LETTERS TO THE EDITOR

Subungual splinter haemorrhages: A new sign of the antiphospholipid coagulopathy?

Sir: We recently reported two patients with valve lesions and transient ischaemic attacks, including amaurosis fugax, both of whom showed other features associated with the 'antiphospholipid syndrome'.[1] One of these patients, in addition to clubbing, showed florid subungual splinter haemorrhages with no definite evidence for infective endocarditis. Treatment of culture negative infective endocarditis in addition to anticoagulation, nevertheless, resulted in clinical improvement.

A recent paper has drawn attention to the presence of subungual splinter haemorrhages in four patients with amaurosis fugax and antiphospholipid antibodies,[2] and a similar patient with amaurosis fugax, who was also found to have aortic incompetence, was reported by Kleiner *et al.*[3]

We have recently encountered two further patients with splinter haemorrhages and antiphospholipid antibodies. The first also developed splinter haemorrhages in association with amaurosis fugax in the absence of valve lesions or vasculitis. The patient, a 43 year old white woman, suffered a right sided cerebral thrombosis in August 1988. This had been preceded by seven months of amaurosis fugax accompanied by subungual splinter haemorrhages. These episodes lasted for approximately 20 minutes at a time, and affected the vision of the left eye predominantly. After discharge from hospital she continued to have episodes of amaurosis fugax accompanied by splinter haemorrhages despite the administration of salicylates (aspirin 300 mg daily).

She had had one spontaneous abortion during the first trimester some 10 years previously. There was no family history of other thrombotic events, nor was she thrombocytopenic. She was referred to St Thomas's Hospital in November 1988 because of the discovery of antibodies to cardiolipin. There was no evidence clinically of systemic lupus erythematosus; she showed a positive test for antinuclear antibodies 1/160, but all other antibodies, including those to double stranded DNA and extractable nuclear antigens were absent. She has remained well on a combination of aspirin (300 mg daily) and anticoagulation with warfarin and has had no further episodes. She was regarded as suffering from a 'primary' antiphospholipid syndrome.

The second patient, a 31 year old Israeli woman, has already been reported.[4] She had developed a hepatic infarction in association with a lupus anticoagulant, the only such case reported to date. She stated that at the age of 22 years after only one tablet of oral contraceptive (Microgynon), subungual splinter haemorrhages developed in the nail area of the fingers and toes. About one month later the same preparation was again tried with a similar result. Nine years later on becoming pregnant, they again reappeared, lasted for one month, and then disappeared spontaneously. She subsequently aborted at 20 weeks. There was no valve lesion detectable.

In our first patient the splinter haemorrhages coincided with episodes of amaurosis fugax, as reported in the other patients. In the second, however, there was a clear relation with hormonal influences (oral contraceptives, pregnancy). In neither of these two was any valve lesion present.

Splinter haemorrhages in systemic lupus erythematosus were first reported in 1966 by Fraga and Mintz[5] and were the subject of a recent review by Young *et al.*[6]

Although larger vascular occlusions are more commonly associated with antiphospholipid antibodies,[7] smaller size vessels, such as the retinal[8] or digital or pedal vasculature, with the resultant ischaemic complications of infarctions and gangrene, have been reported.[9] These lesions have been unassociated with vasculitis.

The presence of subungual splinter haemorrhages may similarly represent evidence of platelet thrombi in the smaller vessels to the nail bed in patients with the 'antiphospholipid syndrome'. A similar mechanism may be causing the transient ischaemic attacks. I wish to draw attention to the presence of this sign and to emphasise the importance of careful examination of this group of patients in order to increase its detection.

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Iron chelation in rheumatoid arthritis: clinical and laboratory evaluation

Sir: Chronic inflammatory processes cause a significant change in iron metabolism with a drop in serum iron and a redistribution of iron to the activated reticuloendothelial system. In patients with rheumatoid arthritis (RA) iron accumulates in the synovial membrane, an extension of the reticuloendothelial system, and in synovial fluid.[1] It has been suggested that iron may play an important part in acute and chronic phases of the arthritic inflammatory process.[2] Iron may catalyse free radical production in the joints, leading to lipid peroxidation and membrane disruption.[3] An abnormal accumulation of iron may promote an infiltration of lymphocytes and macrophages into the synovium of affected joints.[4]

Serum concentrations of β_2 microglobulin, a low molecular weight protein (11 815 daltons) associated with the light chains of cellular membrane HLA antigens, have been significantly correlated with the clinical activity of RA and other rheumatic diseases.[5 6] It seems to be a global marker of the number of lymphocytes implicated in the autoimmune processes and of the alteration in the various lymphocytes subsets.[6]

We evaluated serum ferritin and β_2 microglobulin concentrations and other laboratory and clinical indices in patients with RA treated with desferrioxamine, a metal chelating agent with a very high affinity for iron,[7] to assess the usefulness of iron chelation in reducing chronic inflammation.

Eighteen female patients, aged 23 to 64 years, with RA according to the 1987 revised American Rheumatism Association diagnostic criteria, were treated with desferrioxamine (0·5 g twice a day) by subcutaneous injections into the lower anterior abdominal wall for 14 days. No patients had received systemic steroids or immunosuppressive or disease modifying drugs within three months before the enrolment. All were receiving non-steroidal anti-inflammatory drugs (diclofenac 100 mg/day). Active disease was defined by the following criteria: morning stiffness of at least 30 minutes' duration, six or more tender joints, three or more swollen joints, and an erythrocyte sedimentation rate of at least 50 mm/1st h. Eleven patients (group A) had two or three of the four preceding criteria and seven (group B) had all four criteria.

Haematological, biochemical, and immunological measurements and clinical indices were evaluated before the start of treatment, at the 14th day, and at the 28th day.

Serum concentrations of ferritin and β_2 microglobulin were determined by radioimmunoassays.

Statistical analysis was performed using Student's *t* test. The table shows the laboratory and clinical results.

Group A patients had low or normal serum ferritin concentrations (range 10·4–76·3 μg/l) in contrast with group B patients who had high serum ferritin values (ranging from 119·7 to 1075·1 μg/l).

We found no significant differences in serum iron, transferrin, and iron binding capacity between the two groups at the beginning of the study, though serum iron was lower in group A and transferrin and iron binding capacity higher than in group B. Erythrocyte sedimentation rate and β_2 microglobulin were significantly higher in group B ($p<0·05$). There were no significant differences in morning stiffness, grip strength, and Ritchie index between groups A and B, though they were slightly worse in group B.

A notable increase in IgG concentrations was seen in both groups at the 14th day and 28th day.

β_2 Microglobulin concentrations increased at the 14th day in both groups A and B ($p<0·01$), showed no variation at the 28th day in group A, but had decreased significantly by the 28th day in group B compared with the 14th day and with the initial value.

At the end of the study significant improvements of morning stiffness, grip strength, and Ritchie index were seen in both groups of patients ($p<0·01$).

No statistical differences were noted in erythrocyte sedimentation rate, haemoglobin, serum iron, transferrin, iron binding capacity, and complement concentrations compared with basal values.

An ophthalmological examination was normal in all patients studied. Electro-ocular tests were not performed because of the short period of desferrioxamine administration.