Hypertrophic osteoarthropathy following aortic surgery

F Dellestable, P Péré, D Régent, A Gaucher

Clinical history

A 67 year old man presented with a one year history of increasing pain and swelling of his right lower limb. On examination he was apyrexial and there was diffuse inflammatory swelling and tenderness of his right lower limb with effusion of the knee. No clubbing was evident. Aspiration of the knee obtained a clear, mildly inflammatory synovial fluid. There were no crystals and cultures were negative. Initial laboratory investigations revealed: haemoglobin 10.8 g dl⁻¹, erythrocyte sedimentation rate 76 mm/h, C reactive protein 21 mg litre⁻¹; rheumatoid factor, antinuclear antibodies, VDRL negative; serum electrolytes, plasma calcium, alkaline phosphatase, liver function tests, and thyroid hormone concentrations normal. There was no relevant past medical history other than intermittent claudication which had been remedied by an aortobifemoral bypass with a Dacron graft five years previously.

Imaging findings and clinical course

Plain radiographs of the lower limbs were obtained. There was marked periosteal new bone formation along the diaphysis and metaphysis of the right femur, tibia, fibula and metatarsals, the left side being unaffected (figs 1-3).

^{99m}Tc methylene diphosphonate bone scan showed increased linear pericortical activity in the entire right lower limb with associated increased radionuclide uptake in the adjacent soft tissue (fig 4). The rest of the skeleton was otherwise normal. Magnetic resonance imaging (MRI) of the right knee confirmed joint effusion, mild synovitis, and periostitis appearing as a regular line of low signal intensity separated from the underlying bony cortex by a narrow line of high signal intensity (fig 5). The patient refused further investigation and went home.

Differential diagnosis

The imaging features of unilateral localised periostitis in the lower limbs can be observed in a number of disorders including chronic osteo-

Figure 1 Frontal radiograph of distal diaphysis and metaphysis of right femur showing thick, multilayered and irregular periosteal new bone formation (arrows) separated from the subjacent cortex by a thin radiolucent line.

myelitis, syphilis, patent ductus arteriosus with reversal of blood flow,¹ pulmonary metastatic disease from angioblastic meningioma,² chronic venous stasis,³ Crohn's disease,⁴ severe liver diseases (for example, primary biliary cirrhosis, Wilson's disease, biliary atresia),⁵ thyroid acropachy,⁶ polyarteritis nodosa,⁷ diverticular abscess of the colon,⁸ and primary hypertrophic osteoarthropathy.⁹ These disorders were excluded on clinical, radiological, and biological grounds. Although in our patient left distal pulses were palpable and intermittent claudication was not present at initial presentation, an ischaemic left lower limb could not be totally ruled out. Indeed, this potential change in regional vascular distrib-

Hôpital de
Nancy-Brabois,
France:
Clinique de
Rhumatologie and
URA CNRS 1288
F Dellestable
P Péré
A Gaucher

Département de
Radiologie
D Régent

Correspondence to:
Dr A Gaucher, Clinique de
Rhumatologie, Hôpital de
Nancy-Brabois, rue du
Morvan, 54511 Vandœuvre
les Nancy, France.

Accepted for publication
12 August 1996

ution with relatively increased blood flow to the right lower extremity might have accounted for the preferential development of osseous changes

Figure 2 Frontal radiograph of right ankle showing periostitis along cortical surfaces of distal tibia and fibula (arrows) and ossification of the interosseous membrane (arrowheads).

Figure 3 Anteroposterior radiograph of right foot showing linear periostitis of the metatarsal bones (white arrow and black arrowheads) and metatarsophalangeal joints osteoporosis.

in that limb. Thus the initial diagnosis was unilateral periostitis associated with differential arterial perfusion distal to an aortic graft.

Follow up and final diagnosis

Four months later the patient was readmitted for acute ischaemia of his left lower limb with chills and fever of several weeks duration. Blood cultures were positive for *Streptococcus milleri*. An extra-anatomical axillobifemoral bypass was performed with excision of the aortobifemoral graft. A severe infection of the resected graft grew *Enterococcus* and *Corynebacterium xerosis*. Despite lower extremity revascularisation and intensive antibiotic treatment, the patient died from cardiac and septic complications. No necropsy was performed. The final diagnosis was localised periostitis complicating aortic prosthesis infection.

Discussion

Periostitis is the hallmark of hypertrophic osteoarthropathy (HOA), a syndrome classically characterised by clubbing of the fingers and toes, periosteal new bone formation in the tubular bones, painful swelling of limbs, arthralgia, and arthritis.¹⁰ Signs of autonomic disorders, such as sweating, flushing, and blanching of the skin, also may be present. HOA may be divided into two categories¹¹: primary (hereditary or idiopathic) HOA,¹² also called pachydermoperiostosis, and secondary HOA. Major causes of the secondary form include malignant or inflammatory conditions of the lungs, mediastinum, and pleura, congenital cyanotic heart disease, and inflammatory bowel diseases. Whether primary or secondary, the clinical and radiological findings of HOA are generally diffuse, bilateral, and symmetrical, involving both upper and lower extremities.¹³ Secondary HOA that is confined to the lower extremity in a unilateral or bilateral fashion is very rare and has been described in patients with a patent ductus arteriosus with reversal of flow,¹ or an infected aortic graft.¹⁴

Two main theories have been postulated to explain the pathogenesis of HOA.¹¹ The first, the neurogenic theory, suggests that the autonomic nervous system might play a role in HOA in view of the prompt relief of symptoms and signs following surgical vagotomy. The second hypothesis, which is currently favoured, is humoral and proposes that the substance responsible for HOA might be a circulating factor normally present in the venous circulation and also normally inactivated or removed by the lungs. On the basis of this latter theory, a new hypothesis has recently been proposed, suggesting that both clubbing and periostitis could be produced by the release of platelet derived growth factor (PDGF) due to the peripheral fragmentation of megakaryocytes and platelet clumps which are normally trapped by the pulmonary capillary bed.¹⁵ This hypothesis also accounts for HOA complicating an infected aortic graft, as chronic infection may lead to the formation of platelet clumps with secondary release of PDGF in the arterial

Figure 4 (A) Total body ^{99m}Tc bone scan (anterior view) revealing marked linear pericortical hyperactivity confined to the right lower extremity. (B) ^{99m}Tc bone scan (lower part, posterior view) demonstrating diffuse accumulation of the radionuclide in the soft tissue of the entire right lower limb (arrowheads).

blood distal to the prosthesis. PDGF is probably metabolised in the periphery or in the lungs, thus limiting its effect to the lower extremities. The unilateral or bilateral distribution of HOA is supposed to indicate whether the infection involves one or both of the graft limbs,^{16 17} although differential blood flow in the lower extremities might also account for the unilateral localisation of the condition.¹¹

CLINICAL FEATURES

Localised HOA as a manifestation of arterial graft sepsis was first described by King in 1972.¹⁴ Since then several individual case reports have appeared.^{16–22} With the exception of a patient with an axillary-axillary bypass,²³ the infection always occurs in an aortic bifurcation prosthesis. The interval between surgery and clinical occurrence of HOA ranges from several months to 10 years. Most patients present with progressive pain and diffuse swelling of one or both lower extremities, associated with chronic effusion of the knee or ankle. Clubbing of the toes is noted in approximately half the patients.²² Infectious signs and symptoms of vascular graft sepsis (for example, fever, chills, bacteraemia, recurrent abscesses) are often mild and non-specific, thus delaying accurate diagnosis. When positive, repeated blood cultures usually grow a polymicrobial flora of enteric origin, a finding highly suggestive of aortoenteric fistula.²⁰ This potentially fatal complication almost inevitably occurs in the natural course of infected aortic prosthesis

leading to intermittent and modest bleeding¹⁹ or massive gastrointestinal haemorrhage.^{14 18 20}

IMAGING FEATURES

Localised HOA is diagnosed mainly by radiography. The roentgenographic findings are identical to those seen with other forms of HOA but are strictly confined to areas distal to the infected vascular prosthesis. In early disease, plain radiographs may be normal or show mild periarticular osteoporosis and soft tissue swelling, emphasising the presence of synovitis.¹⁷ The predilection for large joint involvement and the absence of joint space narrowing and osseous erosions allow for differentiation between HOA, rheumatoid arthritis, and Reiter's syndrome. Periosteal proliferation along the shafts of long bones is the major radiological finding, appearing first in the distal diaphyseal regions. Initially, periosteal changes appear as a continuous thin line of new bone separated from the underlying bony cortex by a narrow radiolucent line. However, the morphology, extent, and distribution of the periostitis change during the course of the disease.¹⁶ Thus in mild and early cases, few bones are affected (most commonly the tibia and fibula) and the periosteal proliferation is limited to the diaphysis and appears as a single layer of new bone. Subsequently, more bones are involved, metaphysis and epiphysis may be affected, and periostitis becomes multilayered, fusing with the subjacent osseous tissue and leading to cortical thickening.²² In more advanced cases, ligamentous ossification may appear in the interosseous region between the tibia and fibula (fig 2).

Radionuclide bone imaging using ^{99m}Tc methylene diphosphonate is a highly sensitive method of detecting abnormalities of HOA and is very useful in documenting the extent and exact distribution of periostitis.² The scintigraphic abnormalities frequently appear before the roentgenographic findings and may be present before the development of symptoms. Bone scan shows a characteristic abnormal pattern confined in the affected limb with marked pericortical linear concentration of radionuclide tracer along the shafts of the long bones (fig 4A). Increased periarticular uptake of the radionuclide due to associated synovitis may also be observed. Blood pool early static images emphasise the increased vascular perfusion of affected areas.¹⁷ Diffuse accumulation of the radionuclide in the soft tissue corresponding to swelling of the affected extremity and changes in the regional blood flow is occasionally apparent on the delayed images (fig 4B).

Computed tomography is often preferred in the assessment of cortical osseous alterations. However, MRI allows direct visualisation of the periosteal proliferation, faithfully depicts its local relations with adjacent structures, and optimally assesses the bone marrow. On both T1 and T2 weighted images, the periosteal new bone formation appears as a characteristic line of low signal intensity which is initially separated from the subjacent cortex by a

Figure 5 (A) Coronal postgadolinium DTPA T1 weighted image and (B) axial T2 weighted image of the right knee showing periosteal new bone formation along the distal femur appearing as a regular line of low signal intensity (arrows) separated from the underlying cortical bone by a narrow area of high signal. Knee effusion (*) and mild synovial proliferation (largely of low to intermediate signal) are also apparent in (B). Note preservation of normal fatty bone marrow signal on both sequences.

narrow space of high signal intensity (fig 5). This high signal area is considered to represent fat, a finding that correlates well with what is seen pathologically in patients with HOA.²⁴

MRI is superior to other imaging methods in the evaluation of joint effusion (low T1 and high T2 signal) and associated synovitis. In HOA, synovitis is usually mild, chronic, and

non-inflammatory,¹¹ appearing as an inhomogeneous mass of mixed hypo- and intermediate signal on T2 weighted images, whereas an inflammatory or infective synovitis would appear as an high signal intensity proliferation, hardly distinguishable from synovial fluid (fig 5B). Furthermore, in these patients with an infected aortic graft, MRI is very useful to exclude osteomyelitis and soft tissue infection, thus confirming that the periostitis is not only a response to adjacent infection.

MANAGEMENT

Almost all patients with aortic prosthesis infection will, without surgical intervention, succumb from massive gastrointestinal haemorrhage or sepsis. Therefore it is of the utmost importance to establish a definite diagnosis of vascular graft sepsis to reduce the incidence of aortoenteric fistula which is almost invariably the cause of death in this group of patients. Preoperative diagnosis of infected vascular grafts and aortoenteric fistulae may be difficult.²⁵ The most useful investigations for accurate diagnosis of graft infection are gallium or labelled leucocyte scans,²¹ aortography when demonstrating an anastomotic aneurysm or intraprosthesis vegetations,²⁰ and ultrasound and computed tomography of the aorta and graft, which may show a perigraft collection of fluid or gas indicating graft sepsis (fig 6). Enteroprosthetic fistula may be diagnosed by upper gastrointestinal endoscopy as it allows direct visualisation of the point of graft erosion into the bowel lumen.²⁵ However, upper

Figure 6 Contrast enhanced axial computerised tomography scan at the level of the proximal anastomosis of an aortic graft in a 66 year old man, showing a large perigraft collection of fluid (arrowheads) with small gas pockets (curved arrows) suggestive of graft infection. A right retroperitoneal haematoma is also apparent (black arrows).

gastrointestinal barium contrast studies and aortography are sometimes helpful for establishing the diagnosis of fistula by showing extravasation of the contrast material.^{17 25} Surgical management consists of complete removal of the infected graft, closure of the bowel defect if present, and limb revascularisation through an extra-anatomic route (for example, axillobifemoral bypass).²⁵ Intensive antibiotic treatment is started before surgery and continued postoperatively for at least three weeks.¹⁷ With this therapeutic regimen, survival can be achieved in about 50 percent of patients. Of interest is the fact that clinical signs and symptoms and radiographic and radionuclide findings of localised HOA may diminish or even disappear after appropriate treatment.^{17 23} Improvement of this syndrome following resection of the infected graft supports the hypothesis that clubbing and periostitis could be produced by the release of PDGF due to fragmentation and detachment of large platelet clumps from the walls of the infected vascular prosthesis.¹⁵

Summary

Unilateral lower extremity hypertrophic osteoarthropathy may be the initial symptom of an infected aortic graft. Knowledge of this uncommon association should lead to early and accurate diagnosis and appropriate surgical management, thus avoiding the development of aortoenteric fistula, a complication that still carries a significant risk of mortality.

- Williams B, Ling JT, Leight L, McGaff CJ. Patent ductus arteriosus and osteoarthropathy. *Arch Intern Med* 1963; 111:346-50.
- Ali A, Tetelman MR, Fordham EW, Turner DA, Chiles JT, Patel SL, et al. Distribution of hypertrophic pulmonary osteoarthropathy. *Am J Radiol* 1980;134:771-80.
- Lippmann HI, Goldin RR. Subcutaneous ossification of the legs in chronic venous insufficiency. *Radiology* 1960; 74:279-88.
- Oppenheimer DA, Jones HH. Hypertrophic osteoarthropathy of chronic inflammatory bowel disease. *Skeletal Radiol* 1982;9:109-13.
- Pitt P, Mowat A, Williams R, Hamilton E. Hepatic hypertrophic osteoarthropathy and liver transplantation. *Ann Rheum Dis* 1994;53:338-40.
- Bland JH, Frymoyer JW, Newberg AH, Revers R, Norman RJ. Rheumatic syndromes in endocrine disease. *Semin Arthritis Rheum* 1979;9:23-65.
- Lovell R, Scott G. Hypertrophic osteoarthropathy in polyarthritis. *Ann Rheum Dis* 1956;15:46-50.
- Averns HL, Cheung NT, Dawes PT. Painful knees associated with a septic focus. *Br J Rheumatol* 1995; 34:862-4.
- Martinez-Lavin M, Pineda C, Valdez T, Cajigas JC, Weisman M, Gerber N, et al. Primary hypertrophic osteoarthropathy. *Semin Arthritis Rheum* 1988;17:156-62.
- Martinez-Lavin M, Matucci-Cerinic M, Jajic I, Pineda C. Hypertrophic osteoarthropathy: consensus on its definition, classification, assessment and diagnostic criteria. *J Rheumatol* 1993;20:1386-7.
- Resnick D. In: Resnick D, ed. *Diagnosis of bone and joints disorders*, 3rd ed. Philadelphia: W B Saunders, 1995:4421-34.
- Cooper RG, Freemont AJ, Riley M, Holt PJJ, Anderson DC, Jayson MIV. Bone abnormalities and severe arthritis in pachydermoperiostosis. *Ann Rheum Dis* 1992;51:416-9.
- Pineda CJ, Martinez-Lavin M, Goobar JE, Sartoris DJ, Clopton P, Resnick D. Periostitis in hypertrophic osteoarthropathy: relationship to disease duration. *Am J Radiol* 1987;148:773-8.
- King JO. Localized clubbing and hypertrophic osteoarthropathy due to infection in an aortic prosthesis. *BMJ* 1972;iv:404-5.
- Dickinson CJ. The aetiology of clubbing and hypertrophic osteoarthropathy. *Eur J Clin Invest* 1993;23:330-8.
- Walter RD, Resnick D. Hypertrophic osteoarthropathy of a lower extremity in association with arterial graft sepsis. *Am J Radiol* 1981;137:1059-61.
- Voiriot P, Duperval R, Teixeira J, Levesque R, Lambert R. Localized hypertrophic osteoarthropathy due to arterial graft sepsis from an enteroprosthetic fistula. *Rev Infect Dis* 1987;9:376-81.
- Stein HB, Little HA. Localized hypertrophic osteoarthropathy in the presence of an abdominal aortic prosthesis. *Can Med Assoc J* 1978;118:947-8.
- Sorin SB, Askari A, Rhodes RS. Hypertrophic osteoarthropathy of the lower extremities as a manifestation of arterial graft sepsis. *Arthritis Rheum* 1980;23:768-70.
- Dalinka MK, Reginato AJ, Berkowitz HD, Turner NL, Freundlich B, Steinberg M. Hypertrophic osteoarthropathy as indication of aortic graft infection and aortoenteric fistula. *Arch Surg* 1982;117:1355-9.
- Stiles RG, Resnick D, Sartoris DJ, Savoia MC. Unilateral lower extremity hypertrophic osteoarthropathy associated with aortic graft infection. *South Med J* 1988;81:788-91.
- Fauquert P, Moal MC, Guillermit MN, Gourlaouen A, Le Goff P. Ostéoarthropathie hypertrophique monomélisque associée à une infection de prothèse vasculaire. *Rev Rhum* 1990;57:13-6.
- Ho A, Williams DM, Zelenock GB, Braunstein EM. Unilateral hypertrophic osteoarthropathy in a patient with an infected axillary-axillary bypass graft. *Radiology* 1987; 126:573-4.
- Milgram JW. In: Milgram JW, ed. *Radiologic and histologic pathology of non tumorous diseases of bone and joints*. Northbrook, IL: Northbrook Publishing Company, 1990:933-42.
- Bernhard VM. In: Bernhard VM, Towne JB, eds. *Complications in vascular surgery*, 2nd ed. Orlando: Grune & Stratton, 1985:513-25.