CASE REPORTS

Gastric and Colonic Mantle Cell Lymphoma - Incidental Discovery

Dan Pitigoi¹, Victor Stoica¹, Razvan Stoia², Camelia Dobrea²,³, Gabriel Becheanu¹,³, Mircea Diculescu¹

1) Department of Gastroenterology, Fundeni Clinical Institute; 2) St. Berceanu Centre of Hematology and Marrow Transplantation, Fundeni Clinical Institute; 3) V. Babes National Institute of Pathology, Bucharest, Romania

Abstract

A 65-year old patient, with no medical history, was admitted for lower gastrointestinal bleeding. On clinical examination the patient seemed to be in good health. However the examination was completed with a rectosigmoidoscopy revealing the presence of mucosal erosions, ulcerations, multiple papulae. The histopathological examination raised the suspicion of a colonic lymphoma. Gastric biopsies suggested a gastric MALT type lymphoma associated to the colonic lymphoma, but the immunohistochemical profile corresponded to a mantle cell lymphoma. In spite of the general poor prognosis of mantle cell lymphoma, our patient had a good clinical and endoscopic response to the standard cyclophosphamide, vincristine, prednisone (CVP) therapy. The cases of gastric and colonic mantle lymphoma are rare, the response to therapy is poor; fortunately, our patient had a complete resolution after completion of the six cycles of chemotherapy.

Keywords

Gastric – colonic – mantle-cell lymphoma.

Case report

A 65 year-old man was admitted to the Department of Gastroenterology, Fundeni Clinical Institute for lower GI bleeding. The bleeding occurred always after defecation, after a hard stool, it was intermittent, terminal, with red blood and no clots.

On physical examination the patient was afebrile, without peripheric lymphadenopathy, normal pulmonary sounds, arterial pressure 135/85mmHg, pulse 72/min, abdomen without tumor masses, external hemorrhoids, empty rectal ampula, no bleeding. A rectosigmoidoscopy was performed (Fig. 1).

Complete blood tests, ultrasonography, chest radiography and barium enema were performed. Hematological and biochemical values were within normal range but on barium enema two lacunar images of 3.5 and 1.3cm were noticed at the level of the cecum.

Fig 1. a - Endoscopic image from the sigmoid colon with multiple papulae 4-5 mm, some of them were biopsied; b - the rectum, showing ulcerations between hyperemic areas.
The histopathological examination (Fig. 2) revealed the possibility of a colonic MALT type lymphoma. It became mandatory to perform also an upper digestive endoscopy. Biopsies were taken from the antrum and corpus of the stomach; the endoscopist observed the rigidity of the giant gastric folds at biopsy. The histopathological examination of the gastric mucosa showed similar aspects to those seen at the level of the colonic mucosa (Fig. 3).

Immunohistochemical tests (Avidin – Biotyn - Complexe indirect method) were performed. The panel of monoclonal antibodies included: CD20/L26 (pan B cells marker), CD45RO/UCHL1 (pan T cells marker), CD5 (T cells marker, also positive in some B cell lymphomas, like mantle cell and small lymphocytic), CD23 (dendritic cell marker, also positive in small lymphocytic lymphoma) and cyclin D1 (for MCL) – all NeoMarkers, USA antibodies. The malignant cells were positive for CD20 (Fig 4a), negative for CD45RO and CD5, and positive for Cyclin D1 (Fig 4b).

All endoscopical, histopathological and phenotypical data pointed towards the diagnosis of a gastric and colon mantle cell lymphoma. Because bone marrow was involved, it was considered to be a mantle cell lymphoma with extranodal manifestations.

The patient was transferred to the Department of Hematology and underwent standard CVP (cyclophosphamide, vincristine, prednisone) chemotherapy which was relatively well tolerated and after he completed the treatment he returned to renew the endoscopic evaluation. The complete resolution (CR) of the colonic lesions was evidenced, as well as of the cecal tumor masses (Fig. 5)

### Discussion

The entity now known as mantle-cell lymphoma was first described in the 1970s by two groups. Lennert and his colleagues introduced the term “centrocytic lymphoma” for this tumor on the basis of its putative cell of origin, the small,
cleaved cell of the germinal center, or centrocyte. Berard and colleagues used the term “intermediate lymphocytic lymphoma” for the same tumor. Several years later the term “mantle-zone lymphoma” was introduced. Morphological, immunological, and genetic studies have confirmed the identity of the tumor that received these three designations. In 1992 a group of hematopathologists suggested that the term “mantle-cell lymphoma” should be adopted, because the tumor was thought to originate from cells found in normal primary lymphoid follicles and the mantles of secondary follicles. Immunohistochemical studies have been important in identifying a unique profile for mantle-cell lymphoma. Surface immunoglobulin of the IgM type and sometimes the IgD type is present, with either kappa or lambda light-chain restriction. In addition to its pan-B-cell antigens such as CD19, CD20, and CD22, mantle-cell lymphoma has a signature of other antigens (CD5+, CD10-, CD23-, and CD43+) that help to distinguish it from small lymphocytic lymphoma (CD23+) and follicular center-cell lymphoma (CD10+ and CD43-).

The presence of a chromosomal translocation, t(11;14)(q13;q32) in up to 73 percent of the cases of mantle-cell lymphoma has also helped to validate it as a distinct disease. This translocation joins a chromosome 11 region called Bcl-1 to the immunoglobulin heavy-chain gene locus on chromosome 14 and is associated with up-regulation of Bcl-1 messenger RNA in affected cells. The Bcl-1 gene has been investigated separately in the context of parathyroid adenomas and called PRAD1, and it has been studied in the context of cell-cycle proteins and termed cyclin D1. Because probes are not available for all the Bcl-1 breakpoints, it is likely that this rearrangement is even more common than the current data suggest. Recent studies have shown that nuclear cyclin-D1 protein can be detected in virtually all cases of mantle-cell lymphoma with the use of a polyclonal antibody on paraffin-embedded sections, as illustrated by this case. This protein is not detectable in normal lymphoid tissue or in tissue from patients with most of the other non-Hodgkin’s lymphomas that have been studied.

The contribution of cyclin D1 to cell cycle regulation is still under investigation. Like other D-type cyclins, cyclin D1 is thought to act primarily as a growth factor sensor, integrating extracellular signals with the cell cycle machinery. The pathogenetic role of Bcl-1 activation in human neoplasia is suggested by the ability of cyclin D1 overexpression to transform cells in vitro and contribute to B-cell lymphoma genesis in transgenic mice [1].

The application of strict phenotypic criteria to the classification of B-cell lymphoproliferations has revealed that the distribution of Bcl-1 rearrangements, and consequent cyclin D1 overexpression, are selectively restricted to mantle-cell lymphoma throughout the clinicopathologic spectrum recognized by the REAL classification (70% of the cases). Because the diagnosis of mantle-cell lymphoma may be difficult on pure histological grounds, the frequency and specificity of this genetic alteration provide excellent markers for diagnosis of mantle-cell lymphoma. In particular, because cyclin D1 is not generally expressed by normal B cells, positive expression of cyclin D1 in the context of a lymphoproliferative disorder has come to represent a highly specific marker for mantle-cell lymphoma in the clinical practice. The precise identification of mantle-cell lymphoma among nonfollicular small B-cell lymphomas is clinically relevant, because mantle-cell lymphoma is a far more aggressive disease and displays a significantly shorter survival than other histologically related forms [2, 3].

In the United States and Europe, mantle-cell lymphomas account for 1 to 8 percent of non-Hodgkin’s lymphomas and typically occur in patients who are more than 55 years old and male. They often present at an advanced stage of the lymphoma, with generalized lymphadenopathy and frequently with spread of the disease to the spleen, liver, bone marrow, Waldeyer’s ring, and other sites. The peripheral blood is involved in 13 to 38 percent of the cases, and the gastrointestinal (GI) mucosa or submucosa is involved in up to 20 percent of the cases [4].

Mantle cell lymphoma represents 5% of all cases of non-Hodgkin lymphomas. In the past, GI involvement in mantle

![Fig 5a. The absence of cecal tumor masses no papulæ.](image1)

![Fig 5b. Normal aspect of sigmoid colonic mucosa.](image2)
cell lymphoma was estimated at 30%. Recent studies show a GI tract infiltration even in 92% of cases [5].

Our patient presented with disseminated disease with bone marrow and GI disease (stage IV). Prognosis of mantle-cell lymphoma in this stage is poor with overall survival ranging from 36 to 52 months, and fewer than 8% of patients alive at 10 years. The blastoid variant, which is associated with mutations in the CDK inhibitors p16 and p17 and with p53 mutations, has a very poor prognosis with a median survival duration of 18 months. Favorable prognostic factors include the absence of anemia, splenomegaly and also mantle zone architecture [6-8].

The prognosis of mantle cell lymphoma is worse than that of the indolent lymphomas, and in general, the response to chemotherapy is less durable than in other types of diffuse lymphoma. Alkylating agents achieve good response rates with CR as high as 50%, with median duration of 1 to 3 years.

In conclusion, our patient had an infrequent type of non-Hodgkin lymphoma, discovered in an almost asymptomatic phase. Most cases already reported in the literature have large tumor masses and are symptomatic [9-13]. The patient responded well to chemotherapy as defined by clinical, endoscopic and radiological studies (no suspect adenopathies or tumor masses visible on CT). Hopefully the response will be durable in spite of the general poor prognosis for a stage IV mantle cell lymphoma.

References


