colour. Apart from the schizophrenia he had a history of hypercholesterolaemia and sickle-cell trait. His long-term medications were simvastatin and depot flupenthixol. His alcohol consumption was 28 units per week. On examination he was icteric and mildly dehydrated but afebrile. Full blood count on admission showed a normocytic anaemia (haemoglobin 8.2 g/dL, mean corpuscular volume 98 fL), a white cell count of $21.2 \times 10^9/L$ with neutrophilia and platelets $251 \times 10^9/L$. Total bilirubin was 132 $\mu\text{mol/L}$ (normal 0–19) and conjugated bilirubin was 19 $\mu\text{mol/L}$ (0–4). Liver function tests were normal except for an aspartate aminotransferase of 82 iu/L (7–40). Dipstick urinalysis revealed blood and protein. Tests for viral hepatitis were negative. A blood film the following day showed irregularly contracted red cells with puddling, red cell fragments, spherocytes, nucleated red blood cells and hemighosts with 6.9% reticulocytes (0.2–2.0). Direct and indirect Coombs tests were negative and serum haptoglobins were undetectable. The urine contained haemoglobin but not haemosiderin or bilirubin. The results were compatible with non-immune intravascular haemolysis. The sickle-cell trait was confirmed by electrophoresis. His haemoglobin subsequently dropped to 6.4 g/dL, requiring a four-unit blood transfusion, and then remained stable at 13 g/dL.

The patient's admission had been voluntary, and outside the psychiatric unit he had been obtaining cannabis daily and crack cocaine occasionally. In addition, two days before the development of red urine, he had inhaled amyl nitrite ('poppers'). This was the first time he had used poppers for several months, and on previous occasions there had been no similar symptoms. Further investigation, such as measurement of glucose-6-phosphate dehydrogenase (G-6-PD), was impossible because the patient did not attend for follow-up.

COMMENT

We suspect that the severe intravascular haemolysis in this patient resulted from his inhalation of amyl nitrite. A few cases of this sort have been reported previously.^{1–3} The possibility of G-6-PD deficiency cannot be excluded as a contributory factor, although the lack of previous episodes argues against it. Potent oxidants such as cyclic aromatic compounds, chlorate and nitrites can produce haemolytic anaemia in the absence of G-6-PD deficiency by damaging the erythrocyte membrane.⁴ Haemoglobin oxidized from the ferrous to the ferric form is known as methaemoglobin (MetHb) and cannot transport oxygen.⁵ Acute oxidative damage can lead to the formation of Heinz bodies (precipitated haemoglobin aggregates) which are cleared by the spleen and may not be detected on a peripheral blood film. In addition, oxygen transport is hampered by methaemoglobinaemia, due to oxidation of haemoglobin.⁵

Heinz bodies occur after the inhalation of just 30 mL of amyl nitrite,¹ and a high proportion of hemighosts is a marker for poor outcome.⁶

Methaemoglobinaemia can be treated with intravenous methylene blue 2 mg/kg,² and this is advised when the concentration exceeds 30–40%. This method depends on intact G-6-PD and phosphate shunt pathways and is therefore ineffective in G-6-PD deficiency. When MetHb levels and the proportion of hemighosts are high, exchange transfusion may be indicated.

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Recurrent axillary vein thrombosis as a manifestation of syringomyelia

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Neuropathic arthropathy of the shoulder can complicate many diseases in adults and children. In the early stages, the manifestations can raise diagnostic challenges.

CASE HISTORY

A man of 53 sought advice when his right arm became grossly swollen. He gave no history of trauma or shoulder

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pain, although on examination there was limitation of external rotation of the joint. Because neurological symptoms were not reported, examination of the nervous system did not include detailed tests of sensation. A doppler scan of the right arm showed extensive brachial, axillary and distal subclavian vein thrombosis. Routine blood tests gave normal results, as did a full thrombophilia screen including total and free protein S, protein C, antithrombin III, and activated protein C resistance. A radiograph of the shoulder showed a healed fracture of the right acromion. On CT of the thorax and abdomen there was no abnormality although views of the right shoulder were not adequate. An orthopaedic surgeon gave the opinion that the fractured acromion was of long standing. No cause for the right axillary vein thrombosis was identified. The patient received anticoagulant therapy (warfarin) for six months and the swelling in his arm resolved.

Six months after stopping anticoagulants the swelling in his right arm recurred. On this occasion he disclosed that for 2 years he had lacked temperature sensation in the right hand, which could not judge the heat of his bathwater and did not register cold. During this time he had sustained a grade-two burn to the right forearm from a petrol engine. He also recalled an episode in which his right shoulder clicked and became slightly painful while he was lifting heavy objects. There had been no headache, disturbance of vision, speech or sphincters, or paraesthesiae. On this occasion the right arm was tensely swollen, with non-pitting oedema. Peripheral pulses were intact. There was a gross effusion of the right shoulder joint and abduction was limited to 80°. Deep tendon reflexes were diminished in both arms, especially the right, and there was loss of pain in

Figure 1 MRI of the shoulder. Coronal image showing fragmentation of the glenoid with irregularity of the articular surface of the humeral. There is a large effusion extending superiorly

Figure 2 MRI of the cervical spine. Note low-lying cerebellar tonsils (arrow) and syrinx in the cervical and thoracic cord

the right C5, C6 and C7 dermatomes. Temperature sensation was diminished in all dermatomes from C3 to T2 on the right. The other sensory modalities were intact and his gait was normal. Screening tests for syphilis and vasculitis were negative. Doppler colour flow ultrasound revealed thrombosis in the distal axillary and brachial veins and a large unilocular effusion around the shoulder joint with a further collection medially in the upper arm compressing the veins. On radiography the right shoulder had typical features of a neuropathic joint and MRI showed fragmentation of the posterior aspect of the glenoid with irregularity of the articular surface of the humeral head and an extensive tear of the superior rotator cuff. The large effusion in the shoulder joint was compressing the axillary and brachial veins (Figure 1). MRI of the spine (Figure 2) showed an Arnold–Chiari type 1 malformation, and syringomyelia throughout the cervical and thoracic cord. There was no evidence of a cord tumour. On CT of the brain there was mild enlargement of the third and lateral ventricles; the fourth ventricle was normal and callosal dysgenesis was absent. After a further period of anti-coagulant therapy he underwent foramen magnum decompression and duraplasty.

COMMENT

Neuropathic arthropathy, also known as a Charcot joint, is a progressive destructive arthropathy in an area of sensory loss. The commonest cause in the UK is diabetes mellitus, usually affecting the joints of the lower limb. In certain developing countries leprosy and yaws are more important and tabes dorsalis (syphilis) must not be forgotten.¹ Rarer causes of Charcot arthropathy include syringomyelia, head and spinal cord injuries, amyloid neuropathy, ulcerative-mutilating acropathy, post-renal transplant neuropathy, alcohol-related neuropathy and intra-articular steroid injections. Congenital causes include congenital insensitivity to pain, spina bifida and familial dysautonomia of the Riley–Day type.²

In a patient with a neuropathic shoulder joint, the most likely cause is syringomyelia.^{1,3} In this condition, there is interruption of the lateral spinothalamic tract fibres that mediate pain and temperature sensation as they decussate in the spinal cord.⁴ The proximity of the decussating fibres to the syrinx cavity causes the characteristic pain and temperature sensory loss (fibres that decussate caudal to the syrinx are spared so that the sensory loss is ‘suspended’). Neurological evaluation shows abnormalities in deep sensation and absence of the deep tendon reflexes.² After the shoulder joint, the neuroarthropathy affects in decreasing order of frequency the elbow, wrist and fingers.

The damage to joints is believed to result from excessive mobility through decreased muscle tone and ligament hyperlaxity. These predispose to osteophyte development, cartilage loss, and ossification of the ligaments. In most cases the absence of pain means that joint destruction is far advanced, with subluxation, malalignment and instability, by the time of diagnosis. In our patient, such changes were not evident at the time of his first thrombosis. His second axillary vein thrombosis was clearly due to compression by a joint effusion, and this time the neurological signs were clear.

This case illustrates that, in cases of axillary vein thrombosis where there is evidence of trauma to the shoulder joint, examination should include detailed tests of temperature and pain sensation.

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