Angioimmunoblastic lymphadenopathy, sulphasalazine exposure and villous atrophy

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Summary: A woman with inflammatory lesions in the terminal ileum was treated with sulphasalazine. Nine months later she developed angioimmunoblastic lymphadenopathy and was found to have intestinal villous atrophy. Her systemic illness partially responded to oral steroids but a gluten free diet restored clinical and biochemical well being coincident with a return of her villous pattern.

Introduction

Angioimmunoblastic lymphadenopathy (AIL) is a lymphoproliferative disorder the features of which include weight loss, rash, hypergammaglobulinaemia, Coombs positive haemolytic anaemia and generalized lymphadenopathy. The lymph nodes show characteristic histological features (Frizzera *et al.*, 1974). The condition runs a variable clinical course and may be steroid responsive, but often proceeds to lymphoma (Cullen *et al.*, 1979). An association with sulphasalazine therapy or small intestinal villous atrophy has not been reported.

Case report

A 67 year old woman presented in 1977 with malaise, weight loss and lower abdominal colic. Physical examination was negative but investigations showed haemoglobin 9.5 g/dl, a low serum iron, normal folic acid and vitamin B12, erythrocyte sedimentation rate 82 mm/h, and a diffuse increase in gammaglobulin. Occult blood was present in the faeces on eight occasions but full barium and endoscopic studies were normal. Laparotomy in October 1977 (Mr J.F. Kane) showed four circumferential areas of inflammation and oedema in the terminal ileum thought to be compatible with minor lesions of Crohn's disease. A mesenteric lymph node biopsy showed normal histology. Treatment was started with sulphasalazine 2 g daily but this was doubled in April 1978 because of increased colic.

In August 1978 she developed fever and generalized tender lymphadenopathy. Biopsy of an axillary node showed typical features of AIL. By October she was more poorly although the lymphadenopathy was subsiding. Investigations showed a macrocytic anaemia (haemoglobin 9.7 g/dl, mean cell volume 121 fl, reticulocyte count 9%) and a low serum folate ($<1.0 \mu\text{g/l}$) but serum B12 was normal. Her ESR was 142 mm/h and serum electrophoresis showed a diffuse increase in γ globulin. A duodenal biopsy showed partial villous atrophy with crypt hyperplasia and a moderate excess of plasma cells. Her sulphasalazine was stopped and folic acid started with immediate improvement in her well being. The lymph nodes finally disappeared, the macrocytosis resolved, but her ESR remained raised.

In May 1979 her colic returned and she was treated with prednisolone 10 mg daily with considerable improvement. Her symptoms recurred occasionally but at no stage did she have diarrhoea. Her ESR remained elevated. Repeat duodenal biopsy in May 1983 showed continuing partial villous atrophy and she was started on a gluten free diet. Further duodenal biopsy in August 1983 showed a normal villous pattern. For the first time in 6 years she felt entirely well and had a normal haemoglobin and ESR (15 mm/h).

Comment

Angioimmunoblastic lymphadenopathy has been reported in association with allergen or drug exposure. (Cullen *et al.*, 1979; Newcom & Kadin, 1979; Lapes *et al.*, 1976). Our patient had taken sulphasalazine for 9 months before she developed lymphadenopathy and we cannot be certain whether the AIL was a temporary drug induced phenomenon or whether her illness from the outset was AIL. The development of AIL following prolonged use of a particular drug has led to the

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suggestion that chronic antigenic stimulation might be important (Lapes *et al.*, 1976), but hypersensitivity to drugs early in the course of the disease is more common (Newcom & Kadin, 1979). One patient is reported to have developed lymphadenopathy after sulphasalazine but no histology was obtained (Carr-Locke & Ali, 1982).

The ileal lesions found at laparotomy in 1977 were initially thought to be due to Crohn's disease but no other features of this condition have appeared. Her

clinical condition and duodenal mucosa responded dramatically to a gluten free diet. Coeliac disease can be complicated by ulcerative jejunoileitis (Bayless *et al.*, 1967) and it is noteworthy that both coeliac disease and AIL may proceed to lymphoma. The exact relationship between this patient's multiple pathologies remains uncertain but is worthy of reporting as neither sulphasalazine therapy nor small intestinal villous atrophy have previously been linked with AIL.

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