

Primary Colonic Lymphoma With Paraneoplastic Hypercalcemia

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ABSTRACT

Primary colonic lymphoma is a rare tumor accounting for 0.1%–0.5% of all colorectal malignancies. We describe a 63-year-old man whose initial presentation was altered mental status due to hypercalcemia. Physical examination revealed a hard, right-sided abdominal mass. Abdominal computed tomography showed a mass in the ascending colon, which on further evaluation with colonoscopy and biopsy was diagnosed as diffuse large B-cell lymphoma. A diagnosis of primary colonic lymphoma was made based on the Dawson criteria, after ruling out any extracolonic involvement. Workup for hypercalcemia showed elevated calcitriol levels, which is a paraneoplastic manifestation of the lymphoma.

INTRODUCTION

Primary lymphomas of the gastrointestinal (GI) tract are uncommon and account for less than 4% of malignancies affecting the gut. The colon is a rare site for primary GI lymphoma, constituting only approximately 1%.^{1,2} Diffuse large B-cell lymphoma (DLBCL), which is a subtype of non-Hodgkin lymphoma (NHL), is the most common histology. Fifteen percent of patients with NHL develop hypercalcemia at some point during their clinical course but are rarely symptomatic at the time of diagnosis.^{3,4} We report a rare case of symptomatic hypercalcemia, where subsequent evaluation showed an ascending colon mass diagnosed as DLBCL.

CASE REPORT

A 63-year-old man with a history of type II diabetes mellitus, hypertension, and chronic kidney disease stage III (baseline creatinine 1.6 mg/dL) presented to the hospital with worsening confusion for a week. On further review of symptoms after improvement in his sensorium, he endorsed fatigue, intermittent right-sided abdominal pain, subjective feeling of abdominal fullness, and a weight loss of 35 lbs over the previous month. He also had a new-onset constipation of 2 months, having bowel movements only every second or third day. He had noticed black colored, nontarry stools at least 5 times in the previous month. He had a normal colonoscopy 5 years ago. His vital signs on admission were temperature 99°F, heart rate 66 beats/min, respiratory rate 17 breaths/min, and blood pressure 132/64 mm Hg. Physical examination revealed a hard palpable mass in the right flank.

Initial laboratory test results were significant for hemoglobin of 8.2 g/dL, creatinine 3.7 mg/dL, calcium 13.1 mg/dL and ionized calcium of 7 mg/dL. Workup for hypercalcemia showed suppressed levels of serum parathyroid hormone (PTH) (<3 pg/mL), normal 25 OH vitamin D level (41 ng/mL), and a serum protein electrophoresis negative for monoclonal proteins. This PTH independent hypercalcemia was further evaluated by testing for PTH-related protein, which was also normal (<2 pmol/L). So, the calcitriol (1,25-dihydroxy vitamin D) level was estimated, which was high (112 pg/mL), the common causes of which are lymphomas and granulomatous diseases.

Abdominal computed tomography (CT) showed $16 \times 15 \times 15$ cm exophytic mass with central necrosis arising from the distal ascending colon (Figure 1). Colonoscopy confirmed these CT findings (Figure 2). Biopsy from the mass was consistent with DLBCL, which was subclassified as activated B cell (ABC) type based on immunohistochemical characteristics which were positive for CD 20, BCL-2, and MUM-1, and negative for CD 10, BCL-6, and MYC (Figure 3).⁵ Bone marrow biopsy and positron emission tomography CT scan were performed to stage his lymphoma and were negative for any extracolonic spread. So, a diagnosis of primary colonic lymphoma (PCL) was made based on the Dawson criteria.⁶ His tumor was staged as stage 1 based on the Lugano classification.⁷ He underwent a right hemicolectomy, and grossly, the mass measured $20 \times 18 \times 14$ cm with a necrotic center eroding the colonic mucosa, and the resected margins were negative for the tumor (Figure 4). He was started on combination chemotherapy with R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone). Lenalidomide was later added to this regimen because his DLBCL was ABC type.⁸ He was in remission 6 months after starting the treatment.

DISCUSSION

PCL accounts for 1% of all GI lymphomas and 0.1%–0.5% of all colorectal malignancies.^{1,2} Cecum is the most common site of occurrence within the colon (60%–75%), probably because of the abundance of lymphatic tissue, and is followed by rectosigmoid region (8.5%–35%).^{6,9} Although calcitriol-mediated hypercalcemia is well described with NHL, only less than 10 cases have been reported with PCL, probably because of rarity of later.¹⁰



Figure 1. Abdominal computed tomography showing exophytic necrotic mass arising from the ascending colon (arrow).

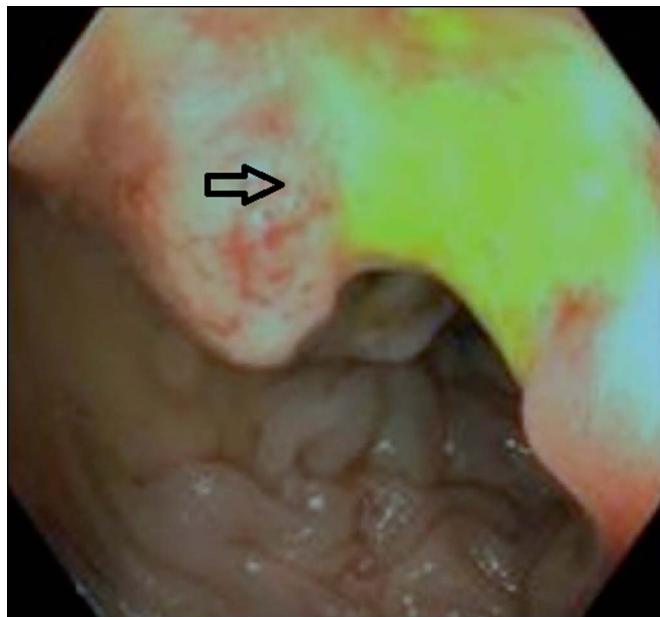


Figure 2. Colonoscopy demonstrating mass in the right colon (arrow).

Immunosuppression and inflammatory bowel disease are the known predisposing risk factors for PCL, but often, none are identified as in our patient.¹¹ The mean age at diagnosis is 55 years, and there is a male predominance. Clinical features described are abdominal pain, altered bowel habits, overt or occult bleeding, and weight loss and are rarely complicated by intussusception and obstruction. However, the lack of any specific symptoms can result in delay in diagnosis, and a third of patients have palpable abdominal mass at the time of presentation, as noted in this case.¹²

CT scan findings could be nonspecific such as polypoid masses, circumferential infiltration, mucosal fold thickening, or extracolonic masses. According to Wyatt et al in his report of 15 patients, the findings that should raise suspicion of colonic lymphoma are cecal tumors with growth into the terminal ileum, tumors that are fairly demarcated from pericolonic fat without invasion of neighboring viscera, and tumors that perforate in the absence of desmoplastic reaction.¹³ Colonoscopic appearance could be a fungating mass, ulcerative lesion, mucosal induration, or nodularity.¹⁴

The Dawson criteria are used to differentiate primary GI lymphoma from secondary GI involvement.⁶ The most widely used staging system is the Lugano classification, which is a modification of the Ann Arbor staging system.⁷ The International Prognostic Index and its variants are the most helpful tools to assess the prognosis.¹⁵ Cell of origin studies in DLBCL is of prognostic importance, with germinal center B cell type having a better prognosis than ABC type.^{16,17} Owing to the rarity of this disease, there is lack of randomized controlled trials to define the most optimal therapy. In most series, surgery followed by multiagent chemotherapy (R-CHOP) has led to improved outcome.¹⁸

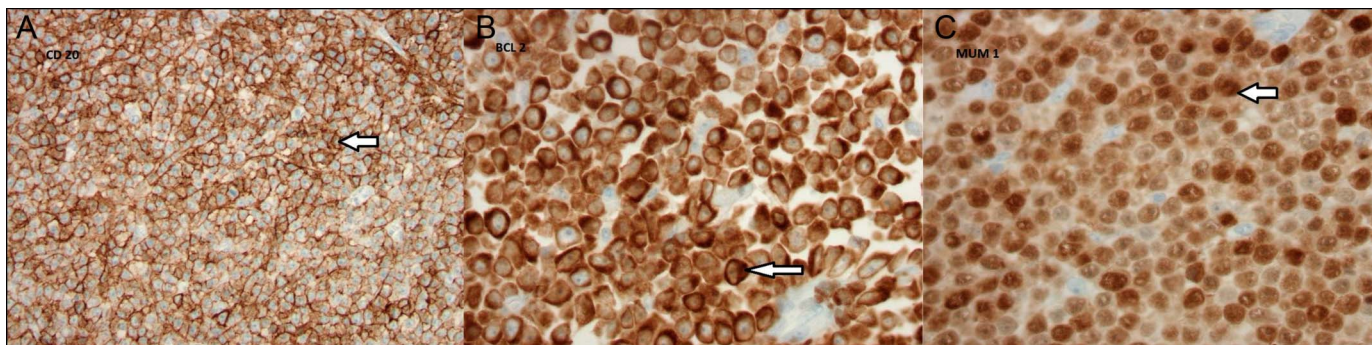


Figure 3. Immunohistochemistry positive for (A) cluster of differentiation 20 (arrow), (B) B-cell lymphoma-2 (arrow), and (C) multiple myeloma-1 (arrow).

Paraneoplastic hypercalcemia in NHL is mostly because of extrarenal production of 1,25-dihydroxyvitamin D facilitated by the 1α -hydroxylase enzymes in the macrophages that surrounds the malignant lymphocytes.^{4,19} By contrast, hypercalcemia is rare in colon carcinoma, unless it is a poorly differentiated carcinoma with or without squamous differentiation or having neuroendocrine features, and the mechanism is by overproduction of PTH-related protein, if not because of skeletal metastasis.²⁰ In conclusion, this is a case report of PCL where the initial presentation was delirium secondary to paraneoplastic hypercalcemia. So, a bulky colon mass with hypercalcemia should raise the suspicion of lymphoma.

DISCLOSURES

Author contributions: T. Augustine wrote the manuscript, revised the manuscript for intellectual content, and is the article guarantor. A. Perisetti, SA Khan, and B. Tharian revised the manuscript for intellectual content. RH Lobo provided the pathology images.

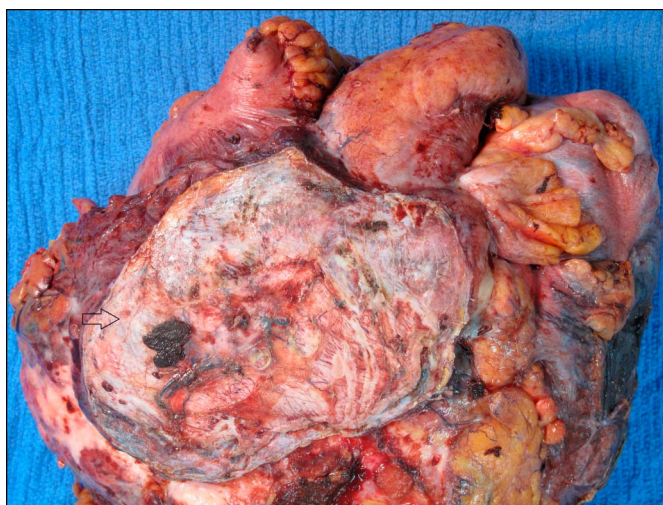


Figure 4. Gross specimen showing colonic mass eroding the mucosa.

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Informed consent was obtained for this case report.

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