Angiotropic Large Cell Lymphoma which Infiltrated to the Adrenal Glands Presenting as Reversible Adrenal Insufficiency

Koichiro Kuwahara, Junichi Fukata*, Masanori Kamio, Toshihiro Mochizuki, Atsushi Tsuchiya and Satoru Tanaka

A 72-year-old man who suffered from recurrent fever was found to have enlarged bilateral adrenal glands on computed tomographic scanning, combined with subclinical adrenal insufficiency. Based on the pathology of bone marrow aspiration, he was diagnosed to have an angiotropic large cell lymphoma (ALCL). Soon after the treatment with a combination chemotherapy, he achieved complete remission of ALCL and size and function of the adrenal glands were apparently normalized. ALCL should be included in the list of differential diagnoses of non-functioning bilateral adrenal swelling with non-specific symptoms such as fever.

Key words: chemotherapy, adrenal incidentaloma, fever

Introduction

Angiotropic large cell lymphoma (ALCL), also known as intravascular lymphomatosis, is a relatively rare but fatal hematologic disorder characterized by massive proliferation of neoplastic mononuclear cells within the vascular lumen. Correct diagnosis is often difficult to make due to the non-specific symptoms, absence of tumor cells in the peripheral blood and its relatively acute clinical course. Although this disease was originally thought to be of endothelial origin (1), a consensus has now been reached that ALCL represents a type of malignant lymphoma (2-4). Since clinicopathological reports of this disease, especially regarding the adrenal involvement, are limited to date, here we report a case of ALCL with bilateral adrenal swelling presenting as partial and reversible adrenal insufficiency.

For editorial comment, see p 3.

Case Report

A 72-year-old man was admitted to our hospital on January 12, 1994, complaining of general malaise and shaking chill. For one month before admission he was recurrently febrile with an afternoon temperature around 39°C. With each episode, the fever continued for about one week and subsided spontaneously. His past medical history included malaria at 37 years of age and appendicitis at age 40. The patient's family history was not contributory. His height was 167 cm and he weighed 57 kg; physical examination revealed the patient to be poorly nourished. His vital signs were as follows: body temperature, 39°C; pulse, 88 beats per minute (regular); and blood pressure, 90/60 mmHg. Examination of his head and neck was unremarkable. No abnormality was found in the chest or abdomen. No hepatosplenomegaly or mass was found in the abdomen. Surface lymph nodes were not pathognomonic and no skin lesion was found. Mental disturbance such as hallucination and confusion were episodically observed even during the period when he was not febrile, but other neurological abnormalities were not noted. Urinalysis was negative. A complete blood count revealed anemia (hematocrit; 27.8%, hemoglobin; 9.5 g/dl) and thrombocytopenia (105,000/jl). White blood cell count was 3,900/mm³ with a normal hemogram. Prothrombin time (PT) was 12.0 seconds, and activated partial thromboplastin time (APTT) was 35.3 seconds with a control of 28.2 seconds. Serum fibrinogen and fibrin degradation products (FDP) levels were 314 mg/dl and 9.8 μg/ml, respectively, and the antithrombin-III level was 66%. Liver function tests were also within normal limits. The serum lactate dehydrogenase (LDH) level was el-
The serum sodium, chloride and potassium levels were 134, 102, and 4.2 mmol/l, respectively. Computed tomography (CT)-scan showed enlarged bilateral adrenal glands (Fig. 1A). Gallium scintigram also showed bilateral large adrenal masses with even trapping of the tracer. Adrenal functions were then evaluated as follows: Adrenocorticotropic hormone (ACTH) was measured by immunoradiometric assay (IRMA), and cortisol, aldosterone, and plasma renin activity (PRA) were quantitated by radioimmunoassay (RIA), using commercial kits. Hormone levels determined using plasma obtained at 9 AM after 1h of recumbent position are shown in Table 1. The serum cortisol level showed an inadequately low cortisol response from 11.8 μg/dl to 14.4 μg/dl at 60 minutes after iv injection of 0.25 μg synthetic ACTH. Among the plasma catecholamines, the adrenaline level quantitated similarly in the morning was abnormally low at less than 5 pg/ml, but those of noradrenaline and dopamine were within normal limits. A bone marrow biopsy revealed hypocellular marrow with large immature lymphoid cells infiltrating and filling the small blood vessels (Fig. 2). Immunohistologically, the abnormal cells showed positive staining to B-cell markers such as LCA, L26, and LN2, indicating the cells to be of B-cell originated ALCL.

The patient received a regimen of chemotherapy termed modified CHOP with cyclophosphamide (840 mg/day × 1 day), doxorubicin HCl (56 mg/day × 1 day), vincristine (1.5 mg/day × 1 day), and prednisolone (70 mg/day × 5 days). After receiving 6 cycles of the regimen over 4 months, the patient became free from the symptoms and lymphoma cells were undetectable in the bone marrow specimen. In the laboratory findings, LDH level was normalized after the first cycle of the regimen and plasma ACTH and serum cortisol levels measured in the morning were normal when measured four months later at 117 pg/ml and 12.8 μg/dl, respectively (Table 1). Plasma aldosterone and renin activity were within normal limits and serum
ALCL with Reversible Adrenal Insufficiency

sodium, chloride, and potassium levels were 141, 106, and 4.1 mmol/l, respectively. Adrenal imaging on CT scan also became apparently normal (Fig. 1B).

Discussion

ALCL is a rare and distinctive form of non-Hodgkin lymphoma characterized by proliferated malignant lymphoid cells within the vascular lumina (4). As a non-Hodgkin lymphoma, ALCL is still a lethal disorder at present which is frequently difficult to recognize with an accurate antemortem diagnosis due to the lack of characteristic symptoms and non-specific laboratory data such as high serum LDH levels. Malignant cells are rarely found in the peripheral blood specimen. In this unusual disorder, however, the lymphoma cells are frequently distributed within the small vessels of systemic organs causing characteristically regional features such as changes of the mental status and skin lesions. Here we presented a typical case of ALCL which has been successfully treated.

The patient was first characterized with the massive bilateral adrenal involvement of ALCL lymphoma cells. In addition to brain and skin, adrenal glands have also been reported to be frequently invaded by the ALCL tumor cell and present as gross tumors. Kayano and Katayama (5) counted the lymphomatous mass lesions in 33 out of 103 ALCL cases reviewed, and found that 17 cases (52%) among the 33 had adrenal involvement, the highest incidence among all of the organs listed; incidentally, the number of both brain and skin lesions was only 2 in this series. In their report it is also impressive that 16 out of 17 adrenal involvements were bilateral. Later Usuda and his colleagues (5) also collected 109 reported autopsies of ALCL and found that out of 19 cases with gross tumors, 13 cases (68%) had tumors in the adrenal glands and among them, 62% were bilateral. Thus, frequent bilateral involvement of the adrenal glands may be a unique feature of ALCL (6).

Meanwhile, it has been generally recognized that adrenal lymphoma is rare; in review of more than 1,400 cases with extra-nodal lymphomas, adrenal involvement was reported to be less than 0.2% (7). Recently, however, adrenal enlargement has become easily detectable due to the development and popularization of diagnostic imaging techniques such as echography, computed tomography, and magnetic resonance imaging. Adrenal incidentalomas found in this way consist of a variety of etiologies (8), and when the adrenals are not definitely been underestimated as a disorder which causes symptoms such as fever of unknown origin has enlarged adrenal glands. Whenever a patient with non-specific symptoms such as fever of unknown origin has enlarged adrenal glands, ALCL should be considered even if the patient has neither brain nor skin lesions. Diagnosis during the early stage of ALCL may make chemotherapy clinically effective even for this lethal disorder.

References