References

Sirs, We thank Drs Pruzanski and Vadas for their interest in our paper and for their positive comments. We would like to add another interesting entity in which phospholipase A2 may have a role—that is, chronic anterior uveitis. In fact, we have studied aqueous humour from seven patients with chronic anterior uveitis for the activity of phospholipase A2. We found levels of phospholipase A2 significantly greater than those in aqueous humour from patients with senile cataracts. It is interesting to note that phosphatidylcholine is readily degraded by aqueous humour phospholipase A2. On the other hand, lysophosphatidylcholine is known to harm the lens in experimental models of cataract development; so another possible role for phospholipase A2 in tissue damage should be added to the list.

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References

Development of morphea in rheumatoid arthritis treated with penicillamine

Sirs, Penicillamine has been used to treat systemic sclerosis and morphea in the past and has been thought to have been of benefit in some cases. I report a patient who developed morphea while taking penicillamine for treatment of rheumatoid arthritis. There is one known previous case report of morphea and another of systemic sclerosis developing during penicillamine treatment.

A 65 year old woman was diagnosed as having rheumatoid arthritis in 1984 affecting the small joints of the hands, elbows, shoulders, neck, and ankles, with confirmatory erosions on x ray. Non-steroidal anti-inflammatory drugs provided little relief, and treatment was started with oral penicillamine, initially 250 mg daily and gradually increased to 625 mg. At this dose and three months after starting penicillamine the patient complained of a red itchy rash on her chest and neck. In view of the persisting activity of the rheumatoid arthritis without evidence of renal or haematological side effects treatment with penicillamine was continued orally at the lower dose of 500 mg daily. The skin rash persisted mildly with irritation. When the penicillamine was reduced to 250 mg daily a year later the patient felt that her skin rash improved. At this time she was seen in the dermatology outpatient's clinic.

Clinically she had morphea lesions, hardened dermal plaques, on both sides of the chest, encircling both breasts, and on both sides of the abdomen (Fig. 1). Symptoms of systemic sclerosis, including Raynaud's phenomenon, dysphagia, and dyspnoea, were absent.

Her full blood count and erythrocyte sedimentation rate were normal with a mildly raised alkaline phosphatase and alanine transaminase consistent with the activity of her rheumatoid arthritis. Her rheumatoid factor and autoantibodies were negative, including antinuclear antibodies and antibodies against extractable nuclear and cytoplasmic antigens. Chest x ray was normal.

Histology of the skin lesion on her chest was consistent with morphea. The keratin was normal and epidermis was mildly atrophic. In the dermis there was condensation of collagen, particularly in the deeper layers, with appendageal structures reduced in number and the remaining ones atrophic. Superficial capillaries were ectatic with an infiltrate of chronic inflammatory cells in a perivascular distribution. Direct immunofluorescent stains for IgG and IgA were also negative.

The penicillamine was discontinued at this time, and nine months later the morphea has remained unchanged with no new lesions appearing. Her rheumatoid arthritis has remained relatively inactive.
Penicillamine appears responsible for this patient’s morphoea as there was a temporal relation, with initial improvement in symptoms on reduction of the dose and no progression of the morphoea on discontinuation.

Generalised morphoea has been described in association with rheumatoid arthritis. The association of morphoea with penicillamine is important, however, as penicillamine was logically used as a lathyrergic agent in the treatment of scleroderma after an effect on the solubility of dermal collagen was observed. Penicillamine inhibits the normal intramolecular cross linking of collagen fibrils and increases the ratio of soluble to insoluble collagen. This led to a study of 14 children with morphoea treated with low dose penicillamine with beneficial results in all patients. Further case reports have not confirmed these results, however.

Treatment with penicillamine has been associated with various mucocutaneous lesions and several mechanisms are responsible for the cutaneous side effects. Penicillamine’s interference with the maturation or synthesis of collagen and elastin has been reported to result in excessive wrinkling, cutis laxa and elastosis perforans serpiginosa and may be of importance as a mechanism in the development of this patient’s morphoea.

Induction of autoimmunity by penicillamine, which can result in pemphigus, pemphigoid, and systemic lupus erythematosus, occurs most commonly in diseases of altered immunity, such as rheumatoid arthritis, and may be due to an effect on regulatory T lymphocyte function. Evidence in support of T cell mediation as a second possible mechanism for the induction of morphoea by penicillamine is illustrated by the cases of two patients who developed morphoea following bone marrow transplants after initial development of acute and chronic skin changes of graft versus host disease. The latter represents immune attack on host antigens (the epithelial cells in the skin) by donor T lymphocytes. The morphoea appeared to represent the final healing stage of longstanding inflammation.

Acute sensitivity reactions to penicillamine present as local or generalised erythematous, macular, and papular or urticarial eruptions. This may account for this patient’s initial skin rash, which subsequently progressed to morphoea.

I would like to thank Dr A W McKenzie, consultant dermatologist, Norfolk and Norwich Hospital, for permission to report his patient.

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