and drainage of the lower right buccal space and multiple dental extractions under general anaesthesia. He was treated with antibiotics for 2 weeks and discharged home after making a full recovery. He is currently under follow-up with monthly visual field testing and regular dental review.

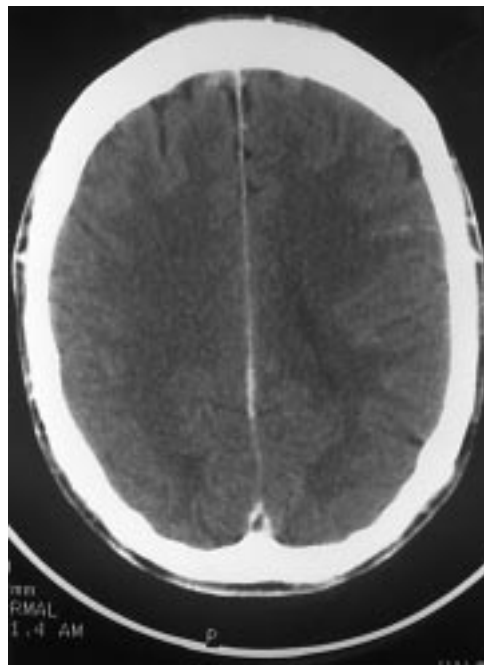


Figure 1 Cranial contrast-enhanced CT

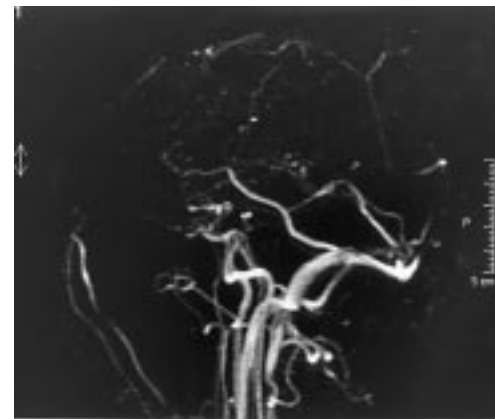


Figure 2

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Questions

- 1 What does figure 1 show? What is this sign called?
- 2 What is the investigation shown in figure 2? What does it show?
- 3 Is there an association between the CT findings and the dental abscesses?
- 4 Are anticoagulants routinely indicated in this condition?

Answers

QUESTION 1

There is a filling defect in the superior sagittal sinus in keeping with superior sagittal sinus thrombosis (figure 1). This appearance is known as the 'delta sign'. On an enhanced brain CT scan, the normal sagittal sinus is homogeneously opaque. Thrombus within the lumen of the sinus appears as a filling defect outlined by contrast, often triangular or delta-shaped, which is known as the delta sign.

QUESTION 2

Figure 2 is a phase-contrast magnetic resonance angiography (MRA) sequence coded for venous flow. This confirms occlusion of the superior sagittal sinus.

QUESTION 3

It is possible that dental abscesses played a causative role in the sagittal sinus thrombosis of our patient. Septic intracranial sinus thrombosis as a complication of upper respiratory tract infections is well recognised.

QUESTION 4

Anticoagulation is not routine in sagittal sinus thrombosis. Management relies on treating the underlying cause and raised intracranial pressure rapidly and effectively.

Discussion

As far as we know this is the first case report of septic sagittal sinus thrombosis associated with dental abscesses. Sepsis is a predisposing factor, most frequently bacterial meningitis or facial sinus infection.¹ Other reported associations include primary thrombocythaemia, homocystinuria, intracranial angiography, dehydration, Behcet's disease, haemolytic anaemia, coagulopathies, inhalational drug abuse, the post-partum period and the oral contraceptive pill.² The natural history of this condition is highly variable with mortality ranging between 10–20%.

At present, venous MRA is probably the definitive examination and the gold standard for diagnosis of dural sinus thrombosis.³ How-

Sagittal sinus thrombosis

- septic complication of bacterial meningitis, facial sinus infection, dental abscess
- 10–20% mortality, worse in sepsis
- diagnosis: cranial CT with contrast ('delta sign'); MRA is the definitive investigation
- treatment is of underlying condition and raised intracranial pressure; anticoagulation is controversial; direct thrombolysis is increasingly used
- other associations: post-partum, dehydration, marasmus, oral contraceptives, inhalational drug abuse, coagulopathies, haemolytic anaemia, primary thrombocythaemia, sickle cell anaemia, Behcet's disease, head injury, homocystinuria

ever, brain CT, which is usually the initial examination, may be diagnostic by demonstrating the 'delta sign' in 70% of cases.⁴ CT or MRI may also identify areas of haemorrhage or venous infarction in the adjacent brain.

The management of intracranial dural sinus thrombosis is still controversial and uncertain. There are no controlled trials of therapy. However, it is important to treat the underlying cause and raised intracranial pressure. Anticoagulants may be indicated early when there is no radiological evidence of haemorrhage.^{2,3} More recently, direct thrombolysis of dural sinus thrombosis has shown a better outcome in these patients.^{5,6}

The decision regarding anticoagulation should be based on the severity of acute presentation, underlying associated conditions, evidence of haemorrhage or venous infarction of adjacent brain tissue on CT or MRI, and advice from neurologists and neurosurgeons should be sought sooner rather than later.

Final diagnosis

Superior sagittal sinus thrombosis as a complication of dental abscesses.

Keywords: superior sagittal sinus thrombosis; dental abscess; papilloedema; anticoagulation

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Abnormal skull X-ray in a child with growth retardation

A S Kashyap

A 41-month-old female child was referred to the endocrine clinic for evaluation of poor growth, and delayed motor and mental milestones. She was the only child born out of a non-consanguineous marriage. There was no history of hypothyroidism or goitre in the parents. There was no family history of congenital hypothyroidism. Clinical evaluation revealed a lethargic child with dry skin, open anterior fontanelle, protuberant abdomen and short limbed dwarfism. Her bone age was less than 2 years and height age was 20 months. Her skull X-ray is shown in the figure.



Questions

- 1 What is the diagnosis?
- 2 What abnormalities are shown in the skull X-ray ?
- 3 What other skeletal abnormalities are seen in this condition?

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Figure Skull X-ray lateral view

Answers

QUESTION 1

This patient has congenital hypothyroidism. Detailed clinical evaluation revealed, in addition to the above findings, an enlarged tongue, coarse facial features, generalised hypotonia, hoarse cry, and delayed relaxation of tendon jerks. There was no goitre. Serum thyroid-stimulating hormone levels were 51 mU/l (normal 0.5–5 mU/l), serum thyroxine levels were 10 nmol/l (64–154 nmol/l) and serum triiodothyronine (T_3) levels were 0.2 nmol/l (1.1–2.9 nmol/l). Sodium [^{99m}Tc]pertechnetate scintiscanning revealed negligible uptake in thyroid region. This investigation profile is consistent with thyroid dysgenesis or agenesis leading to sporadic congenital hypothyroidism. Congenital hypothyroidism has an incidence of 1 in 3500–4000 and is easily picked up by neonatal screening. If diagnosed and treated at an early stage the manifestations of hypothyroidism can be reversed and/or prevented.

QUESTION 2

The skull X-ray displays intrasutural or wormian bones along lambdoid (broad arrow) and coronal sutures (narrow arrow). The anterior fontanelle is visualised (delayed closure of anterior fontanelle, arrow head). These are typical skull X-ray findings in congenital hypothyroidism.¹ Wormian bones disappear when bone age reaches 5 years. These bones may also be seen in cleidocranial dysplasia, pyknodysostosis, acro-osteolysis (Hajdu-Cheney syndrome) and osteogenesis imperfecta.

In congenital primary hypothyroidism, the skull may be brachycephalic (a result of endochondral growth retardation at the base of skull). The sella is small and bowl shaped in young children and larger and rounded (cherry sella) in older children due to rebound hypertrophy of the pituitary gland. The paranasal sinuses are underdeveloped and facial bones are hypoplastic. An increased thickness of bones of the cranial vault with narrow diploic space may be seen. Development of teeth is delayed; primary teeth remain for several years beyond the normal time for exfoliation. Comparable delay occurs in appearance of permanent teeth. Unerupted teeth are structurally abnormal and are subject to caries. Dental defects tend to parallel the delay in ossification of the skeleton. The poorly developed jaw shows gross dental crowding.

Epiphyses are retarded in appearance and closure. When ossification or epiphyseal dysgenesis does occur, it is often from multiple sites within the epiphysis. This leads to a spotted or fragmented appearance on X-ray. This feature is most commonly seen in femoral and humeral heads, and in the navicular bone of the foot. Epiphyseal disturbances, particularly in the femoral head, persist beyond a bone age of 8 years. Femoral epiphyseal dysgenesis may resemble Perthe's disease, though Perthe's disease is usually unilateral. The incidence of slipped capital femoral epiphysis is increased in these cases of hypothyroidism.² The long bones

Bone and skeletal manifestations of hypothyroidism

Skull

- delayed closure of fontanelle
- relatively large sella
- poorly developed paranasal sinuses
- brachycephaly
- delayed dentition and dental caries
- wormian bones

Skeleton

- dwarfism
- increased density

Epiphyseal centres of ossification

- retarded growth
- multicentric and irregular
- delayed fusion and stippled appearance
- epiphyseal dysgenesis (fragmented epiphyses)

Spine

- kyphosis
- flattening of vertebral bodies
- increased width of intervertebral space
- bullet-shaped vertebral bodies (usually L-1 and L-2)

Long bones

- short-limbed dwarfism
- dense transverse bands at metaphyseal ends

Pelvis

- narrow with coxa-vara

are short and this leads to disproportionate (short limbed) dwarfism. Dense transverse bands at metaphyseal ends may be present very early in life, but they tend to disappear by a bone age of 6 months. The pelvis is often narrow with coxa-vara deformity.

In severe involvement, bullet-shaped vertebrae are seen (usually T-12 or L-1). This is due to some degree of flattening of vertebral bodies with forward slipping of one vertebra over another, resulting in thoracolumbar gibbus. Disc spaces may be widened. Diffuse osteoporosis of vertebral bodies leads to the appearance of 'picture framing' of vertebral bodies. Increased density of the skeleton is seen in some cases.

Discussion

The thyroid hormone is important for regulation of normal growth, development and maturation of tissue. In hypothyroidism pathological changes include a marked decrease in cartilage cell proliferation. The osseous tissue abuts the cartilage zone; this forms a barrier to longitudinal growth of the bone. Growth failure is due to both impaired protein synthesis and reduction in insulin-like growth factor-1 levels.³ The decrease in protein synthesis is reflected in retardation of skeletal and soft tissue growth. Thyroid hormone deficiency thus impairs secretion as well as effectiveness of growth hormone.

Thyroid hormone effects on bone growth are direct and indirect. Proof of direct effect of thyroid hormones on bone growth needs to be demonstrated by thyroid receptors in bone cells and responses to thyroid hormones *in*

vitro. Osteoclasts and osteoblasts have been shown to have a specific *in-vitro* response to T_3 . Little is known about the expression of thyroid receptor (TR) in developing bone and cartilage. In studies of osteosarcoma cells, expression of TR beta mRNA was greater than TR alpha mRNA in mature osteoblasts, whereas the opposite was true in fibroblast precursors of osteoblasts.⁴ This provides support for bone responsiveness to T_3 . Retinoid X receptor, a cofactor involved in the interaction of TR with T_3 -responsive element, has also been found to be expressed in osteoblasts.⁵

Thyroid hormone influences bone development and growth indirectly via growth hormone (GH) secretion and action. GH secretion and synthesis are stimulated *in vivo* by thyroid

hormone. This effect is due to direct interaction of TR- T_3 complex with GH gene regulating its expression. Thyroid hormone treatment has been reported to more than double the nocturnal GH values in hypothyroid children.⁶ Reversal of blunted GH response to GH-releasing hormone stimulation in hypothyroid children following treatment with thyroid hormone indicates a direct influence of thyroid hormone on GH secretion at the level of the pituitary rather than the hypothalamus.

Final diagnosis

Congenital hypothyroidism.

Keywords: wormian bones; hypothyroidism

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A respiratory complication of diabetic ketoacidosis

N Younis, M J Austin, I F Casson

A 37-year-old man with type 1 diabetes presented with a few days history of persistent vomiting and lethargy associated with thirst and polyuria. He was not on any regular medication apart from insulin. He had omitted his insulin over the last 24 hours.

Clinical examination revealed him to be dehydrated with a tachycardia of 120 beats/min and blood pressure 130/80 mmHg. He was dyspnoeic with a respiratory rate of 32 breaths/min; the pattern was characteristic of Kussmaul's respiration. Laboratory investigations showed a metabolic acidosis with arterial blood gases pH 7.08, bicarbonate 10.7 mmol/l, base excess -22.6 mmol/l and plasma glucose 32.4 mmol/l. Ward testing for urinary ketones was strongly positive (+++ by ketostix). A chest X-ray was performed (figure).



Figure Chest X-ray

Questions

- 1 What does the chest X-ray show?
- 2 What clinical signs would you look for?

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Answers

QUESTION 1

The chest X-ray shows mediastinal emphysema with characteristic lines of radiolucency around the mediastinal pleura. There is also radiological evidence of subcutaneous emphysema in the soft tissues in the neck.

QUESTION 2

Surgical emphysema is frequently palpable in the neck and may be more widespread involving the face, chest or arm. Hamman's sign is variously described as a crepitous, crackling or crunching sound, synchronous with systole that may be heard with the stethoscope. Pleural effusion may accompany mediastinal emphysema caused by oesophageal rupture.

Discussion

Pneumomediastinum is a well recognised but infrequent complication of diabetic ketoacidosis.¹⁻⁴ The incidence of this complication is unknown. In most but not all reports there is a history of persistent or severe vomiting.^{1,3} The prognosis is excellent and there is prompt regression of the pneumomediastinum following correction of the ketoacidosis.¹⁻³ It is thought that in diabetic ketoacidosis hyperventilation induced by acidosis or by severe vomiting causes changes in the intra-alveolar pressure gradient within the lungs.⁵ The rise in intra-alveolar pressure causes rupture and subsequent dissection of air escaping alongside perivascular sheaths into the mediastinum; air enters into fascial planes particularly in the neck causing subcutaneous

Pulmonary abnormalities in patients with diabetes mellitus

Infections

- zygomycosis (mucormycosis)
- mycobacterioses
- bacterial and viral infections

Physiological changes

- reduced elastic recoil of the lungs
- reduced diffusion capacity of the lungs for carbon monoxide
- diminished bronchial reactivity
- elevated arterial oxygen saturation
- elevated arterial oxygen tension
- disordered breathing patterns: central hypoventilation, sleep apnoea

Others

- pulmonary oedema
- aspiration pneumonia
- pulmonary xanthogranulomatosis
- pneumomediastinum and pneumothorax

emphysema.⁵ Our patient had no specific symptoms to suggest the diagnosis of pneumomediastinum. Thus, unless a chest X-ray is performed, the diagnosis can be missed. Other recognised pulmonary complications of diabetes mellitus are listed in the box.

Final diagnosis

Pneumomediastinum as a complication of diabetic ketoacidosis.

Keywords: pneumomediastinum; emphysema; ketoacidosis; diabetes

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An unusual case of transient ischaemic attacks

B R Archana

A 29-year-old man, with no significant history, presented with a 2-month history of episodic facial numbness on the left side associated with left-sided weakness and expressive dysphasia, lasting about 1 minute. There were no visual disturbances. He was a martial arts enthusiast and led a very active life. He denied any recent trauma to his head or neck. He was a non-smoker and consumed less than 2 units of alcohol a week.

Examination revealed a young man with a pulse rate of 90 beats/min, and blood pressure of 120/80 mmHg. There was no rash, petechiae or lymphadenopathy. Thoracic, cardiovascular and abdominal examinations were normal. No carotid bruits were heard. Nervous system examination revealed normal higher mental functions and no cranial nerve involvement. Motor examination was normal except for an equivocal left plantar response. Sensory examination revealed a patch of altered sensation over the left side of the face. The optic fundi were normal.

The results of the routine laboratory investigations revealed a haemoglobin of 15.1 g/dl, and glucose of 5.7 mmol/l. Electrolytes were within the normal range. Computed tomography of the brain appeared normal. An electroencephalogram showed intermittent slow wave activity in the right anterior and temporal regions. Magnetic resonance imaging (MRI) of the brain (figure 1) revealed multiple areas of high attenuation in the corona radiata and right temporal regions suggestive of ischaemia. A further investigation was performed (figure 2).

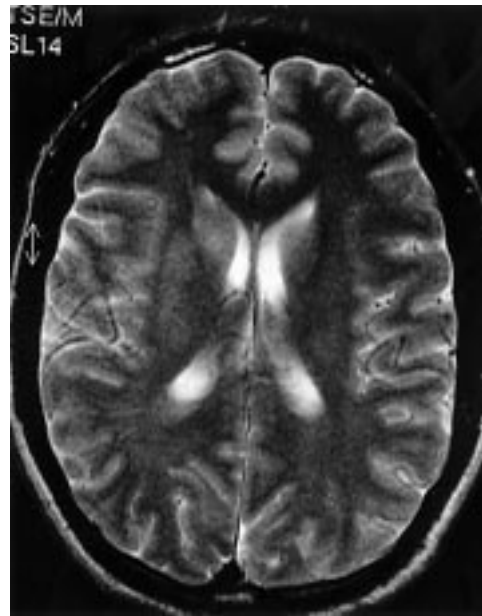


Figure 1 Brain MRI

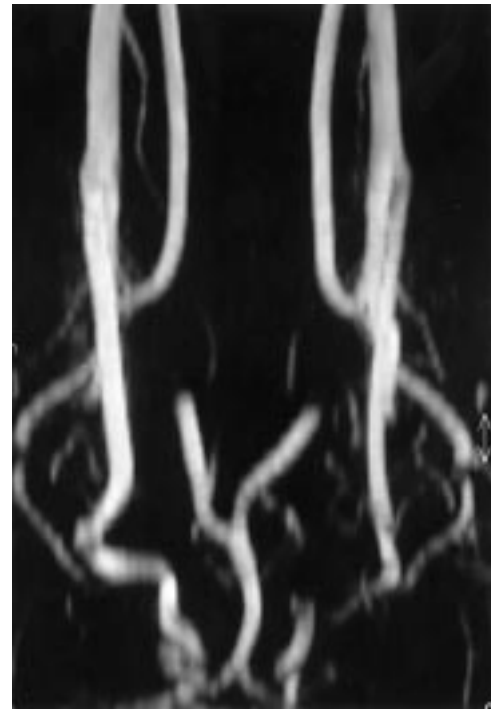


Figure 2

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Questions

- 1 What investigation is shown in figure 2 and what does it suggest?
- 2 What further investigations are appropriate?
- 3 What is the management and prognosis?

Answers

QUESTION 1

Magnetic resonance angiography suggesting bilateral carotid artery dissection.

QUESTION 2

Carotid Doppler studies confirmed the findings. Echocardiography revealed a normal heart.

QUESTION 3

Anticoagulant treatment is often used for a few months when the dissection involves the extracranial segment of the carotid artery. The prognosis of carotid dissections depends on the presence and severity of ischaemic brain damage. Normalisation of the vascular abnormalities is frequent and is an excellent argument in favour of the prognosis.

Discussion

Arterial dissection results from bleeding into the vessel wall. Some cases are associated with cervical trauma or have evidence of underlying vascular disease. In the above case, strain on the neck due to martial art manoeuvres might have been the cause. The extracranial segment

of the internal carotid artery is the vessel most commonly involved. Intracranial carotid dissections are much rarer. Carotid dissection occurs predominantly in young or middle aged adults and shows no sex predominance. Although clinical manifestations can range from isolated headache to rapidly lethal stroke, the most common and suggestive syndrome associates 'local' symptoms (such as head or neck pain, Horner's syndrome, pulsatile tinnitus or cranial nerve palsies) and delayed symptoms of cerebral ischaemia in the territory of the internal carotid artery. Dissection can be bilateral or associated with dissection of the vertebral artery. Angiography has long been considered the gold standard for the diagnosis. As this procedure carries a risk of cerebral complications, noninvasive diagnostic approaches such as MRI and ultrasound are being increasingly used.² Intra-arterial angiography is no longer necessary.

Final diagnosis

Bilateral carotid artery dissection.

Keywords: carotid artery dissection; transient ischaemic attacks

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Myocardial infarction, seizure and an abnormal head CT scan

Nithianandam Selvaraj, David A Drachman, Paula Ravin, John R Knorr

A 60-year-old woman was admitted with acute substernal chest pain. Electrocardiographic findings and creatine kinase values were consistent with an acute anteroseptal myocardial infarction. She underwent a coronary angiogram and percutaneous transluminal coronary angioplasty (PTCA) with stent placement. Two hours following the procedure, the patient developed right-sided partial motor seizures with secondary generalisation. A head computed tomography (CT) scan was obtained immediately to rule out a stroke.

Her medical history was significant for coronary heart disease, hypertension, asthma and seizures. Her last seizure was almost 10 years ago. She had taken an anti-epileptic medication in the past and had stopped it on her doctor's advice. There was also a remote history of alcohol and intravenous drug abuse. Prior to this admission, she was taking zestril, metoprolol, bupropion for smoking cessation, premarin, and steroid inhalers. After admission, she received aspirin, ticlid, intravenous nitroglycerin and abciximab (ReoPro). Abciximab was started during her PTCA.

When examined four hours after her seizure, she was alert and oriented. Her speech and language functions were normal. Cranial nerve examination did not reveal any abnormalities. On motor testing, she was noted to have a right pronator drift. Her muscle strength was entirely normal. Sensation was preserved throughout. Muscle stretch reflexes were 2+ and symmetrical. Babinski sign was present on the right side. The left plantar reflex was normal. Coordination was intact. No signs of meningeal irritation were present.

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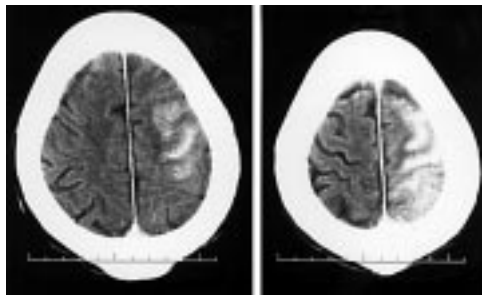


Figure 1 CT scan

Questions

- 1 What is the radiological diagnosis, taking into account the patient's hospital course?
- 2 What are the possible aetiologies of her seizure?
- 3 What is the further management?

Answers

QUESTION 1

The CT scan of the head shows hyperdensity involving the left cerebral hemisphere. Although this was meant to be an unenhanced CT, the fact that the patient had received a contrast agent (Hypaque) for her coronary angiography makes this CT, in fact, a contrast-enhanced study. It is important to recognise this when interpreting the abnormal findings. To the inexperienced eye this may look like subarachnoid haemorrhage or a haemorrhagic cerebral infarction. On close examination, however, it is evident that the hyperdensity involves mainly the white matter rather than filling the sulci (see figure 2).

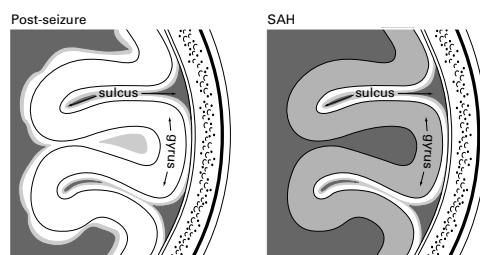


Figure 2 As shown in this schematic diagram, the CT appearance in our patient is not subarachnoid haemorrhage (SAH) because the hyperdensity mainly occupies the gyri and not the sulci

The absence of sulcal enhancement and the absence of blood in the interpeduncular cistern makes the diagnosis of subarachnoid haemorrhage unlikely. As the lesion does not correspond clearly to a vascular territory and has both diffuse white matter and cortical involvement, the diagnosis of a haemorrhagic infarct is less likely. Furthermore, the radiographic findings are out of proportion to the patient's relatively normal neurological status. This also has to be taken into account when interpreting the abnormal CT findings.

QUESTION 2

The aetiology of the seizures in this patient is unclear. The differential diagnosis is shown in the box.

Differential diagnosis

- contrast medium-induced seizure
- relapse of a pre-existing seizure disorder
- bupropion-induced seizures
- abciximab-induced seizures

The patient had a history of generalised seizures many years ago. She has been seizure-free for at least 10 years without any medications; in

the past seizures may have been related to alcohol withdrawal. Hence, it is unclear if this seizure was related to the history of seizures.

Bupropion is known to cause seizures in 0.1–0.4% of patients taking the drug. The risk in patients with a history of seizures may be even higher. We do not know if the drug was causally related to the current episode.

Abciximab (ReoPro) is being used increasingly in cardiac patients. It is the Fab fragment of the chimeric human–murine monoclonal antibody 7E3. It binds to the glycoprotein IIb/IIIa receptor of human platelets and inhibits platelet aggregation. It is used as an adjunct to PTCA for the prevention of acute cardiac ischaemic complications. Nervous system side-effects reported include cerebral ischaemia (0.3%) and coma (0.4%). Although it is theoretically possible that cerebral ischaemia can predispose to seizures in patients taking abciximab, seizures have not been reported with the use of this drug.

Neurotoxicity from intravascular contrast, in particular the ionic high-osmolar agents has been described previously. Contrast medium-induced seizures are also well described in the literature and it is probably the most likely aetiology for seizures in our patient, although a combination of mechanisms is possible.

QUESTION 3

One reasonable approach would be to monitor the patient clinically and if her neurological status did not change, repeat a non-contrast CT in 24 hours. In our patient, a non-contrast CT repeated the next day (figure 3) was entirely normal.

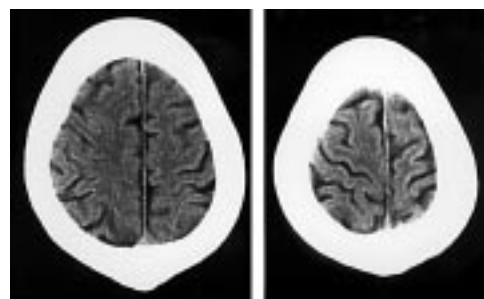


Figure 3 Non-contrast CT scan

The hyperdensity noted in the initial CT had completely disappeared. The minor residual neurological deficits noted post-ictally (Todd's paralysis) completely resolved over 24 hours. As the CT changes were unilateral, we presumed that the ictal activity originated from the left hemisphere. However, an electroencephalogram (EEG) obtained to look for a left hemispheric focus was completely normal. The patient was discharged home after her cardiac status was stable. Phenytoin treatment was begun as the aetiology of her seizures was unclear, pending further evaluation.

Discussion

Contrast-enhanced CT scans of the brain obtained on patients soon after seizures are often abnormal. The changes on CT may be either hypodensities or hyperdensities. Various authors have described reversible radiographic signs after seizures.¹⁻³ All these changes typically disappear over time, most within 1–2 weeks. The underlying mechanism is believed to be a transient disruption of the blood–brain barrier (BBB).

In vitro studies have shown that both electrically and pharmacologically induced seizures cause transient breakdown of the BBB.⁴ During prolonged seizure activity, BBB disruption leads to increased water content in brain tissue (cerebral oedema), especially in the hypothalamus and hippocampus. Both local and systemic changes account for the cerebral oedema. Relative hypoxia due to increased ictal metabolism, with an increase in local pCO₂ and lactate, results in local vasodilatation and loss of autoregulation.⁵ Systemically there is an increase in blood pressure and decrease in blood pH, again resulting in decreased cerebral autoregulation and local hyperaemia.⁶ It has also been reported that the degree of disruption of the BBB is proportional to the duration of seizure activity. Systemic hypertension during seizures, in combination with disrupted BBB, can lead to cerebral oedema, causing hypodense lesions and, in the presence of contrast agents, abnormal-appearing hyperdensities on CT scanning.

Sage and colleagues have demonstrated increased permeability of the BBB after large intracarotid contrast injections.⁷ Scott has previously reported that intravenous administration of contrast material for head CT may precipitate generalised seizures, especially in cases of metastatic neoplasm of the brain.⁸

Neurologic complications after cardiac catheterisation are well known. Contrast agent neurotoxicity presenting with focal seizures with CT head findings similar to subarachnoid haemorrhage has also been reported.⁹ Contrast-medium-induced seizures are well described in the literature and their incidence has been reported to be about 0.2–0.5%.¹⁰ They are typically self-limiting and do not require prolonged anticonvulsant treatment.

In our patient, the hyperdensity noted in the CT done soon after the seizure was probably due to leakage of contrast agent through the disrupted BBB. It does not indicate a cerebral infarction or haemorrhage. The patient's relatively intact neurological status and the resolution of the abnormalities on CT within 24–48 hours confirm our conclusions. The unilateral CT changes make one wonder if the ictal activity originated from the left hemisphere. However, an EEG performed 32–48 hours after the ictus failed to reveal any left hemispheric seizure focus. It is arguable that the EEG might have shown an abnormality if the study had been done soon after the ictus.

It is important to be aware of this possibility when interpreting abnormal CT scans performed soon after seizures. Failure to recognise this may lead to erroneous diagnosis and unwarranted expensive investigations. Proper diagnosis is not only cost-effective but will also avoid unnecessary distress both for the patient and the physician.

Final diagnosis

Anteroseptal myocardial infarction, contrast medium-induced seizure, and false-positive CT abnormalities due to post-seizure disruption of the blood–brain barrier.

Keywords: seizure; myocardial infarction; blood–brain barrier; contrast media

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Growth failure: an unusual clinical problem

Shailendra Kumar Singh, Santosh Kumar Singh, Richa Chaturvedi, Manoj Chaudhari, M Rai, S K Singh, J K Agrawal

A 9-year-old boy presented with short stature and progressive genu valgum (figure 1). He had frontal bossing, rachitic rosary and widening of wrist. X-Rays of the wrist (figure 2) and knee joint (figure 3) showed cupping, fraying and widening of metaphyses. Laboratory investigations showed serum calcium 9.4 mg/dl, phosphorus 2.2 mg/dl, chloride 105 mmol/l, potassium 3.0 mmol/l, alkaline phosphatase 1004 IU/l, and albumin 4.1 g/dl. 24-Hour urinary calcium excretion was 302 mg. Intact parathyroid hormone (iPTH) level was 50 pg/ml. Blood pH was 7.32 and urine pH 8.0. Intravenous pyelogram was normal. A longitudinal ultrasound scan of the kidneys is shown in figure 4. A test was done to confirm the diagnosis.

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Figure 1 The patient (reproduced with his father's permission)



Figure 2 X-Ray of the wrist



Figure 3 X-Ray of the knee joint



Figure 4 Longitudinal ultrasound scan of kidney

Questions

- 1 What does the abdominal ultrasound show?
- 2 What is the most likely diagnosis?
- 3 Name the test for confirmation of diagnosis.
- 4 How should this patient be managed?

Answers

QUESTION 1

The ultrasound scan of the kidneys shows hyperechoic renal pyramids with normal echotexture of the cortex. Renal size on both sides appear normal with normal central sinus echos. Pelvicalyceal system of both kidneys are normal. These features are suggestive of medullary nephrocalcinosis.

QUESTION 2

The diagnosis is distal renal tubular acidosis (RTA) with rickets. The patient had normal iPTH and hyperchloraemic acidosis with nephrocalcinosis in the presence of clinical and biochemical changes of rickets.

QUESTION 3

The confirmatory test is the NH_4Cl challenge test: 0.1 g (1.9 mmol) NH_4Cl /kg body weight is administered orally and blood and urine pH are followed for up to 6 h. In distal RTA the urine pH remains higher than 5.5.

QUESTION 4

The disease can be treated with sodium bicarbonate or Shohl's solution (Na^+ and K^+ citrate solution). The dose should be 0.5–2.0 mmol/kg body weight in four to five divided doses daily. The dose should be raised until acidosis and hypercalciuria are controlled. The patient should be followed by measurements of serum chloride, pCO_2 in blood, and urinary calcium excretion, approximately twice yearly. Potassium supplementation is normally not required. The requirement of alkali usually rises during intercurrent illnesses. Corrective osteotomy may be done only when the rachitic changes have healed.

Discussion

RTA is a disorder of renal tubules in which the renal excretion of acid is reduced out of proportion to reduction of glomerular filtration rate.¹ Metabolic acidosis results but, in contrast to renal failure, the anions that accompany surplus hydrogen ions in the blood such as sulphate and phosphate, are excreted normally and are unavailable to balance the fall in serum bicarbonate. Therefore the kidneys reabsorb chloride in unusually large amounts and serum chloride rises to preserve electroneutrality in the extracellular fluid. The result is hyperchloraemic acidosis, and unmeasured anion gap is normal.^{1,2} There are at least four types of RTA.

Summary points

- distal RTA is a rare condition
- in cases of rickets, if there is nephrocalcinosis in association with hyperchloraemic acidosis and alkaline urine, one should always suspect distal RTA
- the diagnosis is proved by a positive NH_4Cl challenge test
- sodium bicarbonate or Shohl's solution is the cornerstone of treatment

Distal RTA is characterised by hypokalaemic hyperchloraemic metabolic acidosis and is due to selective deficiency in H^+ ion secretion in the distal nephrons. Despite acidosis, urinary pH is high and it cannot be acidified below 5.5.³ Urinary excretion of NH_4^+ is decreased and the urinary anion gap is positive. Chronic acidosis lowers tubular reabsorption of calcium, causing renal hypercalciuria.⁴ The hypercalciuria, alkaline urine and low level of urinary citrate cause calcium phosphate stones and nephrocalcinosis.⁵ Growth in children is stunted because of rickets. The bone disease is due to the acidosis-induced loss of bone mineral and inadequate production of $1,25(\text{OH})_2 \text{D}_3$.¹ Since kidneys do not conserve potassium or concentrate the urine normally, polyuria and hypokalaemia occurs. The diagnosis is suggested by rickets or osteomalacia, hyperchloraemic acidosis, alkaline urine and calcium phosphate stones or nephrocalcinosis. NH_4Cl challenge (see above) confirms the diagnosis. Although systemic acidosis worsens, urine pH does not fall below 5.5.

Distal RTA is treated with sodium bicarbonate and/or Shohl's solution (Na^+ and K^+ citrate), as stated above. The total dose of alkali should be raised until acidosis and hypercalciuria are both eliminated and patients should be followed by measurement of serum chloride and pCO_2 in blood and urine calcium excretion approximately twice yearly. K^+ supplementation is required only when there is hypokalaemia-mediated muscle weakness and respiratory depression.¹

Final diagnosis

Rickets with distal renal tubular acidosis.

Keywords: renal tubular acidosis; nephrocalcinosis; ammonium chloride challenge test; rickets

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Mediastinal fatty tumour

John D Urschel, Dorothy M Urschel

A 60-year-old man complained of dyspnoea and recurrent pulmonary infections. He was an ex-smoker. Medical history was unremarkable. He denied cough, haemoptysis, and chest pain. Physical examination did not show any abnormalities. Basic laboratory studies and an electrocardiogram were normal. A chest X-ray showed a subtle mediastinal abnormality (figure 1), so a computed tomography (CT) scan of the chest was done. It showed a large mass in the mediastinum (figure 2).



Figure 1 Chest X-ray shows a subtle abnormality overlying the left heart border

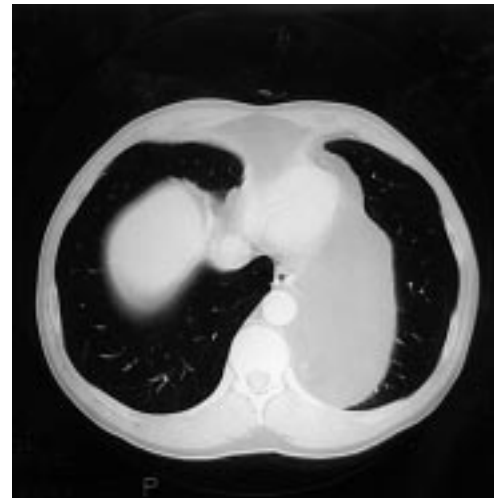


Figure 2 CT scan showing a large mediastinal mass

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Questions

- 1 What is the differential diagnosis?
- 2 What biopsy techniques are appropriate?
- 3 What is the treatment?

Answers

QUESTION 1

The CT shows a homogenous mass with a tissue density consistent with fat. The differential diagnosis of mediastinal fatty tumours includes lipoma, liposarcoma, thymolipoma, and herniated peritoneal fat (hiatus or diaphragmatic hernia). Thymolipomas arise in the thymus gland (anterior mediastinum). Small fatty 'masses' in the inferior-posterior mediastinum often represent hiatus hernias, but it is unusual for large mediastinal fatty masses to be hernias. Large hernias usually consist of stomach or bowel, in addition to herniated peritoneal fat. The main differential diagnoses in this case are lipoma and liposarcoma.

QUESTION 2

Needle biopsies, either fine needle or core, are often inadequate for accurate diagnosis of lipomatous tumours. Low-grade liposarcomas are difficult to distinguish from benign lipomas on needle biopsy. Larger tissue specimens, from incisional or excisional biopsies, are usually required.

QUESTION 3

Complete excision (resection), when feasible, is the preferred treatment for lipomatous mediastinal tumours. This provides the pathologist with adequate tissue for diagnostic purposes, and the procedure is therapeutic as well.

Discussion

Mediastinal lipomas and liposarcomas are rare.¹⁻³ They comprise less than 1% of all mediastinal tumours. A small tumour may be asymptomatic, but as the tumour increases in

size compression of intrathoracic structures causes symptoms. Our patient's dyspnoea, for example, was relieved by tumour removal. Liposarcomas invade adjacent organs, so they are more likely to be symptomatic than benign lipomas, which simply compress adjacent structures.

Given the difficulty of accurate diagnosis with needle biopsies of lipomatous masses, complete excision is the diagnostic and therapeutic procedure of choice whenever possible. However, if the CT scan suggests that complete resection cannot be accomplished, there is little point in proceeding with a surgical procedure that leaves tumour in situ.² In this situation an attempt at needle biopsy, or thoracoscopic incisional biopsy, are appropriate diagnostic procedures. Our patient's tumour was completely excised through a limited muscle-sparing thoracotomy. Final pathology showed a benign lipoma. The resection provided a diagnosis, relieved symptoms (dyspnoea) and prevented potential future problems from tumour growth.

Recurrence of a completely resected benign mediastinal lipoma is unlikely. However, if a liposarcoma had been found, the prognosis would have been quite poor.¹ Mediastinal liposarcomas often invade adjacent vital organs, and microscopically complete tumour resection is difficult. Unfortunately, adjuvant treatment with radiation therapy or chemotherapy has not been very effective in intrathoracic mediastinal liposarcomas.^{1 4}

Final diagnosis

Benign mediastinal lipoma.

Keywords: lipoma; liposarcoma; mediastinal tumours

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Cavitary lung lesion in a patient with Sjögren's syndrome

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A 51-year-old woman was admitted to the hospital after 5 days of fever, cough, minor greenish sputum and right pleuritic pain. A non-smoker, she had a history of non-insulin-dependent diabetes and Sjögren's syndrome. Her temperature was 39°C and her blood pressure was 160/75 mmHg. Pulmonary auscultation revealed right rales. The physical examination was otherwise unremarkable.

The white blood cell count was $12\,930 \times 10^9/l$ (88% neutrophils, 10% bands and 2% lymphocytes). The haemoglobin level was 8.8 g/dl and the erythrocyte sedimentation rate was 118 mm. The PaO₂ when the patient was breathing ambient air was 63 mmHg. A Gram stain of the sputum revealed Gram-positive cocci. Three blood cultures obtained on admission yielded *Streptococcus pneumoniae*. The isolate was characterised as serotype 35. A chest X-ray taken on admission disclosed a parenchymal infiltrate in the right lower lobe (figure 1). A X-ray taken 14 days later displayed a cavity with an air crescent sign. A computed tomography (CT) scan showed lung tissue within the cavity (figure 2).



Figure 1 Admission chest X-ray



Figure 2 Thoracic CT scan

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Questions

- 1 What is the diagnosis?
- 2 What pulmonary alterations are associated with Sjögren's syndrome?
- 3 What is the management?

Answers

QUESTION 1

The diagnosis is pneumococcal pneumonia complicated by pulmonary gangrene. Although a definitive diagnosis of pulmonary gangrene requires pathological confirmation, the radiologic findings are typical. The presence of a fluid-filled cavity in which irregular pieces of sloughed lung parenchyma float like icebergs is virtually diagnostic

QUESTION 2

The pulmonary abnormalities associated with Sjögren's syndrome are listed in the box.

Pulmonary alterations associated with Sjögren's syndrome

- xerotrachea
- chronic bronchitis
- atelectasis
- recurrent pneumonia
- interstitial alveolitis
- lymphoid interstitial pneumonia
- bronchiolitis obliterans with/without organising pneumonia
- interstitial fibrosis
- lymphoma
- amyloidosis
- pulmonary hypertension

QUESTION 3

Although successful medical management of pulmonary gangrene has been described, the majority of cases have been treated surgically, either by drainage or resection. Our patient was treated with antibiotic therapy (penicillin G 4 million U six times daily for 4 weeks and tobramycin 80 mg intravenously bid during the first 2 weeks) and percutaneous drainage.

Discussion

Pulmonary gangrene involves massive necrosis of lung parenchyma secondary to an overwhelming inflammatory pyogenic process that

is mediated by thrombosis of small and large arteries. The presence of lung tissue within a cavity is the result of secondary pulmonary infarction. The most frequently involved microorganisms are *Klebsiella pneumoniae* and *Streptococcus pneumoniae*. Other pathogens may be involved, including other Gram-negative bacilli, *Mycobacterium tuberculosis* and anaerobes.^{1,2} *S pneumoniae* has been described as the responsible microorganism in 11 cases, including the present one.

The pathophysiology of pulmonary gangrene is not well defined. The mechanism is multifactorial, including both microorganism and host factors. Serotype 3 pneumococci are known to cause more severe necrosis than other types.³ In our patient, not only were serotype 35 pneumococci isolated, moreover, she suffers from a primary Sjögren's syndrome. Pulmonary abnormalities in patients with primary Sjögren's syndrome have been well documented.⁴ Peripheral airways can be involved and the result is respiratory tract infection. Another factor associated with Sjögren's syndrome is the presence of pulmonary vasculitis. The vasculitis process, by means of local activation of the coagulation cascade, could explain the thrombosis and accompanying infarction. This is the first documented case of pulmonary gangrene associated with Sjögren's syndrome.

Although definitive diagnosis requires pathological confirmation, the typical roentgenographic picture is virtually diagnostic.² The most useful procedure is CT, which shows the presence of lung tissue within the cavity. This cavity occurs in the upper lobes in 80% of cases.

The optimal therapeutic approach to infectious pulmonary gangrene has not been delineated accurately because of the extreme rarity of the condition. Antibiotic therapy alone may be effective, but in many cases urgent surgical measures are required.⁵ In this case, percutaneous drainage was a useful therapeutic procedure and no surgical measures were necessary.

Final diagnosis

Pulmonary gangrene.

Keywords: Sjögren's syndrome; pulmonary gangrene

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A case of painful thigh

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A 29-year-old previously fit Asian man presented with a 3-month history of diffuse pain in the right thigh, with no obvious swelling or paraesthesia. He had no pyrexia, nocturnal sweats or any significant weight loss. He had no history of travel abroad nor had he any contact with tuberculosis. Physical examination revealed a thin man with a temperature of 37°C and no palpable lymphadenopathy. Systemic examinations were otherwise unremarkable. Examination of the right thigh did not reveal any tenderness or swelling but straight leg raising on the right was restricted to 40° (active) due to pain. Straight leg raising on the left was normal. There was no objective sensory impairment or abnormal reflexes in the lower limbs.

Initial investigations showed a haemoglobin of 11.8 g/dl with a mean corpuscular volume of 62.3 (thalassaemic trait). His white cell and differential counts were normal. Plasma viscosity was raised at 2.2 (normal range up to 1.7). The following tests were normal or negative: rheumatoid factor, antinuclear factor, immunoglobulin electrophoresis and quantitative immunoglobulin assay, blood culture and creatine kinase; C-reactive protein was elevated at 61.9 mg/l (normal range 0–6). Radiographs of the chest, thoracic and lumbosacral spine and hip did not show any abnormality. An isotope bone scan (Tc99) was normal. Computed tomography (CT) of his lumbosacral spine failed to reveal any abnormality apart from a mild disc prolapse.

He was advised strong analgesics and physiotherapy and at review, 3 weeks later, an ill-defined painless fluctuant swelling on the right lateral thigh was discovered. A diagnostic aspiration revealed pus which was negative on Gram stain. Subsequent Zeil Nielson stain was also negative. An ultrasound scan of the right thigh showed extension of a cavity towards the right groin suggesting the possibility of a psoas abscess. A further CT scan of the abdomen (figures 1 and 2) failed to demonstrate any collection over the psoas or inside the pelvis and there was no connection with any intra-abdominal structure or the hip joint. However, the CT scan of the thigh muscles revealed a collection within the muscle planes of the glutei on the right extending to the right mid thigh (figure 3). A thoracic CT scan did not show any mediastinal, hilar or axillary lymphadenopathy. The lung fields were clear.

Seven hundred mls of pus was drained from the loculated swelling. There was no lymphadenopathy or intra-abdominal extension of the abscess cavity. The 'cavity' was loculated between the gluteus maximus and medius muscles.

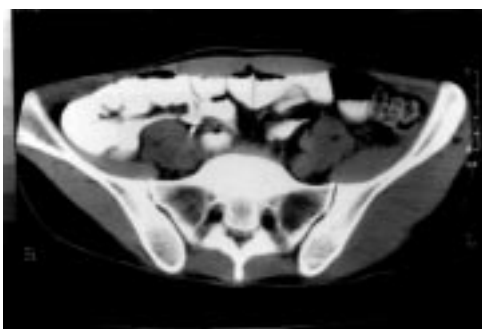


Figure 1 Abdominal CT scan

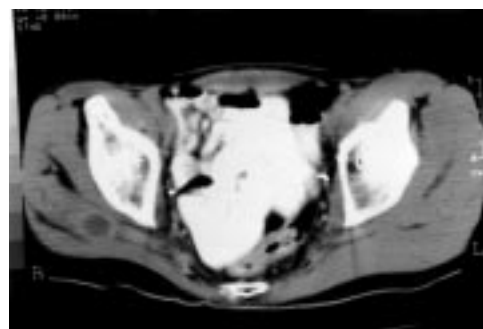


Figure 2 Abdominal CT scan

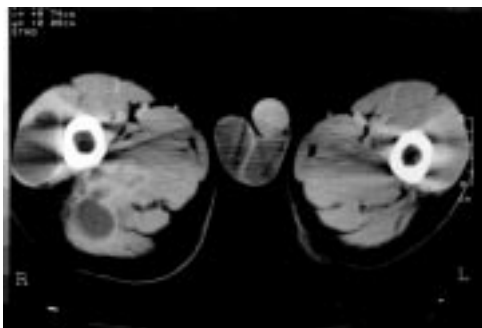


Figure 3 CT scan of the thigh muscles

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Questions

- 1 What do the CT scans in figures 1 and 2 show?
- 2 What is the most likely diagnosis on the basis of the CT scan findings?

Answers

QUESTION 1

Figure 1 shows the normal outline of the psoas muscles with no evidence of intra-abdominal collection. Figure 2 shows a space-occupying lesion within the right gluteal region, which could either be an abscess cavity or a necrotic mass, not in communication with either a joint or intra-abdominal structure.

QUESTION 2

The most likely diagnosis is intramuscular abscess caused by a tubercular infection as the diagnostic aspiration yielded pus which was negative on Gram stain and also ordinary bacterial culture. The aspirated pus, however, showed profuse growth of acid fast bacilli, on culture. He was treated with rifampicin, ethambutol, isoniazid and pyrazinamide with complete resolution of his symptoms and no recurrence.

Primary intramuscular tubercular abscess is extremely rare and one should make a positive attempt to exclude intra-abdominal collection as psoas abscess may track down the groin or the thigh and present a similar clinical picture. It is not uncommon in patients who are immunosuppressed.

Discussion

Primary skeletal muscle tuberculosis is extremely rare and earlier studies have reported only four cases of muscle tuberculosis in 2224 autopsy specimens from tubercular patients and one in 60000 cases of all types of tuberculosis.^{1,2} By far the commonest site of involvement of the skeleton is the spine (50% of cases), followed by hip and the knee. Our patient did not have any focal lesion on the spi-

nal CT scan and there was no evidence of any psoas abscess.

The involvement of skeletal muscle in tuberculosis is usually by a direct extension from a neighbouring joint or rarely by haematogenous spread. The pathophysiological mechanism is not clear but it is possible that high lactic acid content of muscles, absence of reticulo-endothelial cells and lymphatic tissue in muscles associated with very rich blood supply may help towards the localisation of the bacteria in the muscles. Our patient was unusual as he had no systemic symptoms of any illness, no evidence of spinal tuberculosis, and no psoas abscess, which is one of the commonest presentations of swelling in the upper part of the thigh.

Discitis with or without psoas abscess is a common presenting feature in only 5–10% of cases of musculoskeletal tuberculosis. It is important to remember unusual presentations of tuberculosis in the appropriate racial background. It is important also to include symptomatic areas for scanning other than the typically described sites of spinal tuberculosis. Our patient was also somewhat unusual as he had no clinical or serological evidence of primary immune deficiency. He was neither a drug addict nor had any abnormal sexual behaviour. Although psoas abscess is a common cause of a swelling in the thigh, rare causes such as primary intramuscular tubercular abscess should also be considered in the differential diagnosis of painful swellings.

Final diagnosis

Intramuscular abscess caused by a tubercular infection.

Keywords: intramuscular abscess; tuberculosis

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An unusual case of hypercalcaemia

R Gama, J Wright, G Ferns

A 53-year-old woman presented to her general practitioner with a 3-month history of lethargy. She was taking lithium carbonate (900 mg daily for 9 years) and carbamazepine (400 mg daily for 3 years) for manic depressive illness, and thyroxine (50 µg daily for 4 years) for primary hypothyroidism. She smoked 20 cigarettes a day. There was no abnormality on examination. Investigations revealed hypercalcaemia (serum calcium 3.05 mmol/l). Subsequent relevant investigations are shown in the table. Chest, abdominal, hands and skull X-rays revealed no abnormality.

Table Biochemical and haematological investigations

<i>Test</i>	<i>Result</i>	<i>Reference range</i>
Albumin (g/l)	40	37–55
Corrected calcium (mmol/l)	3.16	2.1–2.5
Uncorrected calcium (mmol/l)	3.16	2.1–2.6
Phosphate (mmol/l)	0.54	0.8–1.4
Intact parathyroid hormone (pmol/l)	13.2	0.5–5.5
Magnesium (mmol/l)	0.9	0.65–1.0
Creatinine (µmol/l)	90	45–120
Alkaline phosphatase (IU/l)	111	30–130
Protein electrophoresis	normal	
Haemoglobin (g/l)	129	115–160
ESR (mm)	2	< 5
Lithium (mmol/l)	0.7	0.5–1.2
Thyroxine (nmol/l)	102	60–160
Thyroid stimulating hormone (mU/l)	1.8	0.3–4.5
Thyroid microsomal antibodies	negative	
Bilirubin (µmol/l)	< 20	< 20
Aspartate aminotransferase (IU/l)	35	< 45
Gamma glutamyl transferase (IU/l)	108	< 55

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Questions

- 1 What is the cause of the hypercalcaemia?
- 2 What further investigations would you request?
- 3 How would you manage the hypercalcaemia?

Answers

QUESTION 1

An inappropriately elevated parathyroid hormone concentration in the presence of hypercalcaemia and normal renal function is diagnostic of primary hyperparathyroidism (HPT). Since the patient was on lithium, this raises the possibility of lithium-induced primary hyperparathyroidism.

QUESTION 2

Thallium-technetium subtraction scans and ultrasound scans are the more commonly used techniques to aid pre-operative localization of a possible adenoma. Computed axial tomographic scans and magnetic resonance imaging scans are also available, selective neck venous sampling for parathyroid hormone may be used and arteriography is rarely used. There is, however, some debate about the value of routine pre-operative localisation procedures in patients without previous neck surgery. In this case ultrasound of the neck and a thallium-technetium subtraction scan showed no abnormality.

QUESTION 3

Mild asymptomatic hypercalcaemia in elderly patients may just require monitoring of serum calcium. Indications for surgery include young patients, complications of HPT (bone disease, renal disease, urinary calculi, resistant hypertension, resistant peptic ulceration), symptomatic hypercalcaemia or persistent marked hypercalcaemia (serum Ca > 3.00 mmol/l). This patient was referred for surgical correction of her HPT because of her marked hypercalcaemia. Pre-operative evaluation confirmed HPT but it was noted that she was on lithium. Surgery was deferred and, after discussion with the psychiatrists, the lithium was discontinued and her manic-depressive illness managed with carbamazepine. This led to resolution of the hypercalcaemia within one month, which supported the diagnosis of lithium-induced HPT. We also considered the possibility that her primary hypothyroidism was lithium-induced but the patient refused to stop thyroxine therapy.

Discussion

Lithium is widely used in the management of acute mania, resistant depression, and prophylaxis of unipolar and bipolar affective disorders. Primary hyperparathyroidism is more prevalent in patients on lithium therapy.¹ This

Endocrine complications of lithium therapy⁵

- thyroid disease: primary hypothyroidism (5–15%)
- goitre (5%)
- thyrotoxicosis (rare)
- nephrogenic diabetes insipidus (20–25%)
- hyperparathyroidism (2.7%)
- diabetes mellitus (rare)

increased prevalence may be due to unmasking of pre-existing parathyroid disease or to a direct effect of lithium on the parathyroid glands. Since hypercalcaemia can occur within a few days or several years of lithium therapy, it has been suggested that there are two varieties of lithium-induced HPT; an early onset HPT due to unmasking of an adenoma and a late-onset HPT due to parathyroid hyperplasia with possible end-point adenomatous change due to chronic lithium stimulation.² Lithium may promote hypercalcaemia by two mechanisms. Lithium directly stimulates the secretion of parathyroid hormone,³ which may partly explain early-onset HPT. Lithium also decreases intracellular calcium uptake, thus reducing parathyroid sensitivity to circulating calcium levels leading to an increase in parathormone concentration.⁴ This resetting of the 'calciostat' may explain the pathogenesis of late-onset lithium-induced HPT by a mechanism similar to that found in other forms of HPT. Discontinuation of lithium usually corrects the HPT, but it need not be discontinued in mild asymptomatic uncomplicated hypercalcaemia provided serum calcium is monitored.¹ The usual indications for surgery in HPT apply to lithium-induced HPT persisting after withdrawal of lithium or when it is medically inadvisable to stop lithium therapy.¹

In summary, this case illustrates the importance of recognising lithium-induced HPT which may be reversible on stopping lithium and thus avoiding potentially unnecessary neck surgery.

Final diagnosis

Lithium-induced primary hyperparathyroidism.

Keywords: lithium; calcium; hyperparathyroidism

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