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Case Report

Unusual Bilateral Adrenal Tumors: Primary Adrenal Diffuse Large B-cell Lymphoma

Ya-Lun Ke[1]*, Jui-Feng Hsu[2], Yu-Ching Wei[3,4], Hui-Hua Hsiao[1]

[1]Division of Hematology and Oncology Medicine, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan
[2]Division of Hematology and Oncology Medicine, Department of Internal Medicine, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan
[3]Division of Pathology, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan
[4]Division of Pathology, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan

Abstract

Primary adrenal non-Hodgkin lymphoma is an extremely rare disease confined wholly or chiefly to extranodal involvement. We report the case of an old woman who presented with progressive malaise and was diagnosed with primary adrenal diffuse large B-cell lymphoma pathology using laparoscopic adrenalectomy. Enhanced computed tomography and positron emission tomography revealed bilateral adrenal involvement.

Keywords: Adrenal insufficiency, diffuse large B-cell lymphoma, primary adrenal lymphoma

Introduction

Involvement of the adrenal gland in lymphoma is uncommon. Furthermore, primary adrenal lymphoma (PAL) is also rare, accounting for <1% of all non-Hodgkin's lymphomas and 3% of primary extranodal lymphomas.[1] Because of its rarity, the clinical and pathologic features and therapeutic options of PAL are undefined. Moreover, PAL does not have a strict definition, and it is difficult to determine whether an adrenal lymphoma is truly primary or merely a local manifestation of a generalized disease.[2,3] Hence, we discuss a case with bilateral adrenal diffuse large B-cell lymphomas (DLBCLs) treated with systemic chemotherapy. Ethical approval for this study was obtained from our hospital, and we informed both the patient and her family regarding this study and obtained their written informed consent (IRB number: KMUHIRB-E(I)-20200303).

Case Report

A 79-year-old woman with hypertension, optic nerve stroke, and traumatic subarachnoid hemorrhage without obvious sequelae was brought to the emergency department (ED) of our hospital with complaints of progressive malaise and anorexia for several months. She was able to walk without assistance but needed some rest. Intermittent fever up to 38.9°C was noted at the ED,

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Address for correspondence: Dr. Ya-Lun Ke, Division of Hematology and Oncology Medicine, Department of Internal Medicine, Kaohsiung Medical University Hospital, No.100, Tzyou 1st Rd., Sanmin Dist., Kaohsiung City 80756, Taiwan.
E-mail: a9601082@gmail.com

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but neither vomiting nor diarrhea was observed. Her physical examination otherwise showed unremarkable results. Laboratory results showed no abnormalities, except for leukocytosis (16,040/μL), elevated C-reactive protein (73.8 mg/L), and increased lactate dehydrogenase (LDH, 317 IU/L). Enhanced abdominal computed tomography (CT) revealed bilateral adrenal gland tumors (left predominant, 6.3 cm) and established hypodense masses [Figure 1], and she was admitted to the infection ward for further evaluation.

Antibiotics were then prescribed for a suspected intra-abdominal infection. Further laboratory surveys showed a normal metabolic profile, including cortisol (21 μg/dL), plasma renin activity (4.08 ng/mL/h), aldosterone (10.88 ng/dL), and vanillylmandelic acid (5.71 mg/day). Furthermore, levels of the tumor markers CA 19-9 (<0.8 U/mL), CA 125 (8.5 U/mL), and chromogranin A (38.2 ng/mL) were normal.

Laparoscopic left adrenalectomy was performed, and the pathology results revealed DLBCL, non-germinal center (non-GC) subtype, with immunohistochemical (IHC) staining results positive for CD20, BCL2, BCL6, MUM1, and Ki67 [Figure 2] and negative for cMYC, CD3, CD10, and cytokeratin. We determined whether the Epstein–Barr virus (EBV) was present using serum Epstein–Barr virus capsid antigen IgG (EB-VCA IgG), and the result was positive. Positron emission tomography was compatible with the clinical diagnosis of DLBCL and high-uptake lesions, involving bilateral adrenal glands and intra-abdominal lymph nodes, in stage IV disease [Figure 3]. A bone marrow examination showed no evidence of malignant involvement. Therefore, the patient was given systemic chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP). Follow-up CT revealed an interval decrease in the lymphoma size involving the right adrenal gland after four cycles of R-CHOP.

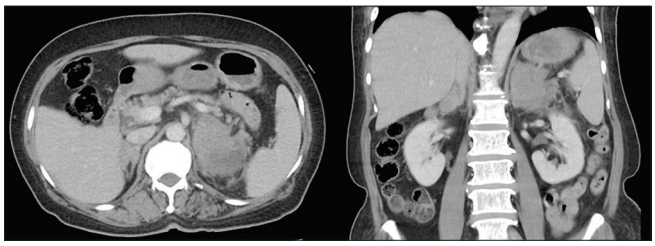

Figure 1: Enhanced abdominal computed tomography showing hypodense bilateral adrenal gland tumors (arrow) with left predominance (6.3 cm)

Discussion

PAL is extremely rare, with fewer than 200 cases in the English literature,[1] and the most common PAL is non-Hodgkin's lymphoma, especially the non-GC subtype of DLBCL.[2,3] DLBCL is predominant in men and elderly individuals and is mostly bilateral.[2,3] The most common clinical manifestations are B symptoms, pain, and fatigue, and only a few cases are found incidentally.[2,3] Elevated LDH is related to bilaterality.[3] Furthermore, PAL with adrenal insufficiency and a significant association with bilateral adrenal involvement have been reported in previous reviews.[2,3] In contrast, the incidence of adrenal insufficiency is low in other adrenal tumors.[2] Generally, destruction of at least 90% of the adrenal parenchyma is required for adrenal insufficiency presentation.[2,4,5] However, even a small PAL can result in adrenal insufficiency.[2] In fact, 60%–70% of the patients with adrenal lymphoma present with biochemical or clinical adrenal insufficiency, irrespective of tumor size.[5] Alterations of the adrenal gland microenvironment are assumed to be caused by cytokines secreted by lymphoma cells.[2,4] Immune dysfunction, EBV infection, and mutations in *p53* and *c-kit* genes have been implicated in the pathogenesis.[3,5] In our case, the patient was diagnosed with primary bilateral non-GC DLBCL and presented with positive serum EB-VCA IgG, progressive malaise, and increased LDH. However, she had a normal cortisol level, and no evidence of adrenal insufficiency was indicated.

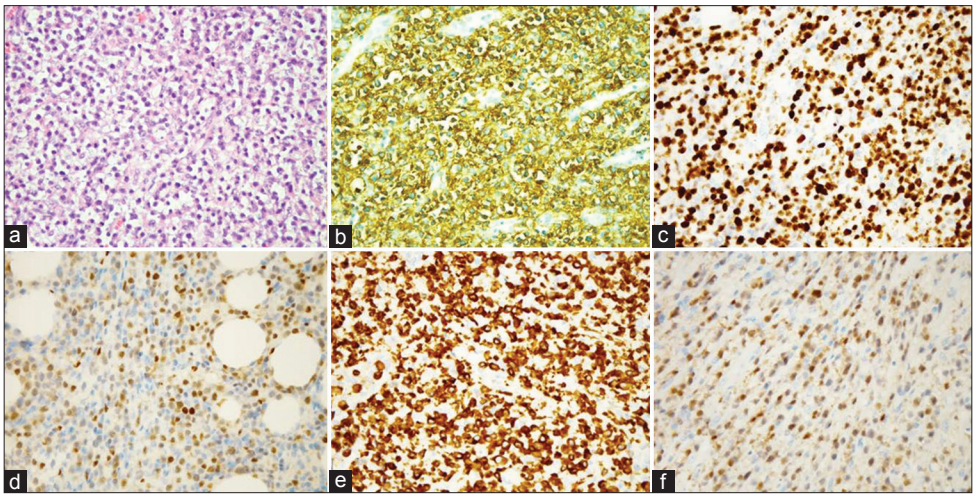

Figure 2: (a) Tumor specimen characterized by predominantly large cell size, vesicular nuclei, and prominent nucleoli (×400). positive expressions of (b) CD20; (c) Ki-67, 85%; (d) Bcl-6; (e) Bcl-2; and (f) MUM1 (IHC, ×400)

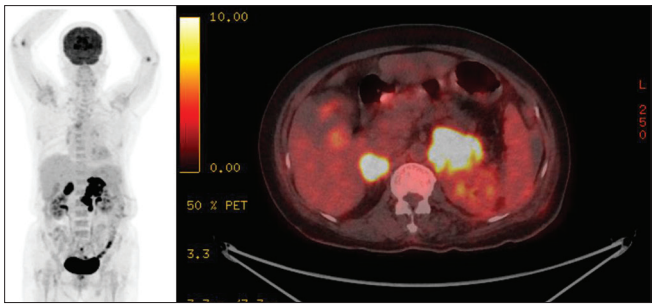

Figure 3: Positron emission tomography revealed high fluorodeoxyglucose uptake over bilateral adrenal tumors

According to imaging findings described in a previous review, PAL is a metabolically hyperactive, hypovascular tumor presenting as hypoechoic heterogeneous masses on ultrasound, with predominantly low-density and slight-to-moderate enhancement on CT.[3] Magnetic resonance imaging findings are characterized by low-signal intensity on T1 and high-signal intensity on T2.[3,5]

The staging system for PAL is not conclusive. The Ann Arbor Staging System may not be suitable for this condition because neither high-risk international prognostic index score nor advanced-stage disease in this system has any effect on overall survival.[1,6] Hence, the modified Lugano staging system for gastrointestinal lymphoma, which results in significantly improved predictability of overall survival, has been considered.[4,6]

Optimal treatment of primary adrenal DLBCL is currently open to debate.[6] The R-CHOP regimen is by far the most commonly administered chemotherapy protocol.[6-8] According to previous reports, advanced stage, large tumor size, adrenal insufficiency, bilateral adrenal involvement, and increased LDH are related to a poor prognosis in PAL.[5-8] Unexpectedly, no difference has been observed in overall survival between unilateral and bilateral involvement.[9] In addition, no significant benefit has been noted in patients who undergo adrenalectomy compared to those who are treated with chemotherapy alone. Nevertheless, the prognosis of primary adrenal DLBCL remains poor.[1,6,9]

In conclusion, we presented a rare case of bilateral PAL without adrenal insufficiency after laparoscopic left adrenalectomy. Because of its rarity, the appropriate staging system and optimal management are inconclusive. Consequently, further investigations and assessments are warranted.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initial will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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