Case Report-II

Enteropathy Associated T-Cell Lymphoma

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ABSTRACT

Celiac disease is rare in India as compared to the western population. Patients with long standing celiac disease are prone to develop occult intestinal lymphoma which can be diagnosed early only on the basis of clinical acumen. Presentation in this cohort is sudden deterioration with clinical symptoms such as weight loss, abdominal pain, intractable diarrhea or emergencies like obstruction or perforation. Lesions may be seen as nodules, plaques, or strictures in the intestine. The disease is confined to the abdomen, with no peripheral lymphadenopathy or pulmonary infiltrates. A variety of regimens, including CHOP have been used, but better combinations needs to be investigated. Early diagnosis and appropriate timely intervention is an important factor to improve the poor prognosis of these patients.

INTRODUCTION

Primary gastrointestinal lymphoma, of which 1/3 rd occur in small bowel, accounts for 5% of all lymphomas and 10 –15 % of small bowel malignant tumour in the adult.[1] Primary T-cell gastrointestinal lymphomas are rare, and, although various histologic types have been reported, the only defined clinicopathologic entity is enteropathy-type intestinal T-cell lymphoma. The association between malabsorption and lymphoma was first described in 1855 by Sir William Gull, who suggested lymphoma as a cause of steatorrhoea, but it was Gough in 1962 suggested that intestinal lymphoma was a complication of adult celiac disease[2,3] and that widespread mucosal derangement of the small bowel, found in idiopathic steatorrhea, was itself a premalignant condition. Isaacson and Wright[4] coined the term "malignant histiocytosis of the intestine" (MHI) and it has been modified to enteropathy-type intestinal T-cell lymphoma. by the World Health Organization International Classification Project [5] in 2001.

CASE: A 60 yr old male with history of Celiac disease presented with diarrhea and weight loss (12 kg in 1 year). He had biopsy proven diagnosis of Celiac disease in 1991 & was on gluten free diet since then. In 2002 he had persistent low grade fever which subsided after starting empirical anti Kochs treatment (AKT) medication and had restarted wheat in 2002 on advice of local doctor. In October 2004 he had history of low grade fever, weight loss, barium meal follow through (Fig-1) showed stenotic lesions in ileum and was started on AKT but this

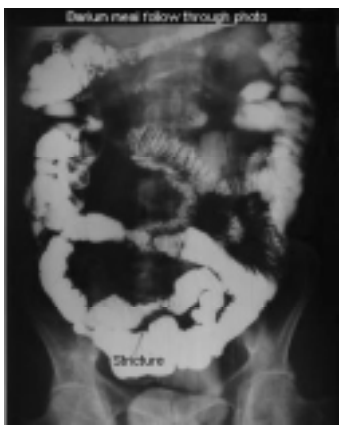

Fig-1: Barium meal follow through showing ileal stenosis

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time symptoms did not resolve. In January 2005, CAT scan of abdomen (fig-2) showed stenosis in ileum. He was seen at this hospital in August

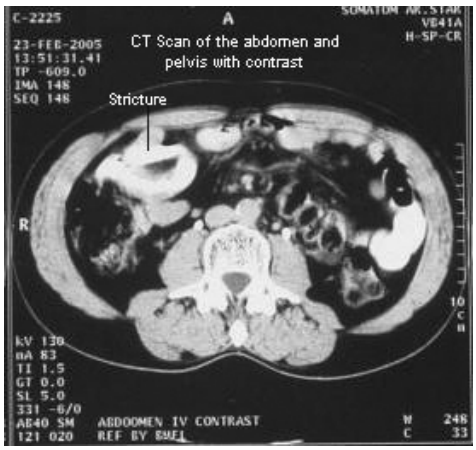

Fig-2: CAT Scan Abdomen showing ileal stenosis

2005. It was decided to explore the patient in view of long standing history of strictures with inadequate response to AKT. A diagnostic laparoscopy was performed and in the course of small bowel walk, terminal ileum was stuck to bladder hence surgery was converted to minilaprotomy and findings were: 2 strictures, 1 foot from Ileocaecal junction and thickened ileum loop of 1 foot between two strictures (fig-3) which was stuck to the dome of the bladder. No obvious enlarged lymph node was seen. The ileal loops were resected and abdomen was closed

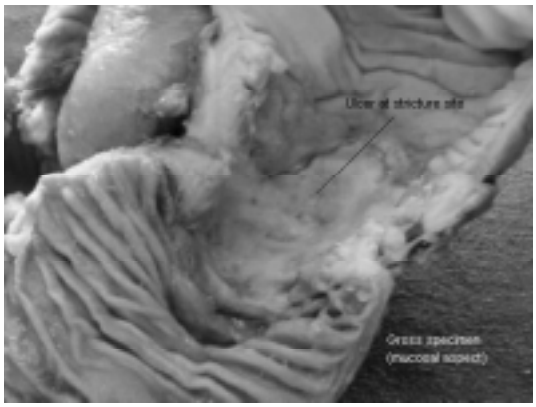

Fig-3: Gross specimen showing mucosal aspect of ileal loop containing stricture & thickening

Histo pathology of resected specimen revealed a high grade anaplastic large cell lymphoma with extensive mucosal ulceration. Submucosal arterioles showed infiltration of the walls by large neoplastic lymphoid cells resembling 'embryonic body'. There was extensive infiltration of the muscle wall, the serosa and mesenteric fat with marked fibrosis and desmoplasia. Adjacent ileal segments showed mild to moderate blunting of the villi, patchy mild to moderate increase in the lymphoplasmacytic infiltate in the lamina propria and increase in intraepithelial lymphocytosis immediately adjacent to ulcers. Ileal mucosa away from the ulcer was unremarkable. The tissue from dome of the bladder showed fibrofatty tissue with many scattered atypical lymphoid cells. Immunohistochemistrically the neoplastic lymphoid cells expressed CD3 and UCHL (CD45Ro) but not CD20. Histopathological diagnosis was Enteropathy Associated T Cell Lymphoma. (EATCL)

Bone marrow examination did not show infiltration. PET scan showed diffuse uptake in small and large bowel which can be due to inflammatory aetiology. Blood investigation were normal except low albumin.

Post operative course was uneventful. Patient has completed chemotherapy using cyclophosphamide vincristine, doxorubicin and dexamethasone regimen.

DISCUSSION

Celiac disease is relatively common in Europe; with an incidence of approximately 1 in 2,000 in the United Kingdom and 1 in 300 in Ireland. Celiac disease is characterized by a gluten-sensitive enteropathy, resulting in symptoms of malabsorption. In infancy it manifests after weaning on to gluten-containing food. In adults, it is seen in the third and fourth decades. If

wheat protein is withdrawn from the diet, the histologic changes of enteropathy usually reverse, with clinical symptomatic improvement [6] Holmes et al have shown that treatment of enteropathy with more than 5 years of gluten-free diet will reduce the risk of development of intestinal lymphoma to that of the general population[7] making this an important part of the treatment of the celiac patient.

According to Harris et al [2] lymphoma was most likely to develop in male, older than 40 years, with a history of celiac disease in excess of 10 years and not adhering to a gluten-free diet. However, Brandt et al [8] suggested a mean interval of 3 years. The newly diagnosed adult with celiac disease consequently requires careful follow-up; one in 20 had developed lymphoma within 4 years of diagnosis, and, with age older than 50 years, the risk was one in 10.[9]

It would seem that low-grade neoplastic cells may be present, but clinically silent, in the bowel for long periods.

Most cases are CD3+, CD7+, CD4-, and CD8-. However, a number of cases have been reported with CD8 positivity. Positive staining with the monoclonal antibody human mucosal lymphocyte-1 is characteristic of this subset.[10] In cases in which large immunoblast-like cells predominate, CD30 expression is characteristic and can be a useful marker to distinguish tumour cells in an inflammatory background. Genotypic studies have confirmed monoclonal T-cell receptor beta gene rearrangement. Treatment response in EATCL patients is much less favourable, complete remissions could be reached only in about 50% of EATCL patients with earlier lymphoma stages, and most of these have lymphoma relapse after a mean period of 28 months. Treatment consists of chemotherapy for patients with stages EI and EII. For patients with stages EIII and EIV, radiotherapy (30 Gy involved-field radiotherapy) is scheduled after initial chemotherapy. Six cycles of CHOP (cyclophosphamide 750 mg/m2, doxorubicin 50 mg/m2, and vincristine 1.4 mg/m2 day 1; fab. prednisolone 100 mg days 1 to 5) chemotherapy are given every 3 weeks. In patients with poor clinical condition, palliative treatment with corticosteroids is recommended. Treatment is started with 60 to 100 mg methylprednisolone; dose reduction depends on the clinical response to corticosteroids. The limited response to CHOP chemotherapy even in early-stage EATCL patients indicates that selected patients could possibly benefit from high dose chemotherapy with stem cell transplantation.[11] However tumour progression and death during chemotherapy are common in EATCL patients; a considerable proportion of patients, especially at late stages, do not complete chemotherapy. Furthermore in about one third of EATCL patients, chemotherapy cannot be initiated, mostly because of the poor clinical condition of the patients. Therefore it is doubtful that more aggressive regimens can be initiated in a major proportion of EATCL patients to overcome the unsatisfactory response to CHOP.

Cumulative 2-year survival in patients with EATCL at stages EI and EII who received CHOP is higher than in those who do not receive CHOP (49% v 14% $P < .05$), but is similar in EATCL patients at stages EIII and EIV whether treated with CHOP or not.[12] Associated malabsorption and malnutrition make tolerance of chemotherapy difficult, and it is advisable to resect the intestinal lesion in EATCL to prevent complications such as gastrointestinal bleeding and perforation during chemotherapy.[13]

Nutritional support with parenteral or enteral feeding should always be considered in these patients. Efforts should therefore be made to diagnose enteropathy-type intestinal T-cell lymphoma early. The diagnosis should be considered in all patients who present in midlife with celiac disease and in those who experience a clinical deterioration after a period of stability on a gluten-free diet.[14]

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