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Requests for reprints to: Dr D. B. Wheldon, Bacteriology Department, John Radcliffe Hospital, Headington, Oxford OX3 9DU, UK.

Letter to the Editor

Angioimmunoblastic lymphadenopathy and hypercalcaemia

We were interested to read the paper by Brearley *et al.* (1979) describing, in addition to the usual clinical features associated with angioimmunoblastic lymphadenopathy (AIL), the haematological and in some cases marrow abnormalities found in seven patients with this syndrome. As the spectrum of abnormal findings associated with this condition broadens we should like to report a recently encountered case in which a persistently raised serum calcium was found, as we are unaware of hypercalcaemia having been reported previously in cases of AIL.

A 27-year-old man presented with generalised hilar and para-aortic lymphadenopathy and fine pulmonary mottling. His initial serum calcium was in the normal range, but persistently raised levels in the order of 3·05 mmol/l (12 mg/100 ml) were soon recorded associated with a serum phosphorus of 0·8 mmol/l (2·5 mg/100 ml) and urinary calcium excretion of 31·0 mmol/24 h (1240 mg/24 h). Serum parathormone was 1·05 ng/ml (reference range up to 1 ng/ml with a normal serum calcium). This presentation initially suggested a diagnosis of sarcoidosis but axillary lymph node biopsy showed a diffuse alteration of nodal architecture by a mixed cellular proliferation of immunoblasts, plasma cells, lymphocytes, and some epithelial aggregates in association with an arborising vascular proliferation with endothelial hyperplasia and some periodic acid Schiff's positive material in vessels, lumens, and walls—the histological features of AIL as described by Lukes and Tindle (1975). Serum IgM, IgA, and IgG were all raised, and immunoperoxidase studies on the lymph node showed polyclonicity of the cellular infiltrate.

Initially, haematological investigations showed little abnormality but within two and a half months of the onset of the disease investigation revealed: haemoglobin 7·2 g/dl; leucocytes $3·8 \times 10^9$/l ($3800/mm^3$) with 31% lymphocytes and 16% eosinophils; platelets 17×10^9/l ($1700/mm^3$); positive direct Coombs test; demonstrable rouleaux and cold agglutinins. Bone marrow aspiration was unsuccessful at two attempts. Treatment with steroids, transfusion, and cytotoxic drugs was ineffective, and the patient died three months after the onset of the disease from a klebsiella septicaemia. The serum calcium remained raised throughout this terminal phase of the disease.

Hypercalcaemia occurs in myelomatosis but is rare in lymphoma and leukaemia (Walker, 1974; Jayaraman and David, 1977). Evidence indicates that a bone-resorbing factor such as ectopic parathormone (Heath, 1976) or osteoclast-activating factor (Mundy *et al.*, 1974) is active in these diseases even in the presence of bony metastases. In this case with hypercalcaemia the serum parathormone is inappropriately high and is compatible with primary or ectopic parathormone secretion. Co-existent primary hyperparathyroidism seems unlikely in view of the initially normal serum calcium, its sudden increase, and absence of supportive radiological evidence. Since AIL may progress to immunoblastic sarcoma ectopic parathormone secretion is a probable hypercalcaemia-inducing mechanism. The release of osteoclast-activating factor may, however, be an additional mechanism since, as well as being demonstrated in patients with myelomatosis and lymphomas (Mundy *et al.*, 1974), it has been produced by phytohaemagglutin stimulation of normal lymphocytes (Chen *et al.*, 1976). This observation may be especially pertinent since the whole histological appearance of angioimmunoblastic lymphadenopathy is that of a marked exaggeration of lymphocytic transformation.

M. J. SWORN
R. BUCHANAN
D. A. F. MCGILL

Departments of Pathology and Medicine, The Royal Hampshire County Hospital, Winchester, Hants

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