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Case Report

Primary Adrenal Insufficiency Secondary to Bilateral Adrenal Lymphoma

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Abstract

Involvement of adrenal glands in lymphoma is rare; the patient may have variable presentations. We report a case of a 62-year-old Saudi female who presented to our center with a few-week history of fatigue, weight loss, subjective fever, and a recent change in skin color. On examination, she looked dehydrated and had a drop in blood pressure with postural change and hyperpigmentation of the skin of the face and hands. Morning cortisol levels were low, and adrenocorticotropic hormone levels were high, which indicated primary adrenal insufficiency (PAI). An adrenal computed tomography (CT) scan revealed bilateral adrenal enlargement. After excluding pheochromocytoma, a CT scan-guided trucut biopsy of the adrenals confirmed non-Hodgkin lymphoma. The patient was started on steroid replacement therapy, and after stabilization, a plan was made to initiate chemotherapy for the treatment of lymphoma; unfortunately, the patient died shortly after diagnosis because of rapid progression of the disease. Adrenal lymphoma can present with PAI and should be considered in the presence of bilateral adrenal enlargement; it is an aggressive tumor and carries poor prognosis if the treatment is delayed.

Keywords: Adrenal, bilateral, lymphoma, primary

Background

Primary adrenal insufficiency (PAI) is a rare condition. The described prevalence in Western countries is 39–144 per million individuals.[1] The age of onset varies, with a median of 34 years according to a cross-sectional study.[2] The presentation of PAI secondary to infiltration of both the adrenal glands by cancer is even rarer, and one of the common cancers that may involve the adrenal gland is lymphoma. We report a case of a 62-year-old woman who presented with symptoms and signs of PAI secondary to diffuse bilateral non-Hodgkin lymphoma of the adrenal glands.

Case Report

A 63-year-old Saudi female patient with long-standing diabetes mellitus type 2 requiring insulin and hypertension diagnosed in a primary health-care center presented to Qatif Central Hospital in the East of Saudi Arabia Emergency Department with a 6-month history of vague complaints that included fatigue, body ache, poor appetite, weight loss, and subjective fever and a 3-week history of postural dizziness, asthenia, and frequent loose bowel motions. The family noticed a gradual decline in insulin requirement with frequent hypoglycemia in the previous 1–2 months, and they also noticed the darkening of sun-exposed areas over the face and hands. The patient sought medical help during her illness and was prescribed antidepressants with no improvement.

Clinically, she looked depressed and dehydrated and showed a postural drop in blood pressure (110/72 mmHg) in a supine position and 85/60 mmHg in a setting position. She was noticed to have mucocutaneous hyperpigmentation over the mucosa and palmar crease [Figure 1]. The head-and-neck examination was not relevant, as it showed no organomegaly or lymphadenopathy in the cervical or axillary areas, and there was no lower limb edema. The initial assessment focused on ruling out adrenal insufficiency versus sepsis or hidden malignancy. An extensive workup was performed, and significant findings included low serum sodium (117), high serum potassium (5.7), normal blood cultures, and normal renal and

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liver panels. The morning adrenocorticotropic hormone (ACTH) was high at 190 pmol/L (5–60) with a low morning cortisol of 8.36 nmol/L (6.2–19.4); other hormonal profiles were not remarkable. A Synacthen test was not available in the center, but signs and symptoms such as high ACTH and low morning cortisol confirmed PAI. The most common etiology of Addison's disease is autoimmune destruction of the adrenals, usually present in younger patients, specifically in female patients; because the patient lacked other autoimmune diseases, an adrenal computed tomography (CT) was ordered to exclude a secondary cause of adrenal destruction other than autoimmune disease. The CT showed diffuse bilateral adrenal enlargement with low attenuation in the noncontrast study, and the findings were heterogeneous, with a few enlarged abdominal lymph nodes, suggesting an infiltrative process [Figure 2]. A CT-guided trucut biopsy of the right adrenal gland was performed after excluding pheochromocytoma and revealed nongerminal center (activated) B-cell-like diffuse large B-cell lymphoma (DLBCL). Immunohistochemical markers showed that CD20 was strongly positive in neoplastic cells, CD5 was positive in background T-cells, CD10 and BCI-6 were both negative, and MUM1 was strongly positive in neoplastic cells [Figures 3 and 4]. The patient was started initially on an intravenous (IV) hydrocortisone stress dose of 50 mg every 8 h for 24 h and then 25 mg via IV every 8 h for the next 24 h. She eventually showed a significant clinical improvement in the form of stability of blood pressure and resolution of hyponatremia and hypoglycemia. The patient had no more diarrhea and was able to stand and move alone. After the resolution of the symptoms and stability of the patient's general condition, she was shifted to a maintenance dose of steroids. She required a higher physiological dose to stay asymptomatic. She required 20 mg cortisol tablets in the morning and 10 mg cortisol tablets in the evening with fludrocortisone 0.05 mg OD. She was referred to a tertiary health center for further staging and was started on active treatment for lymphoma.

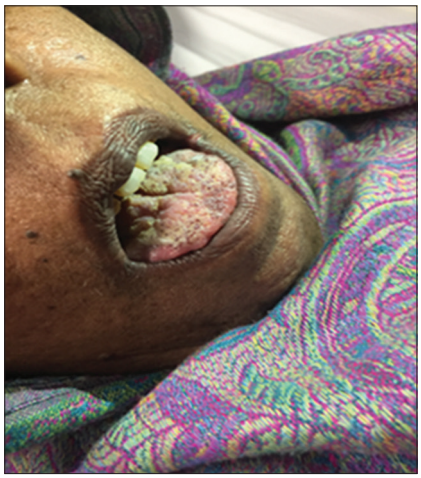

Figure 1: Hyperpigmentation of the tongue and oral mucosa

Discussion

PAI secondary to the destruction of the adrenal glands can arise due to multiple etiologies. The most common etiology is

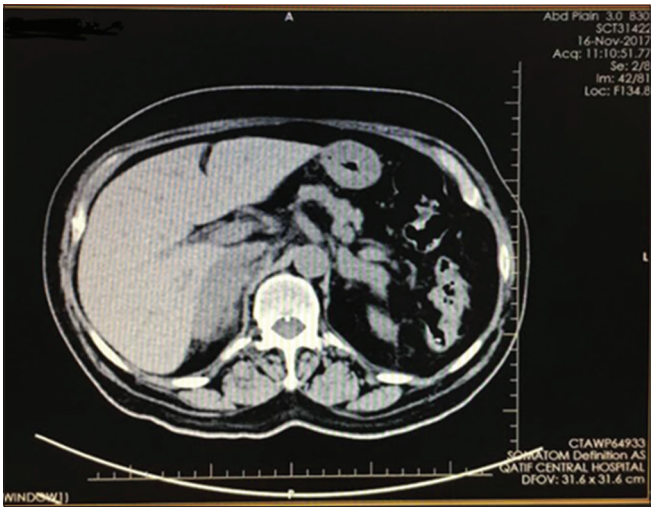

Figure 2: No contrasted adrenal computed tomography showing bilateral adrenal enlargement, and the areas are hypodense and maintain their overall shape

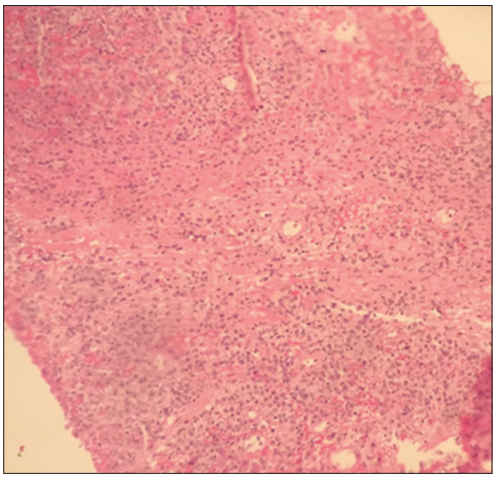

Figure 3: Histopathology with immunohistochemistry markers H and E stain: Diffuse large B-cell lymphoma

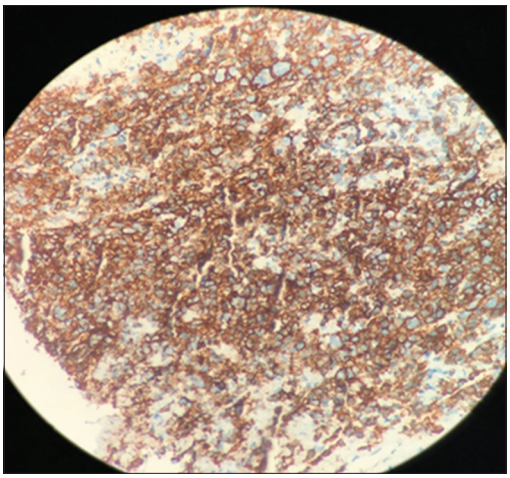

Figure 4: Histopathology with immunohistochemistry markers, CD20: Strongly positive in the neoplastic cells

an autoimmune disease, which represents 70%–90% of cases. When the disease was discovered in 1885, tuberculosis was its most common cause, but it is now the cause of less than 20% of cases worldwide. Other rare causes of PAI are adrenal hemorrhage, infarction, other infectious diseases, drugs, or metastatic cancer or lymphoma.[3,4]

Our patient presented with signs and symptoms of PAI, and the etiology in this age group could be isolated idiopathic or autoimmune.[5] In accordance with the Endocrine Society, clinical practice guideline of 2016 for the diagnosis of PAI, the diagnosis of the underlying cause, should include a validated assay of autoantibodies against the 21-hydroxylase enzyme, but this was not available in our center. Other causes of PAI should be sought out.[6] Therefore, an adrenal CT scan was requested, and it showed bilateral adrenal enlargement, which raised the suspicion for nonimmune-mediated PAI, in which the adrenal glands are expected to be either normal early in the course of the disease or atrophied. However, bilateral adrenal enlargement could result from granulomatous infectious causes, such as tuberculosis, histoplasmosis, or blastomycosis, or be due to acute adrenal hemorrhage and infarction or cancer invasion into the adrenal glands.[7] In the literature, lymphoma has been reported to involve the adrenal glands and to result in PAI in multiple case reports.[8] It is a cancer that arises from white blood cells and has been traditionally divided into two large subtypes: Hodgkin and non-Hodgkin lymphoma. B-cell lymphoma is the most common subtype of non-Hodgkin lymphoma; almost 85% of patients with lymphoma have this variant. Lymphomas can potentially arise from any lymphoid tissue located in the body; however, primary adrenal non-Hodgkin lymphoma is extremely rare,[8] representing less than 1% of the cases. The two most common subtypes are DLBCL (78%) and peripheral T-cell lymphoma (7%) according to the 2008 WHO definitions.[9]

Both the adrenal glands may be involved in more than 70% of cases when PAI should be ruled out. In our patient, CT-guided trucut biopsy confirmed the diagnosis of the non-Hodgkin lymphoma DLBCL. The disease is rare and rapidly progressive, and aggressive intervention should not be delayed. Although our patient deteriorated rapidly and passed away before starting the chemotherapy regimen, the literature shows improved outcomes with the advent of rituximab-containing chemotherapeutic regimens. A review of 31 patients from 14 Korean institutions who were treated for adrenal DLBCL with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone suggests encouraging results in which the achievement of complete remission is predictive of survival.[9,10]

Conclusion

The involvement of the adrenal glands in lymphoma is rare, and DLBCL is the most common type of lymphoma. The patient can present with variable symptoms and a wide range of findings. PAI as the first presentation, as was seen in our patient, is extremely rare.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed

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Conflicts of interest

There are no conflicts of interest.

References

1. Erichsen MM, Løvås K, Skinningsrud B, Wolff AB, Undlien DE, Svartberg J, *et al*. Clinical, immunological, and genetic features of autoimmune primary adrenal insufficiency: Observations from a Norwegian registry. J Clin Endocrinol Metab 2009;94:4882-90.
2. Ross IL, Levitt NS. Addison's disease symptoms – A cross sectional study in urban South Africa. PLoS One 2013;8:e53526.
3. Irvine WJ, Barnes EW. Adrenal insufficiency. Clin Endocrinol Metab 1972;1:549-94.
4. Zelissen PM, Bast EJ, Croughs RJ. Associated autoimmunity in Addison's disease. J Autoimmun 1995;8:121-30.
5. Spinner MW, Blizzard RM, Childs B. Clinical and genetic heterogeneity in idiopathic Addison's disease and hypoparathyroidism. J Clin Endocrinol Metab 1968;28:795-804.
6. Bornstein SR, Allolio B, Arlt W, Barthel A, Don-Wauchope A, Hammer GD, *et al*. Diagnosis and treatment of primary adrenal insufficiency: An endocrine society clinical practice guideline. J Clin Endocrinol Metab 2016;101:364-89.
7. Wheatley T, Gallagher S, Dixon AK. Adrenal insufficiency and bilateral adrenal enlargement: Demonstration by computed tomography. Postgrad Med J 1985;61:435-8.
8. Ram N, Rashid O, Farooq S, Ulhaq I, Islam N. Primary adrenal non-Hodgkin lymphoma: A case report and review of the literature. J Med Case Rep 2017;11:108.
9. Rashidi A, Fisher SI. Primary adrenal lymphoma: A systematic review. Ann Hematol 2013;92:1583-93.
10. Kim YR, Kim JS, Min YH, Hyunyoon D, Shin HJ, Mun YC, *et al*. Prognostic factors in primary diffuse large B-cell lymphoma of adrenal gland treated with rituximab-CHOP chemotherapy from the Consortium for Improving Survival of Lymphoma (CISL). J Hematol Oncol 2012;5:49.