Autosomal dominant undifferentiated spondyloarthropathy not related to the HLA system

We were interested to read the article by Kidd and colleagues1 on familial aggregation for undifferentiated spondyloarthropathy associated with HLA-B7. The authors described a single family in whom numerous members had a non-specific arthropathy or enthesopathy, or both, which fulfilled the European Spondylarthropathy Study Group criteria for spondyloarthropathy2 in the absence of the HLA-B27 tissue type, coexistent psoriasis, or inflammatory bowel disease. They suggested that 'undifferentiated' spondyloarthropathy can be associated with genetic factors other than HLA-B27. We are in total agreement.

A few years ago, we studied a French family of 83 members distributed over five generations divided into four main branches, among whom 18 adult members had destructive arthropathy and enthesopathic changes.3,4 In all patients, the disease began between the ages of 18 and 32 years. It affected predominantly the wrists, fingers, shoulders, and peripheral entheses and progressed as an oligoarthritis, with intermittent inflammatory episodes lasting for one to three months. Axial involvement of the cervical and lumbar spine and the sacroiliac joints was also seen, but was not prominent. The sites of involvement seemed to be influenced by mechanical factors. The right wrist was generally the first joint to be affected. Destructive abnormalities, followed by bony proliferation, and intra- or extra-articular bony ankylosis were the main radiological features of this familial arthropathy (figure).

The transmission of the disease was dominant and autosomal, with 100% penetration. The clinical and radiological features were strikingly similar in all patients with successive generations and different branches of the genealogical tree, suggesting monogenic transmission. HLA typing of 12 patients and 13 healthy family members was performed. No HLA antigen was linked to the disease. None of the affected subjects had antigens B27, DR4 or DR7. The disease was not transmitted with any particular HLA haplotype.

Tests for rheumatoid factor yielded negative results. There was no history of psoriasis or chronic enteropathy in the members of this family. In none of the 18 patients did the arthropathy fulfill the American Rheumatism Association criteria.5 A diagnosis of ankylosing spondylitis was also eliminated, because the New York criteria were not fulfilled.6 This familial arthropathy could belong to the class of undifferentiated spondyloarthropathies proposed by Bensen and Calin.7 The spondyloarthropathies have in common a non-specific inflammation of the entheses, involving both the chondrified and the calcified parts. After a destructive phase, which causes bony erosion, repair takes the form of ossification.8,9 An inherited abnormality in the collagen matrix of the entheses may predispose to destructive arthropathy and enthesopathic changes. Linkage analysis on COL2A1 as the disease causing locus in this family.10 Further studies are needed to identify the genetic locus responsible for the disease.

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Treatment of refractory reflex sympathetic dystrophy with pamidronate

Reflex sympathetic dystrophy (RSD) is a condition affecting part of the whole of a limb, and is characterised by pain, vasomotor disturbance and trophic changes. RSD can persist for months or years and be severely disabling. It is characterised by local osteoporosis, which corresponds to osteoclast hyperactivity. Calcitonin, an anti-osteoclastic drug, has been shown to help some patients. Pamidronate, a second generation bisphosphonate, is a potent anti-osteoclastic agent, which is the rationale for using it in the treatment of RSD.

In an open prospective study, we evaluated the efficacy of pamidronate in the treatment of refractory RSD. Eleven patients (three men and eight women; mean age 51.3 (SD 12.8) years) suffering from RSD of at least six months duration (mean of 14.6 (10.3) months) refractory to calcitonin and physical therapy, were included. All patients fulfilled Doure's criteria for the diagnosis of RSD.1 The involved sites were the foot (n = 5), the hand (n = 2), the upper limb (n = 2), the knee (n = 1), the lower limb (n = 1). In eight cases, the RSD was related to local injury. Six patients had had to stop work because of RSD.

Radiographs of the affected sites showed osteopenia in all cases. The patients were given 30 mg of intravenous pamidronate in 500 ml of saline over four hours, daily, for three consecutive days. The patients received no standard treatment for their RSD from one month before the administration of pamidronate until three months after it. Patients were assessed by the same observer at baseline and after one and three months. Evaluation included: visual analogue scale for pain (VAS), and a physician global assessment (no improvement, moderate, significant or excellent improvement) based on objective signs on clinical evaluation (hyperhidrosis, tissue changes, joint stiffness). Blood cell count and serum calcium (corrected with serum albuminemia) were measured before, during, and one and three days after the administration of pamidronate.

The mean VAS decreased from 58.8±100 (20-2) before therapy, to 41.1±100 (26-8) at one month (p < 0.05; Wilcoxon signed rank test) and 33.8±100 (29) at three months (p < 0.01). In the physician global assessment, the results were: no improvement (n = 4), moderate improvement (n = 1), significant improvement (n = 3), and excellent improvement (n = 3) at one and three months. Three of the six patients who had had to stop work had returned to work after three months. We were unable to find predictive factors for efficacy (age, gender, affected site, degree of osteopenia). Pamidronate was well tolerated, apart from classical minor adverse effects: two patients had a transient fever, two patients had brief, asymptomatic hypocalcaemia (2-05 mmol/l) and one patient had hypocalcaemia (2 mmol/l) associated with parasthesia which resolved rapidly with oral calcium treatment (1-4g/day).

It is not possible to say whether the observed improvements were attributable to the treatment, the natural history of the disease, or psychological factors, as pamidronate was not compared with placebo in a double blind trial. However, more than 50% of the patients suffering from chronic disease, previously refractory to treatment, showed significant or excellent improvement while taking pamidronate, suggesting that it was effective.

In conclusion, this study suggests that pamidronate is a safe and effective drug for the treatment of some refractory cases of RSD. Further double blind trials are required to confirm these results.

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Pericardial tamponade preceding cutaneous involvement in systemic sclerosis

Cardiac involvement in systemic sclerosis may be primary, or secondary to involvement of other organ systems. Primary cardiac involvement in systemic sclerosis may be manifested as pericardial disease, myocardial disease, conduction system disease and cardiac arrhythmias.1 Cardiac symptoms do not usually appear until late in the disease, but exceptionally may precede the recog-