A rare case of Small Intestinal (Duodenal) diffuse large B-cell lymphoma (DLBL) in an elderly patient presented with gastrointestinal bleeding

Sukhjindher Chauhan[1], Talha Jilani[1], Tony Alarcon[1], Youssef Ghobrial[1], Homayon Iraninezhad[1], and Ann M. Wierman[1]

[1]MountainView Hospital

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Abstract

This case report highlights an incidence of small intestinal DLBCL of the duodenum in an 87-year-old woman presenting with a 2-month history of melena and dysphagia to solid foods and laboratory findings of normocytic anemia. The patient had EGD and biopsies revealed DLBCL.

Introduction

Non-Hodgkin lymphoma (NHL) constitutes around 80% of all lymphomas. Over 30 subtypes of NHL have been identified, out of which diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma remain the most commonly occurring. DLBCL accounts for around 30% to 40% of all non-Hodgkin lymphomas and is common in elderly patients. Traditionally, the presentation of DLBCL includes enlarged lymph nodes or a rapidly growing mass along with fever, night sweats, and weight loss. In addition, extranodal involvement, most frequently in the stomach, is also common [1, 2]. However, primary NHLs, such as DLBCL, rarely affect the small intestine, particularly the duodenum, and may present with nonspecific clinical manifestations, which makes it difficult to establish an early diagnosis and initiate timely management.

In this case report, we describe a case of low-grade duodenal DLBCL in an elderly patient who presented with dysphagia and black stools. The patient was diagnosed via duodenal biopsy and was started on an R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone) chemotherapy regimen. The patient showed a good response to the treatment regimen.

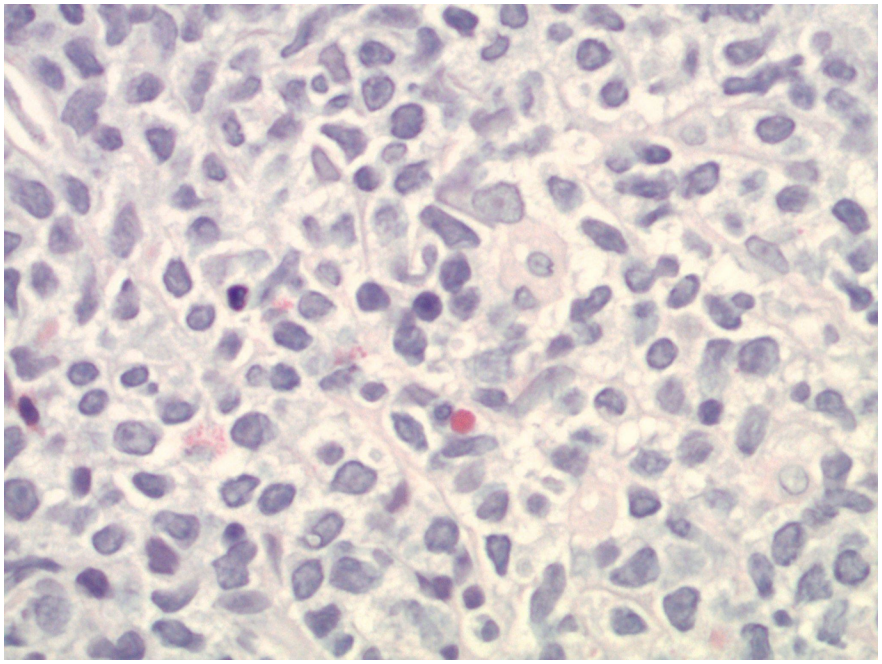
Case Presentation

An 87-year-old woman with a past medical history significant for duodenal ulcers, atrial fibrillation on rivaroxaban, smoking history with COPD, not on home oxygen therapy, chronic generalized pain, and fibromyalgia on NSAIDs and opioids analgesics, presented to the hospital with the chief complaint of black stools and dysphagia to solids. The patient reported a loss of appetite, weight loss of about 10 lbs, and insomnia. She denied any family history of cancer.

On admission, the patient was febrile and her vitals were within normal limits. The physical examination was remarkable for conjunctival pallor. Her abdomen was soft, non-tender, and non-distended, and normal bowel sounds were heard on auscultation. Her complete blood count was remarkable for normocytic anemia with a hemoglobin level of 10.7 g/dL and a mean corpuscular volume (MCV) of 87 fL. The comprehensive metabolic panel and coagulation profile were relatively normal. Iron studies demonstrated serum iron 45 mcg/dL, total iron binding capacity (TIBC) 291 mcg/dL, iron saturation 9 %, and ferritin 12 ng/mL, which was consistent

with iron deficiency anemia. Due to the presence of dysphagia, melena associated with weight loss, and iron deficiency anemia, esophagogastroduodenoscopy (EGD) was ordered. EGD revealed presbyesophagus, a small hiatal hernia, erosive gastritis, and multiple large ulcers located in the duodenal bulb, and the second and third parts of the duodenum. The first and second portions of the duodenum were deformed. Biopsies of the stomach and duodenum were obtained, and the patient was started on omeprazole 40 mg twice a day. Rivaroxaban was held in the setting of acute upper gastrointestinal (GI) bleeding.

The results of the stomach biopsy revealed mild inactive gastritis with no intestinal metaplasia or dysplasia. *Helicobacter pylori* were not detected. The duodenal ulcer biopsy showed atypical lymphoid infiltration shown in Figures 1a and 1b.



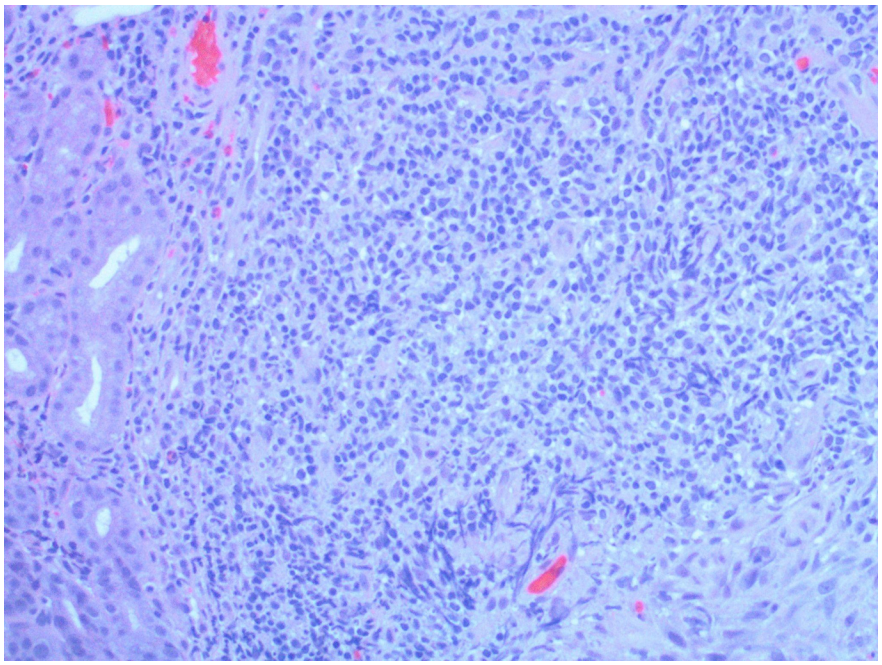


Figure 1a and 1b: Duodenal Biopsy histopathology results demonstrated lymphocytic infiltration.

Fluorescence in situ hybridization (FISH) was performed using probes specific for rearrangement involving BCL6, t(11:14), t(14:18), and MALT1, which are reported in low-grade small B-cell lymphomas. The break-apart signal pattern 1R1G1F was observed with BCL6 break-apart probe in 82 % of the analyzed nuclei (the normal reference range is <11.6 %). This represented an abnormal result indicative of a BCL6 gene rearrangement with an unknown gene and was suggestive of B-cell lymphoma. Immunohistochemical staining was positive for CD23, CD20, Bcl-6, and focally for Bcl-2. The bone marrow cytogenetics test demonstrated an abnormal female karyotype. Two cells from the culture stimulated with IL2 and DSP30 showed clonal abnormalities, while 18 cells show a normal karyotype. The abnormalities included three copies of the long arm of chromosome 3 along with loss of material from the short arm of chromosome 17, which is a poor prognostic indicator for DLBCL.

Based on the laboratory results, a diagnosis of low-grade B-cell lymphoma of the duodenum associated with a poor prognosis was established. The patient was started on chemotherapy using the R-CHOP regimen (rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone. The patient received 4 cycles of chemotherapy and responded well despite the poor prognosis.

Discussion

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL) and accounts for around 30%-40% of all NHL cases. It is a neoplasm of B lymphocytes and comprises a heterogeneous group of clinically and pathologically distinct entities that result in the proliferation of germinal or post-germinal malignant B cells. [1, 2] The neoplasm is typically composed of a diffuse infiltrate of large, transformed blasts that resemble germinal center centroblasts and/or immunoblasts. DLBCL usually develops *de novo* due to a variety of genetic alterations. The most common abnormality involves rearrangements and mutations of the BCL6 gene at the 3q27 locus. [3] In some cases, DLBCL may develop as a result of the transformation of other NHLs, such as chronic lymphocytic leukemia/small lymphocytic lymphoma. This is known as the Richter transformation. [4] Immunosuppression (for example, an acquired immunodeficiency syndrome (AIDS), autoimmune disorders, organ transplantation), pesticides, dyes, and ultraviolet radiation may also increase the risk of the development of DLBCL. [3]

DLBCL typically presents at an advanced stage and has a median age of 60 years. [5] It is an aggressive disease that typically presents with rapidly enlarging lymphadenopathy and constitutional symptoms, including fever, night sweats, and weight loss. However, extranodal involvement is common and may be seen in up to 50% of patients. The gastrointestinal (GI) tract is the most common extranodal site to be involved. [6] The majority of extranodal GI NHLs occur in the stomach, followed by the small bowel and colon. [7] In the small bowel, the ileum is most commonly affected (60%-65%); while the duodenum is an uncommon location for primary GI NHL (6%-8%). [8] Patients with small intestinal NHL may present with nonspecific symptoms, such as abdominal pain, diarrhea, gastrointestinal bleeding, and weight loss. [9]

Since the clinical features of small intestinal DLBCL are highly nonspecific, an endoscopy is usually performed to identify any suspicious lesions and to obtain biopsies. [10] The tumor may appear as a circumferential bulky mass in the intestinal wall and may ulcerate and perforate into the adjacent mesentery. [11] The diagnosis of DLBCL can be established based on an excisional lymph node biopsy or by analyzing samples obtained from an affected organ via an incisional biopsy. [12] Histology and immunophenotyping, as well as staining for B-cell markers, are required for diagnosis. Morphologically, DLBCL is characterized by sheets of atypical lymphoid cells with large nucleoli and abundant cytoplasm. The cells usually express pan-B cell antigens, such as CD19, CD20, CD22, CD45, and CD79a. The different genetic rearrangements in BCL6, BCL2, and/or c-MYC genes can be identified using fluorescence in situ hybridization (FISH). [13] Bone marrow cytogenetic studies can also be used to determine nonrandom chromosomal aberrations in patients with DLBCL and can assist in the prognostic stratification of this condition. For instance, total or partial trisomy 3 is a frequent chromosomal aberration observed in patients with diffuse large B cell lymphoma. Similarly, as was the case with our patient, loss of genetic material from the short arm of chromosome 17 may be seen in some patients with DLBCL and is considered to be an indicator of poor prognosis. This is because chromosome 17 contains the tumor suppressor gene *TP53* (17p13). Inactivation of this gene leads to uncontrolled cell proliferation and has been associated with decreased overall survival and reduced progression-free survival in patients with DLBCL. [4] Once the diagnosis of DLBCL is established, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) can be used to stage the disease. [10]

Due to the low incidence of *de novo* duodenal DLBCL, there are no guidelines available for the treatment of small intestinal DLBCL and the optimal treatment remains unknown. Patients with advanced diseases require more aggressive treatment. Surgery is reserved for patients with complications such as small bowel perforation, small bowel obstruction, or intractable bleeding, for both limited-stage and advanced disease. Surgery followed by adjuvant chemotherapy was historically considered the preferred treatment modality. However, since the lymphomas are highly chemosensitive, surgical resection is now rarely used and is typically reserved for the management of complications, such as bowel perforation, small bowel obstruction, or severe bleeding. The most commonly used chemotherapy regimen is R-CHOP, which is a combination of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. [9, 10, 14] In patients with unfavorable prognostic factors, DA-EPOCH-R (dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab) may also be a beneficial treatment option [10, 15]. Response to treatment is measured using data collected from the post-treatment history, physical, and imaging (PET/CT) scan results. After the chemotherapy is completed, restaging and evaluation of complete remission should be done. Patients should be followed up at periodic intervals to monitor for complications related to treatment and for assessment for possible relapse. [16]

Our patient who presented with dysphagia and melena had iron deficiency anemia, likely due to recurrent intestinal bleeding caused by duodenal DLBCL. The biopsy findings along with the FISH and cytogenetic results confirmed the diagnosis and the patient was started on systemic chemotherapy with R-CHOP. Despite having the poor prognostic indicator of chromosome 17 partial deletion, the patient responded well to this treatment regimen. This case report highlights the fact that small intestinal DLBCL is a rare yet aggressive disease that can present with nonspecific symptoms, which may hinder diagnosis and prompt treatment. However, timely initiation of chemotherapy can result in favorable patient outcomes. Therefore, available diagnostic modalities should be used for the early identification and initiation of appropriate treatment in

these patients.

References

1. Susanibar-Adaniya S, Barta SK. 2021 Update on Diffuse large B cell lymphoma: A review of current data and potential applications on risk stratification and management. *Am J Hematol.* 2021;96(5):617-629. doi:10.1002/ajh.26151
2. Li S, Young KH, Medeiros LJ. Diffuse large B-cell lymphoma.*Pathology.* 2018;50(1):74-87. doi:10.1016/j.pathol.2017.09.006
3. Friedberg JW, Fisher RI. Diffuse large B-cell lymphoma. *Hematol Oncol Clin North Am.* 2008;22(5):941-ix. doi:10.1016/j.hoc.2008.07.002
4. Nedomova R, Papajik T, Prochazka V, Indrak K, Jarosova M. Cytogenetics and molecular cytogenetics in diffuse large B-cell lymphoma (DLBCL). *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* 2013;157(3):239-247. doi:10.5507/bp.2012.085
5. Solimando AG, Annese T, Tamma R, et al. New Insights into Diffuse Large B-Cell Lymphoma Pathobiology. *Cancers (Basel).* 2020;12(7):1869. Published 2020 Jul 11. doi:10.3390/cancers12071869
6. Padala SA, Kallam A. Diffuse Large B Cell Lymphoma. In:*StatPearls.* Treasure Island (FL): StatPearls Publishing; August 2, 2021.
7. Howell JM, Auer-Grzesiak I, Zhang J, Andrews CN, Stewart D, Urbanski SJ. Increasing incidence rates, distribution and histological characteristics of primary gastrointestinal non-Hodgkin lymphoma in a North American population. *Can J Gastroenterol.* 2012;26(7):452-456. doi:10.1155/2012/480160
8. Lo Re G, Federica V, Midiri F, et al. Radiological Features of Gastrointestinal Lymphoma [published correction appears in Gastroenterol Res Pract. 2016;2016:9742102]. *Gastroenterol Res Pract.* 2016;2016:2498143. doi:10.1155/2016/2498143
9. Shirwaikar Thomas A, Schwartz M, Quigley E. Gastrointestinal lymphoma: the new mimic. *BMJ Open Gastroenterol.* 2019;6(1):e000320. Published 2019 Sep 13. doi:10.1136/bmjgast-2019-000320
10. Lodhi HT, Hussain Q, Munir A, Zafar F, Khan ZH. Primary Gastrointestinal Diffuse Large B-cell Lymphoma. *Cureus.* 2018;10(9):e3258. Published 2018 Sep 5. doi:10.7759/cureus.3258
11. Ghai S, Pattison J, Ghai S, O'Malley ME, Khalili K, Stephens M. Primary gastrointestinal lymphoma: spectrum of imaging findings with pathologic correlation. *Radiographics.* 2007;27(5):1371-1388. doi:10.1148/rg.275065151
12. Pfreundschuh M. How I treat elderly patients with diffuse large B-cell lymphoma. *Blood.* 2010;116(24):5103-5110. doi:10.1182/blood-2010-07-259333
13. Liu Y, Barta SK. Diffuse large B-cell lymphoma: 2019 update on diagnosis, risk stratification, and treatment. *Am J Hematol.* 2019;94(5):604-616. doi:10.1002/ajh.25460
14. Zaarour M, Busack C, Munker R. Obstructing Duodenal Diffuse Large B-cell Lymphoma with Peritoneal Lymphomatosis with Exceptional Response to R-CHOP. *Cureus.* 2019;11(5):e4621. Published 2019 May 8. doi:10.7759/cureus.4621
15. Pejša V, Prka Ž, Lucijanić M, et al. Rituximab with dose-adjusted EPOCH as first-line treatment in patients with highly aggressive diffuse large B-cell lymphoma and autologous stem cell transplantation in selected patients. *Croat Med J.* 2017;58(1):40-48. doi:10.3325/cmj.2017.58.40
16. Sussman J, Varela NP, Cheung M, et al. Follow-up care for survivors of lymphoma who have received curative-intent treatment. *Curr Oncol.* 2016;23(5):e499-e513. doi:10.3747/co.23.3265