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Case Report

Primary diffuse large B-cell lymphoma of the cecum ☆,☆☆

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ABSTRACT

When found in the cecum or rectosigmoid junction, primary colorectal B-cell lymphoma is a rare malignant non-Hodgkin's lymphoma often associated with an unfavorable prognosis. Due to the nonspecific clinical symptoms, these uncommon tumors are often left undefined or misdiagnosed, resulting in delays in treatment and adverse patient outcomes. Contrast-enhanced computed tomography is the most commonly used medical imaging process for primary colorectal lymphoma, but due to the rarity of this disorder, accurate imaging diagnosis remains a clinical challenge. In this article, we report the case of a 70-year-old male who was diagnosed with primary B-cell lymphoma of the cecum. We focus on improving diagnosis through the utilization of radiological imaging modalities, particularly computed tomography (CT) and fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (18-F-FDG PET/CT). While imaging modalities are important in recognizing colonic lymphomas, there are no pathognomonic imaging features for lymphoma; therefore, biopsy remains necessary for diagnostic confirmation.

Introduction

Diffuse large B-cell lymphoma (DLBCL), a malignant cancer of B cells, is the most common non-Hodgkin's lymphoma (NHL) phenotype and typically arises from the lymph nodes. Although extremely rare, this extranodal cancer can develop as a primary lesion in the colon or rectum, accounting for 0.2%-1.0% of colonic malignancies [1]. Primary colonic lymphoma is usually seen in older individuals with a mean age of diagnosis of 55 years and has a generally poor prognosis [2]. Because it is so uncommon, there is no standardized

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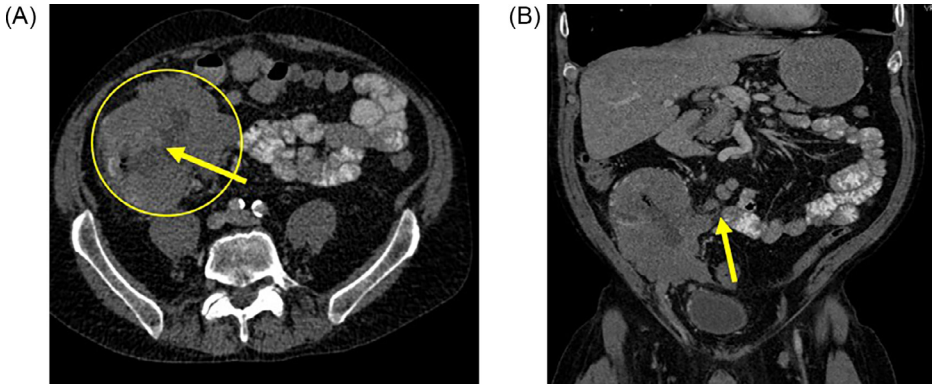

Fig. 1 – A 70-year-old male with a 1-month history of mild right lower quadrant pain and 24-pound weight loss. (A and B). Axial and coronal contrast-enhanced CT scans of the abdomen and pelvis demonstrated a 10.7 x 8.7 cm solid mass with possible early central necrosis. The mass extends to the terminal ileum.

clinical treatment for primary colonic lymphoma but surgery combined with chemotherapy is the usual approach. Preprocedural diagnosis can be challenging due to various nonspecific clinical symptoms such as abdominal pain, weight loss, diarrhea, nausea, and vomiting, as well as a palpable mass [3]. Here, we report the case of a 70-year-old male diagnosed with primary DLBCL of the cecum who was treated with 6 cycles of rituximab and low-dose cyclophosphamide, doxorubicin, vincristine, and prednisone (R-miniCHOP) + etoposide, a reduced-dose chemotherapy regimen. We consider the use of radiological imaging modalities and histopathological findings as diagnostic tools.

Case report

A 70-year-old male with a past medical history of severe chronic obstructive pulmonary disease (COPD), hyperlipidemia, benign pulmonary nodules, and a former smoking history of 24 pack-years presented to his local primary clinic after a month of persistent mild right lower quadrant abdominal pain radiating to the right groin and an unintentional 24-lb. (10.9 kg) weight loss over the previous 2 months. Upon physical examination, he had no palpable lymphadenopathy, denied postprandial pain, or nausea/vomiting, and his abdomen was soft, nontender, with bowel sounds apparent. No significant family history or predisposing factors were noted. A subsequent CT scan of the abdomen and pelvis (CTAP) with IV contrast showed evidence of a large cecal mass measuring 10.7 × 8.7 cm with marked circumferential proximal right colonic wall thickening extending into the terminal ileum, extra colonic spread, and surrounding lymph node enlargement concerning for colon cancer (Figs. 1A and B). There was also evidence of high-grade stenosis involving the proximal superior mesenteric artery, central mesenteric lymphadenopathy, and focal fatty eventration along the hepatic segment. Approximately 2 weeks after the initial presentation, the patient underwent an urgent diagnostic colonoscopy with biopsy, which displayed a nearly obstructing large circumferential friable ulcerated mass in the cecum. Polyps were removed from the transverse, descending, and sigmoid colons. Immunostains

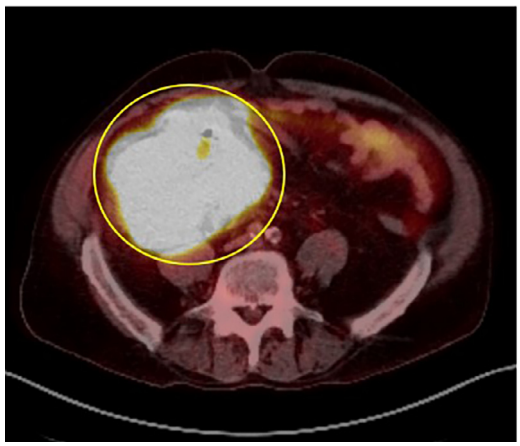

Fig. 2 – A PET/CT was obtained to better define the extent of the tumor and potential distant spread. The PET/CT demonstrates that the large mass is hypermetabolic consistent with malignancy and a differential diagnosis including lymphoma.

CD3 and CD20 showed mixed T- and B-lymphocyte populations in lamina propria, consistent with reactive lymphoid aggregate. The findings suggested an ischemic-type injury and, lacking evidence of malignancy possibly due to a sampling error, the patient was scheduled for a repeat colonoscopy with biopsy.

To monitor the patient's previous pulmonary nodules, a contrast-enhanced CT scan of the chest was completed. A new spiculated nodule was revealed on the right lower lobe (RLL) of the right lung, raising suspicion of primary lung cancer. A biopsy was positive for small cell neuroendocrine lung carcinoma.

A fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (18 F-FDG PET/CT) scan (Fig. 2A) was subsequently conducted to further review the colonic mass and lung carcinoma. The colonic mass exhibited a long segment, intensely hypermetabolic, nonobstructing circumferential wall thickening in the ascending colon and

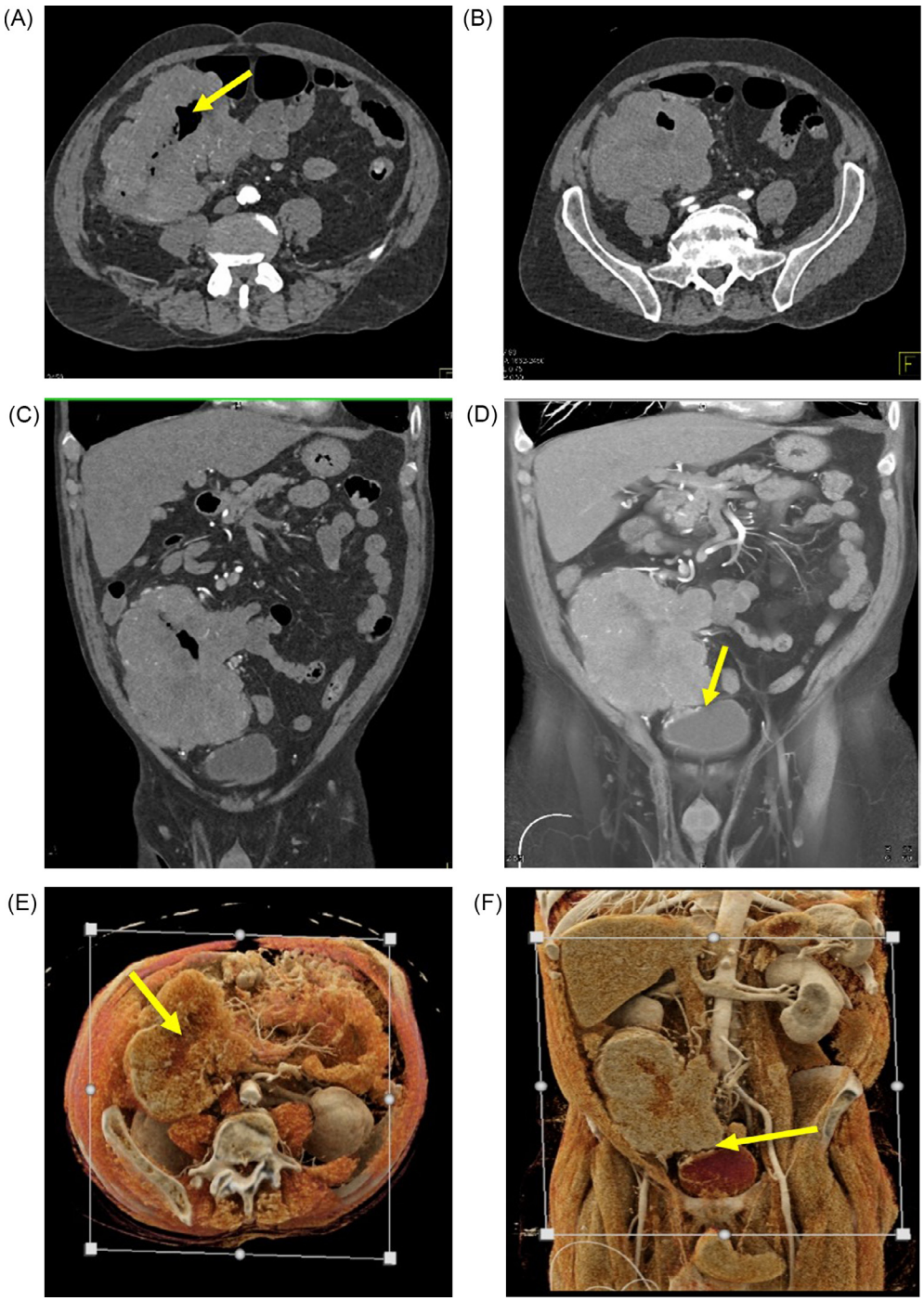

Fig. 3 – A repeat contrast-enhanced CT scan of the abdomen and pelvis was performed due to worsening symptoms and concern for GI bleed. (A–D) Axial, coronal. and volume-rendered images define increasing tumor necrosis and mass enlargement since the prior study. (E and F) Images with cinematic rendering better define the tumor extent with necrosis as well as tumor progression including bladder involvement.

hypermetabolic mesenteric lymph nodes. There were additional hypermetabolic lymph nodes around the colonic mass. Circumferential wall thickening of the bladder increased from the CTAP 3 weeks prior. These findings were primarily suspicious for colonic lymphoma.

Two months after the initial presentation, the patient had an onset of melena, hematochezia, and chronic constipation and underwent a CTAP with and without contrast (Figs. 3A–D). The results demonstrated areas of progressive contrast opacification suggestive of a gastrointestinal bleed from the portal vein surrounding the bulky mass (approximately 15.3 × 11.3 cm) involving the terminal ileum and cecum, consistent with B cell lymphoma. Moreover, 3D rendering (Figs. 3E and F) highlighted a large bulky tumor with ulceration in the right lower

quadrant, which appeared to involve the distal small bowel and cecum. Some peripheral enhancement appeared at the edge. The tumor extended downward and abutted the right dome as well as the right side of the bladder, and the right testicular vein was encased, resulting in a partial hydrocele. Despite the size of the mass, the bowel was not obstructed. On venous phase imaging, the bulky tumor involved the distal bowel, ileum, cecum, as well as right colon and showed increased enhancement, which suggested a bleeding site.

Two weeks after the gastrointestinal bleeding episode, a repeat colonoscopy with biopsy was conducted. A large, nearly obstructing cecal mass blocking a view of the ileocecal valve was observed. Pathologically, sections demonstrated colonic mucosa involved by an atypical diffuse lymphoid proliferation consisting of large, pleomorphic lymphocytes with vesicular chromatin and a moderate amount of cytoplasm. Apoptotic bodies and necrosis were also apparent. Immunostains were positive for CD20, MUM-1, and BCL-6 and negative for CD10, CD30, BCL-2, Cyclin D1, AE1/AE3, INSM1, and P53. The atypical cells were positive for c-Myc (>90%). ISH for EBV (EBER) was negative. FISH results were abnormal and indicated a rearrangement involving the MYC gene region in 46% of nuclei and fusion of MYC and IGH in 55% of nuclei. No rearrangement of BCL2 or BCL6 and no fusion of BCL2 and IGH was observed. Primary DLBCL of the cecum stage IV diagnosis was confirmed given the extensive involvement.

The treatment plan includes six cycles of R-miniCHOP + etoposide, a reduced-dose chemotherapy regimen. The patient was also started on valacyclovir. Since the initiation of chemotherapy, his GI bleed resolved, his abdominal pain improved, and no significant adverse effects were noted except dyspnea. A follow-up CT showed a decrease in circumferential wall thickening of the cecum, resolution of previously seen mass compression of the right bladder wall, and a reduction in the size of the RLL mass. For the carcinoma in the RLL, the patient was started on stereotactic body radiotherapy followed by chemotherapy. Overall, the patient is on regular follow-up with imaging and blood work and is doing well.

Discussion

Here, we review a case of primary lymphoma of the colon, a rare cancer comprising 0.2%-1% of all colonic malignancies [4]. These tumors are predominantly NHLs and have been frequently observed in immunosuppressed patients such as those suffering from human immunodeficiency virus (HIV), inflammatory bowel disease/ulcerative colitis, or immunosuppression due to organ transplant [4]. Most NHLs are gastrointestinal (5%-10%) and occur in the stomach (68%-75%), followed by the small intestine (15%-20%), and the remainder in the colon, esophagus, and rectum [1]. DLBCLs, the most common subtype of extranodal NHL, proliferate quickly and are more aggressive than other B-cell lymphomas [5]. They are most often seen in middle-aged men within the right colon [6]. According to Krol et al. [7], if the NHL originates in an extranodal site, it can be further classified as a primary extranodal NHL as long as it is dominant. Due to the abundance of lymphoid tissue, the cecum is the most common extranodal site of involvement for colorectal lymphomas, followed by the rectum, ascending colon, and descending colon [4,8].

We report the case of a 70-year-old male with a past medical history of severe COPD, hyperlipidemia, pulmonary nodules, and a prior 24-pack-year smoking pattern who presented to his local primary clinic after 1 month of persistent mild right lower quadrant abdominal pain radiating to the right groin and an unintentional 24-pound weight loss over the previous 2 months. Primary colonic lymphomas, which have a male predominance, most frequently present with generic symptoms including abdominal pain, weight loss, and altered bowel habits [4,9]. Lower gastrointestinal bleeding occurs in 13%-82% of patients, and the tumor reaches over 5 cm in diameter in more than half of patients [10]. The nonspecificity of these symptoms and the infrequency of intestinal obstructions lead patients to present late with more advanced disease stages, delaying diagnosis in 33%-65% of cases and worsening overall patient outcomes [10]. Intestinal obstruction rarely develops due to the characteristic feature of perforation without desmoplastic response in lymphomas, making early detection of this cancer difficult [11].

Imaging modalities, CT in particular, are essential for determining the extent of tumor invasion and spread, aid in localizing colonic lymphomas, and provide information regarding tumor depth, size, and lymph node involvement [8]. Common imaging features of primary colonic lymphomas appear as localized, extraluminal, and large masses [12]. Because they can present with patterns similar to other colonic tumors or inflammatory diseases, it is more difficult to determine lymphoma as a differential diagnosis. Some of the patterns include a bulky polyploid, focal infiltrative tumor, or aneurysmal dilatation [13]. Colorectal lymphomas can display concentric circumferential intestinal wall thickening, well-defined margins, mucosal nodularity, aneurysmal dilatation, focal strictures, or ulcerative forms with fistula formation [4]. Helpful in the differentiation from adenocarcinomas is perforation without desmoplastic response, as well as clearly established margins with preserved fat planes and no involvement of adjacent structures [11]. As in our case, colonic lymphomas are usually seen near the ileocecal valve, can grow into the terminal ileum, and are typically larger than adenocarcinomas [13]. If a diffuse infiltration or bulky mass is present with the preservation of fat planes and without obstruction, lymphadenopathy, or multiple site involvement, lymphoma should be considered in the differential diagnosis [8]. Sometimes, colonic wall infiltration may be confused with inflammatory thickening, and if a patient has associated mesenteric adenopathy, it is important to note that it is usually bulkier than that associated with other disorders such as Crohn's disease [8]. If there is no associated adenopathy, it can be difficult to distinguish it from adenocarcinomas of the colon, although adenocarcinomas do not typically cause such extensive colonic wall thickening [8].

PET/CT can be helpful when monitoring the disease's response to therapy and staging [14]. Features that arise on PET/CT are patterns of uptake with nodular, focal, or diffuse hypermetabolic activity [15]. Our patient's PET/CT of the colonic mass showed features consistent with colonic lymphoma: long segment (10 cm), intensely hypermetabolic, nonobstructing, circumferential wall thickening (4 cm) in the

ascending colon, and a hypermetabolic mesenteric lymph node, without any lytic/sclerotic osseous lesions.

Ultimately, because the tumor was advanced, our patient was treated with R-miniCHOP + etoposide and started on valacyclovir. With the addition of rituximab to the CHOP regimen, treatment with R-miniCHOP has remained the standard of care and is a safe, effective therapy for patients with a DLBCL diagnosis, especially for CD20-positive B-cell lymphomas [1]. Due to the absence of intestinal obstruction, intestinal perforation, or hemorrhage, surgical resection was not indicated for our patient. If the probability of recurrence is high or if the treatment response is not complete, stem cell or bone marrow transplantations may be conducted [1].

Conclusion

Primary colonic lymphoma is a rare, aggressive cancer with a generally poor prognosis. The radiological features presented in this case can serve as a valuable tool in helping radiologists develop high clinical suspicion and determine an accurate differential diagnosis. However, although imaging modalities are important in recognizing colonic lymphomas, it is important to note that there are no pathognomonic imaging features for lymphoma; hence, biopsy is required for diagnostic confirmation [6,12].

Author contribution

All authors contributed equally to the writing of this manuscript.

Patient consent

The patient reported in the manuscript signed the informed consent/authorization for participation in research, which includes the permission to use data collected in future research projects such as the presented case details and images used in this manuscript.

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