Cancer complicating Behçet’s disease treated with chlorambucil

Sir, O’Duffy et al recommended long term surveillance of chlorambucil treated patients with Behçet’s disease for infertility, leukaemia, and other malignant lesions. We have seen two patients with Behçet’s disease treated with chlorambucil who developed malignant disease, definite in one case and probable in the other.

The first patient, a 42 year old man, has been followed up for 14 years. The features of Behçet’s disease included oral ulceration, necrotic pseudofolliculitis, skin hypersensitivity to needle prick, and anterior and posterior uveitis with hypopyon leading to complete blindness. He was treated for five years with chlorambucil, with an initial daily dose of 0-2 mg/kg for three months and 0·1 mg/kg for 54 months. Chlorambucil was stopped because of azoospermia.

Nine years later lumbar right and hip pains developed. Radiographs showed lytic lesions in the right ilium, the upper end of the right femur, and the pedicles of the D12 and L3 vertebrae and widening of the upper mediatinum. Fibre optic bronchoscopy was normal. There were no neoplastic cells in bronchial aspiration. Bone marrow biopsy showed infiltration with adenocarcinoma without indication of its origin. The patient died eight months later; autopsy was not performed.

Patient 2, a 44 year old man, has been followed up for three years for Behçet’s disease, including oral and genital aphthosis, venous thrombosis, posterior uveitis, and hypersensitivity to needle prick. The patient was treated daily with chlorambucil in a dose of 0·2 mg/kg for 18 months, during which visual acuity and ophthalmoscopic examination became normal. Nine months after cessation of treatment the patient complained of chest pains. Chest radiography showed a parahilar opacity infiltrating the pulmonary parenchyma with ‘cancer-leg-shaped’ margins. A chest radiography had been normal nine months earlier.

Significant loss of weight was noted. Hard, irregular hepatomegaly developed, and the patient died within three months. Autopsy was not performed.

Azoospermia is frequent in chlorambucil treated Behçet’s disease, occurring in 10 out of 20 patients in our experience. Leukaemia has been reported in association with cyclophosphamide treatment, but other cancers have not been reported previously in patients with Behçet’s disease treated with immunosuppressives.

In our patients the risk of malignant change was probably increased by the administration of chlorambucil in high dose for a long time. The first patient became blind despite long term treatment with chlorambucil and developed both azoospermia and cancer. This form of treatment must be used with care and exclusively for manifestations with a poor prognosis such as severe uveitis and meningocencephalitis resistant to other treatment.

Correspondence

Borrelia isolated from cerebrospinal fluid in a French case of Lyme disease

Sir, Lyme disease was recognised in 1975 in Lyme, Connecticut by Steere and Malawista. Since then several cases have been reported in Europe. Nobody on this continent, to our knowledge, has isolated the causative agent of the disease from the cerebrospinal fluid (CSF) as previously observed in rare cases. We report here one observation.

A man aged 42 developed a characteristic erythema chronicum migrans after a tick bite on the right leg. The tick was removed by the patient. The rash was associated with fatigue and myalgia. A few days later he developed arthritis of his right ankle that lasted five days. Twelve days after the bite painful paraesthesias with numb burning sensation of the lumbar area and of the right leg (L5 and S1 distribution) initiated a meningoradiculitis. Six days later the patient developed vertigo and noted a slow pulse. On admission the electrocardiogram showed a complete atrioventricular block with an escape rhythm of 20/min with right bundle branch block (QRS interval: 0·12 s) necessitating the placement of a temporary transvenous pacemaker (one week). Echocardiography and myocardial pyrophosphate scintigraphy were normal. A significant...
increase of the creatine phosphokinase (CPK) indicated myocarditis: CPK 2865 IU/l, CPKMB 288 IU/l. The CSF contained 24 white blood cells/mm³ (24×10⁹/l) (94% lymphocytes, 6% monocytes) with an increased level of protein: 1.50 g/l. A spirochaete began to grow in BSK II after the second week and a borrelia was identified. It had a diameter of 0.2 µm and a length between 4 and 22 µm. By immunofluorescent assay high titres of IgG antibodies against Borrelia bugdorferri were detected in serum collected three weeks after the beginning of the illness (1/160), and two months later (1/320). The patient's phenotype was A2, B5, DR5. He received oral penicillin therapy (10 million U/day) for 15 days, and recovered.

For the first time in France a borrelia has been isolated from the CSF during Lyme disease. This isolation strengthens the role of borrelia as the aetiological agent responsible for the clinical signs in the acute phase of the disease. The late clinical manifestations could be secondary to an immune reaction triggered by the spirochaete, especially among patients who have the B cell alloantigen DR2. In France the carrier is unknown, but Ixodes ricinus occurs worldwide and its involvement is suspected.

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References

Tendon rupture in systemic lupus erythematosus

SIR, Although it is impossible to disprove Dr Richards' comments, we feel that they are unlikely. Our patient sustained a minimally displaced fracture which required supportive strapping only. She was seen in follow up on four occasions by the orthopaedic and rheumatology services before presentation with tendon rupture. This review was in a research clinic setting where musculoskeletal problems are specifically sought. The patient insisted that muscle swelling did not occur until seven months after the fracture. We feel, therefore, that spontaneous tendon rupture is the most likely diagnosis in this case.

SIR, I read with interest the recent paper by Byron and Kirwan on the feasibility of conducting a study to determine whether low dose corticosteroids modify the course of rheumatoid arthritis.1 The authors solicited the views of your readers regarding the acceptability of long term use of prednisone (7.5 mg) in relation to potential side effects.

An increasing body of evidence suggests that prolonged corticosteroid therapy accelerates the development of atherosclerosis.2 Even low doses of corticosteroids may result in significant side effects such as hypertension, hyperlipidaemia, and impaired glucose tolerance.3 4 Each of these adverse effects is a recognised coronary risk factor.

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Corticosteroids in rheumatoid arthritis

SIR, I read with interest the letter by Hanly and Urowitz1 on the spontaneous rupture of the long head of biceps tendon in a 35 year old woman with SLE on long term corticosteroid therapy and who had suffered a fracture of the neck of the left humerus some seven months previously. It is perhaps straining our credibility too much to ask us to accept this as spontaneous rupture of the tendon when presumably the cause of the fracture (we are not told) was traumatic in nature. Rupture of the long head of biceps can remain undetected and is not apparent until the patient flexes the elbow or supinates the forearm against resistance, manoeuvres which would be impossible to carry out at the time of the fracture. I would surmise that the rupture of the tendon may have occurred at the time of the fracture and remained undetected particularly if at follow up she was not always seen by the same doctor, or that the weakened tendon snapped in the convalescent phase when she was performing shoulder and arm exercises. In either case the tendon would not have ruptured had it not been for the fracture and so can hardly be called spontaneous.
Borrelia isolated from cerebrospinal fluid in a French case of Lyme disease.
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*Ann Rheum Dis* 1986 45: 789-790
doi: 10.1136/ard.45.9.789-b

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