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Case Report

Enteropathy-Type T-Cell Lymphoma Refractor to Chemotherapy: A Case Report

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Abstract

Peripheral T-cell lymphomas not otherwise specified (PTCL-NOS) comprises a heterogeneous group of haematological tumors, which originate from mature T-cells, and constitute 15 to 20% of all non-Hodgkin's lymphomas in adults. Herein, we report a case of PTCL-NOS of the small bowel developed on celiac disease. It was, firstly, revealed by a strangulated Hernia. The treatment was a surgical resection and cyclophosphamide, doxorubicin, vincristine and prednisone CHOP chemotherapy. The tumor had recurred. It was revealed by acute intestinal occlusion. The histological and immunohistochimical study showed PTCL-NOS with different immunophenotype.

Key words:

Peripheral T-cell lymphomas; chemotherapy; small bowel

Introduction:

Peripheral T cell lymphoma not otherwise specified (PTCL-NOS) is a rare tumor originating from mature T cells. It constitutes a heterogeneous group of hematological neoplasms accounting 15 to 20 % of aggressive lymphomas and 7 to 10 % of all non Hodgkins lymphoma. It presents as advanced disease [1]. It has a widespread localization in the body. Only few cases were reported in the literature in the small intestine. This disease entity remains largely unclear in regards to its clinical behavior, its histological features, its immune-phenotypes and its treatment modalities. It is characterized by widespread dissemination, aggressive behavior and very poor outcome. The years overall survival ranges between 25 and 45%.

This paper documents the remarkable clinical course of a patient with celiac disease, since 18 years, who had developed peripheral -cell lymphoma NOS of the small bowel, treated by surgical resection and chemotherapy. The relapse was as peripheral T cell lymphoma NOS with different immunophenotype.

Case report:

A 47-year-old woman with the history of celiac disease with a free-gluten diet, since 18 years suddenly complained of abdominal pain. She was admitted to our hospital as an emergency case. The physical exam showed a painful and irreducible hypo gastric mass measured 3cm of diameter. The diagnosis was astrangulated umbilical hernia. The operative examination found, a small bowel mass, localized at 28 cm from the angle of Treitz associated with multiple lymphadenopathy. The patient underwent a resection of 30 cm of the small bowel.

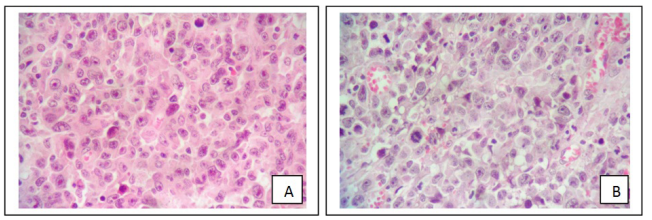
Pathology:

The resected segment of small bowel measured 30 cm and contained a 3 cm sub mucosal mass. The lymph node dissection found 6 nodes.

Histologic sections showed lymphoid proliferation infiltrating the ulcerated mucosa, sub mucosa, and muscularispropria. The lymphoid cells were large. Nuclei were atypical. Nucleoli were prominent (A,B). Mitoses were frequent (B) (50 mitoses/10 fields at high magnification). There were not features of celiac disease (ie, increased intraepithelial lymphocytes, villous atrophy, and crypt hyperplasia).

The immunohistochemical study showed tumor cells were positive for pan T markers: CD2, CD7 and CD43 and cytotoxic markers: perforin and granzyme B. They were strongly positive for CD30, but negative for ALK. The staining was negative for: CD3, CD5, CD4, CD8, TiA1, CD56, CD20 and EMA.

The proliferative fraction was high with 80% of tumor cells marked. The diagnosis was T Cell Lymphoma, NOS.



A, B : proliferation of lymphoid large cell with proeminent nucleoli and numerous mitoses

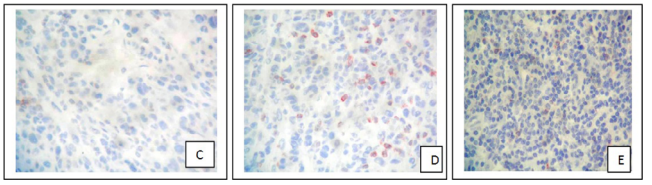
After this immediate partial small-bowel resection, cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) chemotherapy was started. However, the disease was highly refractory and was exacerbated one year later. In fact, the patient developed acute intestinal occlusion and was admitted and operated, in our hospital, in emergency. The operative exam showed a jejunal mass invading the transverse mesocolon. She underwent a resection of small intestine.

On the macroscopic examination, the specimen after fixation measured 7 cm for the small intestine. It contained an indurated and perforativesubmucosal tumor which measured 2 cm in the greatest diameter.

The microscopic examination showed that the tumor was composed of pleomorphic, medium to large lymphoid cells with sternbergoide appearance. A polymorphic inflammatory infiltrate rich in mature lymphocyte is frequently present; Necrosis and a high mitotic rate are seen.

The immunohistochemical study showed that the immune-phenotype's lymphoma had changed. In fact, cell tumors were positive for CD3, CD4 and CD30. They were negative for CD20, CD5 and CD56.

The patient died in a septic shock associated with a panperitonite.



C, D : tumor cells were respectively negative for CD20 and CD56, E: Weak positive staining of CD3

Discussion:

PTCL are a group of uncommon neoplasms deriving from post-thymic (mature) T-Cell. These disorders are among the most aggressive of all lymphoid tumors. Few cases in the literature were reported with a digestive location.

The median age was 60 years (range, 19-87 years), with a male predominance, and the majority of the patients (69%) presented with advanced stage disease [2]. Clinical presentation depends on location. Both strangulated Hernia and acute intestinal occlusion are complications of intestinal PTCL.

In the literature, few cases were reported in association with celiac disease, but no case in intestinal location had immune-phenotype change after CHOP chemotherapy.

The association between celiac disease and malignant lymphomas is not confined to enteropathy T cell lymphoma but includes other types of T cell non Hodgkin lymphoma and, especially T cell lymphoma NOS. There is no standard salvage for relapsed or refractory PTCL-NOS and the prognosis is very poor.

The biological mechanisms behind the development of enteropathy T cell lymphoma in the celiac disease have been extensively explored. Cellier et al have suggested a transitory stage of gluten refractory disease with abnormal clones of intraepithelial T lymphocytes.

PTCL-NOS are often difficult for pathologists to diagnose. Not only are these tumors rare in most geographical areas, but they also exhibit a wide variety of morphological and clinical features [3]. The composition of T cells may be very heterogeneous with a considerable number of T reactive inflammatory cells and the lack of useful marker of clonality[4]. No specific criteria were given for diagnosis. Immunohistochimic study is important to diagnosis.

PTCL manifest the immunophenotypic features of post-thymic T lymphocytes. On immunohistochemistry, PTCL-NOS show expression of T-cell antigens usually with phenotypic aberrations consisting in loss of one or more of the pan T-cell antigens (CD2, CD3, CD5 or CD7) [8,9]. CD7 is most commonly absent, while CD2 is the last to be lost, and thus is usually the most reliable pan-T marker. The phenotype of the cells is CD4+ in about 65% of cases and CD8+ in 15% of cases; double-positive and double-negative tumours are less common, each accounting for about 10% of cases [54]. PTCL can express CD30 irrespectively of anaplastic morphology as well as cytotoxic markers, including TIA1, granzyme B, perforin, CD56 and CD57[6,7]. In our case, firstly, tumor cells were positive for pan T markers (CD2, CD7 and CD43), cytotoxic markers (perforin and granzyme B) and CD30, but negative for ALK, CD3, CD5, CD4, CD8, TiA1, CD56, CD20 and EMA. After the CHOP chemotherapy, tumor cells became positive for CD3, CD4 and CD30 and negative for remaining markers.

Despite the phenotype changing, we have considered the same diagnosis for the first and the second tumor. We suggest that chemotherapy can interfere with the immunophenotype of PTCL-NOS. The large randomised intergroup trial that, in

the early 1990s established CHOPS as the standard regimen for large cell lymphoma included also (a minority of) PTCLs, but the impact of immunophenotype was not assessed [14].

PTCL-NOS represent a wide variety of infrequent clinicopathologic and immunophenotype syndromes that share a dismal prognosis. Several studies have been done to assess the contribution of a number of clinical and histological factors to the prognosis. Systemic symptoms and bone marrow infiltration have been found to correlate with a poor prognosis in a single study [10]. The size of cells has long been debated as a prognostic factor.Someauthors considered that PTCL-NOS withlarge cell had a poorer prognosis than PTCL-NOS with medium or small size cell[11-14].

In conclusion, the understanding of the molecular pathogenesis may allow in the next future the recognition of distinct entities among the PTCL-U. An improved understanding of the biology of the PTCLs should, in turn, improve our ability to develop better treatments for these disorders to improve their prognosis.

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