CASE REPORT

Successful treatment of the post-traumatic osteolysis of distal clavicle with alendronate

Mika T.K. Mularia,b,*, Kimmo Mattilac, Guoliang Gu b, Kai Parkkola a, H. Kalervo Väänänenb

Health Care Unit, Archipelago Sea Naval Command, Turku, Finland
b University of Turku, Institute of Biomedicine, Department of Anatomy, Kiinamyllynkatu 10, FIN-20520 Turku, Finland
c Diagnostic Imaging Centre, Turku University Hospital, Turku, Finland

Accepted 6 March 2006

Introduction

Osteolysis of the distal clavicle may result from a number of local and systemic diseases. Progressive systemic sclerosis, rheumatoid arthritis, gout, Gomang’s disease, infection and hyperparathyroidism may all lead to locally restricted bone destruction. Osteolysis of the distal clavicle has also been reported in patients with a history of weight lifting, baseball, handball, pneumatic jackhammer use and also spinal cord injury. In these cases, the longstanding stress on upper extremity has been suggested to lead to repetitive microtrauma with a consequence of osteolysis.

Shoulder trauma with acromioclavicular (AC) separation leads to distal clavicle osteolysis with an incidence of 1–21%. However, osteolysis has also been repeatedly described in patients with no radiological pathologies after the injury. Although usually self-limiting within 18 months, post-traumatic osteolysis may lead to irreversible vanishing of the distal 0.5–3 cm of the clavicle. However, a recent case report suggested that conservative therapy may not only lead to healing of the distal clavicle, but also to normalization of joint space dimension. The pathogenesis of the disease remains unknown. Therefore, it is not surprising that the therapies described in papers concerning the disease show great variability. Although immobilisation is generally accepted as the first line therapy and although it may decrease the duration of the lytic phase, it may not suppress the early manifestation of the disease. However, reliable studies focusing on the effect of other current therapies such as anti-inflammatory agents, cryotherapy, intra-articular corticosteroid injections, short wave diathermy and operative resection of the distal clavicle are still missing.

Alendronate is a nitrogen-containing bisphosphonate that has a high affinity to bone hydroxyapatite. It mediates its anti-resorptive effect by being locally released from the bone surface during bone resorption and thereafter inhibiting the mevalonate pathway in the osteoclast. This leads to the impaired prenylation of proteins, disturbed osteoclast function and cessation of bone resorption. For these reasons, bisphosphonates are widely used in prevention and treatment of primary and corticosteroid-induced...
Osteoporosis, Paget's disease of bone and hypercalcemia caused by malignancies and metastases—diseases where the loss of bone is the pathological hallmark.

The present paper describes a patient with a history of trauma-induced osteolysis of the distal clavicle, and its successful treatment with alendronate administration. Our results suggest that by inhibiting pathologically increased osteoclastic bone resorption, bisphosphonate therapy is relevant in preventing further bone degradation after the diagnosis of the post-traumatic osteolysis.

**Figure 1** Twelve hours after the trauma conventional radiographs revealed gradus I subluxation in the left acromioclavicular joint (B). The joint was 4 mm wide on the left and 3 mm on the contralateral side (A). At 8 weeks progressive osteolysis of the clavicle was observed at its acromial extremity. Conventional radiographs showed cortical bone erosions and widening of the joint up to 6 mm (D). MRI showed fragmentation of the subchondral bone, cystic formation, bone marrow oedema in the distal clavicle and joint effusion on T2-weighted fat-suppressed coronal images (C). Four weeks after the initiation of the alendronate treatment, cortex reformation and bone fragment ossification were obvious (E). After 11 weeks of alendronate administration, clavicular bone marrow oedema had diminished. Cystic lesions of the subchondral bone in distal clavicle and a mildly prominent joint capsule were still observed (F, proton density-weighted axial image). Conventional radiographs proved further healing of the clavicle (G). c: clavicle; a: acromion; ssm: supraspinatus muscle.
Case report

A 20-year-old male accidentally hit his left shoulder on the ground during military service in December 2001. At the emergency unit, the acromioclavicular (AC) joint was tender and the distal clavicle was slightly prominent. Radiographs revealed a type I AC-separation injury with a mild vertical displacement. The AC distance was 3 mm on the right and 4 mm on the left (Fig. 1A and B). Abduction of the upper left extremity was painful. At this time, all inciting activities were avoided and occasional non-steroidal anti-inflammatory drugs were administered for the pain.

After 8 weeks, the stabbing shoulder pain during sleep and daytime activities persisted. Abduction and rotation movements of the left arm were now painless, but compression of the distal clavicle was painful. Radiographs suggested post-traumatic osteolysis (Fig. 1D).

Three weeks later, the AC distance was 5–6 mm, and with stress provocation test 6 mm. The MRI revealed marrow oedema in the distal clavicle, joint effusion and erosions of the subchondral cortical bone (Fig. 1C). Acromion and the glenohumeral joint were unaffected. Crepitus over the left AC joint was obvious. Due to the pathologically proceeding loss of bone, we initiated oral administration of alendronate (Fosamax®, Merck & Co. Inc., Whitehouse Station, NJ, U.S.A) to slow down the increased osteoclastic activity. During the first week, 70 mg was administered on two successive days. Thereafter, the weekly dose was 70 mg.

After 15 weeks of the incident, extensive abduction was still slightly painful, but compression of the AC joint was painless. In conventional radiographs, the acromioclavicular distance was still 6 mm. Sclerotic cyst formation and bone fragment ossification and fusion with the clavicle were also evident (Fig. 1E). Thus, the progression of clavicle osteolysis was ceased during the first month of alendronate administration.

After 11 weeks of alendronate therapy, conventional radiographs showed a 5 mm widening of the AC joint in stress radiographs (Fig. 1G). Oedema had diminished in the clavicle although small erosions at the distal clavicle were observed. There was no effusion or synovitis in the AC joint, and cortical bone had been re-formed (Fig. 1F). Although almost fully functional and painless, some physical stress such as heavy burden was still provocative of stabbing pain in the shoulder. No crepitus was observed and the healing of the process was evident. No anisocoria was observed at any time during follow-up.

Discussion

A wide diversity of therapies on the post-traumatic osteolysis has been described. However, reliable evidence showing their effect is missing. Although a self-limiting disease with a good prognosis, understanding the pathogenesis of the post-traumatic osteolysis is of importance in the view of discovering and practising an adequate therapy. Unfortunately, this issue is currently covered in a mist as well.

Histological sections of the osteolytic clavicle after more than 6 months after the injury have shown hyperplastic synovium, vascular proliferation, oedematous tissue, bony remodelling and chronic inflammatory cells but no sign of necrosis, hemorrhage or acute inflammation. Asano et al. reported the presence of inflammatory cells in bone marrow of both clavicle and acromion, fibrous tissue with vascular proliferation covering the distal clavicle and the presence of multinuclear giant cells 5 months after the injury, while Levine et al. showed that after 18 months of the initial trauma there was evidence for vascular proliferation, periosteal hypertrrophy, villous hyperplasia and tiny fragments of necrotic bone. Others have suggested bone and articular cartilage destruction and replacement by fibrous tissue, detritus in marrow spaces, subchondral cyst formation and sclerotic bone generally viewed as indicative of avascular necrosis.

Osteoclasts are the only known cells capable of effective bone resorption. Thus, it could be either an increase in the number of osteoclasts or up-regulation of the activity of the pre-existing osteoclasts or both, which leads to the posttraumatic osteolysis of distal clavicle.

Several mechanisms by which trauma induces osteolysis have been suggested. An injury may lead to an autonomic nervous system dysfunction resulting in secondary changes in blood supply. The suggestion is supported by observations of anisocoria among patients. The resulting hypervascularity in the joint may lead to catabolic hyperemia, ischemic necrosis of bone, and finally osteoclastic bone resorption. However, disturbances in neuropeptide secretion may also play a more direct role in orchestrating bone remodelling, since neuronal cells containing peptides affecting the behaviour of osteoblasts and osteoclasts are present in bone. Denervation also affects fracture healing and local neuropeptide expression in bone, which emphasises the potential role of nerve damage in post-traumatic osteolysis.

The stimuli leading to post-traumatic osteolysis are likely to involve many cell types present in bone. Osteoblasts, bone marrow stromal cells and macrophages as well as other cells could release inflammatory cytokines such as IL-1, IL-6 and TNF-α, which lead to osteoclast activation either directly or indir-
ectly via osteoblasts and RANK-ligand-NF-κB or M-CSF signalling pathways. It is thus exciting that several authors have reported the existence of inflammatory cells in the bone marrow of distal clavicle during the post-traumatic osteolysis. A chronic inflammation may also lead to a local lactate production and acidic environment formation, which would stimulate osteoclasts and contribute to the mineralized matrix dissolution directly as well.

Our results suggest that no matter what mediators are associated with the osteolytic process, the cellular pathway in osteolysis involves in the end the activity of the osteoclast and as long as the pharmaceutical agent can inhibit the osteoclast function, improvement could be anticipated. Thus, it is likely that not only alendronate but also other bisphosphonates may have a beneficial effect in treating and preventing post-traumatic osteolysis. However, although inhibiting resorption, no direct anabolic effect of alendronate on bone has been shown. Therefore, it is likely that the change from a 6 mm to a 5 mm diastasis in the injured acromioclavicular joint of the current patient was not likely a direct cause of alendronate treatment but rather a radiographic finding noted by the restoration of bone mass where the bone resorption had ceased. Finally, although the patient’s radiographic and symptomatic findings significantly improved during the alendronate treatment, without a concurrent control patient or group of patients we cannot state for sure if alendronate caused these improvements. Further randomized and placebo-controlled prospective trial is thus needed to confirm or reject this theoretically appealing way of treatment.

Acknowledgements

We thank Drs. Pasi Pyrhönen, Petteri Multimäki and Olli Kiviluoto for their kind support and Pirkko Huuskonen for revising the language of the manuscript. The present study was financially supported by the Academy of Finland.

References