Bilateral Adrenal Lymphoma with Neoplastic Angioendotheliosis

Mitsuru KUBO, Masafumi KOGA, Takashi FUJII, Tadashi KANEKO*, Ken-ichi YAMASHITA** and Tatsuo KOKUBU

We report a case of bilateral lymphoma of the adrenal glands. A 61-year-old man was admitted to our hospital in clinical shock with anuria. Endocrine examination indicated a diagnosis of Addison’s disease. Large tumors were found bilaterally in the suprarenal area, and a needle biopsy was performed, and the diagnosis was malignant lymphoma. Treatment with chemotherapy achieved a moderate response. He was discharged, but died 1 month later. On autopsy, microscopic examination showed extensive intravascular infiltration of lymphoma cells. We considered this to be a case of bilateral adrenal lymphoma with neoplastic angioendotheliosis.

(Key words: non-Hodgkin’s malignant lymphoma, Addison’s disease, large B-cell lymphoma, immunostain, acute renal failure)

Introduction

The diagnosis and classification of some malignant lymphomas remain difficult. Non-Hodgkin’s malignant lymphoma has an extranodal origin in 10–25% of cases and an endocrine origin in 3% (1). Several cases of primary malignant adrenal lymphoma associated with Addison’s disease have been reported (2–23). These cases were described to have a poor prognosis. Neoplastic angioendotheliosis (NAE) was first reported by Pfleger and Tappeiner (24). This condition was characterized by intravascular infiltration by large cells. Currently, these cells are regarded to be B-type malignant lymphoma cells. Here, we describe an unusual case of bilateral adrenal large cell lymphoma. The patient responded well enough to chemotherapy to be briefly discharged, but died suddenly due to massive hematemesis. On autopsy, microscopic examination showed extensive intravascular infiltration by lymphoma cells. We concluded that this patient represents a rare case of bilateral primary adrenal lymphoma with NAE.

Case Report

A 61-year-old man presented with a 1-month history of gastric discomfort and decreased appetite. After several episodes of convulsions of sudden onset, he was admitted to our hospital on July 5, 1989. Clinical findings on admission were shock with anuria and a decreased level of consciousness. Blood pressure was 78/40 mmHg, heart rate was 103 beats/min, and body temperature was 36.4°C. He complained of a dull pain in his lower abdomen, but on palpation the abdomen was soft and flat. There was no superficial lymphadenopathy. Laboratory examinations revealed that the glutamine-oxaloacetic transaminase (GOT) was 54 U/l, lactate dehydrogenase (LDH) 1,129 U/l, blood urea nitrogen (BUN) 62 mg/dl and the creatinine 5.0 mg/dl (Table 1). Serum electrolyte values were sodium 126 mEq/l, potassium 4.6 mEq/l, and chloride 97 mEq/l. The erythrocyte sedimentation rate was 47 mm at 1 hour and the C-reactive protein level was 17.8 mg/dl. Based on these findings, diagnosis on admission was mild hepatic dysfunction, renal failure, and inflammatory reaction. Transfusion was performed and catecholamines and hydrocortisone were administered to improve shock. He recovered from shock, but the serum creatinine concentration remained elevated at 5–6 mg/dl. On the third hospital day, he developed acute subendocardial infarction. The serum creatinine concentration fell to 1.4 mg/dl and his general condition stabilized on the 7th day. However, a spiking fever developed on the 9th day after admission. Because a low density area in the right adrenal lesion had been noted on ultrasonography at admission, a computed tomographic scan of the abdomen was performed. This showed the presence of large tumors bilaterally in the adrenal regions (Fig. 1). Subsequent endocrine function tests showed suppression of adrenal function and a marked increase in serum adrenocorticotropic hormone (ACTH) level (Table 2). A tentative diagnosis of non-functioning adrenal carcinoma associated with Addison’s disease was made, and confirmation was sought by percutaneous
Table 1. Blood and Biochemical Examination at the Time of Admission

<table>
<thead>
<tr>
<th>CBC</th>
<th>U.A.</th>
<th>15.8 mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>s-Amy</td>
<td>55 S.U.</td>
</tr>
<tr>
<td>Hb</td>
<td>T.chol.</td>
<td>67 mg/dl</td>
</tr>
<tr>
<td>Ht</td>
<td>FBS</td>
<td>105 mg/dl</td>
</tr>
<tr>
<td>WBC</td>
<td>CRP</td>
<td>17.8 mg/dl</td>
</tr>
<tr>
<td>St.</td>
<td>Serum electrolyte</td>
<td></td>
</tr>
<tr>
<td>Seg.</td>
<td>Na</td>
<td>126 mEq/l</td>
</tr>
<tr>
<td>Ly.</td>
<td>K</td>
<td>4.6 mEq/l</td>
</tr>
<tr>
<td>Mo.</td>
<td>Cl</td>
<td>97 mEq/l</td>
</tr>
<tr>
<td>Eo.</td>
<td>Ca</td>
<td>4.3 mEq/l</td>
</tr>
<tr>
<td>Ba.</td>
<td>P</td>
<td>4.3 mg/dl</td>
</tr>
</tbody>
</table>

ESR (1 hr) 47 mm, (2 hr) 85 mm, As-Trap. (O2 31/min insp.)

<table>
<thead>
<tr>
<th>Blood chemistry</th>
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</thead>
<tbody>
<tr>
<td>GOT 54 U//</td>
<td>PH 7.455</td>
<td></td>
</tr>
<tr>
<td>GPT 12 U//</td>
<td>PCO₂ 24.2 mmHg</td>
<td></td>
</tr>
<tr>
<td>ALP 10.9 U//</td>
<td>PO₂ 146.7 mmHg</td>
<td></td>
</tr>
<tr>
<td>LDH 1.129 U//</td>
<td>HCO₃⁻ 16.8 mEq/l</td>
<td></td>
</tr>
<tr>
<td>γ-GTP 28 U//</td>
<td>BE -5.1</td>
<td></td>
</tr>
<tr>
<td>CH-E 0.4 ΔPH</td>
<td>O.B. (-)</td>
<td></td>
</tr>
<tr>
<td>T-Bil 1.1 mg/dl</td>
<td>protein (-)</td>
<td></td>
</tr>
<tr>
<td>T.P. 5.0 g/dl</td>
<td>glucose (±)</td>
<td></td>
</tr>
<tr>
<td>Creati. 5.0 mg/dl</td>
<td>RBC 20–30/HPF</td>
<td></td>
</tr>
<tr>
<td>BUN 62 mg/dl</td>
<td>WBC 0–1/HPF</td>
<td></td>
</tr>
</tbody>
</table>

ESR (1 hr) 47 mm, (2 hr) 85 mm, As-Trap. (O2 31/min insp.)

Table 2. Endocrinological Study

<table>
<thead>
<tr>
<th>ACTH</th>
<th>240 pg/ml (30–60)</th>
</tr>
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<tbody>
<tr>
<td>Cortisol</td>
<td>8.7 μg/dl (3.7–13.0)</td>
</tr>
<tr>
<td>Aldosterone</td>
<td>&lt;10 pg/ml (10.9–62.7)</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>&lt;0.01 μg/ml (&lt;0.12)</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>0.27 ng/ml (0.06–0.45)</td>
</tr>
<tr>
<td>DHEA</td>
<td>0.6 ng/ml (1.2–7.5)</td>
</tr>
<tr>
<td>DHEA-S</td>
<td>&lt;200 ng/ml (500–3,000)</td>
</tr>
<tr>
<td>17-KS (urine)</td>
<td>3.3 mg/day (4.6–18.0)</td>
</tr>
<tr>
<td>17-OHCS (urine)</td>
<td>5.2 mg/day (3.4–12.0)</td>
</tr>
<tr>
<td>VMA (urine)</td>
<td>1.4 mg/day (1.3–5.1)</td>
</tr>
</tbody>
</table>


Figure 1. Computed tomography reveals large tumors in bilateral suprarenal portions.

needle biopsy of the right adrenal tumor. Cytologic examination showed the presence of lymphoid cells, and immunocytochemical stains of their cell surface were positive for Mx-Pan B, LN-1 and MB-1, and negative for LN-2, 4KB5, and UCHL-1 (Fig. 2). A diagnosis of B-cell malignant lymphoma was made. Bilateral pleural effusion developed on August 10, even though no particular findings were seen on chest X-ray at admission. Exploratory pleural puncture revealed the presence of the same malignant cells as in the adrenal tumor biopsy specimen.

Figure 3 shows the clinical course of the patient. Combination chemotherapy (VEPA) was started as follows: vincristine 1 mg i.v., cyclophosphamide 300 mg i.v. and doxorubicin 30 mg i.v. on the first day, and prednisolone 60 mg/day p.o. on days 1 to 4. After chemotherapy, his general condition stabilized and his fever subsided. The size of the tumors decreased by 70% on computed tomography, and the pleural effusions resolved. A second cycle of VEPA was administered on September 20 as follows: vincristine 1.5 mg i.v., cyclophosphamide 500 mg i.v. and doxorubicin 50 mg i.v. on the first day, and prednisolone 60 mg/day p.o. on days 1 to 4. However, the patient showed no response to this second cycle. As he was asymptomatic at this time and his family wished him to come home, he was discharged on October 27. He was readmitted on December 6, 1989, because of worsening renal function. Further chemotherapy was considered, but he died suddenly from massive hematemesis on December 13, 1989. Autopsy was performed.

Pathologic Findings

Bilateral suprarenal tumors were found on autopsy. The maximum diameters of the left and right tumors were 7 and 10 cm, respectively. Both tumors were light gray, associated with bleeding, and invaded into the retroperitoneum (Fig. 4). The kidneys were hypertrophic and weighed 250 g each. Cut sections of the kidney were light gray. No normal adrenal tissue was found in the bilateral suprarenal areas.

Histologically, the tumors consisted of large pleomorphic lymphoid cells. These cells showed extensive infiltration mainly into the vein within the tumors (Fig. 5) and into the kidney and liver (Fig. 6). Malignant cells were also seen in the capillaries of the glomeruli, but were not seen in the bone marrow.

Based on these pathological findings, a diagnosis of B-cell non-Hodgkin’s lymphoma of the diffuse large cleaved-cell type
Bilateral Adrenal Lymphoma

Figure 2. Immunostaining of the cell surface of the right adrenal tumor. Left panel shows LN-1 stain and right panel shows MB-1 stain (×200).

Vincristine 1 mg 1.5 mg 1.5 mg 1.5 mg 1.5 mg 1.5 mg
Cyclophosphamide 300 mg 400 mg 400 mg 500 mg 500 mg 500 mg
Doxorubicin 30 mg 60 mg
Hydrocortisone 500 mg
Prednisolone 5 mg 60 mg 60 mg 50 mg

CRP (mg/dl)

Creat. 5.0 -
4.0 -
3.0 -

LDH 3,000 -
2,000 -
1,500 -

B.T. (°C) 39.0 -
38.0 -
37.0 -
36.0 -

July August September October November December (1989)

Figure 3. Clinical course of the patient.
was made. The cause of death was massive hemorrhage from a gastric ulcer arising at the site of tumor invasion. The lymphoma also invaded into the pleural cavity and pericardium.

**Discussion**

Non-Hodgkin’s lymphoma arising in endocrine glands represents only 3% of extranodal malignant lymphomas (1). Primary malignant lymphoma in the adrenal gland is rare, and only 22 cases have been reported to our knowledge (2-23). The present patient had large bilateral tumors in the suprarenal area, and no other apparent hypertrophic lymph nodes were found in the retroperitoneum. Previous cases of bilateral primary adrenal lymphoma were reported to present as Addison’s disease (2, 7, 8, 11, 15, 16, 22). We did not detect normal adrenal gland tissue at autopsy in our patient, and endocrine examination revealed serious adrenal failure. Under this suppression of adrenal function, the patient first presented with shock, which did not improve until the administration of steroids.

Pfleger and Tappeiner (24) reported a patient suffering from a cutaneous eruption, weight loss and fever. Cutaneous biopsy showed intravascular infiltration by large cells. In their examination of the same patient, Strouth et al (25) reported that the patient had developed neurologic symptoms, and they described the condition as NAE. The large cells were considered to have an endothelial origin (26, 27). Immunohistochemical staining studies performed by Mori et al (28, 29), however, revealed that these large cells were positive for B-cell markers, and several investigators have reported that the large cells in NAE have a B lymphocyte origin (30-32). In the present case, we found that B-type large lymphoma cells had extensively infiltrated the vessels of the kidney, liver and the adrenal tumors themselves. Clinically, NAE is associated primarily with intravascular lesions, but the primary tumor in our patient was apparently of extravascular origin. However, we assumed that the malignant lymphoma in our patient was essentially the same as NAE because of the close resemblance in the infiltration pattern of lymphoma cells. Our patient remained in renal failure for 10 days despite the successful treatment of shock on admission. At autopsy, the kidney was hypertrophic and
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Figure 6. Microscopic findings of the kidney (left) and liver (right). Malignant cells showed extensive infiltration mainly into the vein of the kidney and liver, and also in the capillaries of the glomeruli (HE stain, ×200).

ischemic. Extensive intravascular infiltration by lymphoma cells was seen in both kidneys at microscopic examination. We therefore considered that the renal failure in this patient might have been caused by NAE in addition to adrenocortical failure.

Treatment has not been successful in the cases of bilateral adrenal lymphoma reported to date except for only one case (23). We administered two cycles of VEPA combination chemotherapy, using one half of the usual dosages for the first cycle and full dosages for the second. Response was only moderate, but sufficient to allow discharge.

In summary, we reported an unusual case of bilateral primary adrenal non-Hodgkin’s lymphoma that presented as Addison’s disease. On the basis of the pattern of infiltration by lymphoma cells, the pathologic picture was essentially the same as that of NAE. Brief remission was obtained in response to combination chemotherapy.

References

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