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Successful application of high dose intravenous immunoglobulins in Sjögren’s syndrome associated arthritis

High dose intravenous immunoglobulins (IVIg) have become an important treatment in a number of autoimmune disorders. Both controlled and uncontrolled studies have demonstrated the beneficial effects of IVIg in rheumatic diseases such as dermatomyositis, rheumatoid arthritis, and systemic lupus erythematosus. We report our experience with IVIg in a patient with Sjögren’s syndrome.

A 39 year old man presented for the first time in 1992 with a three year history of painful swelling of both parotid glands without signs of infection. A keratoconjunctivitis sicca which had been confirmed by Schirmer’s test required the use of tear substitutes. In addition, the patient had developed an incapacitating, non-erosive arthritis in the wrists, the metacarpophalangeal and proximal interphalangeal (PIP) joints, the knees, and the ankles. Serological evaluations revealed high titers of anti-nuclear antibodies (ANA) and anti-SS-A and anti-SS-B antibody, and increased titers of rheumatoid factor. Serum IgG was increased to 30.4 g/l without IgG subclass imbalance. The patient fulfilled the four of the 1992 American College of Rheumatology (ACR) criteria for the diagnosis of Sjögren’s syndrome. Treatment with NSAIDs was initiated because of persisting arthritis, but without success. Prednisolone was effective in doses up to 30 mg per day, but had to be withdrawn because of signs of iatrogenic Cushing’s syndrome, including hypertension and impairment. Treatment with methotrexate was refused by the patient because of the risk of impaired fertility.

We therefore decided to institute IVIg treatment. The patient received 30 g of a subhoned IVIg preparation (MEM, Behringwerke AG, Marburg, Germany) on each of days 1 to 4 and 21 to 24. Except for one period of headaches, the IVIg were well tolerated and led to a remarkable improvement in the arthritis which was confirmed by a reduction in the cumulative PIP joint circumference from 562 mm before treatment to 550 mm at day 30, and a simultaneous increase in grip strength from 80/180 mm Hg (left/right) to 280/300 mm Hg. In addition, a distinct resolution of the patient’s parotid gland swelling was noted. Serologically, IVIg treatment resulted in an increase in serum IgG to 56-0 g/l at day 5 and 41-1 g/l at day 30. While titers of ANA, anti-Ro(SS-A), and anti-La(SS-B) antibodies were not affected, the erythrocyte sedimentation rate decreased from 32 mm/1st h to 5 mm/1st h within 50 days, accompanied by a parallel decrease in C reactive protein from 12 to 8-5 mg/l. The beneficial effects lasted for a total of three months. During month 4, moderate joint pain recurred, but it was controlled adequately by NSAID for the ensuing two months. However, at the end of month 4 a severe relapse of arthritis occurred. IVIg treatment was reinitiated, followed again by a distinct relief of joint swelling and pain.

Our observations suggest a beneficial effect of IVIg in a patient with Sjögren’s syndrome associated arthritis, which is one of the most common extraglandular disease manifestations of this symptom complex. Although spontaneous remission cannot be excluded definitively, this seems to be unlikely because the clinical improvement closely followed IVIg administration and was reproducible in a flare of the disease. To our knowledge, this is the first description of the application of high dose IVIg in Sjögren’s Syndrome. As many patients with this condition present with increased IgG levels, they are considered at risk of developing symptoms of hyperviscosity hypothesis: despite high IgG levels before treatment, no major side effects occurred in our patient. Although our observation in a single patient requires confirmation in others, it does suggest an additional therapeutic option for selected Sjögren’s syndrome patients with extraglandular manifestations in whom conventional treatment fails or is contra-indicated.

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Asymmetrical nodular osteoarthritis in a patient with a hemiparesis

A 69 year old woman presented to our department complaining of pain and swelling affecting the fingers of the right hand and which had developed progressively over the preceding 10-15 years. There were no symptoms arising from the left hand, which was affected by a hemiparesis, a consequence of the surgical resection of a brain tumor occurring at the age of 12. On examination, the patient had a left hemiparesis with a mild pyramidal weakness and loss of sensation to light touch. She had Heberden’s and Bouchard’s nodes affecting all the interphalangeal (IP) joints.

Radiographs confirmed the diagnosis of nodular generalised osteoarthritis (OA) with osteophytic lipping, sclerosis, and joint space narrowing of the affected joints (fig 2). Serological tests were normal and erythrocyte sedimentation rate was within normal limits for her age.

Osteoarthritis is the commonest joint disorder in Western populations, and the hand is frequently involved. Nodular generalised OA affects the joints of the hand in a symmetrical manner, the most frequent joint groups involved being the DIP and thumb base joint. In a recent population study, the tendency for involvement of nodular OA of the hand will be found to be symmetrical.

Asymmetrical OA of the hands has been described occasionally in similar circumstances. In 1947, Sjöström and Korkmous described a woman with a median nerve injury of the hand who later developed Heberden’s nodes in all her fingers except those supplied by the injured nerve. Stecher also described it in a hand paralysed by poliomyelitis, and in 1935 Coste and Forrestier reported a case that occurred after a cerebral accident.
There is increasing evidence that the nervous system is involved in the development and maintenance of an inflammatory joint response, though most of the studies have been of rheumatoid arthritis. Activation of nociceptors in a joint results, via an axon reflex, in an antidromic response travelling back down peripheral fibres that terminate around the blood vessels of the joint. Inflammatory compounds are released from these fibres, producing an acute neurogenic inflammation. In vivo antidromic stimulation of articular C fibres is known to lead to vasodilatation and plasma extravasation within the joint. It has been demonstrated that the course of adjuvant arthritis can be affected by neurological modification.

The underlying mechanism of symmetry in arthritis is likely to be neurogenic, though mechanical factors may also play a part. Excess loading of a joint tends to increase the risk of its developing OA, and it may be hypothesised that paralysis and disuse of a joint would spare it from these effects. In polyomielitis, for example, a decreased incidence of hip OA was seen in joints on the paretic side compared with both the normal side of the patient and the hips of normal control subjects. The implication is that a reduction in loading accounts for a decrease in the incidence of OA in these affected hips, but weight bearing through a paralysed hip may actually place the joint under greater risk of repetitive trauma and subsequent OA.

If a neurological response is implicated, it is likely that a unilateral noxious stimulus produces a bilateral spinal response via a central reflex arc, mediated by fibres containing neuropeptides such as substance P and calcitonin gene related peptide (CGRP). Animal work on rats has shown that the induction of an inflammatory stimulus in one joint produces an acute response increase in substance P and CGRP in both the ipsilateral and contralateral dorsal horns. It may be that the role of this mechanism is to protect the contralateral side from a similar insult by means of a pre-emptive release of inflammatory mediators.

Generalised nodular OA is striking in its symmetry. The case presented suggests that a purely mechanical cause for this is unlikely, and that the development of a symmetrical distribution appears to depend on an intact nervous system.

**Figure 1** Photograph of hands, showing unilateral Heberden's and Bouchard's nodes.

**Figure 2** Radiograph of hands, showing unilateral primary nodular osteoarthritis.

Sweet's syndrome associated with undifferentiated connective tissue syndrome

Sweet's syndrome, an acute febrile polymorphonuclear neutrophilic dermatosis that was first described in 1964, is characterised by fever, leucocytosis, tender plaques or nodules, and dense dermal infiltration by neutrophils. Some cases have been associated with malignant neoplasms and autoimmune diseases. Reports suggest that hyper-reactivity reactions to bacterial, tumour, or autoantigens may be involved in the pathogenesis of the syndrome. Undifferentiated connective tissue syndrome (UCTS) was described in 1980 by LeRoy, providing a useful diagnostic category for disorders the clinical and laboratory features of which fail to meet the criteria for known connective tissue diseases. We present an interesting case of Sweet's syndrome associated with UCTS.