

Manubrio-sternal joint problems in rheumatoid arthritis

- infection
- synovitis
- subluxation
- ankylosis
- degeneration

the manubrio-sternal and sternoclavicular joints possess synovium,^{3,4} extension of synovial disease from adjacent costochondral joints, degenerative processes or trauma. Histological and microradiographic analysis has indicated active inflammation of the articulation in some patients and the absence of inflammation and presence of fibrous replacement in others.⁵ Pathological problems with clinical manifestation in the manubrio-sternal joint of patients with rheumatoid arthritis are shown in the box. In the former case, bacteraemia and joint sepsis probably occurred secondary to a urinary tract infection in a joint previously compromised by rheumatoid arthritis. This case also illustrates the difficulty in eradication of joint sepsis despite adequate and prolonged administration of appropriate antibiotics. Both cases demonstrate the importance of excluding sepsis in any disproportionately warm and painful joint in a rheumatoid patient. In both patients, fever and peripheral blood leucocytosis were present, characteristic of infection. These responses may be reduced or abolished in rheumatoid patients especially in those debilitated or immunocompromised. Elimination of infection from a joint requires prolonged high-dose antibiotic administration, repeated arthrocentesis and sometimes arthrotomy and surgical drainage. Infection is rapidly destructive of intra-articular structures, congruity and stability.

We suggest that clinically obvious manubrio-sternal joint arthritis in a patient with rheumatoid arthritis should be regarded as septic until proved otherwise.

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Allergic and toxic reaction to alprazolam

Sir,

We report the case of a patient who suffered an alprazolam overdose, and an allergic reaction probably induced by it.

A 19-year-old woman was found unconscious after ingesting 1.2 mg of alprazolam. Six months previously, she had been taking 0.25 mg alprazolam daily and 20 mg fluoxetine daily for two months. One hour later, at the emergency room, a gastric lavage was done, and treatment with fluids was started. Fifteen hours after drug ingestion, the patient's mental status was characterised by total amnesia of what had happened, and a relative had to relate the story. Alcohol and other drug ingestion was ruled out. The patient then presented a crisis of bronchospasm and laryngospasm, with severe dyspnoea and dysphagia.

Physical examination revealed bilateral palpebral and soft palate angioedema and laryngeal stridor. Pulmonary auscultation showed a reduction of the vesicular murmur and disseminated high-pitched wheezes over both pulmonary fields. Cardiac auscultation and abdominal examination were normal. Maleolar oedema with pain on mobilisation, probably secondary to her fall after taking alprazolam, was observed in the left lower limb.

Laboratory analysis showed: $17.6 \times 10^9/l$ white blood cells (84% polymorphonucleocytes, 9% lymphocytes, 6.5% monocytes, 0.1% eosinophils). The remaining cell count, serum electrolytes and urinalysis were normal. Baseline arterial blood gases showed moderate hypoxaemia ($PaO_2 = 76$ mmHg) corrected after oxygen therapy at FiO_2 of 31%. Chest X-ray and electrocardiogram were normal. IgG, A, M and E levels, complement, C1 inhibitor and protein electrophoresis fell within normal limits. Neither HBV antibodies or antigens nor HIV antibodies were detected.

Successive doses of subcutaneous epinephrine and intravenous corticosteroids, antihistamines, oxygen therapy and inhaled β -adrenergic drugs were administered, with good clinical response. On discharge, eight days later, the patient was asymptomatic. Sensitisation to the most frequent allergens was ruled out through clinical history and skin test. A series of standard prick tests for pollens, house dust mites and molds, latex, foods and hymenopter poisons were negative. Finally, an *in vitro* study with alprazolam was conducted on the patient and on three healthy subjects with a negative basophil degranulation test,¹ and a negative histamine release test.^{2,3} No *in vivo* studies on the patient were conducted, being forbidden by current Spanish legislation.

The loss of consciousness and the transient global amnesia, can be attributed to the sedation and the amnesic effects of the alprazolam overdose. This reaction occurred with a dose slightly higher than the upper limit of the dose range for the treatment of panic disorder.⁴

The symptoms that occurred 15 h after ingesting the drug suggest an allergic reaction to alprazolam. Other factors (material used for gastric lavage, other medications, foods or substances) were ruled out by different standard tests. The previous contact of the patient with alprazolam a few months before, supports the idea of a sensitisation. The timing of the clinical manifestations suggests an

independence of the toxic reaction, considering the elimination half-life of the drug.⁵ Ethical considerations made confirmation through *in vivo* tests of our explanation of this clinical picture impossible.

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Chronic myeloid leukaemia and allogenic bone marrow transplantation in a patient with toxic oil syndrome

Sir,

We have observed the development of chronic myeloid leukaemia in a woman who had been affected 10 years earlier by the toxic oil syndrome, produced by the ingestion of adulterated rapeseed oil, and in whom an allogenic bone marrow transplant had been accompanied by severe toxic manifestations.

The toxic oil syndrome^{1,2} is a multisystemic disease in which the basic lesion is endovascularitis involving vessels of all sizes and located anywhere in the organism. The vascular lesion first affects the intima, followed by inflammatory infiltration and cell proliferation producing, in advanced stages, narrowing and occlusion of the vascular lumen, leading to ischaemia and parenchymal atrophy in some organs (box).^{3,4} No cases of development of leukaemia in patients affected by the toxic oil syndrome had been previously reported.⁴

The 35-year-old woman whose case we present here, was diagnosed as having toxic oil syndrome 10 years earlier. The only sequel at the time that the leukaemia was detected, was a mild, predominantly sensory, neuromuscular involvement in the upper limbs. After the diagnosis of Ph-positive chronic myeloid leukaemia, she started treatment with interferon α -2b, but no cytogenetic remission was observed in subsequent haematologic studies.