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Case Report

Primary adrenal lymphoma infiltrating into pancreas: A rare cause of adrenomegaly

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ABSTRACT

Primary adrenal lymphoma is a rare entity and may be suspected in patients having bilateral adrenal masses, with/without lymphadenopathy, and with/without adrenal insufficiency. We report a rare case of a 45-year-old man who presented with pain in the abdomen, with no signs of adrenal insufficiency and bilateral adrenal masses on imaging. Light microscopy findings with immunohistochemistry and flow cytometry confirmed the diagnosis of diffuse large B-cell lymphoma. The patient was offered cyclophosphamide, adriamycin, vincristine, and prednisolone chemotherapy regimen and doing well till the last follow-up.

KEY WORDS: Adrenal insufficiency, hypoechoic adrenal masses, primary adrenal lymphoma

INTRODUCTION

Lymphoma affecting primarily adrenal gland is a rare entity. However, 20-25% patients can show secondary involvement of adrenal gland with non-Hodgkin's lymphoma (NHL). Adrenal lymphoma may be suspected with bilateral adrenal masses, with/without lymphadenopathy, and with/without any sign of adrenal insufficiency [1,2]. Nearly 70% of patients present with bilateral adrenal masses and 50% present with syndrome of adrenal insufficiency. Most of the cases reported in literature are large B-cell type of lymphoma; centroblastic or immunoblastic [3]. We report a rare interesting case of primary adrenal lymphoma (PAL) infiltrating the pancreas.

CASE REPORT

A 45-year-old man with insignificant past medical history was referred to the surgical outpatient department for episodic pain in abdomen accompanied with fever and fatigue for the last 3 months. There was no clinically significant family and personal history. On general physical examination, the patient appeared conscious, malnourished, and pale. His blood pressure was 128/80 mmHg, and pulse rate was 82 bpm with body temperature of 99°F. Systemic examination of head, neck and chest, and respiratory and cardiovascular system was unremarkable. There was no evidence of lymphadenopathy in cervical, axillary, or inguinal region. The facial region, abdominal region, and skin over the extremities did not reveal

any pigmentation. Per-abdomen examination revealed a non-tender abdominal lump, firm in consistency, measuring 11 cm × 10 cm approximately. Hematological investigations revealed that hemoglobin was 12.3 g/dL, white blood count was 10.44 × $10^3/\mu$L with normal distribution of cells, platelet count was 5.2 × $10^6/\mu$L, and red blood cell indices were within normal limit. Coagulation profile was unremarkable. Erythrocyte sedimentation rate was normal. Serum electrolyte estimation revealed sodium concentration of 132.9 mEq/L (normal range: 135-145 mEq/L) and potassium concentration of 4.55 mEq/L (normal range: 4.5-5.5 mEq/L). Serum phosphate level was 4.1 mg/dL (normal range: 2.5-4.5 mg/dL). Liver and renal function tests were within normal range. Serum lactate dehydrogenase (LDH) level was 436 IU/L (normal range: 110-200 IU/L), and serum cortisol concentration at 8 AM was 11.8 μg/dL (normal range: 5-23 μg/dL). The plasma-free metanephrine level was 30.6 pg/mL (normal range: <90 pg/mL).

Chest radiography was unremarkable for any mediastinal lymphadenopathy or pulmonary pathology. Ultrasonography and computed tomography imaging (CT) of the abdomen revealed bilateral hypoechoic adrenal masses; 12 cm × 8.8 cm × 3.5 cm on the right side and 14.5 cm × 10 cm × 4.5 cm on the left side. The left adrenal mass was found to be infiltrating pancreatic tail [Figure 1]. Surgical laparotomy was performed, and *en-bloc* removal of the left adrenal mass with spleen, left kidney, and pancreatic tail was performed and was received for histopathological evaluation.

The total weight of the *en-bloc* specimen was 700 g. The left adrenal mass weighed approximately 560 g, measuring 18 cm × 9 cm × 9 cm, gray-tan with multiple attached lymph nodes. Cut section of the mass was gray-tan with areas of hemorrhage and necrosis. Cut section of the left kidney and spleen appeared unremarkable on gross examination. Pancreas was adherent to the adrenal mass at the inferior border of pancreatic tail, whereas the other organs appeared free from the main mass. Seven lymph nodes were identified attached to the mass. Multiple sections were submitted from tumor mass for histological examination that showed sheets of monomorphic small round cells having round to oval, occasional cleaved nuclei, with prominent nucleoli and scanty basophilic cytoplasm with occasional mitotic figures [Figure 2a]. The tumor cells were separated by delicate fibrous bands containing lymphocytes and plasma cells. Section from the pancreas showed pancreatic tissue infiltrated by the neoplastic cells [Figure 2b]. These tumor cells were periodic acid-Schiff positive and non-argyrophilic. Sections from the kidney and spleen were unremarkable. Sections from the lymph nodes adjacent to the mass showed the features of reactive follicular hyperplasia. Immunohistochemical stains for cytokeratin-7, CD3, CD5, CD20, CD38, CD68, CD79a, B-cell lymphoma 2 (BCL-2), cyclin D1, leukocyte common antigen (LCA), vimentin, κ light chain, λ light chain, neuron-specific enolase, S100, synaptophysin, and chromogranin (Dako, USA) were performed. The histological sections were pretreated by steaming in citrate buffer solution (Target Retrieval Solution, Dako) for 30 min at 99°C. The monomorphic tumor cells displayed positivity for CD20/38/79a, BCL-2, LCA, vimentin, and κ light chain [Figure 3] and were negative for CD3/5/68, λ light chain, neuron-specific enolase,

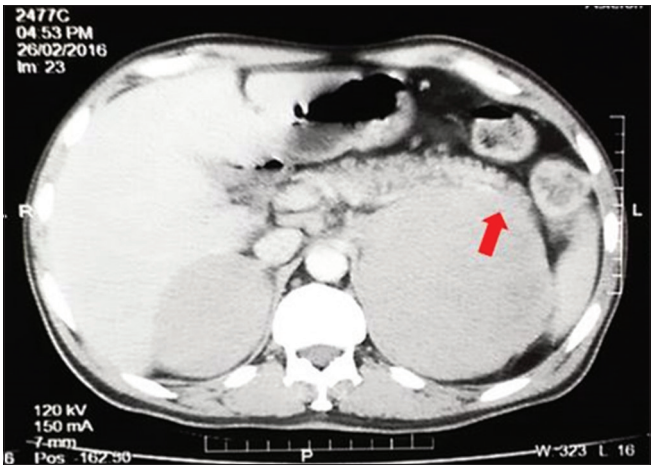

Figure 1: Computed tomography scan image showing bilateral hypoechoic adrenal masses infiltrating the pancreas on the left side (marked by red arrow)

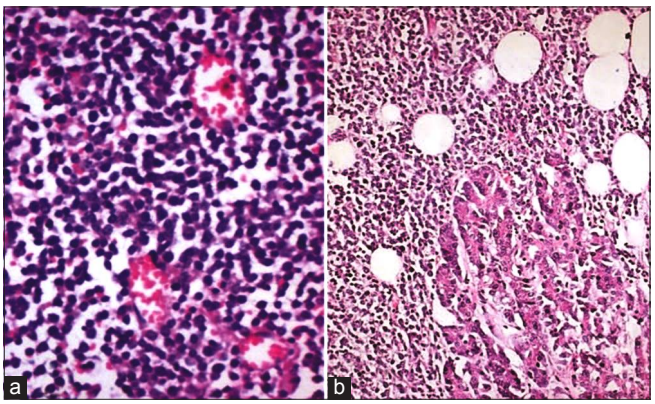

Figure 2: Monomorphic small round cells with round to oval, occasional cleaved nuclei, with prominent nucleoli and scanty basophilic cytoplasm ([a] Hematoxylin and eosin, ×400); tumor cells infiltrating the pancreas ([b] Hematoxylin and eosin, ×100)

synaptophysin, chromogranin [Figure 4], and S-100. Ki-67-labeling index was 70%. The lymphoma was typed as diffuse large BCL (DLBL) (subtype B-cell) type according to the World Health Organization classification. Further evaluation of bone marrow and trephine biopsy showed no infiltration by lymphoma cells. The patient was subjected to cyclophosphamide, adriamycin, vincristine, and prednisolone (CHOP) chemotherapy regimen; vincristine (1.4 mg/m^2) and cyclophosphamide (750 mg/m^2), prednisolone (100 mg/day). He is doing well on the last follow-up 6 months after therapy.

DISCUSSION

Adrenal gland is a frequent site for neoplastic diseases. Differential diagnosis of adrenal mass includes various inactive and active adrenal adenomas, pheochromocytomas, infections, traumatic hemorrhage, adrenocortical hyperplasia, carcinomas, myelolipoma, and metastasis from other organs [1,4]. PAL is a very rare adrenal tumor, representing 3% of all extranodal lymphomas and suspected in individuals with elevated serum LDH, characteristic radiological findings of adrenal gland

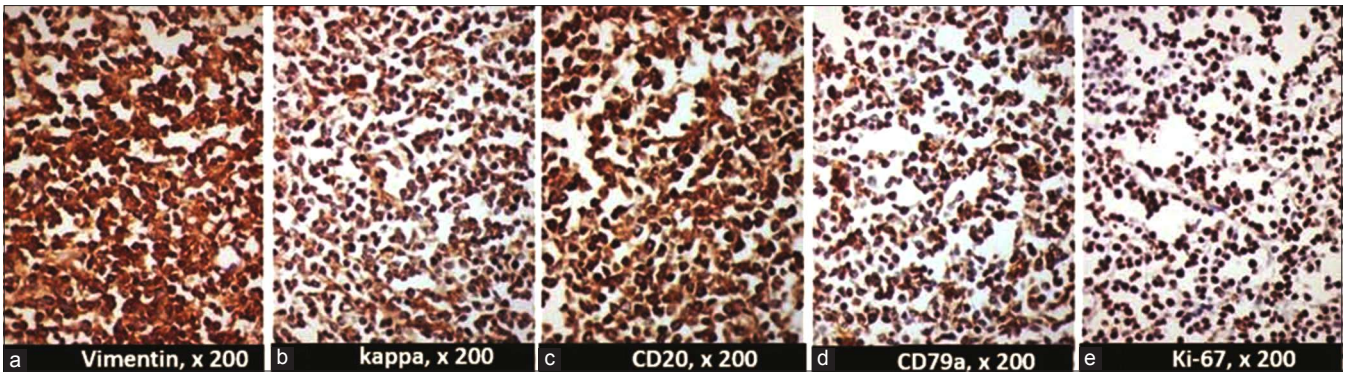

Figure 3: Immunohistochemistry panel of positive markers (immunohistochemistry marker, ×200): Vimentin (a); kappa (b); CD20 (c); CD79a (d); and Ki-67 (e)

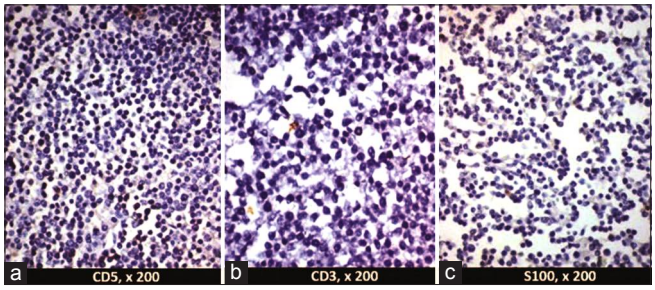

Figure 4: Immunohistochemistry panel of negative markers (immunohistochemistry marker, ×200): CD5 (a); CD3 (b); and S-100 (c)

enlargement with maintained adreniform shape without evidence of extra-adrenal spread and rapid-onset adrenal insufficiency [5,6]. It affects males twice as commonly as females with median age of affection being 68 years (range: 39-89 years). Bilateral cases constitute 70% of the total adrenal lymphomas with a reported median maximum diameter of 8 cm [3,5]. Etiopathogenesis of this disorder is unknown and various hypotheses are proposed. Ozimek *et al*. suggested that PAL arises from previous autoimmune adrenalitis [7]. Ellis and Read have suggested that these tumors may arise from hematopoietic tissue inherent to adrenal gland and an immune dysfunction could predispose to PAL [8].

Clinically, this tumor presents with abdominal pain in 26% cases, fever in 46%, and fatigue and weight loss in 24% patients. Adrenal insufficiency might occur in few patients. Hepatosplenomegaly, lymphadenopathy, concurrent or prior immune dysregulation, and bone marrow involvement are uncommon [9]. However, our patient had unusual presentation of painful abdominal mass, fever, and fatigue without adrenal insufficiency.

Radiologically, these tumors are hypoechoic (on ultrasound), hypodense need to be differentiated from hematoma, infection, adenoma, pheochromocytoma, and adrenocortical carcinoma. Single-photon emission CT by fluorodeoxyglucose scan offers a better modality for evaluation and monitoring of these patients [10]. Patients with advancing age, large tumor size, elevated LDH levels, and presence of adrenal insufficiency at the time of presentation and involvement of other organs usually succumb to the tumor within 1 year [9,11].

Histologically, 70-90% of PALs are of diffuse large B-cell type. The mature small B-cell category comprise >30% of all NHL. These are further classified as nodal, extranodal, and splenic marginal zone lymphoma (MZL), mantle cell lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma, lymphoplasmacytic lymphoma, and low-grade follicular lymphoma [12,13]. The neoplastic cells may appear as monocytoid cells, centrocyte-like cells, or plasmacytoid cells and are distributed in nodular, diffuse, and interfollicular patterns. CD20 and CD79a are the most specific markers for B-lineage derivation. The MZL cells show B-cell markers without expression of CD5, CD10, or CD23, in most cases [12-14].

Donner *et al*. reported a case of primary centroblastic adrenal lymphoma in a 76-year-old man, which was positive for vimentin, cytokeratin, CD20/38/79a, BCL-2, LCA, and κ light chain but negative for CD3/30/CD45/45RO/68, λ light chain, epithelial membrane antigen, chromogranin A, S-100, synaptophysin, HMB-45, and neuron-specific enolase [15]. Our case also revealed similar expression of these markers. Holm *et al*. also reported similar findings in a 60-year-old woman who presented with primary adrenal insufficiency and bilateral homogenous masses on CT scan [11]. Diamanti-Kandarakis *et al*. reported a case of a 71-year-old male who presented with acute abdomen with bilateral adrenal mass and primary adrenal insufficiency. Histological analysis of the tumor revealed large B-cell anaplastic NHL phenotype. However, the patient succumbed to the tumor before any therapeutic intervention [2]. Mozos *et al*. have published a case series of ten patients with PAL. The most common presenting symptoms were abdominal pain and fever. Only one patient had clinically evident adrenal insufficiency. The mean tumor size at diagnosis was 8.5 cm in their study, and 50% of patients had bilateral involvement. All cases presented with stage IE disease without regional nodal involvement. Histologically, eight cases were DLBL (non-germinal center B-cell phenotype), one case each of plasmablastic lymphoma and extranodal NK/T-cell lymphoma, nasal type. Fluorescence *in situ* hybridization revealed Bcl 6 gene rearrangement in 5 (83%) of 6 DLBLs investigated [16].

Therapeutic modalities for adrenal lymphomas include surgical excision, combination chemotherapy, surgery, followed by chemotherapy and/or radiotherapy and corticosteroid

replacement. Rituximab-CHOP chemotherapy regimen is found to be useful in many of the cases. However, most of the patients have a fatal outcome [3].

Our case is unique as it presented with bilateral adrenal masses but without primary adrenal insufficiency. Light microscopy and immunohistochemistry confirmed diagnosis of DLBL (subtype B-cell) lymphoma. The rarity of the case lies in the infiltration of the pancreas by the neoplastic cells, never reported before.

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