A rare cause of bilateral adrenal mass: a case report of primary adrenal lymphoma

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Abstract

Primary adrenal lymphoma (PAL) is extremely rare, representing less than 1% of Non-Hodgkin's Lymphoma (NHL). We present a case of an elderly man who was evaluated for persistent abdominal pain and adrenal insufficiency. The computed tomogram (CT) of the abdomen showed a large bilateral adrenal mass. There were also multiple small lung nodules. The histopathology of adrenal gland showed features consistent with diffuse large B-cell NHL. He received two cycles of rituximab, cyclophosphamide, doxorubicine, vincristine and prednisolone (R-mini-CHOP) followed by five cycles of rituximab, methotrexate, procarbazine, and vincristine (R-MPV) after evidence of brain metastasis on imaging. He responded well to the current treatment at six months follow up.

Introduction

Non-Hodgkin's Lymphoma is a cancer that originates from the malignant transformation of mature and immature cells of immune system, affecting most commonly the B lymphocytes (B cells) and a smaller proportion of T- and natural killer cells. About 40% of patients with lymphoma develop from an extra-nodal site. The extra-nodal form is more common than the nodal form, occurring in 25% of Non-Hodgkin's Lymphoma.[1] The gastrointestinal tract is the most common abdominal site for primary extra-nodal lymphoma, with the stomach accounting for 60-75% of malignant lymphoma.[2] Other common sites of abdominal lymphoma include small intestine, liver and kidneys. Only 4% of Non-Hodgkin's Lymphoma involve the adrenal glands. Primary adrenal lymphoma especially those who present with bilateral adrenal lesions has only been reported in less than 200 cases.[3] In this report, we describe one such case.

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Case Report

A 77-year-old man presented with a three-week history of pyrexia. This was associated with upper abdominal pain and bloating. He had no history of weight loss or loss of appetite. He had a past medical history of coronary artery disease with coronary artery bypass surgery, type 2 diabetes mellitus, hypertension and dyslipidemia. On review of systems, there was no cough, hemoptysis, diarrhea or travelling history.

His temperature was 36.5°C with blood pressure of 128/74 mm Hg and heart rate of 100 beats per minute. His respiratory and abdominal examination was unremarkable. There were no cervical or inguinal lymph nodes palpable. Initial workup showed potassium of 5.5 mmol/L and sodium of 127 mmol/L with normal creatinine and urine analysis (see Table 1). He was started on intravenous glucocorticoids in view of potential adrenal insufficiency as evidenced by hyperkalemia and hyponatremia while in the ward.

Upon further workup for abdominal discomfort, an oesophagogastroduodenoscopy (OGDS) was performed and it showed features suggestive of pan-gastritis and duodenitis with positive Helicobacter Pylori. He was treated with eradication therapy. However, his abdominal pain persisted, a CT abdomen was performed to investigate the cause. It showed multiple large ill-defined hypodense lesions in both adrenal glands, with the right adrenal mass measuing 7.2 x 7.1 x 7.3 cm. The densities at plain, portal venous and delayed phase were 41 Hounsfield unit (HU), 94 HU, and 60 HU respectively. The left adrenal mass measured 5.0 x 4.4 x 5.1 cm with densities at plain, portal venous and delayed phase of 35 HU, 96 HU, and 71 HU, respectively (see Figure 1 and 2).

The right adrenal mass was also compressed onto the retro-hepatic inferior vena cava and proximal left renal vein (see Figure 3). There were multiple small lung nodules ranging from 2 to 4

Table 1. Initial blood test results

Tests	Results	Reference range
Hemoglobin (g/dL)	10.3	13.0 – 17.0
Hematocrit (%)	31.1	40.0 – 50.0
White-cell count (x10^9/ L)	10.2	4.0 – 10.0
Differential count (%)		
Neutrophils	76.5	40.0 – 80.0
Lymphocytes	12.3	20.0 – 40.0
Monocytes	11.0	2.0 – 10.0
Eosinophils	0.1	0.02 - 0.50
Basophils	0.1	0.0 – 2.0
Platelet count (10^3/µL)	282	150 – 410
Erythrocyte sedimentation rate (mm/hr)	51	1 - 15
C-reactive protein (mg/L)	29.9	<5.0
Sodium (mmol/L)	127	136- 145
Potassium (mmol/L)	5.5	3.5 – 5.1
Urea (mmol/L)	9.5	2.78 - 8.07
Creatinine (mmol/L)	89	62 – 106
Calcium (mg/dL)	2.11	2.20 – 2.55
Magnesium (mg/dL)	0.70	0.66 – 0.99
Phosphate (mg/dL)	0.81	0.80 – 1.45
Total Protein (g/dL)	58.2	64.0 – 83.0
Albumin (g/dL)	32.2	35.0 – 52.0
Early Morning Cortisol (mmol/L)	94.8	166 – 507

mm which were suggestive of metastasis (see Figure 4). Further investigations for prolonged fever included blood, urine, and stool cultures which yielded normal results. No other adrenal hormonal studies were taken.

The patient underwent a CT-guided biopsy of the adrenal lesion, which showed diffuse high-grade NHL suggestive of large B-cell lymphoma. The histopathological examination revealed malignant lymphoid cells with large hyperchromatic nuclei displaying one or two prominent eosinophilic nucleoli. The Ki-67 index was more than 90% which indicated high proliferation. Immunohistochemical analysis showed the malignant cells were positive for leukocyte common antigen (LCA) and CD 20 while negative for CD3 and Cytokeratin AE1/AE3 which were suggestive of B-cell lymphoma (see Figure 5).

The diagnosis of primary adrenal lymphoma (PAL) was made. After discussion with the patient, a bone marrow biopsy was not done as it would not have changed the management. His Eastern Cooperative Oncology Group (ECOG) performance status was Grade 2 at diagnosis. He received two cycles of rituximab and a reduced dose of cyclophosphamide, doxorubicine, vincristine, and prednisolone (R-mini-CHOP). However, subsequent MRI of the brain showed metastasis in the right frontoparietal region. The regime was changed to five cycles of rituximab, methotrexate, procarbazine, and vincristine (R-MPV). At 6 months of follow up, his PET scan and MRI showed significant improvement with the regime.

Discussion

Adrenal mass detected on imaging might be difficult to distinguish between lipid-poor adenomas and malignant lesions. However, the majority of adenomas are lipid-rich and can be easily distinguished from pheochromocytoma, adrenocortical carcinoma, and adrenal metastasis. Major international guidelines recommend initial evaluation should include hormonal testing to determine the functionality of the mass and imaging to ascertain features of malignancy.[4,5] In Italy, in 1096 cases collected between 1980 and 1995 the hormonal work-up had demonstrated 85% of adrenal incidentalomas were non-hypersecretory, 9.2% were subclinical Cushing's syndrome, 4.2% were pheochromocytomas, and 1.6% were aldosteronomas.[6] Fewer than 15% of adrenal incidentaloma cases are bilateral. Most of them are benign lesions, such as bilateral cortical adenoma or nodular hyperplasia. However, metastatic lesions, invasive diseases, congenital adrenal hyperplasia, and bilateral pheochromocytoma may also appear as bilateral adrenal mass.[4] It was reported that less than 200 cases of bilateral adrenal mass were attributed to bilateral primary adrenal lymphoma with adrenal insufficiency.[3]

Adrenal biopsy is helpful to identify the underlying cause of adrenal incidentaloma. However, a fine needle aspiration biopsy is often difficult to distinguish between adrenal adenoma and adrenal cortical carcinoma. An adrenal biopsy also runs the risk of tumor dissemination before its resection, if the adrenal mass proved to be an adrenocortical carcinoma.[5] Therefore, biopsy is recommended to be done when diagnosis of adrenal incidentaloma would change the clinical management of a patient.[5] The CT scan of our patient showed several features which were highly suspicious of adrenal mass of non-benign cause. The features include a size of ≥ 4 cm, the HU value on a non-contrast CT scan of ≥ 10 HU, heterogeneous tumor contents, non-uniform enhancement, and possible metastasis. PAL has been reported to have bilateral involvement of adrenal mass with preservation of "adeniform" shape and frequently causes adrenal insufficiency.[7] Other features suggestive of malignant adrenal lesion include low contrast washout rate during the delayed view of a contrast CT scan (absolute washout <60%, relative washout <40%), irregular tumor margin, or presence of surrounding tissue invasion or when there is an abnormal increase in metabolites of steroids, such as dehydroepiandrosterone sulfate (DHEAS).[4]

In this patient, there was a strong suspicion of malignancy with possible metastasis of the lungs from his CT scan. Therefore, there was an urgent need to determine the primary lesion. Most guidelines recommend surgery to remove any adrenal lesion present with radiological features redolent of malignancy to further elucidate its etiology.[4,5,8] However, for patients who are not ideal surgical candidates, conservative approaches are appropriate.[8] Therefore, a CT guided-biopsy was done to confirm the diagnosis of primary adrenal lymphoma.

NHL may be difficult to diagnose as most patients present with non-specific symptoms such as loss of weight and malaise. More than two-third of patients present with painless peripheral lymphadenopathy while about half of them may present with abdominal pain.[9] Diffuse large B cell lymphoma (DLBCL) is the most common histologic category of NHL. NHL in general is highly treatable with current therapy, with five-year survival rates of more than 80% if treated at early stage.[10] Chemotherapy is the mainstay treatment for NHL with surgery reserved mainly for tissue biopsy and patients with complications. Specifically for DLBCL, the standard chemotherapy regimen for treating most patients is R-CHOP.[11] However, for central nervous system lymphoma, chemotherapy regime will depend on patient's factor such as organ function and comorbidities.[12] For those fit for chemotherapy, a Methotrexate-

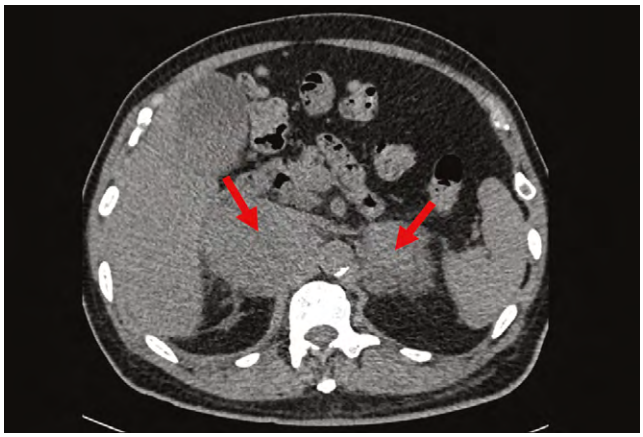

Figure 1. Axial plain abdominal CT scan showing large homogenous hypodense bilateral adrenal masses (red arrow).

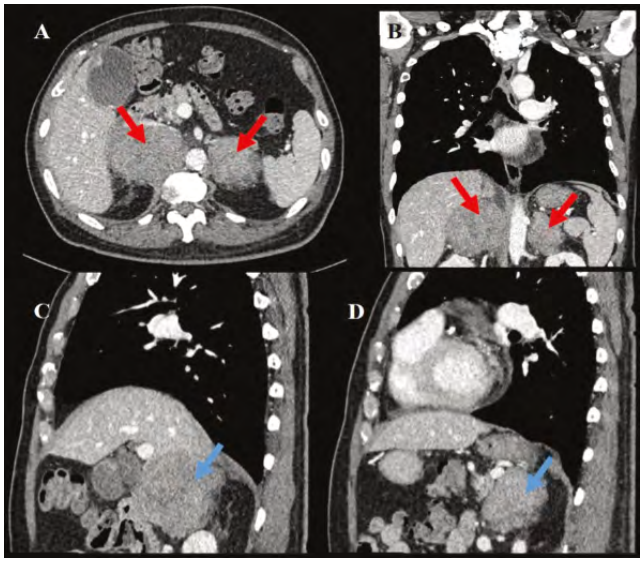

Figure 2. Axial (A), coronal (B) slices of contrasted abdominal CT scan showing large enhancing bilateral adrenal masses (red arrow). Subsequent images (C) and (D) show sagittal images of right and left adrenal masses respectively (blue arrow).

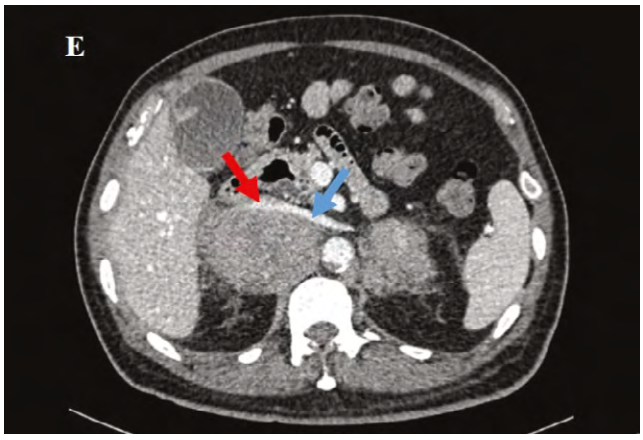

Figure 3. Axial CT (E) showing the right adrenal mass compressing onto retrohepatic inferior vena cava (IVC) (red arrow) and left main renal vein (blue arrow) without compromising the flow.

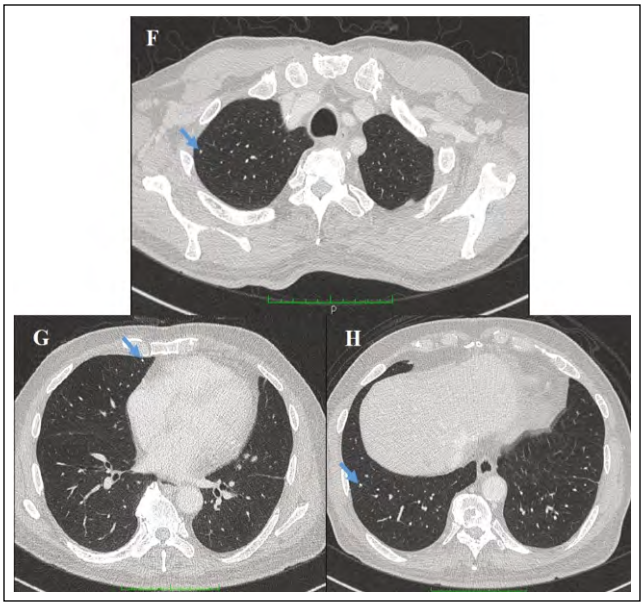

Figure 4. Axial CT thorax in lung window showing tiny nodules (blue arrow) in the right apex (F), medial segment of the right middle lobe (G), and lateral segment of the right lower lobe (H).

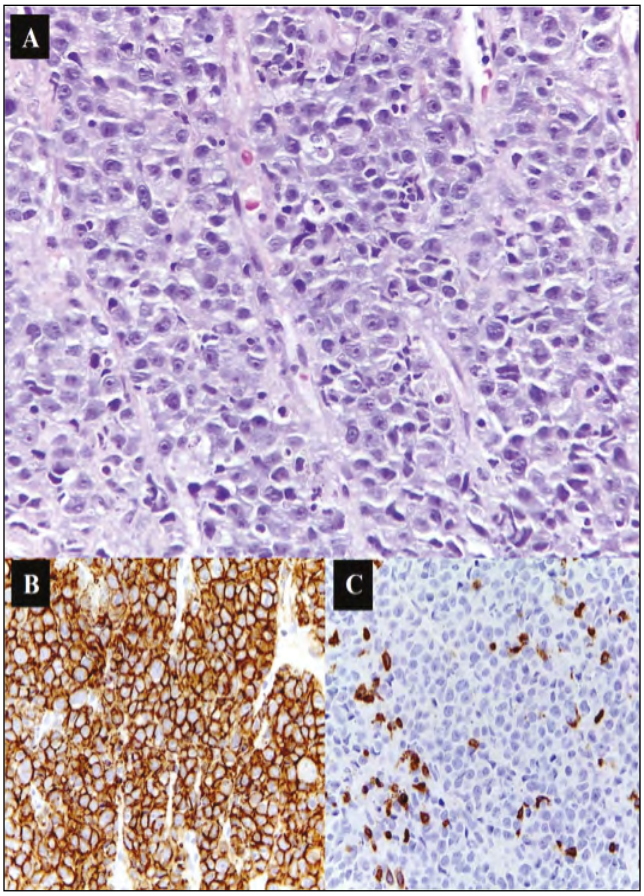

Figure 5. Histopathological examination showing diffuse large B-cell lymphoma (A) expressing CD20 positivity which are stained in brown (B) and negative CD3 which are stained in blue (C) at 400x.

based combination chemotherapy regimen is recommended with choice of regime depending on local preferences.[12] The R-MPV regime has shown to increase survival rate for newly diagnosed primary central nervous lymphoma and even in older adults. Other chemotherapy regimen which have also proven to be effective include temozolomide, etoposide, liposomal doxorubicin, dexamethasone, ibrutinib, and rituximab (DA-TEDDI-R) and MTX, cytarabine, thiotepa, rituximab (MATRIX).[13] As substantial therapeutic progress for lymphoma continues to be made, a high suspicion and prompt diagnosis is therefore undoubtedly imperative for early treatment as evidenced by this case.

Acknowledgements

We would like to thank the patient for his permission to publish this case report.

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