Case Report

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Enteropathy Associated T Cell Lymphoma – A Case Report of An Uncommon Extranodal T Cell Lymphoma

Pathology Section

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ABSTRACT

Enteropathy associated T cell lymphoma is a rare primary intestinal lymphoma. It is often, but not always associated with celiac disease. Intraepithelial T cells are postulated as the cell of origin. It is a rare disease accounting for fewer than 5% of all gastrointestinal tract lymphomas. Recent studies indicate that EATL consists of two diseases that are morphologically and genetically distinct and differ with respect to their frequency of association with celiac disease. Current WHO classification recognises two subtypes of EATL – type 1 (classic) and type 2, based on morphology and immunophenotype. EATL type 1 is a large cell lymphoma which is more common and is more commonly associated with celiac disease compared to type 2. Most common site of involvement is the small intestine. We report a case of EATL type 1, in a 62-year-old female patient who presented with features of intestinal obstruction. However, she did not have spruce like featutes.

Keywords: Celiac disease, Gastrointestinal lymphoma, Small intestine

CASE REPORT

A 62-year-old female presented with complaints of fever, vomiting and loose stools since 15 d. She had no history of abdominal pain, malena, abdominal distension or jaundice. General examination showed pallor. Vitals were stable. Per abdominal examination revealed abdominal distension with tenderness and guarding. Bowel sounds were present. No other findings were noted on systemic examination. Laboratory investigations showed normal hemogram, renal and liver functions. Serum amylase and lipase were also within normal limits. Stool examination revealed occult blood. Abdominal X-ray was done in view of increasing abdominal distension and showed features suggestive of intestinal obstruction. No clear cut history of malabsorption was obtained.

Right hemicolectomy with adjacent ileum was done following a clinical diagnosis of intestinal tuberculosis.

Postoperatively, patient developed lower limb deep vein thrombosis was started on anticoagulants which was stopped due to per rectal bleeding and elevated INR. Later patient developed renal failure, breathlessness and seizures, was started on mechanical ventilation and other supportive treatment. Patient was discharged on request and lost to follow up.

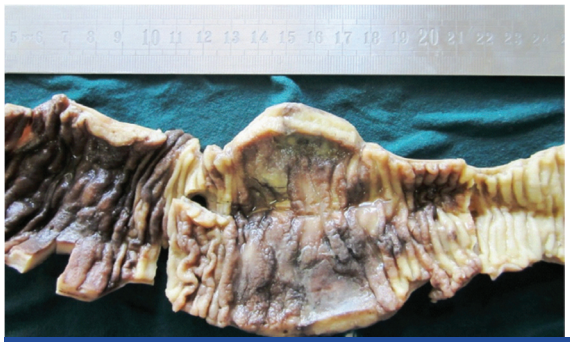
On Gross examination the mucosal surface of small intestine showed multiple foci of ulceration, with focal thickening of wall and constriction of intestinal wall alternating with normal mucosa [Table/Fig-1,2].

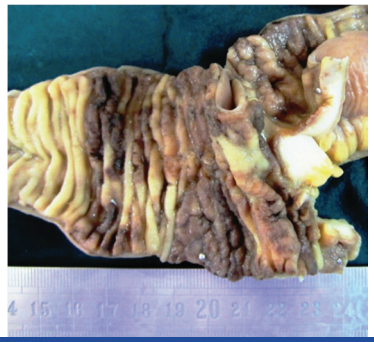
Microscopic examination of small intestinal segment revealed, a lymphoid neoplasm comprising of predominantly medium sized to small abnormal lymphoid cells with coarse chromatin, irregular nuclear contours, some with scant cytoplasm with admixed large cells, some with binucleation and interspersed eosinophils [Table/Fig-3]. Tumour cells were seen diffusely infiltrating into the intestinal smooth muscle fibres of muscularis propria and serosal adipose tissue [Table/Fig-4,5]. Lateral tumour infiltration in between the mucosal crypts with widening of lamina was seen. Few villi were broadened and showed admixed reactive and neoplastic infiltrate along with plasma cells. Isolated lymph nodes from resected specimen and two mesenteric nodes showed tumour infiltration with focal perinodal fat extension.

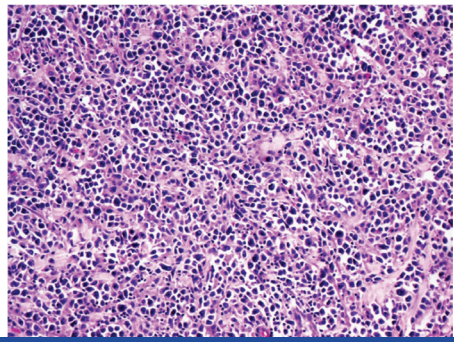
Based on the paucity of large pleomorphic cells and lack of sprue like morphology in the adjoining small intestine, the possibility of EATL type 2 was considered. However, on Immunohistochemistry Tumour cells were CD3 positive [Table/Fig-6] and negative for CD5, CD4, CD8, CD20, CD30, CD56 , TCR-β suggesting EATL type 1.

DISCUSSION

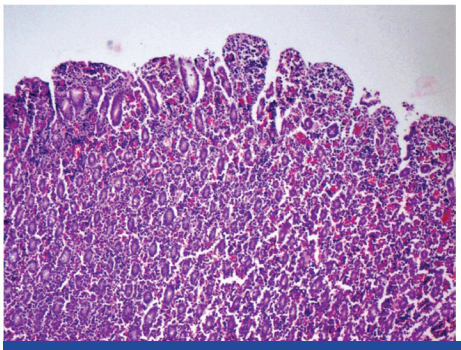
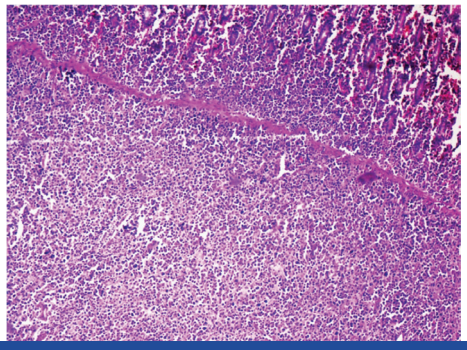
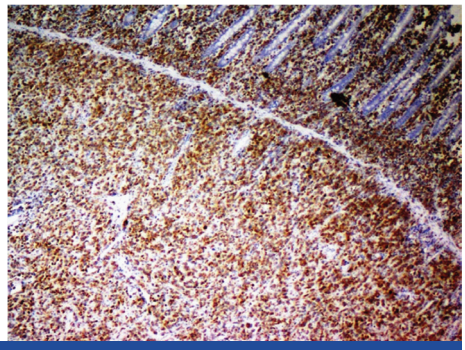
An association between malabsorption and intestinal lymphoma was first reported in 1937 by Fairley and Mackie [1] . In 1978, Issacson and Wright characterised celiac associated lymphoma as a single entity. Later, Issacson used immunohistochemistry and T- cell receptor gene rearrangement studies to demonstrate







[Table/Fig-1]: Multiple foci of ulceration, with focal thickening and constriction of intestinal wall alternating with normal mucosa **[Table/Fig-2]:** Tumor infiltrating into serosal fat **[Table/Fig-3]:** Medium to small abnormal lymphoid cells with coarse chromatin, irregular nuclear contours with admixed large cells [HEMATOXYLIN & EOSIN ; X 200]

[Table/Fig-4]: Tumour cells infiltrating into the mucosa. [Hematoxylin & eosin ; X 40] **[Table/Fig-5]:** Tumour cells diffusly infiltrating into submucosa. [Hematoxylin & eosin ; X 40] **[Table/Fig-6]:** Diffuse stong positivity for cd 3; [X 40]

the T cell derivation of this lymphoma [2]. In 1986, O'Farrelly coined the term 'Enteropathy associated T cell lymphoma' owing to the close association of this lymphoma with villous atrophy of the jejunal mucosa adjacent to EATL [3].

EATL commonly presents in the sixth and seventh decades of life. Men and women are equally affected. Most patients present with bowel obstruction, small intestinal perforation, abdominal pain, weight loss and diarrhoea. The jejunum is most frequently involved followed by other parts of the small intestine, colon and stomach. Tumour is usually multifocal and forms ulcerating nodules, plaques, strictures or less commonly large masses. The mesentry is often infiltrated and mesentric lymph nodes are commonly involved [1,2].

Based on histomorphology and immunophenotype assessment EATL is subclassified as Type 1 (classic) and Type 2.

Type 1 is the more common EATL. It is associated with celiac disease and is common in populations with a high prevalance of the latter. It is rare in Asia, where celiac disease is uncommon. The time period between diagnosis of celiac sprue and onset of lymphoma is quiet variable, ranging from few months to several decades. EATL-1 most commonly presents in patients with a short history of adult celiac disease and /or dermatitis herpitiformis. In a proportion of cases, there is no history of malabsorption and may only show histopathologic evidence of celiac disease in the form of blunted intestinal villi and increased intraepithelial lymphocytes (IEL) at the time of diagnosis of lymphoma. Rarely, patients may have normal or near normal small intestinal epithelium [2], as was noted in the present case.

Classic variant of EATL has a variable morphology and usually shows transmural lymphomatous infiltration by medium sized to large pleomorphic cells with conspicuous nuceoli accompanied by prominent mixed inflammatory infiltrate composed of histiocytes, small lymphocytes, plasma cells and eosinophils along with mitotic figures and necrosis. The mixed inflammatory infiltrate can be dense and at times obscure the lymphoma [2,4].

Immunoprofile of the neoplastic cells is CD3+, CD5-, CD7+, CD8+/-, CD4-, CD56- , TCRβ+/- with variable CD30 expression. The intraepithelial lymphocytes adjacent to the lymphomatous infiltrate when present show the same immunophenotype [2].

Type 2 EATL patients usually do not have a prior history of celiac disease and show villous atrophy. Blunting and intraepithelial lymphocytosis is usually confined to the area of lymphoma whereas the distant mucosa is usually unremarkable and without villous atrophy [4]. It shows monomorphic small to medium sized lymphocytes with slightly irregular nuclei and small nucleoli surrounded by scant pale cytoplasm, infrequent mitosis and sparse inflammatory background. Tumour cells are CD3+, CD4- , CD8+, CD56+ on immunohistochemistry and may express TCR-βF1 or TCRγδ [4,5]. No CD8 and CD56 positivity or TCR-β expression was noted in our case.

EATL has a poor prognosis due to treatment resistance and sepsis or perforation of the bowel at diagnosis or during the course of treatment [6]. The differential diagnosis of EATL includes other T -cell lymphomas with intermediate to large cell morphology including anaplastic large cell lymphoma, extranodal NK/T cell lymphoma, nasal type, peripheral T-cell lymphoma NOS.

Anaplastic large cell lymphoma (ALCL) consists of large lymphoid cells with abundant cytoplasm and pleomorphic often horse shoe shaped nuclei and on immunophenotyping, positive for CD30 and anaplastic lymphoma kinase (ALK) [7].

Extranodal NK/T cell lymphoma of nasal type mostly involve the upper aerodigestive tract, with dissemination to gastrointestinal tract. Morphologically, an angiocentric and angiodestructive growth pattern is frequently present. Immunophentypically, it is CD56 and EBER positive [2,4].

Peripheral T-cell lymphoma , not otherwise specified demonstrates diffuse infiltrates of large lymphoid cells with pleomorphic irregular nuclei and prominent nucleoli. It typically present as nodal involvement, but any site may be affected [2].

The blastoid and pleomorphic variants of Mantle cell lymphoma (MCL) could also be considered. However, MCL mostly present as multiple lymphomatous polyposis and expresss CD20 and cyclin D1 [2].

CONCLUSION

Enteropathy-associated T-cell lymphoma (EATL) is a rare subtype of lymphoma that should be considered when evaluating non-Hodgkin lymphoma of the gastrointestinal tract. Even though both tumour subtypes are associated with poor prognosis, type 1 and type II EATL differ in terms of histologic features, immunophenotype and clinical history. Awareness of these variants is important to avoid incorrect subclassification. However, overlapping features do exist as was seen in this case.

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