MUM-1 and bcl-2 Positive Primary Diffuse Large B Cell Non-Hodgkin's Lymphoma of the Colon

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Abstract
Primary diffuse large B cell lymphoma (DLBCL) presents as a nodal and extranodal disease. The most common extranodal site is the gastrointestinal tract (GI), with the stomach most frequently involved, followed by the small bowel. Primary DLBCL of the large bowel accounts for 0.2%–1.2% of all colonic tumors. We present two patients who underwent radical resections of right colonic tumors. They were diagnosed with primary colonic DLBCL following histological and immunohistochemical testing of the excised tissues, and were determined as being in stage IIE of the disease. The tumors expressed CD20 markers. Both received multi-agent chemotherapy with combined immunotherapy and remain in complete remission at 4 and 5 years.

Keywords: Chemotherapy, colon, hemicolectomy, immunohistochemistry, non-Hodgkin’s lymphoma

Case Report

Primary Non-Hodgkin’s lymphoma (NHL) of the colon is a rare tumor of the gastrointestinal tract (GI) that comprises 0.2%–1.2% of all colonic malignancies. Among primary colonic lymphomas diffuse large B cell lymphoma (DLBCL) is aggressive, distinct and the most frequent subtype of all adult NHL localized in large bowel.1–5 The ileocecal part of the bowel is the most frequently affected site. Due to the small number of published cases, the optimal therapy for NHL of the colon is still undetermined, particularly regarding the necessity of surgical resection, duration of chemotherapy and significance of immunotherapy. Our two cases of DLBCL with primary localisation in colon showed a successful protocol with surgery in combination with immunotherapy.

Case reports

Case 1
A 65-year-old woman presented in January 2009 with intermittent diarrhea followed by obstruction and weight loss of 20 kg over the preceding 4–5 months. Laboratory data showed hypochromic anemia. Lactate dehydrogenase level was normal. Colonoscopy detected a tumor mass narrowing obstructing the ascending colon. A barium enema identified a long stricture of the ascending colon and the right side of the transverse colon with mucosal irregularity suggestive of malignancy. Computed tomography (CT) showed a tumor mass measuring 9.5 × 8 × 8.6 cm in the lower part of right abdomen (Figure 1). The patient underwent right colectomy for suspected colonic adenocarcinoma and had an uneventful recovery. The tumor histology and immunohistochemistry revealed a number of enlarged paracaval lymph nodes, the largest of which measured around 56 × 42 × 60 mm. Bone marrow biopsies were normal. Laboratory analysis found Hb 106 g/L, WBC 6.1–109/l, neutrophils 54%, lymphocytes 46%, platelets 342 × 10⁹/l, (seg 73%, eo 5%, bas 1%, lym 14%, mo 7%), SE 30 mm, and fibrinogen 6.5 g/L. Lactate dehydrogenase level was 498 U/L (normal range 220–460 U/L). The patient received 8 cycles of therapy after which she achieved complete remission. Laboratory tests, biochemistry, bone marrow biopsy, and pelvis CT scans were normalized. She remains in complete remission 4 years later.

Case 2
In February 2008 a 50-year-old woman presented with intestinal obstruction and underwent an emergency right hemicolectomy and terminal ileostomy. Histology found many large cells and diffuse cell growth in keeping with diffuse large B cell lymphoma (DLBCL) expressing the immunophenotype CD20+, CD79alfa+, CD43+, MUM-1+, bcl-2+, cyclin D1-, CD3-, CD5-, CD10-, CD23-, with Ki-67 positivity in over 70% of the tumor cells (Figure 2). Following surgery, it was determined that the patient had stage II disease, IPI score 2. Immunotherapy was administered according to the R-CHOP protocol (rituximab 700 mg 1 day, cyclophosphamide 1400 mg 1 day, adriblastin 90 mg i.v. 1 day, vincristine 2 mg i.v. 1 day, prednisone 100 mg daily days 1 to 5). The patient received 8 cycles of therapy after which she achieved complete remission. Laboratory tests, biochemistry, bone marrow biopsy, and pelvis CT scans were normalized. She remains in complete remission 4 years later.


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Discussion

Primary lymphoma of the colon is a rare malignancy which accounts for around 0.2%–1.2% of all cases of colonic cancers. The stomach is most frequently involved (50%–60%), followed by the small bowel (20%–30%) and the colon/rectum (6%–14%).

Due to their rarity, the literature contains only a small number of case reports and small case series of up to 35 patients, and thus the optimal treatment and clinical outcomes are not completely clear. Furthermore, there is little data on their histology and immunohistochemistry because many of these publications appeared before the World Health Organization Classification. In a recent review of colorectal malignancy, primary colonic lymphoma was found in 29 of a cohort of 6944 patients. Immunohistopathology found that 60% of these had DLBCL, 14% follicular lymphoma, 10% mucosa associated lymphoid tissue (MALT) lymphoma, and 7% mantle cell lymphoma. DLBCL has similarly been found to be the most frequent histopathological subtype in other published series and case reports of primary colonic lymphoma. The tumor cells generally express pan B-cell markers such as CD19, CD20, CD22, CD79a, occasionally MUM-1+, and bcl-2+. The presence of bcl-2 and MUM-1 proteins has been associated with a less favorable prognosis and the possibility of a non germinal center DLBCL subtype, requiring more aggressive treatment. However, our patients had an excellent response to radical surgical excision, and combination immunochemotherapy
which was initiated after histology and immunohistochemical identification of the CD20 marker. Colonoscopy, abdominal ultrasonography and CT scan examination could have helped in detecting the presence and extent of the tumor. However, the appearances of the lesions in DLBCL are very nonspecific, and initially one would usually suspect colonic adenocarcinoma; hence patients often undergo surgery without preoperative histopathology and immunohistochemical examination of lesions, as was the case in our obstructed patient.

The optimal treatment of primary colonic lymphomas remains unclear. Some authors suggest chemotherapy alone with surgery reserved only for complications (such as perforation, obstruction or bleeding). However, emergency surgery for colonic perforation has a high mortality rate and these perforations can often be predicted; hence some authors advocate surgery prior to chemotherapy. A combination of chemotherapy with additional anti-CD20 monoclonal antibodies (rituximab) has been shown to have a beneficial effect and increase survival time in patients with lymphomas expressing CD20.

Our two patients had initial surgical excision followed by 8 cycles of immunotherapy, as their tumors expressed CD20. They remain well and in remission at 4 and 5 years. Our experience echoes that of other reports which have shown better outcomes in patients with primary colon lymphoma. It is likely that a combination of surgery followed by immunotherapy treatment currently offers the best overall survival for primary colonic DLBCL patients.

References