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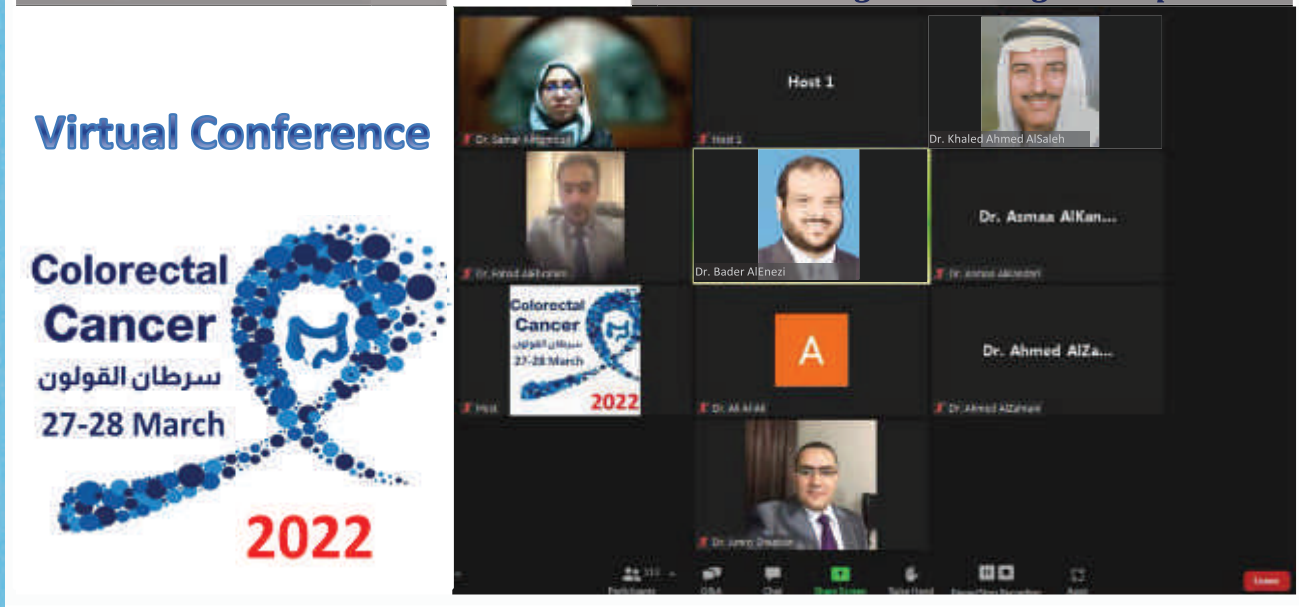

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Table of Contents

Original Articles

Review Article

Case Reports

Conference Highlights/Scientific Contributions

Case Report

Bilateral Primary Adrenal B–Cell Lymphoma Diagnosed by Workup for Primary Adrenal Deficiency

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Abstract

Primary adrenal lymphoma (PAL) often occurs bilaterally and is a rare malignancy of old age. Workup for primary adrenal insufficiency often unmasks this underlying grave pathology. In this article, we present a case of a 73–year–old patient who presented with features of primary adrenal insufficiency and renal colic. Diagnostic abdominal imaging revealed bilateral suprarenal masses as the cause of adrenal gland destruction and the patient's symptoms. FDG PET–CT scan and histopathology confirmed the diagnosis of mature bilateral B–cell primary adrenal lymphomas. Though the patient showed an excellent initial response to the first four chemotherapy cycles, a relapse resulted in metastatic disease. This article highlights the PAL's disease course, imaging features, and management dilemma due to Chemotherapy's side effects and a higher recurrence rate.

Keywords: Primary adrenal lymphoma, Primary adrenal insufficiency, R–CHOP, Role of imaging.

Introduction

Adrenal involvement by lymphoma can rarely present with manifestations of decreased adrenal functions. Primary adrenal lymphoma (PAL) is rare (1–5% of lymphomas) malignancy with fewer than two hundred reported cases in the literature.(1) In 70% of the cases, PAL is bilateral and depicts a poor prognosis despite an excellent initial response to Chemotherapy.(2) Radiologic evaluation to exclude any extra–adrenal lesions and diagnosis confirmation by histopathology is mandatory before initiating the Chemotherapy.(3) This article presents a 73–year–old patient who was incidentally diagnosed with bilateral primary adrenal lymphoma during the workup for abdominal pain and primary adrenal insufficiency

Case Presentation

A 73–year–old male patient presented to the emergency department with right flank pain for the last two months. His past medical history was significant for type II diabetes mellitus. Initially, the pain was mild to moderate in intensity and was relieved with oral analgesics. One week before the presentation, the pain became severe. However, it didn't radiate, and no aggravating or relieving factors were identified. The pain was also associated with nausea, loss of appetite, and a marked weight loss of thirteen kilograms in two months. His vitals were within normal limits; however, bilateral lumber masses were palpable, requiring further radiological investigations. Laboratory tests showed a high ESR of 80 along with primary adrenal insufficiency (hydrocortisone was started as a replacement therapy).

Ultrasound abdomen showed hypoechoic masses in the bilateral adrenal areas with internal vascularity on color Doppler (Figure 1). Nevertheless, there were no obstructing stones. A contrast–enhanced CT of the thorax,

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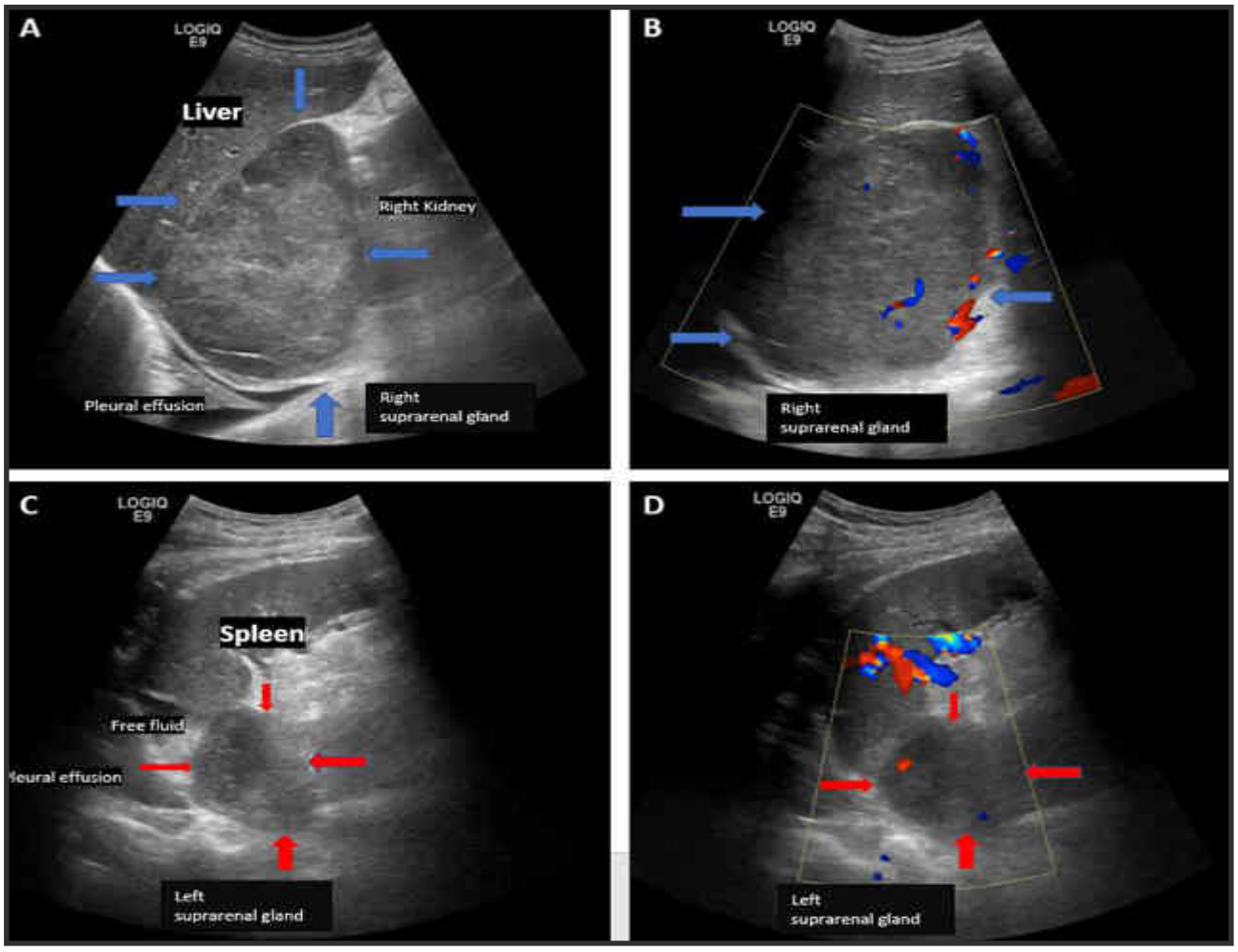

Figure 1: Ultrasound abdomen

A&B: A large heterogeneously hypoechoic mass (blue arrows) in the right suprarenal region with internal vascularity with some degree of indentations on the liver. **C&D:** A heterogeneously hypoechoic mass (red arrows) in the left suprarenal area showing internal vascularity.

abdomen, and pelvis demonstrated two large, hyper vascularized masses replacing the adrenal glands with patchy enhancement (Figure 2). These adrenal masses were indenting and displacing the surrounding structures without any definite infiltration. Furthermore, there were no focal lesions in the abdominal and pelvic viscera or any regional or retroperitoneal lymphadenopathy. These findings suggested an absence of metastasis or other visceral organs' primary malignancy.

The multidisciplinary team decided to proceed with a CT–guided trucut adrenal biopsy to confirm the diagnosis. Analysis of the biopsied tissues by flow cytometry showed a population of monotypic B–cells comprising approximately 28%, showing high light side scatter and expressed CD45, CD19, CD20, FMC7, CD79b, CD38 (partial) with kappa light chain restriction. This monotypic population showed no significant expression of CD5, CD10, CD23, CD34, TdT, or CD200. These findings were suggestive of mature B–cell primary adrenal lymphomas bilaterally (activated type). As a part of staging, the patient underwent an FDG–PET CT scan that revealed an intense uptake by bilateral adrenal masses with an evidence of involvement of renal fascia alongside retrocaval and para–aortic lymph nodes (Figure 3A). Hematology and oncology teams agreed on three weekly R–CHOP (R: rituximab, C: cyclophosphamide, H: doxorubicin, O: vincristine sulfate, also known as oncovin, P: prednisone) therapy and CNS prophylaxis by intrathecal injection of methotrexate.

After four cycles, a significant decrease in the size of masses was seen with a resolution of metabolic activity in the renal fascia and lymph nodes (Figure 3B & 3C). Unfortunately, an echocardiogram showed a significant decrease in ejection fraction from the baseline of 63% to 47%. Further, two cycles were considered with a 50% reduced dose of doxorubicin. A repeated contrast–enhanced CT scan of the thorax, abdomen, and pelvis revealed infiltration of the lymphomatous material in both kidneys, liver, retroperitoneal lymph nodes, and head of the pancreas. Ultimately, the patient developed urosepsis and severe septic shock, progressing to multi–organ failure and death.

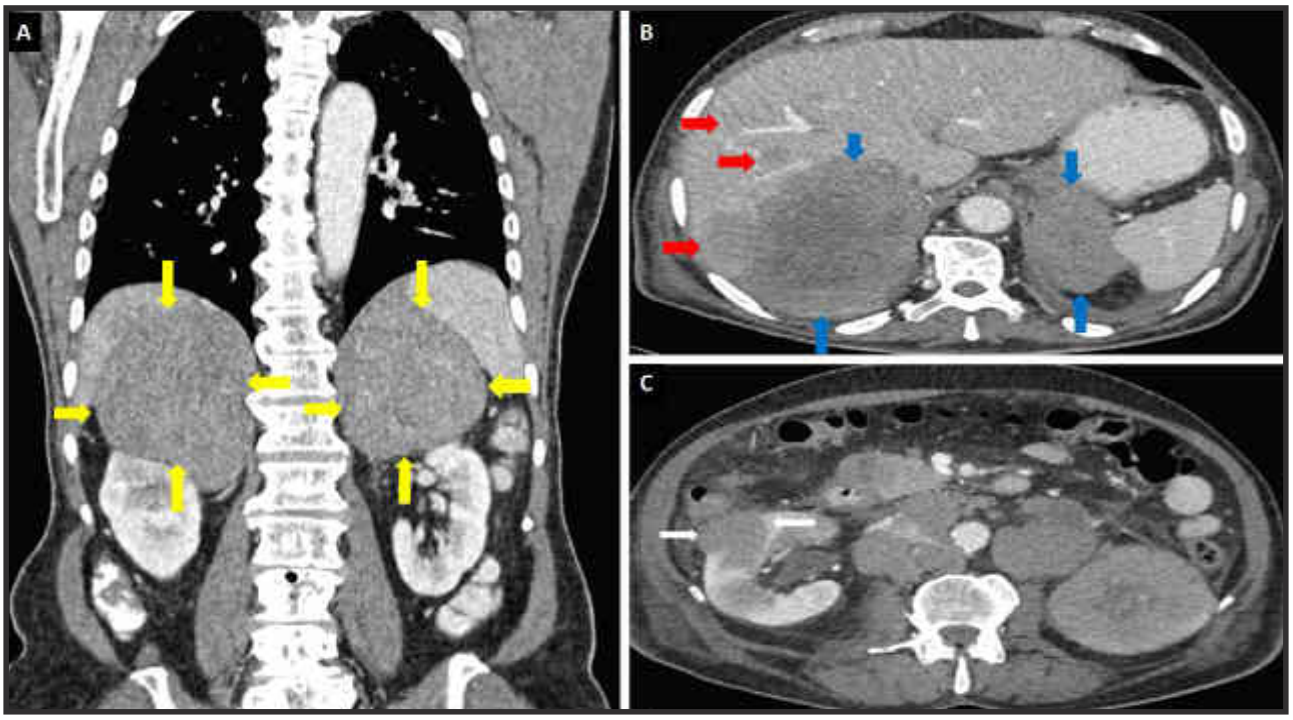

Figure 2: CT scan abdomen and pelvis with intravenous contrast (venous acquisition phase)

A: A selected coronal section of the CT scan, done before starting the Chemotherapy. It demonstrates large, slightly enhancing bilateral suprarenal masses with no definite infiltration of the kidneys. **B & C:** Selected axial sections of the CT scan of the upper abdomen done after six sessions of Chemotherapy. They demonstrate relapse of the bilateral suprarenal masses with internal necrosis (blue arrows). They also delineate metastatic multiple hypodense lesions in the liver (red arrows) and right kidney (white arrows).

Figure 3: Whole Body FDG PET–CT Scan

A: Bilateral large suprarenal masses are completely replacing adrenal glands and showing avid FDG uptake. **B & C:** Post–chemotherapy reduction in the size of the tumors; however, the uptake is still comparable to the pre–chemotherapy images.
Abbreviations: FDG: fluorodeoxyglucose, PET: positron emission tomography, CT: computed tomography.

Discussion

Due to the rich blood supply, metastasis to the adrenal glands is usually seen in clinical practice. The most common origin of adrenal metastasis is breast, lung, kidneys, melanoma, and malignant colonic tumors.[4] Even though the adrenal glands are devoid of any lymphoid tissue, bilateral primary adrenal lymphomas are identified in less than 1% of the Non–Hodgkin lymphomas.[5] Diffuse large B cell lymphoma is the most commonly identified lymphoproliferative neoplasm involving the adrenal glands.[6] PAL is a malignancy of old age with an average age of 70 years at diagnosis. It is more prevalent in males with a male to female ratio of 7:1.[7]

The pathogenesis of PAL is still unclear. However, literature has suggested the association of PAL with autoimmune adrenalitis and viral infections like Epstein Barr virus & JC virus.[8,9] The diagnosis can be challenging because of the vague and non–specific clinical manifestations. Almost 50 to 70% of patients with PAL present with clinical or biochemical manifestations of primary adrenal insufficiency.[10] Usually, the tumor size does not correlate with the degree of adrenal insufficiency.[11] However, the patients exhibit features of adrenal insufficiency when more than 90% of the adrenal glands are already destroyed.[12] Typical clinical manifestations of PAL include abdominal pain, fever, weight loss, hypercalcemia, thrombocytopenia, and adrenal insufficiency.[5] Pathmanathan et al. described that adrenal lymphomas could be large enough to irritate the diaphragm, and the patients can present with intractable hiccups.[13]

A high index of suspicion is required for diagnosis, along with thorough history, physical examination, and biochemical studies. Steroid replacement should be started once adrenal insufficiency is identified to avoid unwanted consequences.[7] CT scan is the initial study of choice. Heterogenous masses >4 cm are suggestive of malignancy.[14] MRI features of lymphoma on the T1–weighted sequence include signal intensity lower than the liver, while on T2–weighted sequences, they appear heterogeneously hyperintense.[15] Histopathological immunohistochemical analysis is required for definitive diagnosis and planning therapy. For this purpose, a biopsy is performed with CT or ultrasound guidance.[4]

Prognosis is generally poor for primary adrenal lymphoma, with the reported 1–year survival rate of about 17.5%, and median survival is about 13 months.[6,16] Chemotherapy is the mainstay of treatment, with the R–CHOP regimen being associated with overall survival rates above 50% at 2–year follow–up.[17] Large Tumor size, advanced age, LDH levels, and adrenal insufficiency are a few of the poor prognostic features.[18]

Conclusion

Primary adrenal lymphoma is a rare malignancy that often presents late in the disease course with vague clinical symptoms and features of adrenal insufficiency. Keeping a low threshold to request abdominal imaging can help in the incidental diagnosis at an early stage and might have better outcomes. An avid FDG uptake on PET–CT has good sensitivity and specificity for the diagnosis. Initial response to Chemotherapy is excellent; however, relapse with metastasis is common and results in morbidity and mortality.

Funding and Conflict of Interest

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