Cyclosporin in Wegener's granulomatosis with renal failure

Sir: In 1987 we presented in this journal the case history of a patient with Wegener's granulomatosis, in whom remission of the disease was achieved with cyclosporin.1 Now, after more than three years' treatment with this immunosuppressive drug no further activity of the disease has occurred. Although we stated that cyclosporophamide is still the drug of choice in the treatment of Wegener's granulomatosis, this positive experience persuaded us to start cyclosporin treatment in another patient with Wegener's granulomatosis resistant to conventional treatment. As the effect of cyclosporin in this patient was even more impressive than it had been in the previous subject we feel it is worth reporting this case history.

In 1982 a 72 year old woman was admitted to our hospital for evaluation of cough, rhinorhoea, fever, and fatigue. Laboratory tests showed a raised erythrocyte sedimentation rate (ESR) of 122 mm/h, thrombocytopenia (platelets 625×10⁹/l), and normal renal function. An xray examination of the chest and sinuses showed no abnormalities. Histopathological examination of a biopsy specimen of the nasopharynx, however, showed destructive granulomatous reaction with necrotising vasculitis, characteristic of Wegener's granulomatosis. Consequently, treatment with cyclophosphamide (100 mg/day) and prednisone (30 mg/day) was started. Six weeks later her clinical condition and laboratory indices had normalised. During the following months the doses of both drugs were tapered slowly, with success.

Unfortunately she withdrew from outpatient clinic control until she was admitted to hospital again in 1986 because of severe fatigue and depression. By that time she had stopped taking prednisone but continued with cyclophosphamide 100 mg/day. Laboratory examination showed a raised ESR (83 mm/h), anemia (haemoglobin 93 g/l), low platelet count (78×10⁹/l), increased serum creatinine (156 µmol/l), and haematuria (15–30 erythrocytes in the urinary sediment); testing for the presence of antineutrophil cytoplasmic antibodies was not done at that time. Her raised ESR and renal failure were considered to be markers of activity of Wegener's granulomatosis. The low platelet count was thought to be manifestations of bone marrow depression due to cyclophosphamide. The administration of cyclophosphamide was stopped and prednisone 30 mg/day was given. Nevertheless, her clinical condition deteriorated and serum creatinine rose to 365 µmol/l. The corticosteroid regimen was changed to methylprednisolone 1500 mg every other day intravenously for 10 days and the addition of azathioprine 25 mg every eight hours, but this did not prevent further progression of renal failure and further rise of serum creatinine to 516 µmol/l.

As Wegener's granulomatosis seemed to be progressive despite intensive treatment we decided—to inform the patient— to start treatment with cyclosporin 5 mg/kg body weight a day and prednisone 40 mg/day. Trough concentrations of cyclosporin (by radioimmunossay and measured in whole blood) ranged from 405 ng/ml to 780 ng/ml. One month later her condition had clearly improved, with decreased values of ESR (48 mm/h) and serum creatinine (213 µmol/l). During the following period cyclosporin trough concentrations were kept at about 600 ng/ml and prednisone was tapered slowly. More than two years after the initiation of cyclosporin this patient, who at that time was aged 79, is doing very well with stabilised serum creatinine concentrations of 190–210 µmol/l and no antineutrophil cytoplasmic antibodies.

In this case of Wegener's granulomatosis cyclosporin seems to have been effective. Interestingly, remission of renal function was achieved by treatment with an immunosuppressive drug for which nephrotoxicity is the most prominent side effect. This observation fits with another case report showing the beneficial influence of cyclosporin for a patient with Wegener's granulomatosis with renal failure.2 Obviously, cyclosporin is an alternative to cyclophosphamide in treatment of patients with Wegener's granulomatosis. Additional studies are necessary to confirm the precise role of cyclosporin in the treatment of this disease.

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An aerobic bacteria in rheumatoid arthritis

Sir: In past years some rheumatologists have thought that an aerobic bacteria have a role in the pathology of rheumatoid arthritis.1 We considered that if such an aerobic bacteria were essential to metabolism in the diseased joint then it should be possible to measure substantial amounts of their metabolic products—short chain fatty acids—in the synovial fluid.

We used a modification of McArthur's gas chromatographic method2 to examine 11 normal synovial fluids obtained during negative explorations on knees for meniscal disease and 15 fluids taken from the knees of patients with classical or definite rheumatoid arthritis. The synovial fluid samples were treated with hydrolase, the short chain fatty acids were extracted with ether and freeze dried at

80°C. Before injection into the gas chromatograph the freeze dried material was redisolved in 8 M formic acid. 2-Ethylbutyric acid was used as an internal standard.

The mean concentrations (range) of short chain fatty acids in normal fluid were found to be: acetic acid 102 (54–149) µmol/l; propionic acid 13 (0–31) µmol/l; n-valeric acid 5 (4–30) µmol/l; n-valeric acid 3 6 (0–18) µmol/l. There were no significant differences between normal and rheumatoid synovial fluids.

Thus it seems that the direct action of aerobic bacteria—for example, Clostridium perfringens and others, which produce short chain fatty acids, is excluded.

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Treatment of polymyalgia rheumatica and giant cell arteritis

Sir: We read with interest Kyle and Hazleman's article on the treatment of polymyalgia rheumatica and giant cell arteritis,1 which sheds some light on the problems of treatment in these two conditions. We would support their views that the lowest doses of steroid possible should be used both in the initial and maintenance treatment, but would like to draw attention to the possible dangers of undertreatment of the ophthalmic manifestations of giant cell arteritis. Although doses may indeed be to some extent based on tradition and anecdote, in such a capricious and visually devastating condition it is anecdotal evidence which has to be taken. That the 'high dose' group had fewer episodes of relapse than the 'low dose' group, but still suffered a significant therapeu- tic failure rate, implies that even higher dose regimens should be considered. Ophthalmologists usually use higher doses of steroid, at least initially, when treating patients who present with the visual sequelae of giant cell arteritis.2 Although quite probably most cases of giant cell arteritis might be managed with a lower dose even than 40 mg prednisolone initially, visual loss with the majority is not the ultimate aim of treatment, when the fate of the rest may be irresistible visual loss.

Sarah A. Day, the acute ischaemic optic neuropathy resulting from giant cell arteritis is often bilateral, with the second eye being affected very shortly after the first. A recent review of 50 cases of anterior ischaemic optic neuro- pathy related to giant cell arteritis3 found that when large doses of steroid (80–120 mg prednisolone initially, followed by the same dose for several days after) were used 95% of patients were protected from disease in the
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