Non-Hodgkin's Lymphoma With Bilateral Adrenal Gland and Brain Involvement Presenting as Primary Adrenal Insufficiency: Report of a Case

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A 73-year-old man with a history of type II diabetes mellitus was hospitalized because of progressive general weakness, anorexia and marked weight loss for 1 month. On admission, lethargy, poor skin turgor and hyperpigmentation of skin were found. Laboratory data showed hyponatremia, anemia and thrombocytopenia. Primary adrenal insufficiency was confirmed by a relative low serum cortisol level during stress test, an elevated adrenocorticotropic hormone (ACTH) level and inadequate response to the rapid ACTH stimulation test. Non-Hodgkin's lymphoma (NHL) of the diffuse large B-cell type with bilateral adrenal gland and brain involvement was diagnosed based on histological study of computerized tomography-guided biopsy of an adrenal mass and emergent craniotomy for a brain tumor with hemorrhage. There was no evidence of involvement with other organs, the lymphatic system or bone marrow. Steroid replacement therapy was started while workup for adrenal insufficiency proceeded. Whole brain irradiation was performed and he received one course of chemotherapy with cyclophosphamide, vincristine, and prednisolone. He died of aspiration pneumonia complicated with septic shock and progression of NHL 2 months later. **(Mid Taiwan J Med 2002;7:250-4)**

Key words

non-Hodgkin's lymphoma, primary adrenal insufficiency

INTRODUCTION

NHL is uncommon but not rare, and all evidence points to it becoming more common than most other malignancies. Adrenal involvement is not uncommon in NHL. In a post-mortem study, the incidence of adrenal involvement was as high as 25% and was usually unilateral [3]; however, adrenal insufficiency as a consequence of adrenal involvement is rare. We report a case of NHL with bilateral adrenal gland and brain involvement in a patient who initially presented with primary adrenal insufficiency.

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CASE REPORT

This 73-year-old retired businessman with a history of type II DM was brought to our hospital because of general deterioration during the previous 1 month. He presented with general weakness, anorexia and marked weight loss. About 1 year prior to this visit, type II DM was diagnosed with fasting plasma sugar 200 mg/dL but with no polyphagia,

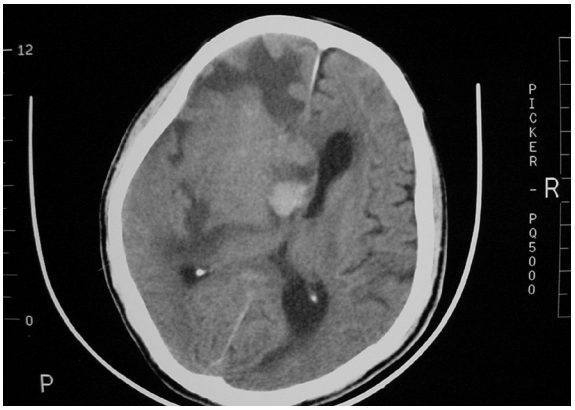

Fig. 1. Brain CT showing a huge brain tumor in the right frontal-temporo-parietal lobes and right basal ganglia with hemorrhage and significant mass effect.

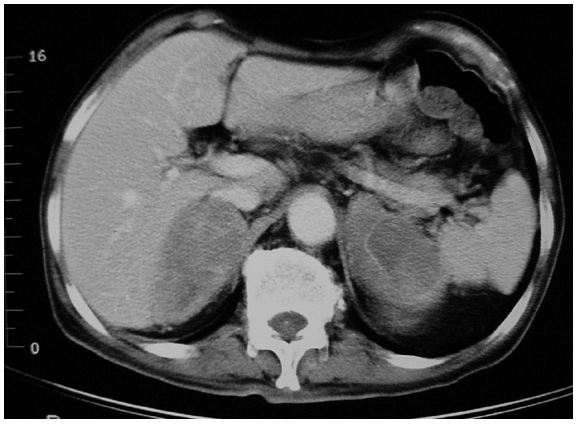

Fig. 2. Abdominal CT scan with intravenous enhancement showing bilateral adrenal mass lesions.

polyuria or polydipsia, although body weight loss and hyperpigmentation of the skin were found. He initially took metformin 500 mg twice a day and fasting plasma sugar was controlled to around 100 to 150 mg/dL. He had stopped using the oral hypoglycemic agent because of anorexia with poor intake the month previous to this admission.

One month prior to this visit, panendoscopy was performed because of anemia, anorexia, and body weight loss of more than 5 kg in 1 month. Superficial gastritis and hiatal hernia were identified. Aggravated hyperpigmentation of the skin was also noted by his family. He was brought to Ching-Chiuan hospital because of his deteriorating general condition and then transferred to our hospital post blood transfusion because of anemia. On admission, his vital signs were all within normal limits. Physical examination revealed clear consciousness, and dry skin turgor with hyperpigmentation over buccal mucosa, lips and skin, especially over the lower limbs, but no evidence of lymphadenopathy. Complete blood count showed a hemoglobin level of 12.8 g/dL, a white cell count of 5150/μL (54.1% segmented neutrophils, 27.1% lymphocytes, 15.8% monocytes, and 2.4% reticulocytes) and a platelet count of 69700/μL. Serum sodium was 129 mmol/L, potassium 4.1 mmol/L and glucose was 100 mg/dL. Clinical suspicion of primary adrenal insufficiency was confirmed by a relatively low serum cortisol level of 7.4 μg/dL (normal, AM: 5–25 μg/dL), a high ACTH level of 283.61 pg/mL (normal, 9–52 pg/mL), and a low cortisol level of 6.6 μg/dL at 30 minutes and 6.1 μg/dL at 60 minutes after the rapid ACTH stimulation test (cosyntropin 250 μg intramuscular injection with a baseline cortisol concentration 6.2 μg/dL). Sudden onset of consciousness change accompanied with left hemiplegia developed during hospitalization and emergent craniotomy was performed because of the detection of a huge brain tumor in the right frontal-temporal-parietal lobes and right basal ganglia which showed hemorrhage on brain CT (Fig. 1). Abdominal CT (Fig. 2) was performed later and revealed bilateral adrenal mass lesions. Histological examinations of a brain tumor specimen (Fig. 3) and a percutaneous CT-guided biopsy specimen from the right adrenal mass (Fig. 4) both showed diffuse large lymphoma cell infiltration.

Immunohistochemical studies showed that these tumor cells positively stained for leukocyte common antigen (LCA) and L-26, a B-lymphocyte marker. Bone marrow study showed no morphological evidence of lymphoma infiltration. Chest radiography and CT scan revealed no abnormalities and there was no evidence of lymphoma outside the adrenal glands and brain. Intravenous hydrocortisone 100 mg was administered daily every 6 hours and whole brain irradiation was arranged following craniotomy. One week

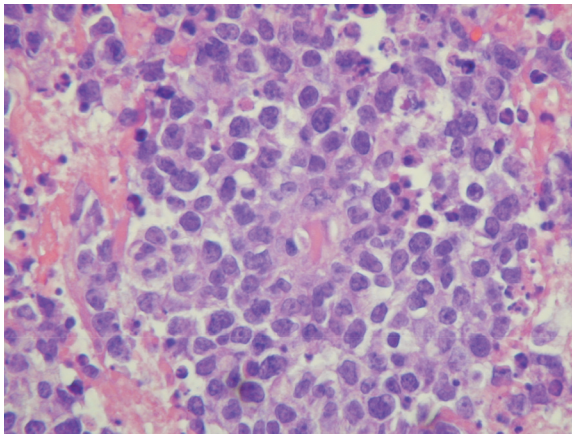

Fig. 3. Histological appearance of a specimen obtained from craniotomy for brain tumor, showing malignant lymphoma, diffuse large B-cell type (H & E stain, × 400).

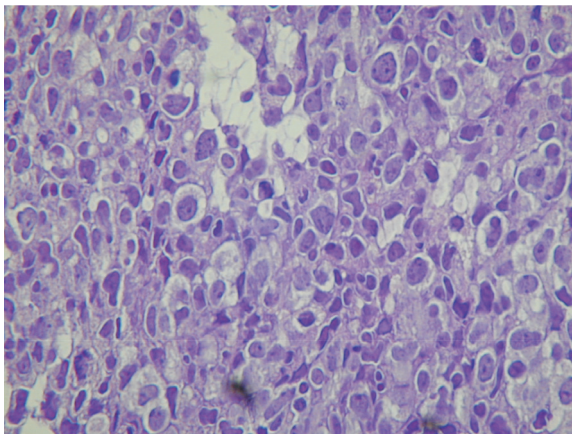

Fig. 4. Biopsy specimen obtained from right adrenal mass, showing malignant lymphoma, diffuse large B-cell type (H & E stain, × 400).

later, the first course of chemotherapy was started with cyclophosphamide, vincristine, and prednisolone. The patient died of aspiration pneumonia complicated by septic shock and progression of NHL about 2 months later. No autopsy was performed.

DISCUSSION

The most common disorders which cause primary adrenal insufficiency include autoimmune diseases, granulomatous diseases, such as tuberculosis and histoplasmosis, metastatic malignancies, hemorrhage associated with anticoagulant therapy or meningococcemia, and other rare hereditary diseases [4]. The adrenal glands may be involved in metastatic cancer, with the most frequent sites of origin of neoplasias being the lungs, breast, gastrointestinal tract and skin [1,2]. Primary adrenal insufficiency due to adrenal involvement is rare as destruction of more than 90% of the adrenal cortex is necessary to cause adrenal failure [5,6]. The clinical manifestations of primary adrenal insufficiency can include anorexia, nausea, vomiting, abdominal pain, fever, weakness, fatigue, lethargy, and mental confusion, or even coma. Hypoglycemia, hyponatremia, hyperkalemia, azotemia, hypercalcemia, and eosinophilia have been found in laboratory studies. Hyperpigmentation of the skin and mucosa may be found in patients with long-standing adrenal insufficiency. Cases of cerebral lymphoma appear to be increasing and is related to both congenital and acquired immune deficiency. Cerebral lymphoma usually presents with symptoms of an intracerebral space-occupying lesion, personality changes, headaches, and lethargy.

NHL in our patient involved the adrenal gland and brain but there was no evidence of superficial nodal involvement. There was also no leukemic blood picture or other organ involvement. Our review of the recent literature found no similar case reports. In our case, primary adrenal insufficiency was diagnosed immediately post admission but the diagnosis of NHL with brain and bilateral adrenal gland involvement was not immediate. Patients with adrenal insufficiency may have symptoms similar to those of patients with a malignant lesion which may explain why we were unable to detect brain and adrenal lesions until obvious sudden focal neurologic symptoms and signs were present. In fact, adrenal insufficiency in the presence of disseminated malignant disease may easily be overlooked and is probably an underdiagnosed entity [7].

The therapeutic modalities for adrenal lymphoma include surgery, combination chemotherapy, surgery followed by

chemotherapy and/or irradiation therapy, and corticosteroid replacement [8,9]. In cerebral lymphoma, radiation is the mainstay of treatment. Old age, initial presentation with primary adrenal insufficiency, huge tumor size, elevated serum LDH level, and involvement of other organs generally carry a poor prognosis [7,9].

The most common cause of primary adrenal insufficiency is autoimmune adrenalitis but primary adrenal lymphomas and other malignant tumors may cause adrenal insufficiency as well. Therefore, adrenal insufficiency should not be attributed to autoimmune adrenalitis without appropriate imaging studies, especially in the elderly and patients with immune deficiency [10]. A detailed history and physical examination are helpful in the detection of occult malignancy and disease. However, the initial manifestations of adrenal insufficiency in patients with NHL are indicative of an aggressive clinical course. Early diagnosis based on a stepwise approach is essential for the appropriate management of these patients.

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開始以腎上腺功能不足表現的兩側腎上腺及腦侵犯之非何杰金氏淋巴瘤：一病例報告

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造成原發性腎上腺功能不足的原因有很多，其中因非何杰金氏淋巴瘤所引起者卻很少見。本文報告一例73歲男性病人，一開始以原發性腎上腺功能不足爲表現，在住院當中意外發生急性意識變化和左側偏癱，後而診斷出是合併兩側腎上腺及腦侵犯之非何杰金氏淋巴瘤。由於腎上腺功能不足及惡性腫瘤在臨床上有許多相同的表現，在這些腎上腺功能不足病人的照顧應該更加警惕，及早診斷和治療眞正病因，將有助病人整體預後的發展及生活品質的改善。（中台灣醫誌 **2002;7:250-4**）

關鍵詞

非何杰金氏淋巴瘤，原發性腎上腺功能不足

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