CASE REPORT

Pleural lymphoma in a patient presenting with malabsorption: an illustration of the clinicopathological behaviour in a case of enteropathy associated T cell lymphoma

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Abstract

A case of enteropathy associated T cell lymphoma (EATCL) is described, which was diagnosed by biopsy of a lymphomatous pleural mass. Retrospective radiological review showed that this lesion had been present when an initial diagnosis of coeliac disease had been made 12 months previously and a detailed description of the natural history of the lymphoma during this period was thus available. The findings show that EATCL may behave in an indolent fashion and masquerade as coeliac disease, delaying the correct diagnosis. The relation of this disorder with coeliac disease and lymphocytic gastritis is discussed with reference to recent published works.

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The cause and definition of enteropathy associated T cell lymphoma (EATCL) and its relation to coeliac disease has been the subject of much debate recently. This is centred around the question of whether or not T cell lymphoma may be a cause or an effect of coeliac disease. The traditional view that EATCL is a complication of coeliac disease¹ is supported by new immunohistochemical evidence that both diseases have similar subsets of intestinal mucosal T cells.² It has been argued, however, that in some cases of adult onset 'coeliac' disease the histological findings of villous atrophy, crypt hyperplasia, and intra-epithelial lymphocytosis may be a response to low grade lymphomatous infiltration.³ Because coeliac disease may be asymptomatic⁴ it is difficult to prove that a monoclonal lymphocytic intestinal infiltrate can develop in previously normal bowel.

Lymphocytic gastritis is a recently described entity characterised by a dense epithelial lymphocytic infiltration⁵ the pathogenesis of which is incompletely understood. It has been associated with coeliac disease, small bowel lymphoma,⁶ and Menetrier's disease.⁷ In one report the subset of T cells present differed from those found in coeliac disease in having low percentage of γ/δ T cells.⁷ Some take the view that it may be a common morphological manifestation of more than one disease.^{6,7}

This report describes the case of a patient who

was initially diagnosed and treated as having coeliac disease and lymphocytic gastritis but who responded poorly to a gluten free diet. A diagnosis of T cell lymphoma was made by pleural biopsy one year later.

Case report

A 74 year old man presented in October 1990 with a two year history of intermittent diarrhoea and weight loss. Investigations showed a raised mean corpuscular volume (MCV -114 fl), low serum B12 (150 ng/l, normal 200-1000), and folate (1.2 μ g/l, normal 2-14). Haematological parameters were otherwise normal. Liver function was normal. Chest x ray showed evidence of previous tuberculosis and some pleural thickening at the left base, which was thought likely to be long standing (Fig 1). Barium enema was normal. Gastroscopy showed a nodular gastric mucosa with aphthous ulceration and superficially normal duodenal mucosa. Gastric biopsy showed a lymphocytic gastritis and duodenal biopsy showed partial villous atrophy with a mixed severe mononuclear cell

Figure 1: Chest x ray at presentation showing blunting of the left costophrenic angle.

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Figure 2: Duodenal biopsy specimen showing partial villous atrophy and intense intraepithelial mononuclear cell infiltrate.

infiltrate consistent with a clinical diagnosis of coeliac disease (Fig 2). A gluten free diet was started and over the next two months there was 2.3 kg weight gain and symptomatic improvement. In the year after diagnosis the improvement in bowel symptoms was maintained but three further gastric and duodenal biopsies at four monthly intervals showed no improvement.

Further weight loss, fever, and upper abdominal pain precipitated re-admission in September 1991. Liver function tests now showed raised alanine transaminase (101 IU, normal 0–35) and alkaline phosphatase (227 IU, normal 25–95). Upper abdominal ultrasound and abdominal computed tomography were normal. Repeat chest x ray showed no change. Liver biopsy showed a predominantly T cell mononuclear cell infiltrate and although the possibility of lymphoma was raised it was considered that this may also have been caused by an inflammatory process. Barium follow through was normal. Infection screen was negative. A trephine bone marrow biopsy specimen showed a slight increase in small lymphocytes but no definite evidence of lymphoma. Finally, computed tomography of the chest showed pleural thicken-

Figure 3: Transverse computed tomography scan of the chest during IV contrast showing a rim enhancing left sided pleura associated mass that corresponds with the area of pleural thickening seen on chest x ray.

ing at the left lung base in an area corresponding to that previously noted on a chest x ray (Fig 3). A biopsy specimen of this lesion showed infiltration of the chest wall by malignant mononuclear cells of T cell phenotype consistent with a high grade non-Hodgkin's lymphoma (Fig 4). Because of the poor response to gluten free diet and the presence of lymphoma it seemed reasonable to consider that the malabsorption was as a result of an enteropathy associated with the lymphoma (EATCL) rather than simple coeliac disease.

The patient then received 'B-CHOP' chemotherapy. Each course of 'B-CHOP' consists of intravenous bleomycin, vincristine, cyclo-

Figure 4: Pleural biopsy specimen showing a malignant mononuclear cell infiltrate. The malignant cells have large vesicular and sometimes multilobed nuclei with prominent nucleoli. Immunohistochemistry showed a T cell phenotype.

Figure 5: (A) left costophrenic angle before B-CHOP chemotherapy; (B) left costophrenic angle after three courses of chemotherapy.

phosphamide, and adriamycin on day 1 with oral prednisolone on days 1–5. There is a course option at four weeks depending on the response of the lymphoma and the extent of bone marrow suppression that is induced. Computed tomography after three courses of chemotherapy showed that the pleural mass had reduced in size. This reduction in pleural thickening could also be seen on the chest x ray (Fig 5) making it very likely that the pleural thickening noted initially in October 1990 and thought then to be unimportant was neoplastic from the outset. Unfortunately the chemotherapy was poorly tolerated, the patient went into a gradual decline, and died in a hospice three months later. Post-mortem examination was refused.

Discussion

This patient presented with malabsorption and small bowel biopsy specimens were consistent with a diagnosis of coeliac disease. The subsequent biopsy of a lymphomatous pleural plaque, visible on previous radiographs, permitted the retrospective deduction of lymphoma at initial presentation. This case is similar to that of Wright *et al*³ in that none of the intestinal tissue provided morphological evidence of lymphoma but differs in the unusual finding of a high grade lymphoma in the pleural lesion. Further similarities can be drawn with two cases described by Wolber,⁶ which had lymphocytic gastritis, small bowel intraepithelial lymphocytosis, and morphologically detectable T cell lymphoma of the small bowel.

A valuable feature of our case is that it provides a detailed profile of the natural history of EATCL over a period of 12 months from initial presentation to the introduction of chemotherapy. This suggests that EATCL may behave in an apparently indolent fashion with a very

slow change in pathological state over many months as measured by clinical state, serial upper gastrointestinal biopsy, radiography, haematology, and biochemistry results. It is also of interest that the pleural lesion, morphologically a high grade lymphoma when biopsied, showed no significant increase in size during the year after presentation. There was some progression of the disease, however, over this period as shown by the slow deterioration in general condition and liver function. Although we have not investigated the clonality of the T cells infiltrating the gut one possibility is that these represented epitheliotropic 'transitional' or 'end' cell phases of the same cell line present in the pleural lesion. This may partly explain the lack of change in the appearance of the duodenal mucosa on serial biopsy in this condition. We consider it to be most unlikely that the pleural lesion is the site of origin of this lymphoma because of the extensive lymphocytic infiltration elsewhere, the long history of bowel symptoms, and the similarity with other described cases.^{3,4} Primary pleural lymphoma has been described, particularly in Japan⁸ but is said to arise most frequently from old inflammatory pleural disease, is usually of B cell type and is usually localised to the pleura.

The conventional view would be that our patient had asymptomatic coeliac disease and developed a lymphoma, which precipitated the initial presentation. The alternative view that the intestinal lymphoma developed as a primary event two years before presentation seems possible in view of the indolent nature of the disease and subsequent findings.

Clearly the combination of malabsorption with small bowel villous atrophy and lymphocytic infiltration is not specific for coeliac disease because EATCL may present in similar fashion. It is probable that the lymphocytic gastritis

present in this case was also a manifestation of lymphoma.

These findings reaffirm the maxim that patients with adult onset 'coeliac' disease who show a poor response to treatment or who deteriorate when receiving treatment should be viewed with a high degree of suspicion. Small bowel biopsy and abdominal computed tomography are essential but often unhelpful in early diagnosis.⁹ In such cases a careful search for secondary extra-abdominal disease may be worthwhile. Unless there is macroscopic, radiologically detectable disease it may be necessary to perform cytogenetic and immunohistochemical studies on biopsy specimens, possibly even obtained from laparotomy,³ to exclude lymphoma.

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