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 neuroanatomical 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 polymyalitis, 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.

Sweet’s syndrome associated with undifferentiated connective tissue syndrome

Sweet’s syndrome, an acute febrile 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 hypersensitivity 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.
A 17 year old Japanese woman was admitted to hospital in June 1990 with thrombocytopenic purpura and Raynaud's phenomenon. Laboratory results revealed decreased numbers of platelets (3 x 10^9/l) and leucocytes (2.3 x 10^9/l), and positivity for serum antinuclear antibody (ANA) (speckled pattern) and antibody to ribonucleoprotein (RNP). Arthralgia, sclerodactyly, nail changes, dry eyes, and dry mouth were not present. Because the findings did not fulfill the criteria of any known connective tissue disease, the diagnosis was UCTS. Administration of high doses of intravenous gammaglobulin with prednisolone 50 mg/day increased the platelet count. Treatment was then changed to administration of betamethasone 0.5 mg on alternate days.

In June 1994, the patient developed a fever and tender cutaneous lesions on the left arm and trunk. She denied having any other recent illness or symptoms preceding this acute episode. The fever did not respond to antibiotics and non-steroidal anti-inflammatory drugs, and the patient was readmitted to hospital. Her body temperature was 39°C, blood pressure 111/69 mm Hg, and heart rate 102 beats/minute. She exhibited slightly oedematous, infiltrated erythematous plaques on the face, trunk, left arm, and legs. An aphthous ulcer was present on the upper lip. Ophthalmological examination revealed no abnormalities. Laboratory investigations showed the following: erythrocyte sedimentation rate 82 mm/1st h (normal value (NV) 4–20 mm/1st h); serum C reactive protein 111 mg/l (NV < 4 mg/l); haemoglobin 114 g/l (NV 115–145 g/l); packed cell volume 34.3% (NV 35–44%); platelet count 136 x 10^9/l (NV 150–400 x 10^9/l); leucocyte count 3.7 x 10^9/l (NV 3.0–9.4 x 10^9/l) with 52% segmented neutrophils, 34% band neutrophils, 13% lymphocytes, and 1% monocytes. The prothrombin time and active partial thromboplastin time were normal, but the serum fibrinogen concentration was increased to 6550 mg/l (NV 1300–4500 mg/l). Serum protein electrophoresis revealed polyclonal hypergammaglobulinaemia with IgG 25.9 g/l (NV 10–21 g/l), IgA 2.6 g/l (NV 1–5 g/l), and IgM 1.6 g/l (NV 0.4–2.9 g/l). The serum complement concentration was increased to 45.7 CH50 U/ml (NV 30–40 U/ml), with C3 0.88 g/l (NV 0.45–0.87 g/l) and C4 0.32 g/l (NV 0.12–0.37 g/l). ANA was present at a titre of 1:256. Platelet associated IgG was increased to 50-0 ng/10^10 platelets (NV 9–25 ng/10^10). Findings were negative for dsDNA antibody, Sm antibody, La antibody, antineutrophil cytoplasmic antibody, lupus anticoagulant, anti-beta2-glycoprotein I, cryoglobulins, and serological test for syphils. HLA typing demonstrated the presence of antigens A24, A31, B51, B54, Cw1, DR4, and DR8. No abnormalities were detected by urine analysis, stool examination, electrocardiography, and chest radiography. Ultrasound tomography showed mild splenomegaly. A biopsy specimen of a cutaneous lesion on the back showed oedematous papillary bodies, and a dense polymorphonuclear leucocyte infiltration with nuclear dusts in the upper and mid-dermis (figure). Vasculitis was absent. These findings led to a diagnosis of Sweet's syndrome. Institution of prednisolone 30 mg/day immediately reduced fever and eruptions without leaving scars. During an attempt to wean the patient from prednisolone, the disease recurred once. However, the patient has remained clinically well taking prednisolone 10 mg/day.

Cases of Sweet's syndrome have been reported more frequently in Japan than in other countries. In Japan, the syndrome is suggested to be associated with expression of HLA-Bw54, as detected in our patient. Conditions underlying Sweet's syndrome have included malignancies and autoimmune diseases such as rheumatoid arthritis, Sjögren's syndrome, subacute cutaneous lupus erythematosus, and drug induced lupus erythematosus. As far as we can establish from search of the literature, our patient is the first case of Sweet's syndrome associated with UCTS. However, during her attack of Sweet's syndrome, this patient presented oral aphthae, which are rarely reported in other countries. This may be suggestive of the presence of subclinical Behçet's disease or systemic lupus erythematosus, though the symptom is relatively common in Japan (30%). In addition, the lack of leucocytosis is not characteristic of Sweet's syndrome. This could be explained by an underlying leucopenia complicated by UCTS as an associated disease in our patient.

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