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Intestinal perforation caused by type II enteropathy-associated T-cell lymphoma

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ABSTRACT

Primary lymphomas of the small intestine are rare. Clinical features at presentation and prognosis are variable. T-cell lymphomas may or may not be associated with enteropathy but if it has been previously diagnosed it can present a range of clinical features, show peculiar evolution and affect prognosis. This report describes the case of a patient with insidious gastrointestinal symptoms, who received no treatment, and with no known gastrointestinal alterations. The sudden and unexpected presentation, despite being common with enteropathy-associated T-cell lymphoma (EATL), meant that the diagnosis was unforeseen. It is important to keep in mind the possibility of this diagnosis in the case of a patient with abdominal symptoms and no previous clinical history of this kind of disorder.

RESUMEN

Los linfomas primarios del intestino delgado son poco frecuentes. Las características clínicas de presentación y el pronóstico son variables. Los linfomas de células T pueden o no estar asociados con enteropatía, pero si se ha diagnosticado previamente, puede presentar una serie de características clínicas, mostrar una evolución peculiar y afectar el pronóstico. Este informe describe el caso de un paciente con síntomas gastrointestinales insidiosos, que no recibieron tratamiento, y sin alteraciones gastrointestinales conocidos. La presentación repentina e inesperada, a pesar de ser común en pacientes con enteropatía asociada a linfoma de células T (EATL), quiere decir que el diagnóstico fue imprevisto. Es importante tener en cuenta la posibilidad de este diagnóstico en el caso de un paciente con síntomas abdominales y sin historia clínica previa de este tipo de trastorno.

INTRODUCTION

Primary lymphomas of the small intestine are rare, accounting for 20-40% of malignant neoplasms found in this site. Clinical features at presentation and prognosis are variable.[1] They can be either of B- or T-cell origin, the former being the most common. T-cell lymphomas may or may not be associated with enteropathy.[2,3] In most cases, T-cell lymphomas that are not associated with enteropathy present as a high-grade malignancy.[4,5] In this report, the case of a man with enteropathy-associated T-cell lymphoma (EATL II) is presented whose major clinical manifestation was intestinal perforation.

CLINICAL SUMMARY

A 46-year-old man with no significant medical antecedents presented with evidence of intestinal obstruction, lower gastrointestinal bleeding, weight loss, and suffering from septic and hypovolemic shock. He died with these conditions short after his arrival at the emergency room.

AUTOPSY SUMMARY

An ileal perforation was found 15 cm from the ileocecal valve. It was 5 cm along its major axis but 95% sealed by the greater omentum. There was an associated transmural neoplastic lesion, which had a well-defined prominence towards the luminal surface, which was ulcerated and 7.3 cm along its major axis *(figure 1)*. Histologically, the lesion had the characteristics of a lymphoid neoplasm with a diffuse growth pattern and infiltrating edges up to the muscle layer *(figure 2)*. It was composed of round-to-polygonal cells of medium-to-large size with scant cytoplasm and large central pleomorphic nuclei, some with vesicular chromatin and prominent nucleoli *(figure 3)*. The adjacent mucosa showed villous atrophy *(figure 4)*. The neoplastic cells were CD3, CD8 and CD56

positive by immunohistochemical staining *(figure 5)*. An increased number of CD4 and CD8 positive intraepithelial lymphocytes (IEL) were detected in the mucosa adjacent to the lesion *(figure 4)*, as well as fibroadhesive peritonitis localized to the area neighboring the perforation. The rest of the organs showed no alterations. Based on these findings a diagnosis of EATL was made.

DISCUSSION

EATL was first described as a neoplasm associated with celiac disease in 1978 by Isaacson and Wright, and Isaacson and collaborators demonstrated its T-cell origin in 1986. It was O'Farrelly and colleagues, however, who coined the term EATL because of the close association of the lesion with villous atrophy in the jejunal mucosa adjacent to the disease.[6-8] At the lymphoma workshop of the XVIth meeting of the European Association for Haematopathology and the Society for Hematopathology was proposed that the EATL could be of two types EATL I and EATL II each one with clearcut differences *(table I)*: the type I has evidence of coeliac disease, usually is alfa-beta, often double-negative for CD4 and CD8, and polymorphous cytological composition.[9] While type II also known as (monomorphic intestinal T-cell lymphoma) usually has not evidence of coeliac disease, has a worldwide distribution, usually gamma-delta, monomorphic, and CD8 and CD56 positive.[10-12]

Primary lymphomas of the small intestine have a different clinical presentation and prognosis, and differ-

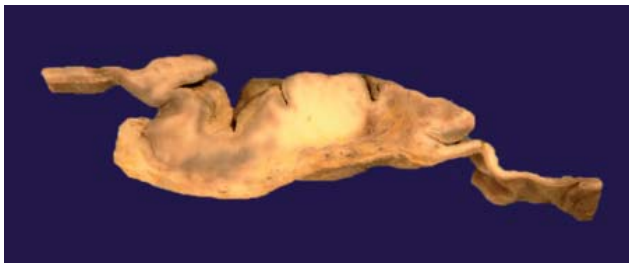

Figure 1. Fragment of ileum with a transmural neoplastic lesion that forms prominence toward the luminal surface.

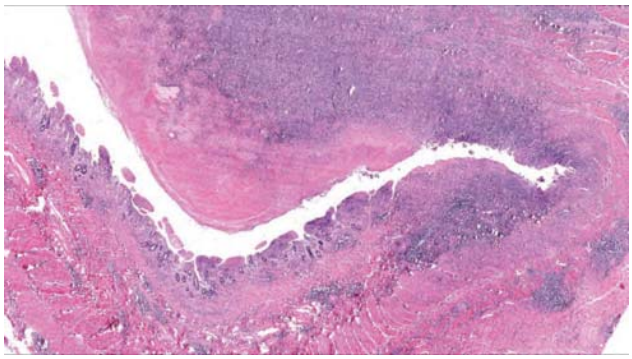

Figure 2. Malignant lymphoid neoplasm with diffuse growth pattern and accentuated pleomorphism of infiltrating borders that extends up to the serous and dissects the muscular fibers.

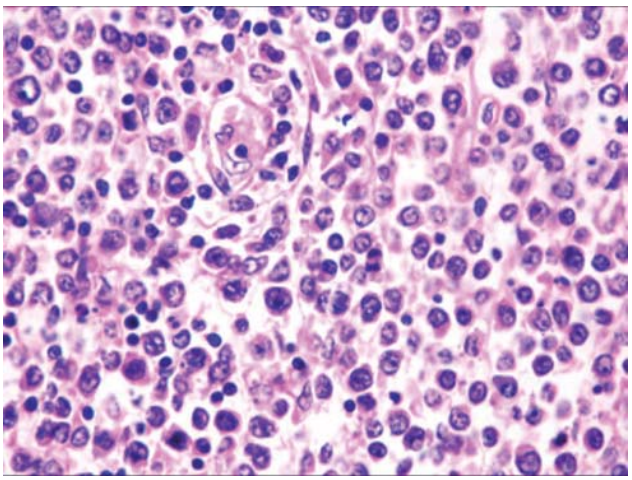

Figure 3. Lymphoma composed of medium to large cells with scant cytoplasm and large central nucleus with granular chromatin. In some of them the nucleolus is evident as well as mitotic figures.

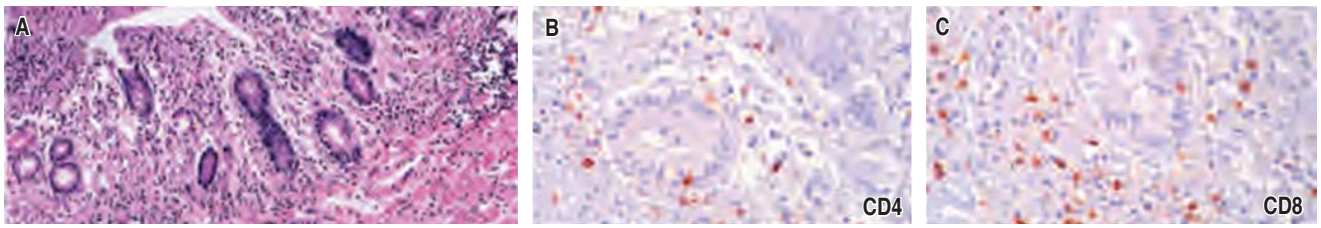

Figure 4. The mucosa adjacent to the lesion shows atrophy of the glands as well as widening of the villi at the expense of intraepithelial lymphocytes (**A)** (HE 40x) that are positive for CD4 (**B)** and CD8 (**C)** (immunoperoxidase 100x).

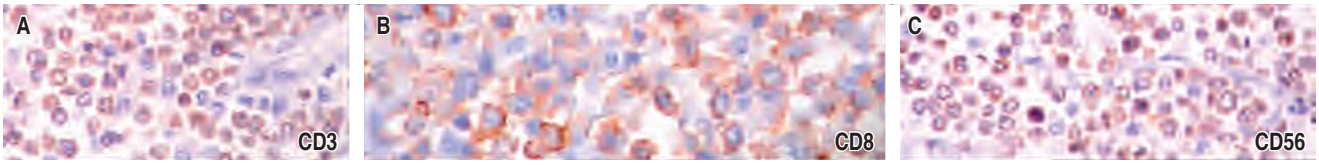

Figure 5. Neoplastic cells showed cytoplasmic positivity for CD3, CD8 and CD56 (immunoperoxidase 40x).

Table I. Characteristics of enteropathy-associated T-cell lymphoma.

Characteristic	Type I enteropathy-associated T-cell lymphoma	Type II enteropathy-associated T-cell lymphoma
Frequency	80-90%	10-20%
Morphology	Variable (large pleomorphic cells)	Small monomorphic cells
Immunophenotype		
CD3	Positive	Positive
CD4	Negative	Negative
CD8	Negative to 20% positive	Positive
CD56	Negative	Positive
HLA-DQ2/-DQ8	90% positive	30-40% positive
Mucosa	Villous atrophy No CD4+ or CD8+ lymphocytes	Villous atrophy Increase in CD8+ lymphocytes
Genetics		
+8q24 (MYC)	27%	73%
TCR rearrangement	Present	Present
EBV	Negative	Negative

TCR = T-cell receptor, EBV = Epstein-Barr virus.

ent pathological features to those observed in lymphomas arising in other locations of the gastrointestinal tract.[13,14]

The lesions may be single or multiple, usually in the form of circumferential small bowel ulcers. Lesions can also be nodules, plaques or stenotic, but rarely appear as big masses. The mesenteric lymph nodes are often enlarged by infiltration or by reactivity to the disease.[1]

Most patients with EATL either type I or II present with abdominal pain, weight loss, diarrhea or vomiting.[1,4] Fever and night sweats. The presence of peripheral lymphadenopathy is frequent, with anemia in over two thirds of cases, often accompanied by a 25% increased level of LDH. Serum albumin is usually diminished. Less than half of cases with celiac disease and lymphoma have the two conditions diagnosed at the same time.[15-17]

Histologically, the lesion widens the villi, and is comprised of small-to-medium cubic cells, with scant eosinophilic cytoplasm and large nuclei, in which hyperchromatic nucleoli can be observed. The presence of mitotic figures and villous atrophy is frequent, as well as crypt hyperplasia in the mucosa adjacent to the lesion.[18]

The diagnosis is almost always made with a laparotomy. Immunoproliferative small bowel disease and coeliac disease[19] should be considered in the differential diagnosis, especially in cases where villous atrophy as well as symptoms predominantly of malabsorption are evident.

Patients are typically treated with a combination of surgery, to remove as much of the tumor as possible, and chemotherapy. Staging is carried out by Axial Computer Tomography (ACT) and a bone marrow biopsy.[20,21]

COMMENT

The frequency of intestinal T-cell lymphoma is approximately 30%, and it is associated with celiac disease in 5% of cases. There is, however, a rare variant where patients have no previous symptoms and which shows characteristic histopathological features, namely, monomorphic cells, increased CD8 and CD56 positivity (80-90%) compared to intestinal T-cell lymphoma associated with celiac disease, and c-MYC amplification.[7] These factors should be considered in the diagnosis of such neoplasms. The prognosis of patients with EATL is poor, with a 2 year overall survival rate of approximately 28%.[19,22]
There are no reports on the frequency of this neoplasm in Mexico.

This report describes the case of a patient with insidious gastrointestinal symptoms, who received no treatment, and with no known gastrointestinal alterations. The sudden and unexpected presentation, despite being common with EATL, meant that the diagnosis was unforeseen. It is important to keep in mind the possibility

of this diagnosis in the case of a patient with abdominal symptoms and no previous clinical history of this kind of disorder.

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