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Netherlands Journal of Medicine 48 (1996) 227–231

The Netherlands
JOURNAL OF
MEDICINE

Brief report

Vertebral bone destruction in sickle cell disease: infection, infarction or both

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Received 12 May 1995; revised 11 August 1995; accepted 15 August 1995

Abstract

Infectious and vaso-occlusive vertebral bone and joint destruction in two patients with sickle cell disease (SCD) are featured by H-shaped vertebrae, kyphotic angulation, osteolysis of endplates and collapse of intervertebral discs as shown by X-ray films and magnetic resonance imaging. Staphylococcal serology supported the diagnosis of staphylococcal osteomyelitis/spondylo-discitis in both SCD patients. The difficulties of establishing the causes and treatment of the osteoarthropathy in these particular cases are discussed in the light of the literature.

Keywords: Sickle cell disease; Osteomyelitis; Septic arthritis; Bone infarctions

1. Introduction

Individuals with sickle cell disease (SCD) are highly susceptible to bacterial infections due to functional asplenism and impaired microcirculation [1,2]. Bone involvement in SCD consists of marrow hyperplasia, microvascular thrombosis, infarction and aseptic necrosis resulting in formation of a nidus on which bacteria may thrive [3,4]. A vicious cycle of local hypoxia and further sickling of red cells may cause an area of bone infarction. Moreover, the anaemia-induced marrow hyperplasia itself may cause stasis in sinusoidal spaces, leading to increased sickling of red blood cells in these areas [4]. Vaso-occlusive destruction, osteomyelitis and septic arthritis all contribute to progressive skeletal damage. In two patients with SCD we describe the osteoarthropathy and the difficulties of establishing its causes.

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Elsevier Science B.V.
SSDI 0300-2977(95)00075-5

2. Case reports

2.1. Case 1

A 31-year-old black female with homozygous SCD presented with a 6-week history of fever, cold shivers, malaise, weight loss, localized mid-back pain, a swollen painful right ankle and a recent productive cough. Three years before she had been treated for a salmonella coxitis and osteomyelitis.

Physical examination revealed fever (38.2°C), thoracic hyperkyphosis, pain on pressure of the 12th thoracic and 1st lumbar vertebra (Th12 and L1), and a warm painful swelling of the right ankle. Abnormal laboratory data were (normal values between brackets): ESR 20 increasing up to 102 mm/h (< 10 mm/h), haemoglobin 6.2 mmol/l (7.3–9.3 mmol/l), Howell-Jolly bodies being present, reticulocyte count 53‰ (5–20‰) leucocyte count 13.6×10^9/l ($4.0–10.0 \times 10^9$/l) with normal differential count and alkaline phosphatase 173 IU/l (25–75 IU/l). Blood cultures were negative, while the antistaphylolysin titre (ASTA) was positive: 8.0 IU/ml (normal: < 2 IU/ml). *Staphylococcus aureus* was cultured in synovial fluid aspirated from the right ankle. Faecal and blood cultures on salmonella were negative. A positive culture of the sputum (Löwenstein) for mycobacterium tuberculosis and an infiltrate on the chest X-ray were consistent with pulmonary tuberculosis. A spine X-ray (Fig. 1a) revealed extensive destruction of Th12–L1 and kyphotic angulation. Magnetic resonance imaging of the spine (MRI, sagittal [1] T1-weighted images, Fig. 1b) showed severe dislocation, imminent compression of the myelum and prevertebral soft tissue swelling. The diffuse low signal intensity of all vertebrae corresponds to active haematopoiesis in the bone marrow. Abnormal H-shaped vertebrae and osteolysis of the endplates were prominent on MRI and X-ray film. A bone biopsy specimen from the spine was not performed because of the imminent myelum compression. Technetium-99m-sodium-pertechnetate scintigraphy showed hot spots in the right ankle, Th12 and L1.

Pulmonary tuberculosis was treated with rifampicin 450 mg, isoniazide 200 mg, ethambutol 1 g and pyrazinamide 1 g, each orally once daily. Staphylococcal arthritis was treated with flucloxacillin 1 g intravenously 6 times daily for 2 weeks followed by clindamycin 450 mg plus sodium fusidinic acid 500 mg, each orally 3 times daily for 6 weeks. During this therapy, fever, malaise, weight loss and painful swelling of the right ankle disappeared, while mid-backpain decreased markedly. The ESR, WBC and ASTA decreased markedly. After 6 weeks of complete bedrest the spine appeared stable enough for mobilization.

2.2. Case 2

A 33-year-old black male with a sickle cell β-thalassaemia (HbA_2 4.2%; HbS 63.1%; HbF 16.2%; HbA 16.5%) presented with a 2-month history of mid- and low-backpain. He was not able to anteflect his back for more than 10 degrees. Abnormal laboratory data were (normal values between brackets): ESR 12 increasing up to 60 mm/h (< 10 mm/h), haemoglobin 7.3 mmol/l (7.8–10.0 mmol/l), reticulocyte count 19‰ (5–20‰), leucocyte count 5.3×10^9/l ($4.0–10.0 \times 10^9$/l) with normal differential count and alkaline phosphatase 117 IU/l (25–75 IU/l). Bacterial cultures from blood, faeces and bone biopsy specimen were negative. ASTA was clearly positive: 5.3 IU/ml (normal: < 2 IU/ml). Spine X-ray (Fig. 2a) showed an almost complete narrowing of the intervertebral disc Th12–L1, the endplates of these vertebrae being destroyed. MRI (sagittal [2] T2-weighted images, Fig. 2b) revealed increased signal intensity of Th12 and L1–2. Findings on both X-ray and MRI are consistent with osteomyelitis and spondylodiscitis. A bone biopsy specimen from the destroyed spine showed a hypocellular and oedematous marrow, haematopoiesis being virtually absent with predominance of lymphocytes and to a lesser extent macrophages. The microscopic picture is consistent with a chronic inflammation.

[1] T1-weighted images = images based on spin-lattice relaxation time.

[2] T2-weighted images = images based on transverse relaxation time.

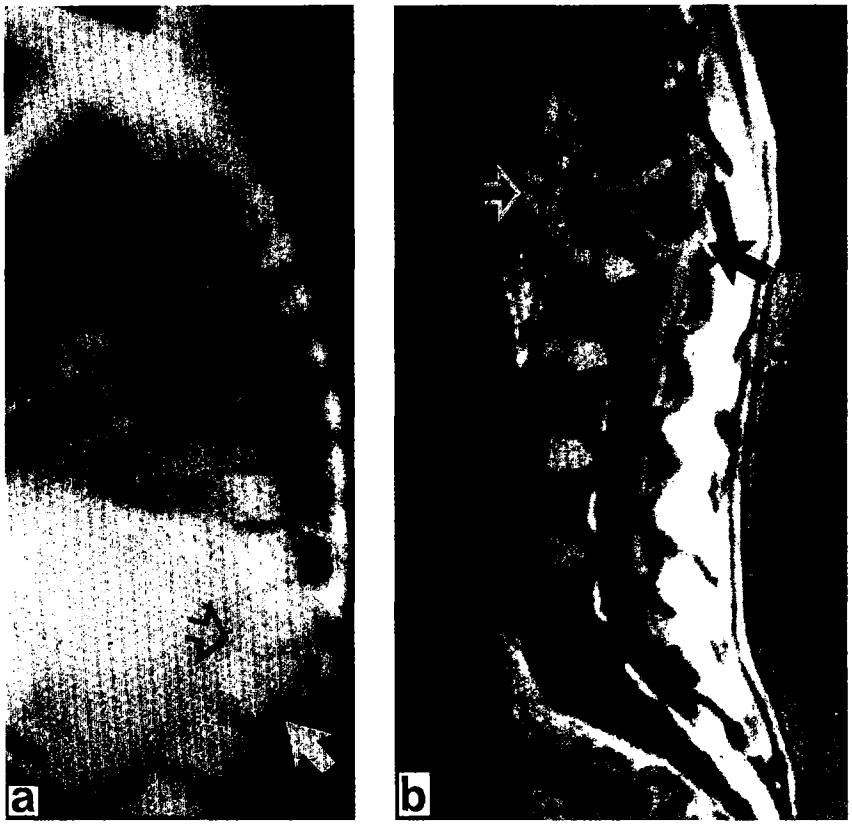

Fig. 1. Case 1. (a) Vertebral X-ray demonstrates severe destruction and dislocation of Th12–L1 (solid arrow), resulting in kyphotic angulation (open arrow). (b) Sagittal T1-weighted MR image shows prevertebral soft tissue swelling (open arrow), imminent compression of the myelum in the kyphotic angulation (solid arrow), H-shaped vertebrae and diffuse low signal intensity of all vertebrae indicating active haematopoietic tissue.

The osteomyelitis and spondylodiscitis of Th12–L1, possibly caused by staphylococcal infection in view of the elevated ASTA, were treated with ciprofloxacin 750 mg and rifampicin 600 mg, each orally 2 times daily for 6 weeks. During this therapy the backpain markedly diminished and the patient became able to anteflect his back for more than 90 degrees; the ESR and ASTA normalized.

3. Discussion

The combination of tuberculosis, septic arthritis, vertebral bone destruction and SCD is rare but not accidental [5,6]. In SCD, salmonella is the major causative organism of osteomyelitis in 70% followed in frequency by *Staphylococcus aureus* [3]. In addition, tuberculous osteomyelitis has previously been described in a patient with SCD presenting with pulmonary tuberculosis [5]. The main presenting symptom in our patients was painful destruction of Th12–L1, in combination with pulmonary tuberculosis and staphylococcus arthritis in Case 1 and spondylodiscitis in Case 2. Since ASTA is highly specific for staphylococcal infection [7], this diagnosis was also very probable in *case 2*. These bone destructions are most likely caused by infection superimposed on infarction. Differentiation between bone infection and infarction appeared to be difficult without local histological and bacteriological findings, since the symptoms and clinical features may be identical [8]. Radiographs may show multiple bone infarcts but also signs of an indolent infection in a vascularly compromised bone [6]. Bone scans

are not helpful in distinguishing bone infarction from osteomyelitis, since normal and increased uptake may be seen in both [1,8].

On the contrary, MRI is more specific in qualifying bone marrow abnormalities, also in SCD [9–11]. Normal marrow in adults has a higher signal intensity on T1-weighted images and a lower signal intensity on T2-weighted images than normal intervertebral discs. This corresponds to yellow, haematopoietic active marrow. Diffusively decreased marrow signal on T1-weighted images, as seen in our patients, reflects hypercellular haematopoietic marrow in SCD. Focal areas with low signal intensity on T1-weighted images and high signal intensity on T2-weighted images correspond to acute marrow infarction. The lesions found in both cases were located around the intervertebral disc Th12–L1 and have the classical signs of spondylodiscitis in an advanced stage: osteolysis of the endplates, diminished height of the discs, osteolysis and deformity of the vertebrae leading to kyphotic angulation and prevertebral soft tissue swelling. In Case 2 foci with increased signal intensity on T2-weighted images suggested infarction, histologically reflected by strongly suppressed haematopoiesis, superimposed by infection. The H-shaped vertebrae, characteristic of SCD in general, are caused by repeated microinfarctions in the central subchondral vertebral bone during childhood.

In conclusion, since excellent clinical responses were observed in both cases during antibacterial treatment, infectious factors rather than infarction appeared to be determinative in the development of the painful bone lesions. The value of staphylococcal serology is demonstrated. MRI may reveal classical signs of bone infection and infarction in SCD, as

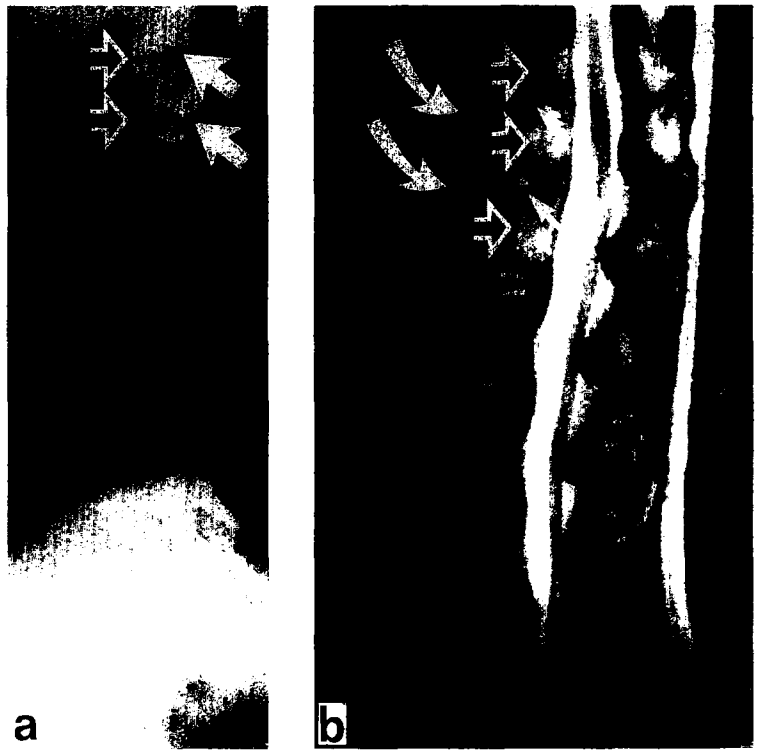

Fig. 2. Case 2. (a) Vertebral X-ray demonstrates moderate destruction of Th12–L1, with narrowing of the intervertebral discs (open arrows) and destruction of the endplates (solid arrows). (b) Sagittal T2-weighted MR image shows destruction of the endplates (solid arrows), increased signal intensity of Th12, L1 and L2 (open arrows) and prevertebral soft tissue swelling (curved arrows).

described in both cases. Early detection and treatment of osseous infections may inhibit progression of skeletal damage in SCD.

Acknowledgement

We gratefully acknowledge Prof. Dr. J.C. Birkenhäger for critically reading the manuscript.

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