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Case Report

Primary Splenic Diffuse Large B-Cell Lymphoma: A Case Report and Literature Review of a Rare Condition

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Keywords

Primary splenic lymphoma · Diffuse large B-cell lymphoma of the spleen · Splenomegaly · Non-Hodgkin's lymphoma of the spleen · Lymphoma · Malignancy

Abstract

Introduction: Primary splenic lymphoma is a rare lymphoproliferative disorder that involves the spleen, exhibits diverse clinical presentations, and lacks a clear consensus in terms of management strategies. ***Case Presentation:*** We present the case of a 52-year-old patient with a complex medical history marked by multiple chronic medical conditions. The patient was diagnosed with primary splenic lymphoma, specifically the diffuse large B-cell subtype. Treatment for our patient involved a shortened course of chemotherapy (4 cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone [R-CHOP] followed by two doses of rituximab) due to issues related to compliance and treatment-related complications. This was followed by consolidative radiotherapy without resorting to splenectomy. ***Conclusion:*** Remarkably, despite using a shortened course of R-CHOP, the patient achieved complete resolution, and a positron emission tomography scan conducted at the end of the 6-month posttreatment period confirmed sustained complete remission.

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Introduction

The spleen can serve as the location for primary or secondary involvement by lymphomas, including Hodgkin's lymphoma and non-Hodgkin's lymphoma (NHL) [1]. The predominant type is often large-cell/immunoblastic lymphomas, followed by chronic lymphocytic leukemia/small lymphocytic lymphoma [2]. The clinical presentation and treatment options differ depending on the subtype. Historically, most cases involving the spleen, whether primary or secondary, were addressed through splenectomy. This was done either due to resistance to chemotherapy treatment or as a therapeutic splenectomy [3]. The authors have completed the CARE Checklist for this case report, which is attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000537780).

Case Presentation

Our patient is a 52-year-old heavy smoker with a known medical history of type 1 diabetes mellitus complicated by amputation of his left big toe (diabetic foot), diabetic nephropathy resulting in CKD stage III, hypertension, ischemic stroke in July 2021 with residual left-sided weakness, bronchial asthma, and schizophrenia diagnosed in 2011, with prolonged uncontrolled course with multiple recurrences, being off-treatment since his stroke in 2021. He presented in April 2022 with a 2-day history of fever and general fatigue with no other notable symptoms. Upon initial assessment, his vitals were within normal range, and his physical examination showed non-tender splenomegaly but no lymphadenopathy, while the rest of his physical examination was unremarkable.

Initial laboratory tests showed leucocytosis, normocytic anemia, with high lactate dehydrogenase (LDH) and C-reactive protein, with renal parameters similar to his baseline (summarized in Table 1). We assessed the patient with an abdomen ultrasound, which showed an enlarged spleen of 15 cm with a mixed iso-hypoechoic heterogeneous structure with internal vascularity measuring 11 × 7.6 cm. MRI of the abdomen showed an enlarged spleen, a 15-cm focal splenic lesion with peripheral diffusion restriction impressive of malignant neoplasm, showing peri-splenic and para-aortic lymph nodes (Fig. 1a).

NM whole-body FDG positron emission tomography (PET) CT on April 25, 2022, showed FDG-avid splenic mass lesion with regional hypermetabolic lymphadenopathy with no hepatic, bone marrow, or distal nodal involvement. The radiologic impression was lymphoma versus primary splenic malignancy (angiosarcoma) (Fig. 1b-i).

The patient underwent an ultrasound-guided splenic lesion biopsy in June 2022, which showed sheets of hypercellular lymphoid tissue (Fig. 1c) consisting of a dual population of aggregates of large lymphocytes of centroblast morphology and smaller lymphocytes of centrocyte morphology in the background. The immunohistochemical studies showed the following: positive reactivity in the centroblasts for CD20 (Fig. 1d), CD79b, and PAX5, which are B-cell markers; and positive reactivity for BCL6 (Fig. 1e) and CD10 (Fig. 1f), which are germinal center markers that are usually positive in diffuse large B-cell lymphoma (DLBCL) of the germinal center type.

The Ki-67 (Fig. 1g) rate, a proliferation index, is 60% (high), as is usually seen in high-grade lymphomas. He underwent a bone marrow examination, which showed cellular bone marrow with trilineage hematopoiesis and no evidence of lymphoma involvement.

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Table 1. Laboratory tests at initial presentation for the patient with primary splenic diffuse large B-cell lymphoma

	Value	Normal range
WBC, μL	29.7×10^3	$4–10 \times 10^3$
Hgb, g/dL	7	12–15
PLTs, μL	180×10^3	$150–400 \times 10^3$
Absolute neutrophils count, μL	24.3×10^3	$2–7 \times 10^3$
Absolute lymphocytes count, μL	3×10^3	$1–3 \times 10^3$
Urea, mmol/L	14.7	2.5–7.8
Creatinine, μmol/L	241	44–80
Sodium, mmol/L	137	133–146
Potassium, mmol/L	4.8	3.5–5.3
CRP, mg/L	231	0–5
LDH, U/L	544	135–225
Hepatitis C antibody	Negative	
HCV RNA PCR	Undetectable	
HBs antigen	Negative	
HBs antibody	Negative	
HBc antibody	Negative	
HIV P24\antibody combo test	Negative	

WBC, white blood cells; Hgb, hemoglobin; PLTs, platelets; CRP, C-reactive protein.

Thus, based on all the above, his lymphoma was stage II-S bulky disease. The team planned to give the patient four cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) with a reduced dose of vincristine based on neurological assessment.

His first and second cycles were given on June 23, 2022, and July 17, 2022, and both were complicated with hyperkalemia, which was managed medically. His third cycle went smoothly without complications, while the fourth cycle given on September 11, 2022, was complicated by acute kidney injury that improved with conservative measures.

Following the fourth cycle, the patient was admitted for right-hand cellulitis and superficial thrombophlebitis. Both were treated conservatively without complications of note. It should be noted that during the four cycles, the treating team had issues managing the patient's poor compliance, and the psychiatry consultation team followed him strictly during each cycle.

An interim whole-body PET CT on September 29, 2022, showed complete metabolic remission in the initial lymphoma manifestations (Fig. 1b-ii). The decision was made to de-escalate the therapy to single-agent rituximab for two doses following PET CT results due to complicated chemotherapy courses, poor compliance, and mental incapacitation.

Both doses of rituximab were given on October 18, 2022, and November 9, 2022, without complications of note. After the chemotherapy, the patient was referred for consolidation radiotherapy to splenic mass because of bulky disease at staging.

He received radiotherapy to the spleen and para-aortic lymph nodes, 30 GY in 15 fractions from December 6 till December 26, 2022 (rapid arc technique with daily cone-beam CT for treatment verification). At the end of treatment, NM whole-body FDG PET CT on May 13, 2023, showed complete metabolic remission: no pathologic uptake was seen as in the initial scan (Fig. 1b-iii).

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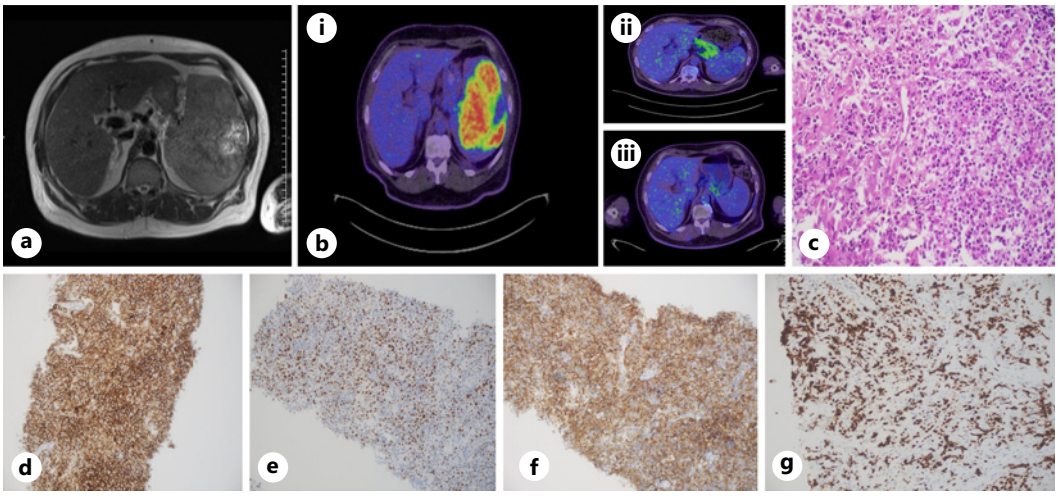

Fig. 1. a Initial MRI of the abdomen. **b-i** Whole-body FDG PET CT. **b-ii** Interim NM whole-body PET CT. **b-iii** End of treatment, NM whole-body FDG PET CT. **c** Hypercellular lymphoid tissue (large lymphocytes and centroblasts). **d** Abnormal B lymphocytes showed strong positivity with CD20 at 20X power field. **e** Positive BCL6 at 20X power field. **f** Positive CD10 at 20X power field. **g** A KI-67 index: 60%.

Discussion

Splenomegaly is considered a common finding on clinical examination and radiologic studies of the abdomen, with a wide range of causes that include but are not limited to infections, infiltrative processes, hyperfunctioning spleen, extramedullary hematopoiesis, portal hypertension, and finally malignancies [4]. Malignancies involving the spleen are usually categorized into primary or metastatic neoplasms, with the majority being primary, while metastatic lesions are identified less frequently [5].

However, one study by Pugalenthi et al. [6] showed that splenic lesions found on examination of splenectomy specimens were malignant in 63% of the patients, with 66% being metastatic from other locations within the abdomen. Furthermore, primary splenic neoplasms can be divided into hematologic and rarely non-hematologic origin, like angiosarcoma and primary mesenchymal splenic malignancies [5].

Hematologic malignancies of the spleen can be subdivided into lymphoid and non-lymphoid. While the involvement of the spleen by lymphoid malignancies is common, a true definition of primary splenic lymphoma (PSL) is still controversial. On the one hand, some authors like Dasgupta et al. [7] advocated that true PSL is a lymphoma involving only the spleen with adjacent splenic lymph nodes and that a 6-month disease-free period should be established postsplenectomy. In contrast, other authors like Kehoe and Straus [8] were less stringent in diagnosing PSL by not requiring a survival-free period postsplenectomy.

PSL constitutes a subtype of NHL. It is considered rare, especially the subtype of DLBCL, which was reported to be around 1% of all NHL in previous studies [9]. In a review by Byrd et al. [10] examining the database for diagnosis of early-stage PSL DLBCL between 1973 and 2013, most identified patients were male Caucasians with similar diagnosis rates before and after the rituximab era.

One interesting association noted by Shimono et al. [11] was the higher detection rate of hepatitis C virus (HCV) from splenic samples for patients with PSL DLBCL in comparison to samples from lymph nodes of patients with non-splenic primary DLBCL, which could support the role of HCV in PSL. Our patient had negative HCV serology and negative HCV PCR.

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The clinical presentation of PSL varies from asymptomatic or incidentally discovered splenic masses found on imaging to more rare forms of presentations like splenic abscess [12] and ascites [13], in which PSL should be considered a differential. Bairey et al. [14] described PSL DLBCL's most common presentation features, which included mainly abdominal pain and splenic mass associated with high LDH levels.

Our patient presented with classical B-symptoms of fever and night sweats and was found to have an abdominal mass that turned out to be a non-tender splenomegaly. His laboratory tests were impressive for high LDH with a presentation value of 544 U\L.

To confirm the diagnosis of splenic lymphoid malignancies, splenectomy was considered indispensable [15]. However, due to its invasive nature, the noted morbidity and mortality (reported as 12% and around 1%, respectively) [16], more authors are advocating for ultrasound-guided core needle biopsies of splenic lesions [17] as it can be accurate in providing adequate tissue samples for histologic confirmation (accuracy reaching up to 90%) and at the same time being a safe overall option with minor and major complications rates of 1.9 and 0%, respectively [18].

The available literature showed that the most used chemotherapy regimen for PSL\DLBLC patients was similar to non-splenic DLBCL, which was based mainly on R-CHOP or polatuzumab R-CHP [19]. In this case, we report our experience in treating a patient diagnosed with stage II-S bulky DLBCL with a shortened course of R-CHOP (4 cycles) followed by a single agent of rituximab, with the rationale being that the patient had compliance issues due to his underlying psychiatry comorbid, in addition to chemotherapy-related complications (acute kidney injury and electrolytes disturbances).

Despite this, the patient showed great response and complete resolution by the time the end of treatment PET scan was carried out. This type of good clinical outcome, as measured by the end of treatment PET at 6-month intervals posttreatment, can be an encouraging sign to consider shorter courses of chemotherapy as it will be difficult to follow the standard six cycles of chemotherapy in some patients, whether it is due to treatment-related complications or in some unique circumstances, the challenging noncompliance that arise from handling of complex patients like patients with active underlying psychiatric illnesses as in our case.

Recent clinical trials examined the possibility of using a shorter course of R-CHOP therapy. In the FLYER clinical trial reported by Poeschel et al. [20], they used a regimen of four cycles of R-CHOP followed by two doses of rituximab as a single agent. The included patients were localized and non-bulky DLBCL with PS 0-1, normal LDH value, and aged 18–60 years.

This study showed the non-inferiority of this regimen to the standard six cycles of R-CHOP that were used in the control arm, with 3-year event-free survival reaching up to 89% in the treatment arm, similar to the control arm. Furthermore, patients in this trial who were in the treatment arm (four cycles R-CHOP) had fewer hematologic and non-hematologic adverse outcomes such as infections, which indicates a better safety profile.

Our patient was treated with four cycles of R-CHOP followed by two doses of rituximab as in the FLYER trial. As illustrated above, splenectomy has long been a cornerstone in diagnosing and managing PSL [21]. The importance of splenectomy is advocated for as a combination with chemotherapy as it achieved better outcomes in terms of cancer-specific survival and overall survival, as in the study done by Yonghao et al. [22] compared to either splenectomy or chemotherapy alone.

In our case, our patient did not undergo splenectomy as he was refusing invasive surgical options. While the role of post-chemotherapy consolidative radiotherapy as a first-line treatment is not well defined in primary splenic DLBCL, it was traditionally considered

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for patients with advanced nodal or extra-nodal DLBCL (stages III-IV) [23] or for patients with residual masses post-chemotherapy [24] with improved survival outcomes in both studies examined populations. In our patient's case, we referred him to radiotherapy despite his stage being II because he had bulky disease.

Conclusion

The use of a shortened chemotherapy option followed by consolidative radiotherapy could be a potentially less invasive, safer all-around option for patients with PSL who have complex chronic medical conditions that increase their risk for treatment-related side effects or have, in some cases, factors that limit their ability to adhere to treatment like schizophrenia or other psychiatric conditions. However, further studies are needed to confirm these findings.

Statement of Ethics

The Hamad Medical Corporation's Medical Research Centre approved the case report under the number MRC-04-23-583. Written informed consent was obtained from the patient to publish this case report and any accompanying images.

Conflict of Interest Statement

On behalf of all authors, the corresponding author states that there is no financial or nonfinancial conflict of interest to be declared.

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Author Contributions

Mohammed Najdat Seijari: manuscript writing, literature review, final manuscript approval, and corresponding author. Samer Kaspo: history and physical, manuscript writing and editing, case identification and conceptualization, and literature review. Amro Elfaieg: manuscript writing and editing. Awni Alshurafa: history and physical examination and case follow-up. Sarah A. Elkourashy: case selection, case identification and conceptualization, obtaining informed written consent, prescribing medicine, and clinical follow-up.

Data Availability Statement

The article and supporting materials include data supporting this study. Further inquiries can be directed to the corresponding author if needed.

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