MATTERS ARISING

Exposure to chemicals and systemic sclerosis

Occupational exposure to various chemicals, including vinyl chloride, silica dust, epoxy resin, benzene, trichloroethylene, propylene glycol, and a later solvent, has been described as a potential provoking factor of systemic sclerosis (SSc) and scleroderma-like disorders. However, the precise contribution made by occupational environmental factors to the occurrence of scleroderma remains unclear.1

Susceptibility to these agents may differ widely in distinct areas of Europe, as a result of different employment patterns and environmental differences, as the following examples indicate. Several cases of exposure to solvents have been described, including that reported by Garcia-Zamalloa and colleagues in the Annals.2 Predisposing work has been described,3 except in the study by Yamagke and Ishikawa.4 In the Hungarian population, a remarkable predominance of women has been found among patients with SSc who were previously exposed to chemicals.5-8 23 of our 180 patients with SSc had exposure to solvents in their case history; only three of them were men. During the epoch of ‘socialist industrialisation’ in the 1950s and 1960s widespread exposure of female workers from rural areas were employed to do menial jobs in the urban areas, with a concomitant higher risk of exposure to solvents and other chemicals.

After a latent period of several years, these patients developed SSc indistinguishable from ‘true’ systemic sclerosis. Now, with the improvement of working conditions in Hungary, the number of cases with exposure to chemicals seems to be decreasing.

Vinyl chloride disease seems to be relatively frequent among British workers exposed to this agent.9-11 Conversely, in Hungary, vinyl chloride disease has been found to be extremely rare, in spite of the presence of well detectable exposure to this chemical: 464 workers were exposed to vinyl chloride in Kozinbacika (north-eastern Hungary) for more than 10 years on average, but only one case of vinyl chloride disease has been described, despite regular and well documented screening for the presence of this disorder. Another group of 60 workers has been found to be exposed to trichloroethylene without any signs of scleroderma related disease.

Genetic markers are useful tools for relating chemically induced SSc-like vinyl chloride disease. Susceptibility to this disorder is increased in the presence of HLA-DR5 or a gene in linkage disequilibrium with it and an antigen associated with the haplotype A1 B8, while DR3 favours the progression over the disease,10 as seen among the British workers.

The heterogeneity of clinical symptoms, distribution of major histocompatibility complex alleles, and autoantibody profiles in SSc suggest that this disorder may represent a group of distinct diseases, and that the characteristic genetic and environmental pre-

LETTERS TO THE EDITOR

Acquired scleroderma anaemia associated with penicillinase therapy for rheumatoid arthritis

Penicillinase has been successfully used in the treatment of rheumatoid arthritis since 1964.1,2 Most of the serious reactions have been haematological and include agranulocytosis, thrombocytopenia, and aplastic anaemia.3 The incidence of some adverse side effects, such as thrombocytopenia, rashies and proteinuria, has been shown to be unacceptable high with high dose treatment.

We report a case of acquired scleroderma anaemia following treatment with penicillinase for rheumatoid arthritis.

A 50 year old man with a five year history of rheumatoid arthritis and non-insulin-dependent diabetes mellitus developed more active joint disease associated with rheumatoid nodules and erosive changes revealed by radiography. His joint disease had been controlled on ibuprofen 600 mg three times daily, but in June 1988 penicillinase 125 mg once daily was added to his regimen. The dose was gradually increased, by 125 mg at monthly intervals, to 500 mg once daily. At no stage was he taking phenacetin or paracetamol.

Before he commenced taking the penicillinase, the patient’s full blood count had been stable with a haemoglobin concentration of 13·2 g/dl, platelet count 351 × 10^11/l, leucocyte count 9·3 × 10^11/l and erythrocyte sedimentation rate 35 mm/1st h. The film was mildly microcytic with a cell volume (MCV) 76 (f1) and hypochromic. The white cell differential was normal.

Two months after he started treatment, his haemoglobin had decreased to 9·9 g/dl and showed hypochromia and microcytosis (MCV 78 f1). He then began a course of iron therapy and the haemoglobin temporarily increased to 12 g/dl in November 1988. By January 1989 his haemoglobin decreased again to 10·8 g/dl with the typical microcytic picture (MCV 70 f1) and by February 1989 it had decreased further, to 7·0 g/dl. At this stage, the film showed a dimorphic picture with some hypochromia, some macrocytosis, and the presence of sideroblasts. There were some nucleated red cells and the white cells and platelets were normal. Because of the appearance of the blood film, the possibility of scleroderma anaemia was raised.

Clinically, there was no evidence of blood loss and an endoscopy was normal. His arthritis was considered to be well controlled on therapy, with a C reactive protein 29 mg/l (NR < 20 mg/l) and a C3 degradation product 15 U/ml (NR 5-12 U/ml); vitamin B12 and folate levels were normal, serum iron 33 mmol/l (NR 14-34 mmol/l), and iron binding capacity 34 mmol/l (NR 43-72 mmol/l). Bone marrow aspirate and trephine revealed a hypocellular marrow with markedly reduced erythropoiesis, gross dyserythropoiesis and 24% ringed sideroblasts. The karyotype of the disorder is one of the megakaryocytic series were normal. During the period of investigation the haemoglobin decreased to a minimum of 4·9 g/l. The patient’s penicillinase regimen was continued and he began taking pyridoxine 100 mg twice daily. He required a blood transfusion to control his symptoms, but subsequently maintained his haemoglobin at about 12·5 g/dl, with a normal MCV (81 f1). A repeat bone marrow aspirate at two months was hypercellular, and although there was mild dyserythropoiesis, ringed sideroblasts were not present.

During subsequent follow up, the patient’s joint disease flared. To control this problem, he decided initially to treat him with prednisolone 5 mg once daily, and more recently, with hydroxychloroquine.

Patients with acquired idiopathic systemic scleroderma anaemia have common features of all three haemopoietic cell lines. The changes are most marked in the red cell lineage, with at least 15% of nucleated erythrocytes in the marrow being ringed sideroblasts.4 The peripheral blood shows a dimorphic picture with poikilocytosis, basophilic stippling and some hypochromic features, although the overall MCV is often slightly increased. The karyotype may be abnormal and there is a predisposition to develop acute leukaemia.5

Secondary scleroderma change occurs in a wide variety of conditions, but the number of
Exposure to chemicals and systemic sclerosis.

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