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Primary Gastric Atypical Burkitt Lymphoma: A Rare Case Report

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Abstract

The abdomen, particularly the ileocecal region, is the most commonly affected disease site in sporadic Burkitt lymphoma (BL). Involvement of the stomach is very rare. Primary gastric atypical Burkitt lymphoma has not been described in the literature, to the best of our knowledge. In this case report, we discuss a patient with atypical Burkitt lymphoma involving the stomach. The immunohistochemical stains showed positive results for CD20, PAX5, BCL6, CD10, and high ki-67. The fluorescence in situ hybridization (FISH) test revealed a positive result for c-MYC gene rearrangement, but there was no evidence of the typical translocation associated with Burkitt lymphoma involving the IgH, kappa, or lambda genes.

Keywords

atypical Burkitt lymphoma, gastric lymphoma

Introduction

Burkitt lymphoma (BL) occurs at an incidence of 2.5 cases per million adults, making it a very rare and aggressive lymphoma of mature B cells.[1] In adults, Burkitt lymphoma is most commonly found in the abdomen, followed by the jaw and central nervous system. In the gastrointestinal (GI) tract, it is typically found in the small or large intestine, with localization in the gastric area being rare.[2-4] There have been only a few reported cases.[5,6]

The similarities in morphology between BL and diffuse large B-cell lymphoma (DLBCL) present a diagnostic and therapeutic challenge for clinicians.[2] The rarity of these lymphomas also poses a significant challenge for oncologists and pathologists in determining treatment strategies for these patients. We herein report a rare case of atypical Burkitt lymphoma in the stomach.

Case Presentation

A 52-year-old male with a past medical history of hypertension, bleeding peptic ulcer disease with *Helicobacter pylori* infection, congestive heart failure, chronic kidney disease presented to the hospital after 3 episodes of hematemesis. He also complained of 20-lbs unintentional weight loss in the past 2 years night sweats. He was found to have a drop of hemoglobin of 2 points from 10 to 8 g/dL. He was admitted to the hospital for management of an upper gastrointestinal bleed. On physical examination, a 2- to 3-cm anterior cervical neck swelling was noted. A computed tomography scan (CT) of the neck revealed a 4.4-cm soft tissue mass in the left neck in proximity to the left internal jugular vein and left common carotid artery (Figure 1C). A computed tomography scan of the chest, abdomen, and pelvis revealed a mass in the porta hepatis measuring 4.7 cm × 3.7 cm suspicious for malignant adenopathy (Figure 1A). The patient underwent esophagogastroduodenoscopy (EGD) that revealed a gastric cardia mass (Figure 2). Biopsy of the mass showed high grade atypical Burkett lymphoma of stomach: the intermediate-sized atypical lymphocytes are infiltrated in the lamina propria of the gastric mucosa. The lymphocytes are monotonous with mild nuclear pleomorphism showing focal starry sky pattern (Figure 3A and B). The neoplastic cells are diffusely positive for B-cell markers of CD20 and PAX5 (Figure 3 A and B). The proliferative index of the neoplastic B-cells approaches approximately 100% stained by Ki67. The germinal center markers CD10 and BCL-6 are diffusely positive in the neoplastic cells. FISH test was positive for rearrangement involving MYC gene in approximately 48%

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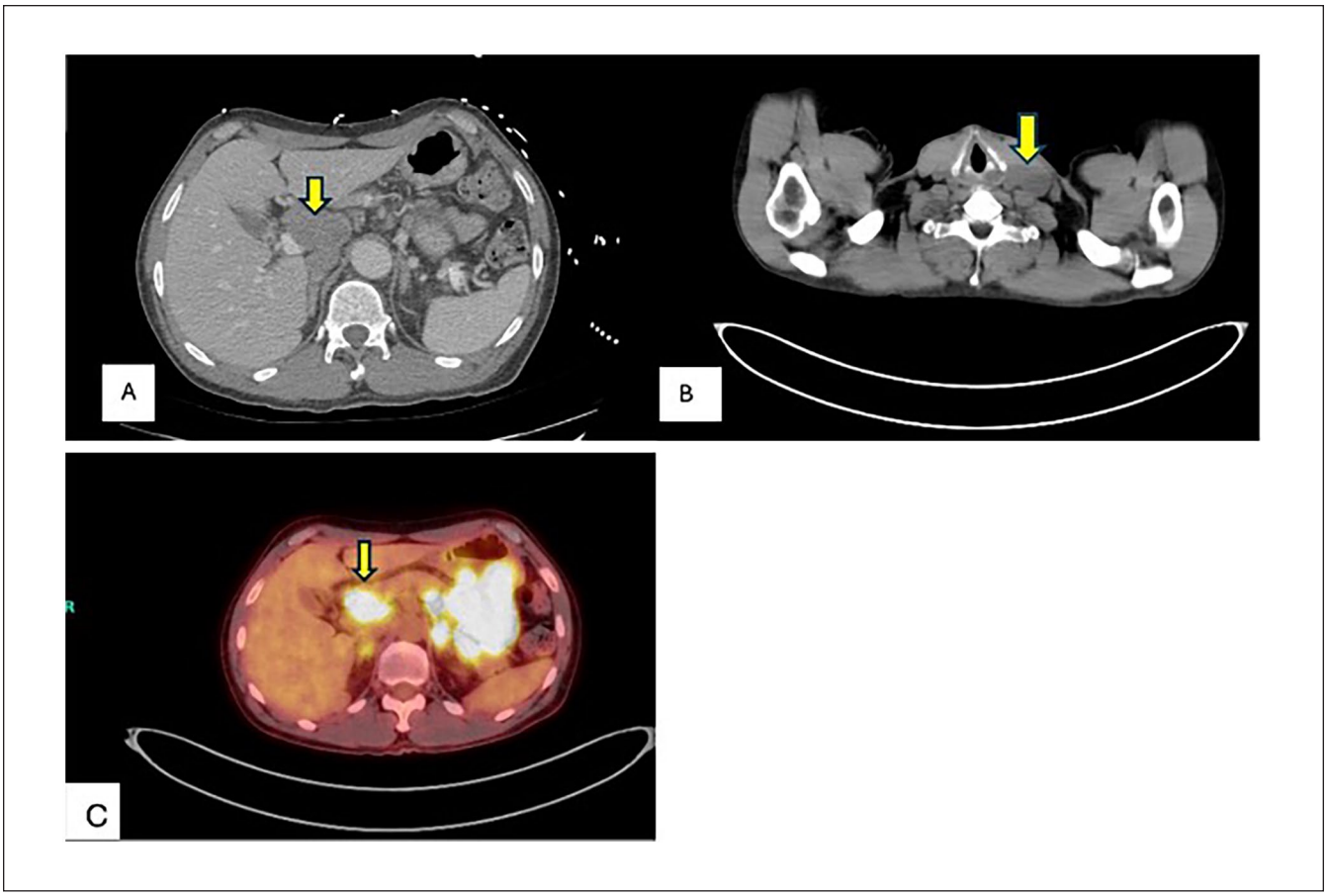

Figure 1. (A) Arrow pointing to 4.7 cm × 3.7 cm mass in the porta hepatis in CT scan. (B) Arrow pointing to low attenuation/cystic lesion in the base of the neck. (C) Hypermetabolic lymph nodes (arrow) seen in the peri gastric fat, porta hepatis, and mid to upper abdominal retroperitoneum.

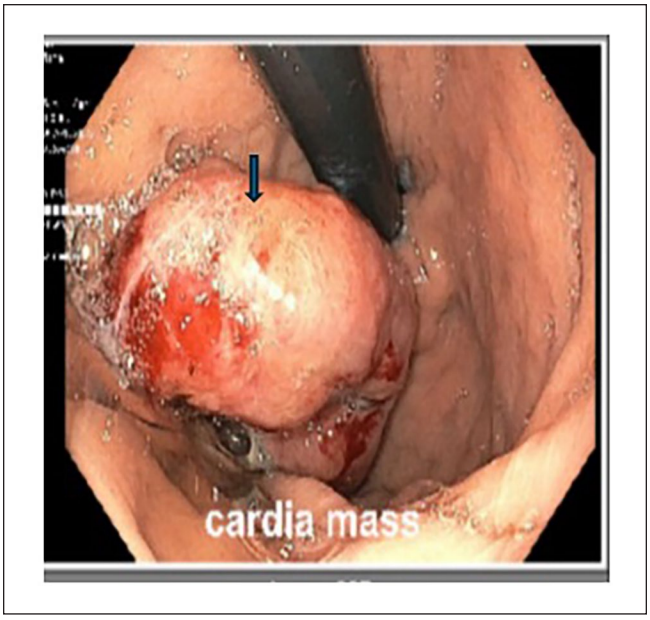

Figure 2. EGD showing gastric mass (arrow).

of the neoplastic B cells and no co-mutation on BCL2 or BCL6 were found. The neoplastic B cells are not immunoreactive to BCL-2, CyclinD1, CD5, CD43, CD30, and MUM-1. These immunophenotypes are consistent with atypical Burkett lymphoma with germinal center phenotype and c-MYC gene derangement. positron emission tomography (PET) scan done prior to initiation of therapy showed robust abnormal hypermetabolism associated with abnormal non-concentric mural thickening involving the posterior wall of the stomach corresponding to biopsy-proven lymphomatous involvement. Hypermetabolic lymph nodes were seen in the perigastric fat, porta hepatis, and mid-to-upper abdominal retroperitoneum (Figure 1A and C). Photogenic centrally hypodense and well-circumscribed structure in the posterior triangle of the left level II-IV neck was noted (Figure 1B). After discussion of the patient's case at the hospital's tumor board, his primary oncologist decided to treat with cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab (R-CHOP). A PET scan after 6 cycles of R-CHOP revealed marked interval decrease in the intensity and amount of hypermetabolic thickening of the stomach (Figure

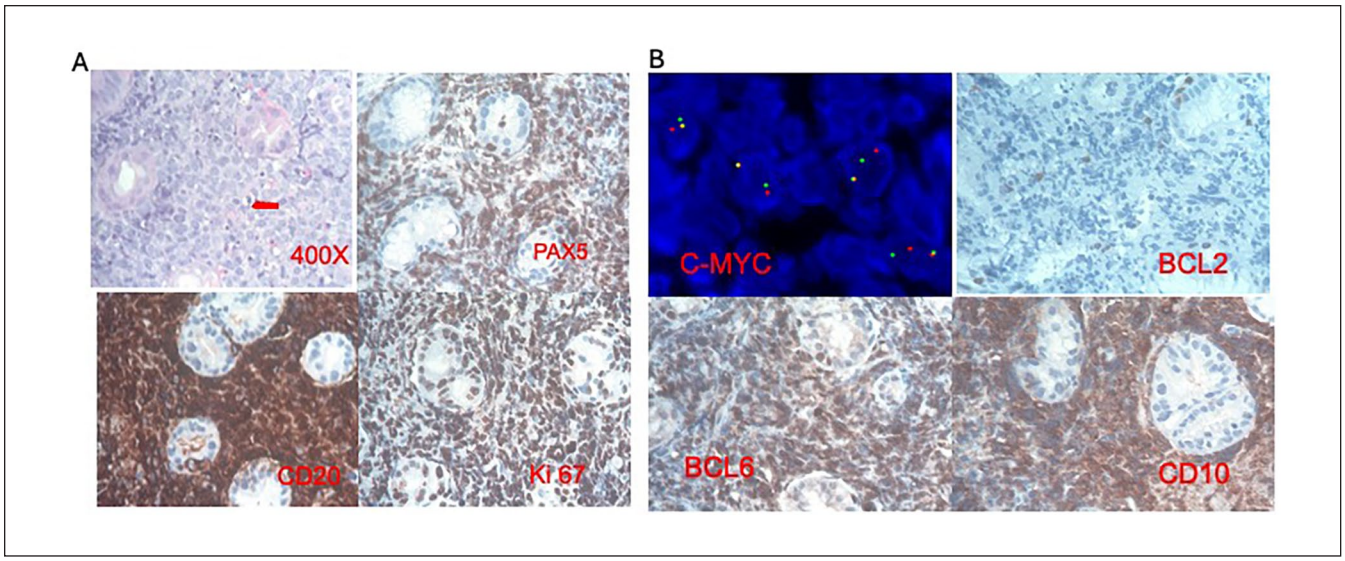

Figure 3. (A) Atypical Burkitt lymphoma of stomach: the intermediate-sized atypical lymphocytes (arrow) are infiltrated in the lamina propria of the gastric mucosa—showing a starry sky appearance. The lymphocytes are monotonous with mild nuclear pleomorphism (400×). The neoplastic cells are diffusely positive for B-cell markers (Pax5, CD20). The proliferative index of the neoplastic B-cells approach to approximately 100% stained by Ki67. (B) Atypical Burkitt lymphoma of stomach: 1 c-MYC gene breaks apart in approximately 48% neoplastic B cells. The neoplastic B cells (arrow) are not immunoreactive to BCL-2, CyclinD1, CD5, CD43, CD30, and MUM-1. The GC markers CD10 and BCL-6 are diffusely positive in the neoplastic cells. These immunophenotypes are consistent with atypical Burkett lymphoma.

4A and C). Interval resolution of the additional hypermetabolic foci in the abdominal and retroperitoneal lymph nodes was noted. The patient tolerated 6 cycles of R-CHOP very well with no significant adverse effects from the therapy, resolved B-symptoms, and significantly reduced neck swelling (Figure 4B).

Discussion

Three distinct clinical subtypes of BL are immunodeficiency-related, sporadic, and endemic.[2,5] The endemic form presents primarily as a jaw or facial bone tumor but may also frequently involve the ileum, cecum, ovaries, and breasts. Immunodeficiency-related Burkitt lymphoma typically presents with signs/symptoms related to the immunodeficiency and more likely to involve the lymph nodes, bone marrow and central nervous system.[5] The sporadic form may present with massive disease and ascites.[4] The sites commonly involved are the distal ileum, cecum, mesentery, kidneys, testis, ovary, breast, bone marrow, or central nervous system. Some cases may have jaw or facial bone involvement.

The morphology in classic BL demonstrates uniform, medium-sized cells with round nuclei similar to that of macrophages. They contain between 2 and 5 basophilic nuclei. A basophilic cytoplasm with multiple vacuoles can be demonstrated with Giemsa and Wright staining. The characteristic "starry sky pattern" is revealed due to the high mitotic rate. The hallmark feature of BL is the presence of a classic translocation between IgH and MYC genes (t8;14)(q24;q32).[2] Approximately 80% of cases demonstrate this translocation with variant translocations involving MYC and kappa with lamda in the remainder. Variant translocations involving MYC and the kappa light chain locus (2p11-12) or the lambda light chain locus (22q11)—specifically t(2;8)(p11-12; q24) or t(8;22)(q24; q11)—also lead to the activation of MYC.[23,24] It is well recognized that some cases of aggressive, mature B-cell non-Hodgkin's lymphoms exhibit morphologic features similar to Burkitt lymphoma, but with more variability in nuclear and cytoplasmic characteristics compared to typical Burkitt lymphoma. These cases also overlap with the morphologic spectrum of diffuse large B-cell lymphoma. Differentiating between these subtypes is challenging, with consensus among expert hematopathologists averaging only 53%.[25] In the 1994 Revised European American Lymphoma classification, aggressive mature B-cell non-Hodgkin's lymphomas that showed Burkitt-like morphology but did not possess all the characteristic immunophenotypic features of classic Burkitt lymphoma were classified as Burkitt-like lymphoma or atypical Burkitt lymphoma.[26] In the 2001 World Health Organization (WHO) classification, aggressive mature B-cell non-Hodgkin's lymphoma encompassed both Burkitt lymphoma and atypical Burkitt lymphoma/Burkitt-like lymphoma.[27] In our case, the morphology showed only focal areas with a typical starry sky appearance. In addition, there was the presence of a broken c-MYC gene and without showing rearrangement in BCL2 or BCL6 in 48% of the cells. These findings support the diagnosis of atypical Burkitt lymphoma or Burkitt-like lymphoma. The presence of classical Burkitt lymphoma germinal center markers, such as CD20+ and BCL6+, supported the diagnosis of atypical Burkitt

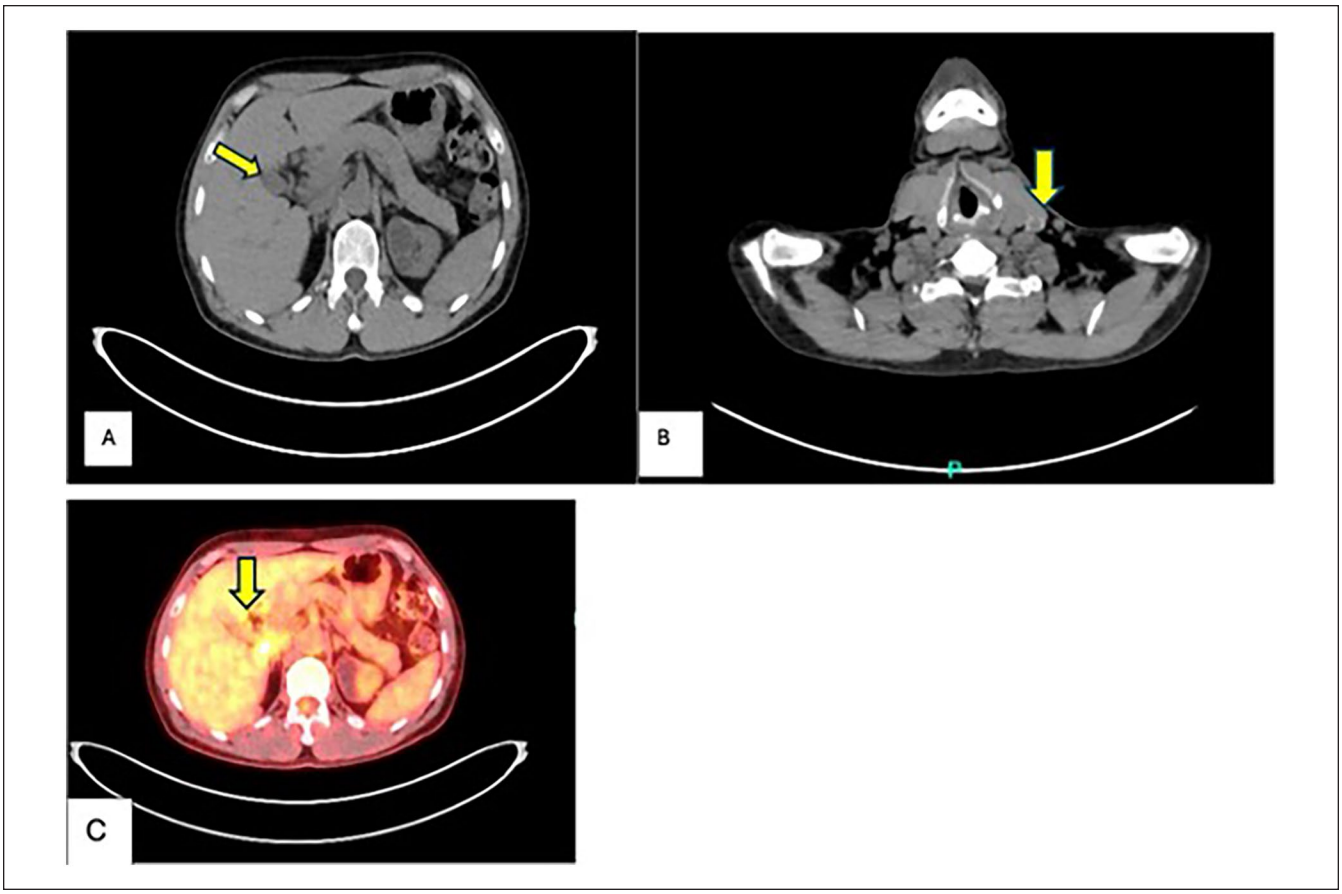

Figure 4. (A) Arrow pointing to posttreatment hepatic mass resolution in CT scan. (B) Arrow pointing to posttreatment interval decrease in the size of cystic lesion in the base of the left neck. There are new calcifications within this lesion. (C) Posttreatment PET (hypermetabolic lymph node resolution).

lymphoma/Burkitt-like lymphoma over diffuse large B-cell lymphoma or the provisional entity of B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma in the subsequent 2008 WHO classification.[28] Several studies have reported worse outcomes for atypical Burkitt lymphoma/Burkitt-Lymphoma subset after regimens typically used for diffuse large B-cell lymphoma, instead of short, intensive, multiagent regimens designed for Burkitt lymphoma.

Approximately 30% to 50% of extranodal non-Hodgkin lymphomas (NHLs) involve the gastrointestinal tract. Among these, gastric lymphomas are more prevalent than intestinal lymphomas, with diffuse large B-cell lymphoma being the most common, followed by low-grade marginal zone lymphoma of MALT type.[28,29]

Gastric Burkitt lymphoma is an extremely rare manifestation of Burkitt lymphoma, with data existing primarily in the form of case reports in the literature.[5,6-22] Large studies demonstrated no cases of gastric Burkitt lymphomas.[8] Table 1 showed the summary of reported cases of gastric Burkitt lymphoma, with their c-MYC gene rearrangements and treatment outcomes. Studies of the sporadic variant show an association with Epstein–Barr virus (EBV) in 20% of cases, although a causal relationship with gastrointestinal Burkitt lymphoma has not been well established. Some case studies have reported *H Pylori* as a causal factor of gastric Burkitt lymphoma with eradication therapy leading to complete remission.[10] As observed in our patient, *H Pylori* infection may have contributed to the pathogenesis of his disease.

Diagnosing Burkitt-like lymphoma can be difficult because the features of Burkitt lymphoma and diffuse large B-cell lymphoma can overlap. While Burkitt lymphoma can usually be distinguished morphologically from diffuse large B-cell lymphoma, some cases may show similarities and involve rearrangements of the MYC, BCL2, or BCL6 genes.[30] Some of these may represent an aggressive variant of diffuse large B-cell lymphoma that arises from transformation of an underlying follicular lymphoma or may also be known as double-hit lymphoma.[29,30] While MYC rearrangements may occur in other lymphomatous processes, such as diffuse large B-cell lymphoma (nearly 10% of cases), they are always present in Burkitt lymphoma.[2] The tumor cells in our patient, which histologically most closely resembled Burkitt lymphoma cells, present a significant challenge to pathologists and oncologists. This is because the cyclophosphamide, doxorubicin, vincristine, and

Table 1. Clinical Characteristics of Reported Cases of Gastric Burkitt Lymphoma.

A	B	C	D	E	F	G
No.	c-MYC	Age	Sex	Treatment	Outcome	Ref
1	Positive (no description)	52	Male	R-CODOX/ R-IVAC	Obstruct ion was resolved	5
2	Positive (no description)	61	Female	R-hyper CVAD/MA	CR	13
3	Positive for rearranged MYC gene	42	Male	dose-adjusted R-EPOCH	CR	14
4	Unknown	60	Female	Gastrectomy	Died	15
5	Unknown	21	Male	Cyclophosphamide, Vincristine, and Adriamycin	Gastric perforation	16
6	Unknown	39	Male	R-CHOP	Non-Hodgkin lymphoma, diffuse large B-cell lymphoma to BL, patient passed	17
7	IGH-MYC fusion	28	Male	Patient refused chemo treatment	Patient passed	18
8	Unknown	45	Male	Cyclophosphamide, Ifosfamide, Doxorubicin, Etoposide, Ara-C, Methotrexate, and Vincristine	CR	19
9	Unknown	42	Female	Cyclophosphamide, Adriamycin, Vincristine, rituximab	Gastric perforation	20
10	Unknown	56	Male	CEOP	CR	21
11	Unknown	52	Male	CODOX-M	CR	22
12	Unknown	76	Male	3 different protocols	Patient passed	23
13	Positive (no description)	46	Male	Unknown	Unknown	24
14	MYC gene locus rearrangement (not IgH/MYC)	59	Male	R-hyperCVAD	Patient passed	27

prednisone (R-CHOP) treatment protocol is inadequate for tumors with a Burkitt lymphoma-like behavior.[29] Furthermore, these aggressive variants are often associated with a poorer prognosis and require more intensive treatment.[29] The decision to treat is often decided based on clinician experience. We believe further diagnostic refinements are needed to arm clinicians with the tools necessary to select appropriate treatments. We agree with the findings of Nowakowski et al[19] that molecular characterization should take centerstage for personalization of therapy to achieve optimal efficacy outcomes. Patients whose tumors have features that more closely resemble Burkitt lymphoma are treated with an intensive, short-duration combination chemotherapy rituximab-cyclophosphamide and cytarabine, vincristine, doxorubicin, methotrexate (R-CODOX-M) whereas those that more closely resemble diffuse large B-cell lymphoma are treated with R-CHOP.[29,31,32]

Conclusion

Burkitt lymphoma (BL) and diffuse large B-cell lymphoma (DLBLC) are 2 different diseases that can be reliably diagnosed using established guidelines. However, there are cases that fall into the spectum in between BL and DLBCL which represents the real diagnostic challenge for clinicians. Despite frequent changes in the WHO guidelines for the classification of this continuum of diseases, uncertainties endure. A comprehensive evaluation of the patient's clinical presentation, histopathology, and cytogenetics is crucial for accurately diagnosing these lymphomas—particularly given the frequent updates to the diagnostic criteria. Further studies are also required for identifying the optimal treatment regimens for these patients.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics Approval

Ethics approval to report this case was obtained from Brookdale Hospital IRB Review Board.

Informed Consent

Written informed consent for patient information to be published in this article was obtained from the patient.

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