Case Report

Chronic Diffuse Sclerosing Osteomyelitis Treated with Risedronate

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ABSTRACT. We describe a 21-year-old woman with chronic diffuse sclerosing osteomyelitis (CDSO) of the left femur. The patient presented with shortening of the left leg and intractable pain that was unrelieved with conventional analgesia. Radiological imaging and open bone biopsy confirmed the diagnosis of chronic diffuse sclerosing osteomyelitis. Treatment with risedronate was commenced and a dramatic response in the patient's symptoms and biochemical markers of bone turnover was observed. To our knowledge this is the first case of CDSO treated successfully with risedronate. (J Rheumatol 2005;32:1376–8)

Key Indexing Terms:
CHRONIC DIFFUSE SCLEROSING OSTEOMYELITIS RISEDRONATE

Chronic diffuse sclerosing osteomyelitis (CDSO) is an uncommon condition typically associated with changes in the mandible[1] although it has been reported in other sites, namely the diaphysis of long bones[2]. Women are affected more than men and the typical symptoms include characteristic episodes of pain and swelling that may be chronic and intractable.

Bone deposition rather than resorption is the characteristic feature, resulting in the radiological appearance of a diffuse sclerotic opacity with poorly defined borders[3]. The underlying etiology is unknown, but an infectious etiology has always been suspected, with organisms of low virulence thought to be the causative agent[4]. This theory is currently under review as the results of prolonged courses of antibiotics, including our case, are poor and bacteriological cultures are often negative.

To our knowledge this is the first case of CDSO treated successfully with risedronate.

CASE REPORT

A 21-year-old woman presented with a 15-year history of pain in her left hip radiating down the left thigh to the level of the knee. Over the previous 6 months the pain had become intractable, disturbing her sleep and unresponsive to nonsteroidal antiinflammatory medication and codeine based analgesia. At age 7 years a radiograph of her lumbar-sacral spine and pelvis was performed, which was normal. There was no other medical history of note. Initial examination revealed a one centimeter shortening of her left leg, but hip and knee movements were normal. There was no localized tenderness in her thigh and no evidence of inflammatory joint disease.

Investigations. Initial investigations revealed normal full blood count, and normal urea, electrolytes and creatinine, corrected calcium 2.31 mmol/l (2.10–2.65 mmol/l) and alkaline phosphatase 61 U/l (42–121 U/l). Erythrocyte sedimentation rate (ESR) was raised at 45 mm/h, and C-reactive protein (CRP) was elevated at 62 mg/l. A radiograph of her left femur revealed extensive cortical thickening of the femoral shaft (Figure 1) and a 3 phase bone scan showed increased uptake in the corresponding area with no enhanced uptake elsewhere (Figure 2). Magnetic resonance imaging (MRI) of the left femur revealed diffuse cortical thickening with a reduction in the size of the medullary cavity (Figure 3).

No definitive diagnosis could be made, and because the patient was having ongoing symptoms, an open bone biopsy was undertaken. The exposed femur appeared densely sclerotic with no visible pus or macroscopic evidence of infection. Bone cultures including acid fast bacilli were negative. Histological sections revealed very thickened reactive sclerotic bone. In the marrow there was very little osteoclast activity, but in some areas there was evidence of increased osteoblast activity, but no neoplastic lesion.

The radiological and biopsy appearances were in keeping with Paget's disease, but given the patient's young age and normal alkaline phosphatase level, CDSO was an alternative diagnosis.

Treatment. The patient was given a combination of oral clindamycin 150 mg 4 times daily and ciprofloxacin 500 mg twice daily for 6 weeks. On review the patient reported no improvement in her symptoms, and her blood tests showed ESR 40 mm/h and CRP 52.4 mg/l.

It was then decided to give the patient bisphosphonate therapy. Her baseline markers of bone turnover were serum crosslaps 3760 pmol/l (premenopausal female mean value 2304 pmol/l), ostase 10.3 µg/l (premenopausal female range 8.7-14.3 µg/l) and osteocalcin 33.1 ng/ml (premenopausal female range 4.9-30.5 ng/ml). She received oral risedronate 35 mg weekly. After 4 weeks her symptoms had improved and at 6 months of treatment she reported a dramatic improvement in her symptoms. This correlated with a change in her bone turnover markers: serum crosslaps 1620 pmol/l, ostase 6.2 µg/l, and osteocalcin 20.1 ng/ml and her blood tests showed ESR 10 mm/h and CRP 7.9 mg/l. There was, however, no discernable radiographic or isotope bone scan change. The risedronate therapy was discontinued but her symptoms reoccurred after 4 weeks, correlating with a rise in her bone markers once again back to almost pre-treatment levels and thus the risedronate was recommenced and will continue with the patient under regular review.

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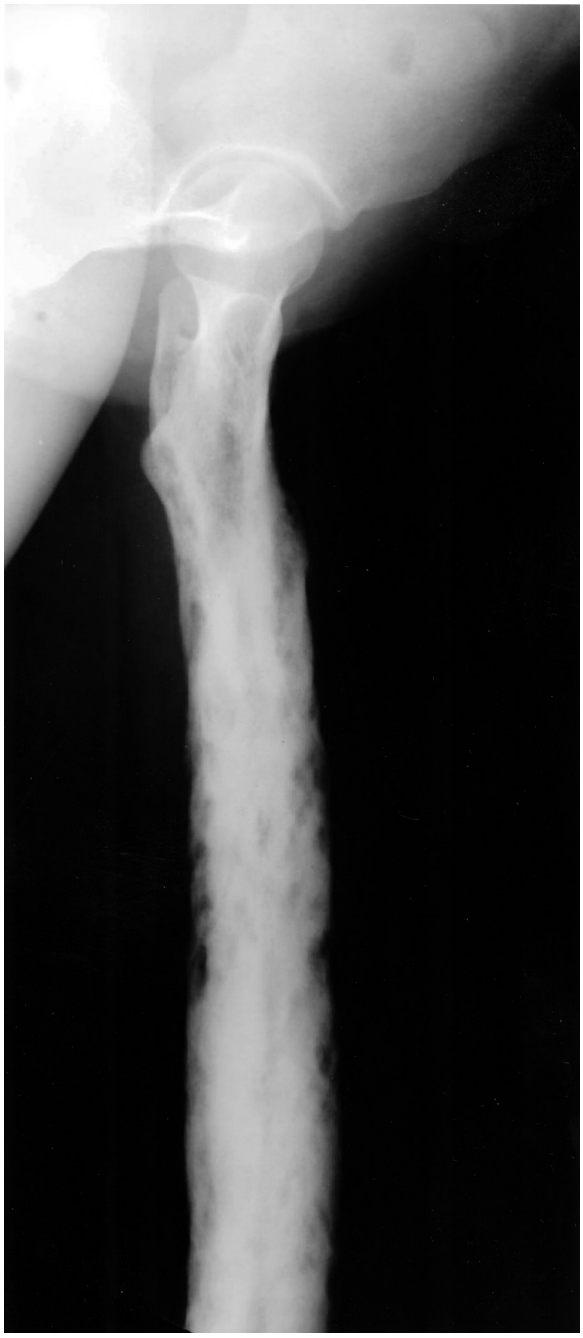

Figure 1. Diffuse cortical thickening and irregularity of left femur.

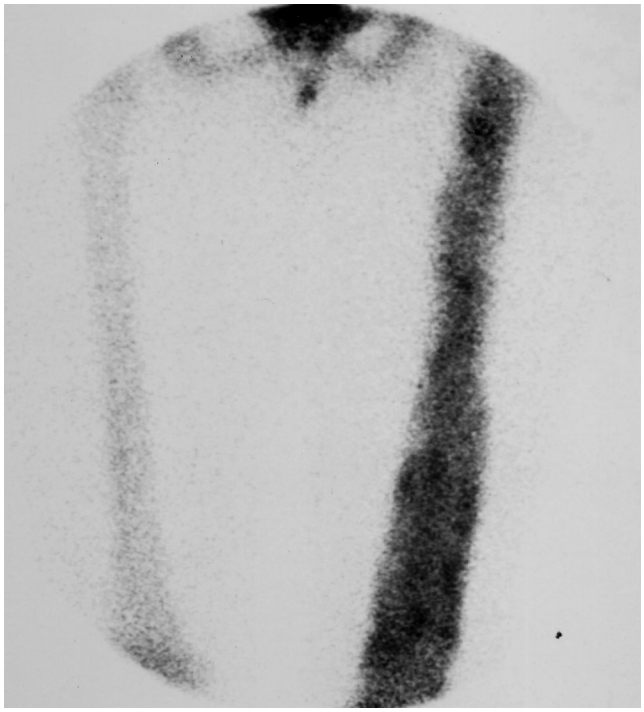

Figure 2. Isotope bone scan showing diffuse uptake in the left femur.

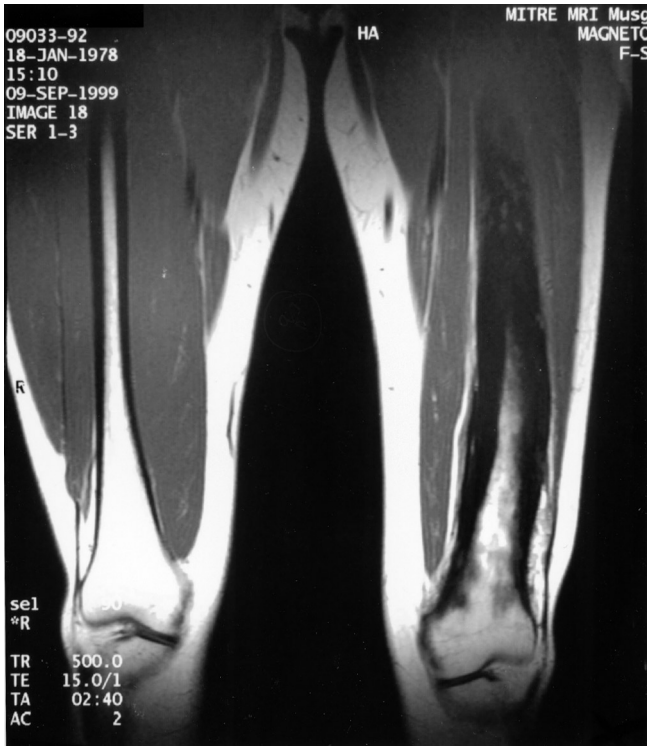

Figure 3. MRI showing cortical thickening of left femur with reduction in medullary cavity.

DISCUSSION

Medical therapy for CDSO is limited. Calcitonin has been shown to have a beneficial effect on the symptoms[5], although the mechanism is unclear as calcitonin is known to act locally by inhibition of osteoclast activity[6] and yet in chronic sclerosing osteomyelitis, osteoblast activity appears to be predominant.

Risedronate has been shown to be effective in the treatment of osteoporosis and Paget's disease[7], both characterized by a relative increase in osteoclast activity. The exact mechanism of bisphosphonates is still unclear and each bisphosphonate may affect remodeling with subtle but important differences[8], but their main action is to inhibit osteo-

clast activity by increasing osteoclast apoptosis directly or indirectly through cellular effects on osteoblasts[9,10].

The early onset of analgesia effect in our case would suggest that risedronate may have analgesic properties, and can be effective locally even in the presence of increased osteoblast activity and sclerosis. This would mirror the effect seen with calcitonin[5]. The lack of change in the isotope bone scan may reflect the short time interval between the bone scans. A further isotope bone scan after 12 to 18 months of risedronate therapy may reveal an improvement.

CDSO is thought to be primarily a disorder of bone deposition, i.e., osteoblast activity. This would be confirmed by the bone biopsy in our patient. However, markers of bone turnover revealed normal osteoblast activity (ostase and osteocalcin) but markedly elevated osteoclast activity (serum crosslaps). Also the dramatic clinical response to risedronate, which primarily acts through inhibiting osteoclast activity, provides evidence that osteoclasts are also involved in CDSO.

Alternative bisphosphonates may be tried. Disodium pamidronate has been shown to be effective in CDSO[11] although there are no reports on the use of alendronate or zolendronate. The use of disodium pamidronate and zolendronate could be reserved for intractable cases due to their increased potency and longer terminal half-lives.

To our knowledge this is the first reported case of CDSO being treated with risedronate, but the therapeutic effect seen with risedronate also suggests that this case could represent an atypical, sclerotic, and localized form of Paget's disease as described[12].

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