The advent of high-resolution imaging techniques has led to the increasingly frequent and unexpected discovery of adrenal masses. Most of these adrenal incidentalomas are nonfunctioning adrenocortical adenomas. If the adrenal masses are hormone-secreting or proved to be malignant, surgical removal is the general rule. Adrenal neoplasms account for 4-12% of adrenal incidentalomas reported in recent series. Among them, primary adrenal lymphoma (PAL) is extremely rare. How ever, the treatment and outcome of PAL is quite different from other adrenal tumors. Here is a case of PAL, diffuse large-B cell type, presenting as bilateral adrenal incidentaloma.

**CASE REPORT**

A 59-year-old woman was a hepatitis B carrier and had an episode of fulminant hepatitis in April 1999. A follow-up ultrasonography of her abdomen in August 2000 disclosed an incidental finding of bilateral adrenal masses. Despite the huge size of the tumor, her adrenal function was intact. Ultrasound-guided biopsy disclosed a picture of malignant lymphoma, diffuse large B cell type. The patient received bilateral adrenalectomy and adjuvant chemotherapy, but succumbed 6 months later. We suggest that, although rare, primary adrenal lymphoma should be considered as a possible cause of bilateral adrenal incidentalomas.

**Key Words**

adrenal incidentaloma; adrenal insufficiency; primary adrenal lymphoma

Although involvement of the adrenals by malignant lymphoma is common, primary adrenal lymphoma is extremely rare. Herein, we report a case of a 59-year-old woman with bilateral adrenal glands en large ment found incidentally on abdominal imaging. Despite the huge size of the tumor, her adrenal function was intact. Ultrasound-guided biopsy disclosed a picture of malignant lymphoma, diffuse large B cell type. The patient received bilateral adrenalectomy and adjuvant chemotherapy, but succumbed 6 months later. We suggest that, although rare, primary adrenal lymphoma should be considered as a possible cause of bilateral adrenal incidentalomas.
99.82 pg/mL (normal 37.5-240 pg/mL), renin < 0.5 pg/mL (normal 2.5-21.4 pg/mL), 8AM ACTH 45.5 pg/mL (normal 9-52 pg/mL), cortisol 36.2 µg/dL (normal 5-25 µg/dL), 10PM ACTH 6 pg/mL (normal < 10 pg/mL), cortisol 9.6 µg/dL (normal < 10 µg/dL). 24-h urinary excretion of catecholamines included epinephrine 4 µg/day (normal 0-24 µg/day), norepinephrine 20 µg/day (normal 10-80 µg/day), and dopamine 108 µg/day (normal 138-540 µg/day), rendering the diagnosis of pheochromocytoma less likely. The 17-hydroxyprogesterone level increased from 1.31 ng/mL to 5.97 ng/mL 1 hour after intravenous injection of 250 µg corticotropin, thereby excluding the possibility of attenuated congenital adrenal hyperplasia (17-hydroxyprogesterone > 8 ng/mL).

Computed tomography (CT) showed enlargement of bilateral adrenal glands with attenuation values of 37.5 Hounsfield units (HU) and 36.7 HU over the right and left side, respectively (Fig. 1). Chemical magnetic resonance imaging (MRI) did not display a loss of signal intensity on opposed-phase images (Fig. 2), indicating the absence of fat component. Gallium-67 citrate scintigraphy showed markedly increased uptake in bilateral supra-renal regions and no other abnormal tracer distribution in the whole body study (Fig. 3). Breast sonography, colon fiberoscopy and whole body bone scan all revealed negative findings. Upper gastro-intestinal endoscopy showed a shallow gastric ulcer, which showed no evidence of malignancy on biopsy of a specimen. Thus, the possibility of a metastatic lesion was unlikely.
To determine the nature of the abdominal masses, ultrasound-guided fine needle aspiration biopsy from the right adrenal was performed. Histological examinations disclosed a picture of malignant lymphoma, diffuse large B cell type, as evidenced by positive immunocytological reactions for leukocyte common antigen (LCA) and L26, but not for CD3. Subsequent bone marrow aspiration and biopsy revealed no evidence of lymphomatous infiltration.

The patient underwent exploratory laparotomy with bilateral adrenalectomy. The right adrenal tumor was 9.0 × 6.5 × 4.0 cm, and the left one was 8.0 × 6.5 × 3.0 cm. Histologic examination showed a diffuse pattern of large neoplastic lymphocytes with vesicular nuclei and large nucleoli (Fig. 4). These neoplastic lymphoid cells were immunocytochemically positive for L26, indicating their B-cell origin. One para-aortic lymph node was also infiltrated with lymphoma cells. Replacement therapy with cortisol acetate and adjuvant chemotherapy with full-dose CHOP regimen were given after the surgery. Unfortunately, the patient died of neutropenic fever 6 months after the diagnosis.

**DISCUSSION**

Primary adrenal lymphoma (PAL) is extremely rare. Only 76 cases have been reported in the medical literature, including the autopsy cases. The disease is more common in males and the mean age at presentation is around 65 years (range: 38 to 87). In all the cases of PAL reported, the incidence of bilateral involvement is about two times that of unilateral involvement, and large cell lymphoma appears to be the most common pathologic finding. Genetic alterations, such as p53 and c-kit genes mutations, are hypothesized as playing a role in the pathogenesis of adrenal lymphomas.

In the 35 reported cases of PAL in which adrenal function results are available, hypoadrenalism accounts for about one third of the cases (13/35) (Table 1). Since it is generally accepted that morning cortisol levels of greater than 19 µg/dL do not need further testing for the adequacy of adrenal function, our patient, who had a morning serum cortisol of 36.2 µg/dL and an ACTH of 45.5 pg/mL, appeared to have intact adrenal function despite the presence of bulky bilateral adrenal masses. Among 24 reported cases of PAL with bilateral adrenal masses, 13 patients were associated with adrenal insufficiency (Table 1). Namely, about half of the patients with bilateral masses still had intact adrenal function, like our patient. The mean tumor size in those patients with bilateral PAL and without adrenal insufficiency was 7.35 cm, whereas in those patients with adrenal insufficiency, it was 8.48 cm. The difference was not statistically significant (p = 0.559, independent samples t-test).

On CT and MRI, PAL may appear as a complex mass with variable density although some reported cases also show a homogeneous density. However, no pathognomonic appearance on CT, MRI or ultrasound indicates lymphomatous involvement of the adrenal glands. In our patient, the density of the adrenal tumors on CT is homogeneous but with relatively high Hounsfield units (HU). Lee et al. reported that a threshold at a level of 10 HU had a sensitivity to specificity ratio of 79%:96% for distinguishing benign from malignant adrenal lesions and suggested that adrenal biopsies should be performed if the attenuation values were greater than 10 HU. Another detection technique is chemical shift MR imaging, which shows a loss of signal in ten sity in benign lipid-containing adrenocortical masses. In our patient, the finding of no significant decrease in signal in-
ten sity on chem i cal shift im ages might be sug ges tive of ma lig nant le sions.

Gal lium scintigraphy has been con sid ered of great value in de tect ing, stag ing and eval u at ing the treat ment re sponse of PAL, on ac count of the high avid ity of Ga-67 for lym pho mas.10 Also, the sym met ric ad re nal vi su al iza -

10

tion on Ga-67 scan with out ex tra-adrenal up take might be highly sug ges tive of a di ag no sis of pri mary ad re nal lym phoma.11 In our pa tient, the find ing of an intensly in creased radiouptake by the bilat eral ad re nals on Ga-67 scan was con sis tent with this hy poth e sis. Re cently, FDG PET was re ported to show ex cel lent di ag nos tic per for -

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mance in dif fer en ti ating ma lig nant from be nign ad re nal le sions with a sen si tiv ity of 100% and spec if ic ity of 94%;12 as com pared with sen si tiv i ties of 90% and 79%, as well as spec ific ities of 100% and 96% for MRI and CT, re -

spec tively.8,13

The prog no sis of PAL is poor. Most pa tients die within one year of di ag no sis and the out come is worse if ad re nal insuffi ciency is present (Table 1).14 The ther a -

peu tic modal ities in clude sur gery, com bi na tion che mo -

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therapy, and sur gery fol lowed by che mo ther apy and/or ra di a tion ther apy. Ra di a tion ther apy alone or sur gery alone ap peared to be in ef fec tive.15 Che mo ther apy alone or sur gi cal resec tion fol lowed by ad juvant che mo ther apy has been re ported to achieve par tial or com plete re mis -

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sion. How ever, there is no con clu sive ev i dence to sug -

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gest which treat ment might of fer the better chance of sur -

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vival. Hence, the role of adrenalectomy is still to be de -

t ermined.

In sum mary, we sug gest that al though a rare dis ease, pri mary ad re nal lym pho mas should be con sid ered as a pos si ble cause of bi lat eral ad re nal incidentalomas. Non-

invasive im a ging tech niques, such as at ten u a tion co ef fi-

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cient of CT, chem i cal shift MR, and Ga scintig raphy, may pro vide clues to the di ag no sis and ex pect ing treat ment. We hope that the treat -

ment reg i mens which achieve max i mum ef fi cacy can be de vel oped through the ac cu mu la tion of these cases.

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Table 1. Primary adrenal lymphomas reported in the English literature as isolated cases with known adrenal function

<table>
<thead>
<tr>
<th></th>
<th>PAL without adrenal insufficiency</th>
<th>PAL with adrenal insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases number</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>Male: female</td>
<td>13:9</td>
<td>11:2</td>
</tr>
<tr>
<td>Site of tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral: unilateral</td>
<td>11:11</td>
<td>13:0</td>
</tr>
<tr>
<td>Age (years) Mean (ranges)</td>
<td>65 (38-87)</td>
<td>67 (57-81)</td>
</tr>
<tr>
<td>Size (cm, in greatest diameter)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 5 cm</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>5-10 cm</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>&gt;10 cm</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>NM</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 3 months</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3-6 months</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>6 months-1 year</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 1 year</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>NM</td>
<td>11</td>
<td>3</td>
</tr>
</tbody>
</table>

PAL = primary adrenal lymphoma; NM = not mentioned.


