Comment

Fraser *et al*¹ in their original description of legionnaires' disease referred to three patients out of 182 with a WCC less than $2.0 \times 10^9/l$, two of whom died. Two other patients had WCCs of less than $6.0 \times 10^9/l$.

During his acute illness our patient had pancytopenia with bone marrow depression. We can only speculate on the part played by legionnaires' disease in producing hypoplastic anaemia. A toxic effect on the marrow may explain the pancytopenia during the acute phase of the illness. Its recurrence within a few weeks of clinical recovery, however, was unexpected and difficult to explain. Marrow hypoplasia might have been present before the development of legionnaires' disease, although this seems unlikely in view of the return of an almost normal blood profile after clinical recovery.

The role of co-trimoxazole in producing the hypoplastic anaemia is probably unimportant as the blood dyscrasias of this drug are quite distinct from that seen in our patient.³

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Polyneuritis associated with azathioprine sensitivity reaction

A reaction with fever, leucocytosis, arthralgia, myalgia, and rash may occur about two weeks after taking azathioprine.¹ The mechanism of this response is unknown but the clinical pattern is similar to that of serum sickness. We report a case of reversible polyneuritis associated with other features of azathioprine sensitivity reaction.

Case report

A 40-year-old man presented with an 18-month history of weight loss, abdominal discomfort, diarrhoea without blood or mucus, aphthous ulcers, and night fever. Crohn's disease was diagnosed by finding rectal granulomata in a biopsy specimen and extensive disease throughout the small bowel on barium follow-through x-ray examination. Outpatient treatment with prednisolone 45 mg and azathioprine 125 mg (2 mg/kg body weight) daily was started. After 19 days he developed fever, arthralgia, and, within 48 hours, a rapidly progressive proximal muscle weakness such that he could not stand even with support. On admission he was febrile with a tachycardia of 140/min and blood pressure 100/50 mm Hg. There was no exacerbation of the Crohn's disease, which symptomatically had improved, but he had developed erythema nodosum over both shins. The proximal weakness was most definite in the hip girdle muscles, particularly the quadriceps (MRC grade 2), with some muscle tenderness but no fasciculation or reflex change and no sensory abnormality. He had a moderate normochromic anaemia of 11.4 g/dl, a neutrophil leucocytosis of $17.2 \times 10^9/l$ ($17\,200/mm^3$), an erythrocyte sedimentation rate of 64 mm in 1 h, a moderate hypoalbuminaemia of 25 g/l, and a serum alkaline phosphatase activity of 134 IU/l (normal 25-100 IU/l). The serum creatinine phosphokinase activity was normal. Electromyography, sampling quadriceps, showed a pattern of denervation with units of normal duration but low amplitude and moderate reduction in interference pattern. Motor conduction in the left peroneal nerve was reduced to 40 m/s (normal 42.1-63.5 m/s).

Azathioprine was stopped but prednisolone continued in the same dosage. The symptoms settled rapidly. Within four days there was no detectable weakness and the white cell count and alkaline phosphatase had returned to normal. He remained well. Five months later electromyograms were normal and conduction in the left peroneal nerve was 55 m/s.

Comment

Peripheral neuropathy has not been reported in association with Crohn's disease without secondary amyloid,² but it is a recognised complication of hypersensitivity reactions to vaccination, immunisation, and drugs such as penicillin.^{3 4} In hypersensitivity reactions a

subclinical neuropathy may be responsible for the common complaint of myalgia, and weakness may be masked by joint pain. Recognised patterns of peripheral neuropathy include mononeuritis, symmetrical motor or sensorimotor neuropathy, and brachial neuropathy, but there may also be central nervous system lesions or cranial nerve palsies, including optic neuritis. Azathioprine is now used in treating immune-mediated peripheral neuropathies and other immunological disorders of the nervous system (polymyositis, myasthenia, multiple sclerosis, polyarteritis). A drug-induced neuropathy should be considered when there is any change of neurological function associated with an azathioprine reaction. In at least one case azathioprine hypersensitivity was associated with "relapse" in a patient with dermatomyositis.⁵ The patient's serum creatinine phosphokinase activity remained normal and the increased weakness may have been due to a drug-related neuropathy.

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Radiological bone changes in T-cell and "common" ALL of childhood

In view of the well-known poor prognosis of T-cell acute lymphoblastic leukaemia (ALL) compared with "common" ALL¹ a difference in radiological bone changes might be expected. Analysis of recent data on incidence and width of the characteristic radiolucent metaphyseal bands in children at time of diagnosis appears to confirm this.

Patients, methods, and results

Routinely taken pretreatment skeletal survey films from 25 consecutive children diagnosed as ALL were "blindly" evaluated by one of us (EMS) and later correlated with the results of membrane marker studies of leukaemic cells aspirated from the bone marrow. The assessment of radiolucent metaphyseal bands was subjective since indefinite margins prevent exact measurement. Nevertheless, it was possible to apply the following criteria using an x-ray film centred over the knee joint in the antero-posterior position at 100-cm f c-s-film distance. Radiolucent metaphyseal bands in the femur or tibia with longitudinal dimensions up to 1 mm in width were scored as +, those between 1 and 2 mm as ++, and those over 2 mm as +++. The results are shown in the table.

Comment

The results show a significantly lower incidence and width of the characteristic radiolucent metaphyseal bands at diagnosis in children

Pretreatment radiological bone changes in 25 children diagnosed as suffering from acute lymphoblastic leukaemia (ALL)

Metaphyseal bands	"Common" ALL (n = 18)	T-cell ALL (n = 7)
None	1	6
+	3	1
++	6	—
+++	8	—

No bands vs bands +, ++, +++:
 χ^2 (Yates corr) = 12.3, $p < 0.001$ (2×2 tables).

with T-cell (ALL) compared with those with common ALL. This could be related to the suggested extramedullary, lymphatic or thymic, origin of T-cell ALL in contrast to common ALL.² Alternatively it could be related to a slower rate of tumour growth in common ALL compared with T-cell disease. It is superficially surprising that other studies have shown either no relation³ between radiological bone changes and prognosis or a shorter remission⁴ in children with multiple bone involvement. In fact, the criteria for classifying degree of bone changes in each of these studies were somewhat different from ours, and by relating their findings to overall remission duration or survival of children treated on a variety of different drug schedules the relation to the adverse subset of T-cell ALL may have been obscured.

We thank Drs M F Greaves and G Janossy, London, for the membrane marker studies.

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Immunological findings during successful treatment of HBsAg-associated polyarteritis nodosa by plasmapheresis alone

Corticosteroids can be of great value in treating polyarteritis nodosa but may cause severe complications due to arteriolar stenosis.¹ A patient of ours with polyarteritis associated with HBs antigen (HBsAg) developed such complications. We then treated her with intensive plasma exchanges (IPE) alone, firstly to try to improve her condition and, secondly, to study the immunological response to this immuno-manipulation.

Case report

A 60-year-old woman was admitted with abdominal pains. She had a six-month history of diffuse arthralgia, myalgia, weakness, loss of weight (10 kg), intermittent fever, and Raynaud's phenomenon. She was treated for three months with prednisolone 30 mg daily because she had HBsAg in her serum and raised serum transaminase concentrations (AST 300 IU/l). She was febrile (38°C), cachectic, and in severe distress because of generalised abdominal pains. White blood cell count was $15 \times 10^9/l$ ($15\,000/mm^3$) with 80% neutrophils, 3% eosinophils. Erythrocyte sedimentation rate 96 mm in 1 h. Arterial blood pressure was 100/80 mm Hg. Other routine laboratory findings were normal. Corticosteroids were stopped. Polyarteritis was suspected, and angiography showed hepatic and renal microaneurysms. At laparotomy 1 m of small bowel with some areas of gangrene but without apparent vascular occlusion was removed. Microscopic examination of bowel, liver, and muscle biopsy tissue showed necrotising vasculitis. Furthermore, liver biopsy showed some residual changes of acute viral hepatitis. The patient did not improve, and 21 days after surgery she was lethargic. She was then given on each of five successive days a session of IPE with a Haemonetics 30-cell separator. At each session 3-4 l of plasma were exchanged for modified gelatine (Plasmin) and fresh frozen plasma. No other treatment was given. A striking improvement occurred after the first IPE and she was asymptomatic when discharged 14 days after the last IPE. Six months later she had only slight abdominal pain and her clinical condition was good. Her blood pressure was 140/80 mm Hg. Angiography showed considerably fewer hepatic and renal microaneurysms. The kidneys were normal in size. She was given seven more sessions of IPE. Twelve months later she was in good health and having no treatment.

Circulating immune complexes (CIC) were measured by the ¹²⁵I Clq-binding assay (normal concentrations < 10%). Reverse passive haemagglutina-

tion system (WHI-HBs Wellcome) was used for detecting HBsAg. Antibodies to HBsAg (anti-HBsAg) were detected by solid phase radioimmunoassay (Ausab, Abbott). The results of the main laboratory investigations are shown in the figure. In addition aspartate transaminase (AST) rose from 15 to 80 IU/l (N < 20 IU) during the second series of IPE and complement, immunoglobulins, and plasma fibrinogen decreased, as already observed.²

Laboratory investigations in patient with polyarteritis nodosa treated by plasmapheresis (IPE). WBC=White blood cell count. ESR=Erythrocyte sedimentation rate. Anti-HBs U=Ausab-Abbott units.

Comment

Recovery in this one patient could have been fortuitous. Nevertheless, the improvement was very striking and abrupt. We have also treated two other patients with HBsAg-negative polyarteritis nodosa in the same way with good results. We are therefore encouraged to carry on with further trials in similar desperate conditions. The lesions of polyarteritis, at least in part, could be caused by CIC.³ We have seen CIC permanently resolve even without immunosuppressive or corticosteroid treatment while CIC concentrations usually rise when IPE is stopped.⁴ Since in our patient HBsAg disappeared and anti-HBsAg appeared at the same time as transaminases and CIC increased temporarily, we assume that an adequate immunological response, as occurs in acute resolving viral hepatitis, was mimicked—perhaps by the withdrawal of the complexes,⁵ in altering the ratio of viral antigen to viral antibodies, or both. So IPE could have acted not only by passively decreasing inflammatory mediators or CIC but also by stimulating immune reactivity.

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