

A Case of Primary Bilateral Adrenal Lymphoma with Partial Adrenal Insufficiency

Keu-Sung Lee¹, Yoon-Sok Chung¹, Kwang Hwa Park², Hyun Soo Kim³, and Hyeon-Man Kim¹

Abstract

Unilateral or bilateral non-Hodgkin's lymphomas arising primarily in the adrenal glands are extremely rare. These lymphomas are usually present with large, bilateral adrenal masses with or without lymphadenopathy, and may be accompanied by adrenal insufficiency in some cases. A review of the literature indicates that patients with primary lymphoma of the adrenal glands usually do not have disease elsewhere, and if present, it is frequently extranodal. We report here an unusual case of primary bilateral adrenal lymphoma with partial adrenal insufficiency.

Key Words: Primary adrenal lymphoma, partial adrenal insufficiency

INTRODUCTION

The malignant lymphoma of the adrenal gland is an extremely rare condition of adrenal gland pathology.^{1,2} It usually occurs as a bilateral adrenal mass without lymphadenopathy, and may be accompanied by adrenal insufficiency in some cases.³ An adrenal lymphoma as well as metastasis, congenital adrenal hyperplasia, and pheochromocytoma of multiple endocrine neoplasia should be considered in cases of bilateral adrenal enlargement.⁴ The most common type of adrenal lymphoma is diffuse large cell lymphoma of B cell lineage.

We report a case of bilateral adrenal lymphoma that strongly suggested that it occurred primarily from the adrenal gland without evidence of systemic metastasis. The patient did not complain of any symptoms of adrenal insufficiency, but laboratory findings revealed that he had partial adrenal insufficiency.

CASE REPORT

Received January 28, 1999

Accepted April 23, 1999

¹Department of Endocrinology and Metabolism, ²Department of Pathology, ³Department of Hematology and Oncology, Ajou University School of Medicine, Suwon 442-749, Korea

Address reprint request to Dr. Y. S. Chung, Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon 442-749, Korea. Tel: 82-331-219-5127, Fax: 82-331-219-5109, E-mail: cys3333@chollian.net

A 54-year-old male was admitted to the hospital complaining of pain in the left upper quadrant of the abdomen for two weeks. Before admission, he had taken an abdominal ultrasonography at another hospital, which showed that he had a retroperitoneal mass. His past medical and family history was not contributory. There was no history of weight loss, fever, night sweat or pruritus.

His height was 161 cm and he weighed 55.2 kg. Physical examination revealed the patient to be moderately nourished. His vital signs were as follows: body temperature, 36.7°C; pulse rate 72 beats per minute. We checked for three positional blood pressures. His supine blood pressure was 140/80 mmHg, sitting blood pressure 140/80 mmHg, and standing blood pressure 120/80 mmHg. Examination of his head and neck was unremarkable. No abnormality was found in the chest. Hepatosplenomegaly or mass was not detected in the abdomen. No lymphadenopathy was noted and no abnormal skin lesion was found.

A complete blood count revealed hemoglobin 13.3 g/dL, hematocrit 39.8%, white blood cell count 5,400/mm³, platelet 163,000/mm³. Prothrombin time was 12 seconds and activated partial thromboplastin time was 28 seconds. The serum aspartate aminotransferase was 33 U/L, alanine aminotransferase was 20 U/L. The serum sodium, potassium and chloride levels were 134, 3.8, and 100 mEq/L, respectively. The serum total calcium was 8.1 mg/dL, and inorganic phosphorus was 2.0 mg/dL. The serum uric

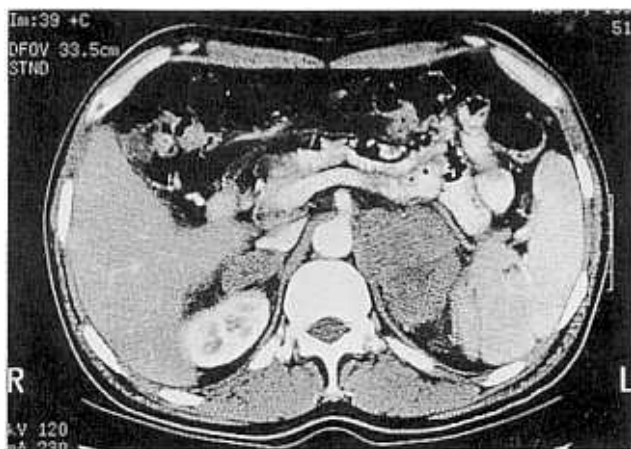


Fig. 1. Abdominal computed tomography revealed an irregular heterogeneous mass in the left adrenal gland approximately 5×7 cm in size, and another mass lesion in right adrenal gland approximately 2.5×5 cm in size.

acid, total bilirubin and total cholesterol levels were 5.1, 1.0, and 135 mg/dL, respectively. The serum albumin level was 3.8 g/dL. The serum β_2 -microglobulin increased to 3,069.10 ng/ml (normal range 881–2421). The serum lactate dehydrogenase level increased to 750 U/L. The serum cortisol (8AM) was 12.1 μ g/dl (normal range 7–25) and the plasma ACTH (8AM) increased to 155 pg/ml (normal range 9–52). The serum aldosterone was 20.38 pg/ml (normal range 20–160). The level of 24 hr urine vanillylmandelic acid was 3.63 mg/day (normal range 0–8), epinephrine, 3.5 μ g/day (normal range 0–20), norepinephrine, 24.8 μ g/day (normal range 0–130), total metanephrine, 0.09 mg/day (normal range 0–1.3), 5-HIAA, 7.3 mg/day (normal range 2–8), and free cortisol, 40.33 μ g/day (normal range 0–100), respectively. The 24-hour urine 17-KS and 17-OHCS decreased to 4.0 mg/day (normal range 8–20) and 1.0 mg/day (normal range 3.6–9.0), respectively.

The chest X-ray was normal without evidence of hilar lymphadenopathy. A computerized tomographic scan showed large bilaterally irregular adrenal mass lesions with single paraaortic lymphadenopathy (Fig. 1). The left adrenal mass was approximately 5×7 cm in size, and was of an irregular heterogeneous nature. The right adrenal mass was approximately 2.5×5 cm in size, with similar characteristics.

We performed bilateral adrenalectomy with clinical impression of adrenal cortical carcinoma. The adrenal

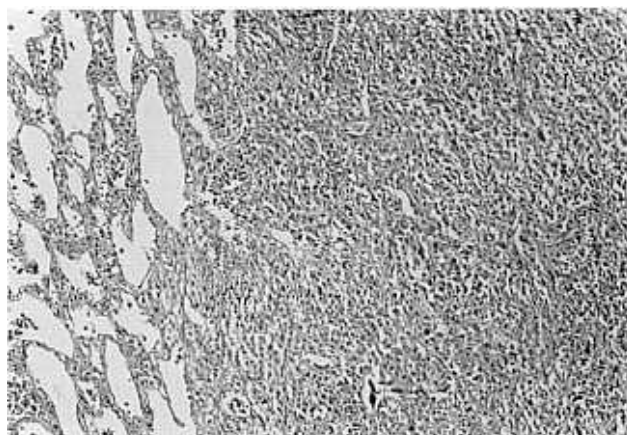


Fig. 2. The adrenal gland was replaced by massive lymphoid cell infiltration. It showed diffuse pattern with sinusoidal involvement (H&E, $\times 100$).

gland was replaced by massive lymphoid cell infiltration. It showed diffuse pattern, with predominant angiotrophism and sinusoidal involvement (Fig. 2). Tumor cells were large cells and showed positive reaction with CD20 on immunohistochemical stain, but CD3, CD30, were negative. In-situ hybridization and PCR for EBV (EBER and EBNA) were negative.

In this case of lymphoma, the clinical staging by the Ann Arbor System was II_E, and the International Prognostic Index was low risk group. The patient received adrenal hormone replacement with prednisolone 7.5 mg (5 mg at 8AM and 2.5 mg at 4PM) after bilateral adrenalectomy. He also received CHOP chemotherapy with cyclophosphamide 750 mg/m² i.v., doxorubicin 50 mg/m² i.v., vincristine 1.4 mg/m² i.v. on the first day, and prednisolone 100 mg p.o. for 5 days. The patient completed 6 cycles of CHOP chemotherapy. The follow-up abdominal computed tomography and ¹⁸F fluorodeoxyglucose-positron emission tomography scan after 6 cycles of chemotherapy revealed no evidence of tumor.

DISCUSSION

Malignant lymphomas arising primarily in endocrine organs are rare, accounting for less than 3% of extranodal presentations.⁵ They are almost always confined to the thyroid gland. Unilateral or bilateral non-Hodgkin's lymphomas arising primarily in the adrenal glands are extremely rare.^{1,2} These lym-

phomas are usually present with large, bilateral adrenal masses with or without lymphadenopathy, and may be accompanied by adrenal insufficiency in some cases.³ The bilateral adrenal lymphoma could develop because of lymphatic tissues existing in both adrenal glands.

The most common type of adrenal lymphoma reported in the literature is diffuse large cell (B cell) lymphoma with bilateral masses.³ Previously, three out of 18 cases were associated with hypercalcemia.^{3,6} Primary adrenal lymphoma occurred predominantly in males with a male-to-female ratio of about 7 : 1.³ Our case was a male subject. Three out of 18 cases were T cell lymphoma.^{3,6} There was a case of a variant form of angiotrophic large cell lymphoma.⁷

At first, this case was not suspected with adrenal lymphoma because of its rarity and absence of B symptoms. Our first clinical impressions were adrenal cortical carcinoma with contralateral metastasis; second, bilateral adrenal metastasis from hidden malignancy; third, bilateral silent pheochromocytoma; and fourth, bilateral involvement of granulomatous disease.

Imaging techniques using computerized tomographic scan are usually able to discriminate adrenal malignancy from benign diseases. Adrenal cortical adenomas are mostly homogeneous, hypodense tumors, round or oval in shape with regular and well-defined margins. Conversely, adrenal cortical carcinomas are mostly inhomogeneous tumors of irregular shape and margins.⁸ In this case, computerized tomographic scan showed inhomogeneous density mass with irregular shape and margins which suggested malignancy rather than benign adenoma, and the serum lactate dehydrogenase increased to levels that were compatible with malignant lymphoma.

Destruction of approximately 90% of the adrenal cortex is necessary before adrenal insufficiency becomes apparent.⁹ For this reason, although solid tumor metastases to the adrenal glands are common, they rarely produce symptoms of adrenal insufficiency. However, in primary adrenal lymphoma, 13 out of 18 patients reported in the literature showed adrenal insufficiency.^{3,6}

In this case, the patient had no symptoms of adrenal insufficiency, such as weakness, anorexia, nausea and vomiting, weight loss, cutaneous and mucosal hyperpigmentation, and occasional hypoglycemia. Adrenal insufficiency can be documented by lower basal serum cortisol levels and elevated plasma

ACTH levels, and finally confirmed by rapid ACTH stimulation test which would reveal peak serum cortisol levels at 30 or 60 minutes less than 18 $\mu\text{g}/\text{dL}$. We measured basal serum cortisol and plasma ACTH levels only once and did not perform an ACTH stimulation test, but the patient showed a high basal ACTH with lower normal cortisol levels. This indicated that he had partial adrenal insufficiency. Kuwahara et al. reported a case of bilateral adrenal lymphoma associated with partial adrenal insufficiency.⁷

Biopsy would ordinarily be sufficient to reach a diagnosis, but in our case we performed bilateral adrenalectomy because we wanted to find any possible hidden intraabdominal malignancy, and we did not want a hypertensive crisis after biopsy of possible pheochromocytoma.

Prognosis of primary adrenal lymphoma and disseminated B cell lymphoma has been very poor.^{3,6} Seven out of 11 patients in the literature who were followed died within 5 months. All patients reported in the literature died within 11 months after diagnosis, despite combination chemotherapy.

In our case, because a bone marrow biopsy was not performed, and there was single paraaortic lymphadenopathy, the possibility remained of malignant lymphoma not originating primarily from the adrenal gland. We report a case of primary bilateral adrenal lymphoma with partial adrenal insufficiency along with a review of the literature.

REFERENCES

1. Choi CH, Durishin M, Garbadawala ST, Richard J. Non-Hodgkin's lymphoma of the adrenal gland. *Arch Pathol Lab Med* 1990;114:883-5.
2. Bauduer F, Delmer A, LeTourneau A, Guettier C, Alexandre JH, Zittoun R, et al. Primary adrenal lymphoma. *Acta Haematol* 1992;88:213-5.
3. Al-Fiar FZ, Pantalony D, Shepherd F. Primary bilateral adrenal lymphoma. *Leukemia and Lymphoma*. 1997;27:543-9.
4. Barzon L, Scaroni C, Sonino N, Fallo F, Greganin M, Macri C, et al. Incidentally discovered adrenal tumors: Endocrine and scintigraphic correlates. *J Clin Endocrinol Metab* 1998;83:55-62.
5. Freeman C, Berg JW, Culter SJ. Occurrence and prognosis of extranodal lymphomas. *Cancer* 1972;29:252-60.
6. Pimentel M, Johnston JB, Allan DR, Greenberg H, Bernstein CN. Primary adrenal lymphoma associated with

- adrenal insufficiency: A distinct clinical entity. *Leuk Lymphoma* 1997;24:363-7.
7. Kuwahara K, Fukata J, Kamio M, Mochizuki T, Tsuchiya A, Tanaka S. Angiotrophic large cell lymphoma which infiltrated to the adrenal glands presenting as reversible adrenal insufficiency. *Intern Med* 1998;37:73-6.
 8. Angeli A, Osella G, Ali A, Terzolo M. Adrenal incidentaloma. An overview of clinical and epidemiological data from the National Italian Study Group. *Horm Res* 1997; 47:279-83.
 9. Kung AW, Pun KK, Lam K, Wang C, Leung CY. Addisonian crisis as presenting feature in malignancies. *Cancer* 1990;65:177-9.
-