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Atypical presentation of primary adrenal lymphoma with adrenal insufficiency and hypercalcemia in an elderly male: A diagnostic and therapeutic challenge

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Abstract

Background: Primary Adrenal Lymphoma (PAL) is an exceedingly rare form of extra nodal lymphoma that mostly targets the adrenal glands, frequently manifesting with nonspecific symptoms that may result in a postponed diagnosis. PAL may present with adrenal insufficiency, mass effect, and metabolic disturbances such as hypercalcemia, potentially resembling other prevalent adrenal disorders.

Case presentation: We present a case of a 68-year-old male with nonspecific fatigue, weight loss, nausea, and hyperpigmentation. Preliminary laboratory assessments indicated adrenal insufficiency and hypercalcemia. Imaging scans revealed bilateral adrenal masses. A biopsy verified diffuse large B-cell lymphoma (DLBCL) of the adrenal glands, thereby establishing the diagnosis of Primary Adrenal Lymphoma. The patient had chemotherapy and hydrocortisone replacement treatment.

Conclusion: Primary Adrenal Lymphoma must be included in the differential diagnosis of adrenal tumors associated with adrenal insufficiency and hypercalcemia. Timely identification and immediate intervention with chemotherapy and steroid replacement are crucial for enhancing outcomes.

Keywords: Primary adrenal lymphoma; Adrenal insufficiency; Hypercalcemia; Bilateral adrenal masses; Diffuse large B-cell lymphoma; Endocrine emergencies.

Introduction

Primary Adrenal Lymphoma (PAL) is an uncommon variant of extra nodal Non-Hodgkin Lymphoma (NHL), constituting less than 1% of all NHL instances. It primarily impacts elderly males and frequently manifests with nonspecific symptoms, complicating prompt detection [1,2]. The clinical manifestations of PAL differ according on the degree of adrenal involvement and may encompass adrenal insufficiency, stomach pain, and symptoms related to mass effect. PAL may additionally manifest with metabolic irregularities, in-

cluding hypercalcemia, thereby confounding the diagnosis [3]. Due to its infrequency and shared clinical characteristics with other adrenal conditions, such as primary adrenal cancer, metastasis, and infectious adrenalitis, PAL presents a diagnostic challenge [4]. This case report details an uncommon instance of Primary Adrenal Lymphoma (PAL) in an older individual with adrenal insufficiency and hypercalcemia, emphasizing the diagnostic difficulties and the necessity of a multidisciplinary therapy strategy.

Case Presentation

A 68-year-old male with an unremarkable medical history reported to the outpatient clinic with complaints of nonspecific fatigue, unintended weight loss of 10 kg over three months, nausea, vomiting, anorexia, and gradual skin hyperpigmentation. The patient indicated a reduction in appetite and a pervasive sense of weakness, however refuted the presence of fever, stomach discomfort, or night sweats. No prior history of TB, malignancy, or recent infections was documented.

Vital signs and examination: Upon examination, the patient exhibited signs of weakness and dehydration, accompanied by significant darkening of the oral mucosa and palmar creases.

Vital signs recorded were: Blood pressure 85/60 mmHg, heart rate 92 bpm, temperature 36.8°C, respiration rate 18 breaths per minute, and oxygen saturation 96% on ambient air. The abdominal examination revealed no notable findings, with no palpable tumors or pain present. The cardiovascular, respiratory, and neurological assessments were unremarkable.

Investigations: Preliminary laboratory analyses indicated hyponatremia (sodium 126 mmol/L), hyperkalemia (potassium 5.9 mmol/L), and hypercalcemia (total calcium 12.5 mg/dL, adjusted for albumin). The serum cortisol concentration was diminished at 3 µg/dL (normal: 10-20 µg/dL), while Adrenocorticotropic Hormone (ACTH) was raised at 180 pg/mL (normal: 10-50 pg/mL), thereby confirming primary adrenal insufficiency. Thyroid function tests, renal function, and liver function tests were all within normal ranges.

A contrast-enhanced Computed Tomography (CT) scan of the abdomen demonstrated bilateral massive adrenal masses, measuring 6.5 cm on the right and 5.8 cm on the left, exhibiting heterogeneous enhancement. No evidence of abdominal lymphadenopathy or metastases to the liver or kidneys was observed. Due to the suspicion of malignancy, a Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) scan was conducted, revealing significant FDG uptake in both adrenal glands, with no indications of disease in other areas, implying a primary adrenal condition.

A biopsy of the right adrenal tumor was conducted using ultrasound guidance. Histopathological analysis indicated Diffuse Large B-Cell Lymphoma (DLBCL), with immunohistochemistry demonstrating positivity for CD20, CD10, and BCL-6, while being negative for CD3 and CD5, so validating the diagnosis of Primary Adrenal Lymphoma (PAL). The bone marrow biopsy did not indicate lymphoma involvement.

Management and outcome: The patient was diagnosed with Primary Adrenal Lymphoma, exhibiting adrenal insufficiency and hypercalcemia. He was initiated on intravenous hydration and high-dose ste-

roids (hydrocortisone 100 mg IV three times day) to address adrenal crisis and hypercalcemia. Upon stabilization, he commenced the R-CHOP chemotherapy regimen (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone) alongside concomitant hydrocortisone replacement treatment (50 mg orally twice daily).

The patient had good tolerance to the treatment, with no significant ill effects. Following the initial chemotherapy cycle, subsequent laboratory tests indicated normalization of calcium levels (9.5 mg/dL), sodium (138 mmol/L), and potassium (4.3 mmol/L). His symptoms of weariness, anorexia, and hyperpigmentation markedly alleviated. Subsequent CT scans following three cycles of treatment revealed a substantial decrease in the dimensions of the adrenal masses (right 3.2 cm, left 2.9 cm) with no newly identified lesions.

Following the completion of six cycles of treatment, the adrenal masses were undetectable on imaging, and the patient attained complete remission. He maintained a hydrocortisone dosage of 20 mg in the morning and 10 mg in the evening for adrenal insufficiency. At the one-year follow-up, the patient remained asymptomatic with no indications of recurrence.

Discussion

Primary Adrenal Cancer (PAL) is an exceedingly rare cancer type affecting the adrenal glands, frequently manifesting with nonspecific symptoms and adrenal insufficiency [5]. The majority of PAL cases are Diffuse Large B-Cell Lymphomas (DLBCL), primarily impacting older males [6]. The clinical signs of PAL may encompass adrenal insufficiency, abdomen or back pain, fever, weight loss, and, less frequently, hypercalcemia. The etiology of hypercalcemia in PAL remains incompletely elucidated, potentially linked to elevated production of parathyroid Hormone-related Protein (PTHrP) or the direct osteolytic action of lymphoma cells [7].

The diagnosis of PAL is difficult due to its infrequency and the ambiguous characteristics of its presentation. Imaging modalities, including CT and FDG-PET scans, are essential for detecting adrenal masses and excluding metastatic disease [8,9]. A conclusive diagnosis necessitates a tissue sample, which identifies the histological subtype of lymphoma [10].

The management of PAL often entails combination chemotherapy, exemplified by the R- CHOP regimen, including corticosteroid replacement therapy for adrenal insufficiency. The prognosis of PAL is contingent upon various criteria, including disease stage, treatment response, and the existence of adrenal insufficiency [11]. Timely diagnosis and commencement of treatment are crucial for enhancing survival rates in PAL patients.

This case underscores the necessity of incorporating PAL into the differential diagnosis of adrenal masses associated with adrenal insufficiency and metabolic irregularities. A comprehensive strategy involving endocrinologists, oncologists, radiologists, and pathologists is crucial for precise diagnosis and appropriate management.

Conclusion

Primary Adrenal Lymphoma (PAL) is an uncommon yet significant factor in the differential diagnosis of bilateral adrenal tumors associated with adrenal insufficiency and hypercalcemia. Timely identification, swift biopsy, and rapid commencement of chemotherapy are crucial for positive outcomes. This example highlights the necessity for heightened suspicion and a multidisciplinary strategy in the management of uncommon adrenal disorders.

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