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 large solvent, has been described as a potential provoking factor of systemic sclerosis (SSc) and scleroderma-like disorders.1 However, the precise contribution made by occupational environmental factors in the occurrence of scleroderma remains unknown.2

Susceptibility to these agents may differ widely in distinct areas of Europe, as a result of the different environmental factors acting as a common agent.3 Scleroderma-like disease in women is more frequent in rural than in urban areas, and the age distribution was similar among different regions.4

Vinyl chloride disease seems to be relatively frequent among British workers exposed to this agent.5 9 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 Kazincbarcika (northern 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 exposed to trichloroethylene without any signs of scleroderma related disease.

Genetic markers are useful tools for relating chemically induced SSc-like vinyl chloride disease.5 9 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 of 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-disposing risk factors can be totally different in these subgroups. The environmental contribution to scleroderma is unknown, raising the need for a European multicentre case-control study to determine the groups at risk.

LETTERS TO THE EDITOR

Acquired sideroblastic anaemia associated with penicillamine therapy for rheumatoid arthritis

Penicillamine 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.2 3 The incidence of some adverse side effects, such as thrombocytopenia, rash, and proteinuria, has been shown to be unacceptable high with high dose treatment.

We report a case of acquired sideroblastic anaemia following treatment with penicillamine 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 penicillamine 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 penicillamine, the patient’s full blood count had been stable with a haemoglobin concentration of 13.2 g/dl, platelet count 351 x 10^9/l, leucocyte count 9.3 x 10^9/l and erythrocyte sedimentation rate 35 mm/1st h. The film was mildly microcytic with a cell distribution (NA 76 fl) 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 70 fl). 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 without iron therapy. The microcytic picture (MCV 70 fl) and by February 1989 it had decreased further, to 7.0 g/dl. At this stage, the film showed a dimorphic picture with some macrocytosis, microcytosis, and basophilic stippling. 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 sideroblastic 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 0-12), ESR 22 mm/h (NR < 20 mm/h) and C3 degradation product 15 U/ml (NR 5-12 U/ml); vitamins B12 and folic acid levels were normal, serum iron 33 μmol/l (NR 14-34 μmol/l), and iron binding capacity 34 μmol/l (NR 43-72 μmol/l). Bone marrow aspirate and trephine revealed a hypocellular marrow with markedly reduced erythropoiesis, gross dyserythropoiesis and 24% ringed sideroblasts. The trephine showed the typical iron pattern of microcytic, normal, and sideroblastic marrow. The patient had been 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 fl). 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. On this second problem, it was decided initially to treat him with prednisolone 5 mg once daily and, more recently, with hydroxychloroquine.

Patients with acquired idiopathic sideroblastic anaemia have abnormalities of all three haemopoietic cell lines. The changes are most marked in the red cell lineage, with at least 15% of nucleated erythrocyt cells in the marrow being ringed sideroblasts. 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.8

Secondary sideroblastic change occurs in a wide variety of conditions, but the number of
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