Case Report

# Bilateral primary adrenal non-Hodgkin's lymphoma without adrenal insufficiency

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**Abstract**

We are presenting a rare case of bilateral adrenal non-Hodgkin's lymphoma (NHL) that presented as a primary malignancy. An 83-year-old man presented with newly discovered bilateral adrenal incidentalomas, fatigue, and 30 pound weight loss. Of the 116 cases of primary adrenal NHL reported, over half have presented bilaterally and occur with adrenal insufficiency. Therefore, the finding of bilateral adrenal masses requires an urgent work-up of the functional status of the adrenal gland as well as a thorough analysis of the imaging characteristics seen on noncontrast computed tomography (CT) in order to maximize patient survival. Adrenal function testing was normal. Repeat CT imaging revealed rapidly growing lesions with high attenuations; both masses >10 HU. Histological examination of core biopsies discovered malignant lymphoma with no known past history of lymphoma. Our case coincides with the literature, which states that a mass with attenuation >10 HU in the adrenal glands has a high risk of malignancy.

**Key Words:** Extranodal, incidentaloma, primary non-Hodgkin's lymphoma

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**Received:** 19.04.2014, **Accepted:** 27.04.2014

## INTRODUCTION

Any mass >1 cm that is discovered incidentally on imaging is referred to as an adrenal incidentaloma. Up to 2% of the general population undergoing computed tomography (CT) or magnetic resonance imaging are found to have a previously undiscovered adrenal mass;[1] 10-15% of those patients have masses bilaterally.[2] As of the year 2008, only 116 of cases of primary lymphoma had been reported; 70% of these cases have presented bilaterally.[3,4] Of the primary adrenal non-Hodgkin's lymphoma (NHL) cases reported to date, 60-70% present with adrenal insufficiency at the time of diagnosis.[5,6] In the case reported below, the bilateral primary adrenal NHLs were an incidental finding on CT and lacked the associated adrenal insufficiency seen in the majority of cases.

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| Quick Response Code: | Website: www.urologyannals.com |
| | DOI: 10.4103/0974-7796.152942 |

## CASE REPORT

An 83-year-old male presented with bilateral adrenal masses discovered incidentally on abdominal computed tomography angiography (CTA) following abdominal aortic aneurysm repair 7 weeks earlier. Since the repair, the patient reported significant fatigue and an unintentional 30 pound weight loss. The patient denied any pain or associated symptoms. Past medical history was significant for type II diabetes mellitus, hypertension, hypothyroidism, and coronary artery disease. The patient's family history was insignificant for any cancer or urological disease. Review of systems was unremarkable, including denial of episodes of tachycardia, palpitations, flushing, headache, or chest pain. Furthermore, physical exam revealed a soft, nontender abdomen with no organomegaly. Vital signs included heart rate 58, body mass index 20.75, afebrile, and blood pressure 160/80. The basic metabolic

panel obtained 1-week prior showed a sodium concentration of 136 mmol/L (normal range: 136-148), potassium concentration of 4.3 mmol/L (normal range 3.8-5), blood urea nitrogen concentration of 13 mg/dL (normal range: 7-18), serum Cr concentration of 1.0 mg/dL (normal range: 0.6-1.3), and mild serum hyperglycemia with glucose of 118 (normal range: 70-110 mg/dL). Liver function tests were within normal limits and the urine analysis was unremarkable.

The original Helical Transverse CTA of the abdomen showed a 6.5 cm right adrenal mass and a 5 cm left adrenal mass; both with homogeneous attenuation throughout and no calcifications [Figure 1]. A repeat CT with contrast in 5 mm slices was conducted 2 months later and showed a substantial increase in the size of both adrenal masses. The left adrenal mass measured 7.3 × 7.3 × 7.8 cm, while the right adrenal mass increased to 12.3 × 7.6 × 11.2 cm in size [Figure 2]. The repeat CT also showed encasement of the right renal artery and anterior displacement of the inferior vena cava and bilateral renal veins by the right adrenal mass; consequentially causing a mass effect on the porta hepatis. A 1 mg dexamethasone suppression test produced a cortisol level of 2.8 mcg/dL (normal range <5 mcg/dL). 24 h urinary free-cortisol level was 35 mcg/24 h (normal range: 3.5-45 mcg/24 h). ACTH levels were 44.1 pg/mL (normal range: 7.2-63.3 pg/mL). 24 h urine fractionated metanephrines was 10 mcg/24 h (normal range <20 mcg/24 h). Serum aldosterone levels were <1 ng/dL (normal range: 0.0-30.0 ng/dL) and serum dehydroepiandrosterone sulfate levels were 38.4 ug/dL (normal range: 20.8-226.4 ug/dL).

Computed tomography guided core biopsy of the right adrenal gland showed poorly differentiated malignant tumor extending beyond the adrenal gland into the periadrenal adipose tissue. Immunohistochemical staining showed the malignant cells to be 4+ positive for both CD20 and CD45 (leucocyte common antigen) cell markers; all markers for epithelial malignancies were negative.

Following the diagnosis the patient decided to undergo CHOP chemotherapy and to date is still living.

## DISCUSSION

Computed tomography imaging is the primary study leading to the discovery of adrenal incidentalomas. Interpretation of CT studies should be incorporated into the ensuing plan following the discovery of one of these masses. Angeli *et al.* in their study have reported that the maximum diameter of a mass is predictive of both malignancy and overall prognosis, with 90% of adrenocortical carcinomas being >4 cm.[2] Therefore, any mass >4 cm should be treated like a malignancy until proven otherwise. In addition to the diameter of the mass, it has also been reported that the density, shape, and margins should all be used as predictors for malignancy.[2] In 2005, the Cleveland Clinic conducted a large retrospective study in order to determine a cut-off for malignant adrenal masses using HU. This study compared the pathology reports of 299 adrenalectomies to their respective CT imagines and determined a safe cut-off for distinguishing a benign adenoma from a nonadenomatous mass to be <10 HU on nonenhanced CT.[7] The predictability of a benign process is increased further if the mass is homogeneous, noncalcified, with smooth borders.[8] On a delayed contrast-enhanced CT, an absolute contrast medium washout >50% after 10 min is 100% sensitive and specific for a benign adenoma.[7] Using these criteria, clinicians should be able to predict with strong suspicion if the adrenal incidentaloma is a benign or malignant process.

The incidentalomas discovered on the noncontrast CT of the patient in this case had an average attenuation of 53.2 HU and 64.8 HU; each with a diameter >4 cm. Furthermore, the borders of both adrenal masses were irregular and calcifications were absent. Based on the criteria discussed above, the characteristics of our patient's masses as seen on CT are strongly

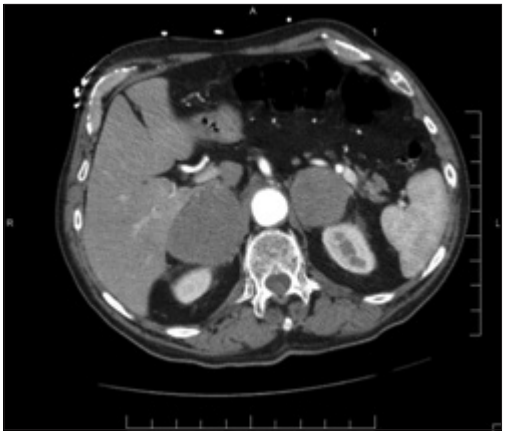

**Figure 1 :** Nonenhanced computed tomography scan from 7/12/13 showing bilateral adrenal masses measuring 6.5 cm and 5 cm

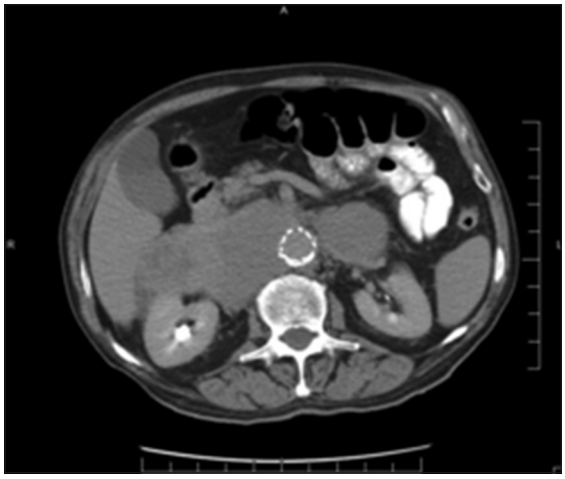

**Figure 2:** Nonenhanced computed tomography scan from 9/25/13 showing a significant increase to 12.3 cm and 7.3 cm

predictive of malignancy. The decision to biopsy the mass was based on the results from a previous study from Grumbach *et al*. They stated that masses with an attenuation >20 HU with no signs of metastasis should be biopsied.[8] Due to the rich blood supply to the adrenal glands, hematopoietic metastasis to these glands is much more common than lymphatic metastasis. Cancer arising in the adrenal tissue is most commonly due to metastatic infiltration of carcinomas originating in the lungs, breast, skin, and colon;[3] all of which our patient lacked. Lymphatic metastasis to the adrenal glands most commonly originates from the retroperitoneal lymph nodes or the ipsilateral kidney,[5] none of which were enlarged on CT.

Primary adrenal NHL represents 3% of all extranodal NHL.[4] This is atypical due to the fact that there is no lymphoid or hematopoietic tissue in the adrenal glands.[5,9] The leading hypothesis for this anomaly is that it arising in the presence of a preexisting autoimmune adrenalitis.[5] This could in fact explain why up to 70% of these malignancies present bilaterally as well as why 60-70% present with adrenal insufficiency.

Although the majority of primary adrenal lymphomas have been shown to cause adrenal insufficiency, metastatic NHL to the adrenals has only been shown to do so on few occasions.[3,5] In their study Gamelin *et al*. they found that of 127 patients with widespread NHL, only 4 had adrenal insufficiency.[10] This is due to the fact that >90% of adrenal tissue must be infiltrated in order to affect function[6] whereas primary adrenal lymphomas tend to be associated with adrenal insufficiency because they often arise in the presence of autoimmune adrenalitis.[5,9] Ellis and Read showed the most common symptoms of bilateral adrenal lymphomas are abdominal pain (67%), weight loss (67%), and fatigue/weakness (44%).[5] All of these symptoms can be seen with adrenal insufficiency. In addition to the presence or absence of adrenal insufficiency, the type of lymphoma and the tumor size impact the presenting symptoms.[4] Our patient presented in this case denied abdominal pain, but reported both weight loss and fatigue despite the lack of adrenal insufficiency.

Treatment options for this disease include, chemotherapy, surgery, surgery followed by chemotherapy/radiation, and corticosteroid replacement. Despite treatment, the prognosis is poor and is worsened by increased serum lactate dehydrogenase, increased age, adrenal insufficiency, and a large tumor size.[3] Our patient elected to undergo chemo therapy and is still living. Similar cases undergoing chemotherapy survived an average of 1-5 months, with one patient going into remission.[2,5] The most common chemotherapy regimen is cyclophosphamide, hydroxy doxorubicin (adriamycin), vincristine (oncovin), and prednisolone (CHOP). Unfortunately, the effectiveness of the CHOP chemotherapy combination over other combinations is not known.

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**How to cite this article:** Simpson WG, Babbar P, Payne LF. Bilateral primary adrenal non-Hodgkin's lymphoma without adrenal insufficiency. Urol Ann 2015;7:259-61.

**Source of Support:** Nil, **Conflict of Interest:** None.