DIAGNOSIS OF OSTEOMYELITIS IN NEUROPATHIC FOOT ULCERS

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We reviewed all patients with a clinically infected foot ulcer attending a specialised neuropathic foot clinic. Neuropathy was confirmed by the inability to feel a 5.07 Semmes-Weinstein hair, areflexia and impaired vibration sense, as measured by a biothesiometer.

Of 40 patients who attended the clinic over a two-year period, six with ischaemic ulcers were excluded. The remaining 34 had plain radiographs of the foot followed by a ^{99m}Tc -MDP bone scan. If the latter was positive, an ^{111}In -labelled WBC scan was performed with planar and/or tomographic dual-isotope studies where appropriate. Bone and WBC scans were performed in 31 patients. In ten, isotope imaging showed infection localised to the soft tissues only and conservative treatment was successful in them all. Eighteen patients were treated surgically with excision of the involved bone, which was sent for culture and histological examination.

Dual-isotope scans had a sensitivity of 93% and a specificity of 83%. ^{99m}Tc -MDP bone scans with the appropriate ^{111}In -labelled WBC scans can reliably determine the site and extent of osteomyelitis in the neuropathic diabetic foot.

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The overall incidence of diabetes mellitus in the UK is 1.2% (Neil, Gatling and Mather 1986), rising to 4% over

the age of 65 years (Mather and Keen 1985). Ulceration of the foot is 50 times more common in diabetes and the incidence of amputation of the lower limb is 25 times greater (Forrest, Jackson and Yudkin 1986). Management of the diabetic foot accounts for a considerable proportion of the spending on health care (Laing, Cogley and Klenerman 1991).

Osteomyelitis increases the risk of amputation but early diagnosis is notoriously difficult in the presence of diabetic osteopathy. Progressive osteolysis characterised by bone demineralisation and destruction may resemble osteomyelitis on radiographs, but there may be no infection and the destruction may merely represent demineralisation. Radiological evidence of bone destruction by itself must not be the basis for amputation (Pogonwska, Collins and Dobson 1967).

PATIENTS AND METHODS

Between January 1991 and December 1992, 40 diabetic patients with foot ulcers which were clinically infected were referred to a special clinic in the Royal Liverpool University Hospital Trust. Such infection is associated with greater than 105 colony-forming units/ml of wound fluid (Wheat et al 1986). Six patients who had peripheral ischaemia were excluded from the study. Light touch sensation was assessed using Semmes-Weinstein hairs (Hansen's Disease Foundation Inc, Carville, Louisiana). These are nylon monofilaments which buckle at a constant pressure and are applied perpendicular to the skin. The 5.07 hair has been identified as the level at which a patient has protective sensation if the hair can be felt (Birke and Sims 1986). The number refers to the logarithm of ten times the force in grams required to buckle the hair. Two out of three responses have to be correct for sensation to be considered to be intact in any area. The areas which we chose were the metatarsal heads, the pulp of the hallux and the medial and lateral heel (Bell 1978).

Impairment of vibration sense was measured using a biothesiometer (Bio-medical Instrument Company, Newbury, Ohio). This is a hand-held machine with a plastic probe, 13 mm in diameter, which vibrates at a constant frequency. The amplitude of vibration varies according to the applied voltage which can be increased until the patient perceives the vibration. The vibration perception threshold (VPT) was measured over the bony prominence of the

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medial malleolus and the pulp of the hallux. The ability to feel vibration decreases with age, but the result can be expressed as a standard deviation score (SDS) from the normal for the patient's age (Bloom et al 1984). Patients with an SDS greater than 2.1 for the combined medial malleolus and hallux are at risk of neuropathic ulceration (Klenerman and Laing 1991).

Ankle reflexes were recorded and a history of previous neuropathic ulceration was noted. Absence of peripheral pulses and a history of intermittent claudication excluded the patient from the study. All patients had their ankle/brachial index measured using a Doppler ultrasound probe. A sphygmomanometer cuff was placed above the ankle and the systolic pressure noted in the posterior tibial artery. This was compared with the systolic pressure in the brachial artery and a ratio obtained.

A microbiological swab was taken from the surface of the ulcer and from its base after curettage. They were immediately placed into Stuart's transport medium and cultured both aerobically and anaerobically in a qualitative and semiquantitative manner on five solid media. These were MacConkey, blood, kanamycin aesculin azide, yeast morphology for aerobes and brain-heart infusion agar for anaerobes. The swabs were inoculated immediately on to the five media using the four-quadrant method.

All patients had anteroposterior and oblique radiographs of the foot and an initial bone scan to demonstrate and localise the abnormality. The scan was performed using a large field-of-view gamma camera three hours after the intravenous administration of 370 to 550 MBq ^{99m}Tc methylene diphosphonate (MDP). The foot was placed directly on the gamma camera and magnified images were obtained using a low-energy, high-resolution collimator.

Those with a positive bone scan had an ^{111}In WBC scan performed within a few days. Autologous WBCs were labelled with 16 MBq ^{111}In tropolone and were then reinjected. Plantar images were taken using a medium-energy collimator 24 hours after reinjection of the labelled WBCs with a 20-minute acquisition time. If the ^{111}In WBC scan was positive, 150 MBq ^{99m}Tc -MDP were then administered and simultaneous dual-isotope imaging performed two hours later using a 64×64 word matrix. A plantar view with the foot resting on the collimator, and an appropriate medial or lateral view were obtained with an acquisition time of ten minutes. The ^{99m}Tc -MDP image was then contoured, and the contour superimposed on the ^{111}In WBC image to determine the site of the sepsis (Fig. 1). Where appropriate a dual-isotope tomographic study was also undertaken using a full 360° rotation. Sixty-four angles were taken with an acquisition time of 30s/angle giving a total acquisition time of just over 30 minutes. Thirty-two transaxial slices two pixels (1.5 cm) thick along the long axis of the foot were reconstructed using a standard technique (Fig. 2).

If the combined isotope imaging showed no evidence of osteomyelitis and the clinical findings suggested infection

limited to the soft tissues, the ulcer was treated with the appropriate antibiotics, as determined by culture and sensitivity of the microbiology swab, and with local debridement and dressings. When the infection had subsided, the foot was placed in a total contact cast until the ulcer had healed.

If the WBC-labelled scan was positive for osteomyelitis or if local therapy failed to heal the ulcer irrespective of the scan result, resection of the involved bone was performed. Amputation was carried out for osteomyelitis of a digit and excision of the ray for a metatarsal infection. The wound was left open to heal by secondary intention and the bone sent for culture and histology. Immediately after amputation the specimen was dissected using sterile instruments. Direct contamination of the bone was carefully avoided. Osteomyelitis was diagnosed in the presence of osteonecrosis, which showed absence of osteocytes in the lacunae in the presence of nuclear staining for other cells in the section, and the replacement of normal marrow with acute inflammatory cells. The proposed protocol for investigation is shown in Figure 3.

RESULTS

All patients had a positive isotope bone scan. Three had gross bone destruction on plain radiographs and evidence of local infection. They had surgical debridement before having an ^{111}In WBC scan. Thirty-one patients had a ^{99m}Tc -MDP bone scan followed by an ^{111}In WBC scan. Of these, 21 had dual-isotope studies of whom 8 had tomography.

Of the 21 patients, 14 had the infection correctly localised to bone. In five patients the infection was correctly localised to the soft tissues, and all of these healed with conservative treatment. In one case the ^{111}In WBC scan suggested osteomyelitis but as the ulcer was responding to local therapy it was not operated on and had healed at review one year later. In another patient the WBC scan suggested that the infection was confined to the soft tissues and conservative treatment was undertaken without success. Osteomyelitis was confirmed on culture and histological examination of the proximal phalanx.

Dual-isotope studies had a sensitivity of 93% and a specificity of 83%. Eighteen patients had successful amputation of an involved digit (6) or ray resection (12). The bone was cultured aerobically and anaerobically and examined histologically. Both bone and wound culture yielded a mixture of aerobes and anaerobes. The most frequently isolated were *Staphylococcus aureus* and an anaerobic *Streptococcus*.

DISCUSSION

The high rate of plantar ulceration in diabetic patients with neuropathic feet is largely due to the uneven distribution of body-weight over the sole (Stokes, Faris and Hutton 1975).

Fig. 1a

Fig. 1b

Fig. 1c

Dual-isotope studies. The upper two images of each set show ^{99m}Tc -MDP activity, on the left before bone contouring and on the right after the contour is computed. The lower two images show ^{111}In WBC activity, on the right in relation to the bone contour.

^{111}In WBC activity lies (a) outside the bone contour indicating soft-tissue infection without involvement of the bone, within the bone contour indicating osteomyelitis (b), and (c) both within and without the bone contour indicating soft-tissue infection and involvement of the bone.

Paresis of the intrinsic foot muscles leads to a cavus foot and distal subluxation of the metatarsal fat pads. Callosities form in the skin over the unprotected metatarsal heads. Repeated minor trauma produces subcutaneous haematoma and these eventually break through the skin to form an ulcer (Brand 1983). Osteomyelitis may be present in up to 68% of diabetic foot ulcers and the incidence may be higher than clinical examination would suggest (Newman et al 1991). It is thought that bone infection occurs by the direct spread of contaminating organisms from an ulcer rather than by the haematogenous route (Sugarman et al

1983).

There is a variety of bony changes on plain radiographs in patients with diabetic neuropathy, including osteoporosis, juxta-articular cortical bone defects, osteolysis of the ends of the bone, destruction of the ends of the bone, destruction of an entire bone, periosteal reaction and cortical sclerosis (Pogonwska et al 1967). Those associated with osteomyelitis may not be seen by plain radiography for 7 to 15 days after the onset of the acute infection (Bonakdar-pour and Gaines 1983). The specificity of plain radiographs in detecting osteomyelitis is only about 50%

Fig. 2

An example of a tomographic study. The scout film is shown on the upper left. Each numbered slice comprises a ^{99m}Tc MDP bone scan on the left and an ^{111}In WBC scan with the bone contour overlaid on the right. Slices 13 and 15 show activity within the bone contour indicating osteomyelitis.

Fig. 3

The proposed protocol for investigating patients with clinically infected ulcers in whom osteomyelitis is suspected.

(Park et al 1982; Seldin et al 1985; Segall et al 1989). Widespread osteopathy of the foot, which may be indistinguishable from osteomyelitis and lead to progressive bone destruction, is often seen in diabetic neuropathy and has a better prognosis than osteomyelitis, from which it must be distinguished (Friedman and Rakow 1971). Metatarsal periosteal reactions are common among diabetic patients and do not themselves indicate osteomyelitis (Williams et al 1988).

The isotopes, ^{87}Sr , ^{67}Ga , ^{99m}Tc -MDP, and ^{111}In , have been used to improve the accuracy of the diagnosis. Strontium is no longer used because of the large amount of gamma radiation emitted. ^{67}Ga -citrate is readily taken up by neoplasia and is widely distributed around the body resulting in high background activity. ^{99m}Tc -MDP is taken up in areas of hyperaemia, which may be a result of cellulitis in soft tissue, healing fractures, or osteitis, and is therefore not specific for bone infection. The uptake of

radio-isotopes is increased in the feet of patients with diabetic neuropathy as a result of increased peripheral blood flow even in the absence of radiological abnormalities, making this a very sensitive test (Edmonds et al 1985). The specificity of ^{99m}Tc -MDP scans in the diagnosis of osteomyelitis can be improved if three-phase imaging is performed with the addition of a radionuclide angiogram and 'blood-pool' images (Maurer et al 1981).

WBCs labelled with ^{111}In are used to detect infection in soft tissue and bone but as an infection becomes chronic, WBC infiltration subsides so that radionuclide accumulation may not occur and the bony involvement may go undetected. Maurer et al (1981) state that an isotope bone scan used alone has a specificity for excluding infection of 56%, but this is raised to 89% when the scan is combined with WBC imaging. They cite, however, the long preparation time, low count rates resulting in low spatial resolution and absence of bony landmarks as disadvantages of WBC imaging.

In our study, the use of bone contouring with a dual-isotope study allows for better localisation of the WBC activity. Eisenberg et al (1989) showed that correlation of three-phase ^{99m}Tc -MDP bone scans with ^{111}In WBC scans had a sensitivity of 100% and a specificity of 81%. Their study involved a standard technique for a five-hour delayed imaging in the three-phase bone scan and marking the foot in the ^{111}In WBC scan, with three routine views obtained for each imaging procedure to ensure clinical accuracy. Infection in the bone or in the adjacent soft tissues was correctly localised using orthogonal projections (Schauwecker et al 1988) in 89% of the cases, and they were able to obtain a sensitivity of 100% and a specificity of 83% for detecting osteomyelitis. Culture of infected bone will determine if infection is present, but contamination from the surrounding soft tissues is difficult to exclude (Caprioli et al 1986). We have used a combination of bone culture and histological examination to overcome this problem, examining material removed at operation.

Dual-isotope imaging, with a sensitivity of 93% and a specificity of 83%, can reliably determine the extent and localisation of osteomyelitis in ulcers in the neuropathic diabetic foot.

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