Unilateral Active Adrenal Tuberculosis Featuring Persistent Intermittent Fever

AKI IKOMA, KAZUYUKI NAMAI, TOMOYUKI SAITO, TAKAHISA KAWANO, TAKAKO SAITO, KEIZO KASONO, HIROYUKI TAMEMOTO, SHIGEKI YAMADA, MASANOBU KAWAKAMI AND SAN-E ISHIKAWA

Department of Medicine, Jichi Medical School Omiya Medical Center, Saitama 330-8503, Japan

Abstract. The adrenal gland is one of the organs which tuberculosis infects. In most clinical settings bilateral adrenal tuberculosis has been clarified after adrenal insufficiency is overt. On the contrary, active adrenal tuberculosis is rarely detected during the survey of infectious disease. A 68-year-old man was admitted because of intermittent fever. The intermittent fever was accompanied with leukocytosis and elevation of C-reactive protein. Serum soluble interleukin-2 receptor was 1920 U/ml, and β2-microglobulin was 4.0 mg/l. Bacterial cultures of blood, sputa, urine, bone marrow and cerebrospinal fluid did not show any particular bacteria. Mycobacterium tuberculosis was negative in culture of sputa, and there was no tuberculin reaction. Plasma ACTH and serum cortisol were 18.5 pmol/l and 527.0 nmol/l, respectively. Abdominal CT scan showed right adrenal mass with a size of 28 × 20 mm, which was low density and had a well-encapsulated homogenous appearance. After the adrenalectomy, histology verified active adrenal tuberculosis. The intermittent fever disappeared, and white blood cells and C-reactive protein normalized. These findings indicate an atypical, rare case of unilateral, active adrenal tuberculosis closely linked to intermittent fever, and without any other organ involvement.

Key words: Adrenal tuberculosis, Adrenal mass, Acute infection

THE adrenal gland is one of the organs which tuberculosis infects [1]. In most clinical settings bilateral adrenal tuberculosis has been clarified after adrenal insufficiency is overt [2]. Namely, the cause of adrenal insufficiency is sought, and long-term tuberculosis infection is suggested because of adrenal calcification on abdominal X-ray film or adrenal enlargement on abdominal CT scan [3–5]. On the contrary, active adrenal tuberculosis is rarely detected during the investigation of organs with acute inflammation. Lam and Lo [6] reported adrenal tuberculosis in 55 patients during a 28-year autopsy experience. Adrenal tuberculosis was diagnosed after adrenalectomy in only 3 patients, and others were confirmed at autopsy.

In the present study we reported a case with unilateral active adrenal tuberculosis. In addition, how to diagnose adrenal tuberculosis by proper bacterial and biochemical examinations and features of computer imaging was retrospectively considered.

Case Report

A 68-year-old man was examined to determine the cause of persistent intermittent fever. At 55 years he was diagnosed as type 2 diabetes mellitus and chronic hepatitis C, and had been treated with diet therapy and oral hypoglycemic agents. His hemoglobin A1c has been kept at 5.3–8.0%. At 67 years an artificial pacemaker was permanently implanted. He had had inter-
Intermittent fever above 38°C since November, 2002. He was admitted to a hospital to examine the cause of fever, but nothing was clarified. Thereafter he visited Jichi Medical School Omiya Medical Center in February 2003 according to the suggestion of his family doctor. There was no fever with white blood cell counts of 8400/cmm and C-reactive protein (CRP) of 49.8 mg/l. He became febrile again, and was admitted to our medical center to further have examined for the pathological cause of unknown fever on February 27, 2003.

Physical findings at hospitalization were height, 163 cm; body weight, 54.3 kg; blood pressure, 142/80 mmHg without postural changes; pulse rate, 70 beats/min; and body temperature, 35.8°C. He was conscious and alert. Operation scar was found on chest because of the implantation of pacemaker. He had tattoo on his back. There was no abnormal finding in lung, heart and abdomen. Cervical, axillar and inguinal lymph nodes were not palpable. No edema was found in pretibia or foot. Neurological examination showed no abnormal findings.

Laboratory studies showed white blood cells were 8050/cmm; red blood cells, 410 × 10⁴/cmm; hemoglobin, 120 g/l; hematocrit, 34.5%; and platelets, 32.0 × 10⁴/cmm. CRP was 0.7 mg/dl; total protein, 75 g/l; albumin, 36 g/l. GOT was 68 U/l; GPT, 69 U/l; LDH, 202 U/l; and total bilirubin, 2.6 mg/l. Serum sodium level was 141 mmol/l; potassium, 4.4 mmol/l; and chloride, 105 mmol/l. Fasting plasma glucose was 4.8 mmol/l; hemoglobin A1c, 6.0%; total cholesterol, 3.08 mmol/l; HDL-cholesterol, 0.92 mmol/l; and triglyceride, 2.80 mmol/l. Plasma ACTH level was 18.5 pmol/l and serum cortisol, 527.0 nmol/l in the early morning. Plasma renin activity was 0.33 ng/L per sec, and plasma aldosterone level, 351.4 pmol/l. Plasma epinephrine and norepinephrine levels were 38.2 pmol/l and 1.71 nmol/l, respectively. Urinary excretions of epinephrine and norepinephrine were 8.5 µg/day and 91.2 µg/day, respectively. Soluble interleukin-2 receptor in plasma was elevated to 1920 U/ml and serum β2-microglobulin was 4.0 mg/l. Bacterial cultures of blood, urine, sputa, bone marrow, and cerebrospinal fluid did not show any particular bacteria. Also, mycobacterium tuberculosis was not found in culture of sputa, and tuberculin reaction test was negative.

Chest and abdominal X-ray films did not show any abnormal finding, other than the implantation of pacemaker. Abdominal echogram depicted gallbladder stone and right adrenal mass. Abdominal CT scan further clarified right adrenal mass. There was an encapsulated, homogenous mass in right adrenal gland, which was 28 × 20 mm in size (Fig. 1). The mass was not calcified, and was slightly heterogenous after it was enhanced by iodine. There was no abnormal finding in the left adrenal gland. No abnormal accumulation in the right adrenal gland was found in gallium scintigram.

Clinical course

Intermittent fever above 38°C had been repeated every several days. Leukocytosis and elevation of CRP were found in a febrile state. There were not
any particular bacterial findings in the cultures of blood, sputa, bone marrow and cerebrospinal fluid. Because serum soluble interleukin-2 receptor and β2-microglobulin were increased, malignant lymphoma in adrenal gland was suspected. Therefore total right adrenalectomy was performed under laparoscopy. The mass hardly adhered to the posterior wall of inferior vena cava. The adrenal mass was 35 × 18 × 20 mm in size (Fig. 2), and histological study showed irregularly shaped caseous necrosis bound by epitheloid histiocytes and Langerhans giant cells (Fig. 3). There was no fungus or acid-fast bacilli in special stains. These findings diagnosed the case as adrenal tuberculosis. After the operation, fever disappeared and inflammatory changes in leukocytosis and elevation of CRP never recurred. The patient was treated with isoniazid 400 mg per day during the post-operative period of 3 months.

**Discussion**

In the present patient intermittent fever along with inflammatory changes strongly indicated infectious diseases. We made an effort to clarify the source of infection and its affected organs systematically, but nothing was found except for right adrenal mass. Tuberculosis was not suspected because there was no culture of mycobacterium tuberculosis in sputa, no abnormal shadow on chest X-ray film and negative tuberculin reaction. We considered three possibilities as below: First, serum soluble interleukin-2 receptor and β2-microglobulin were elevated. These biochemical markers made us suspect malignant lymphoma of adrenal gland, although physical findings and computer imaging did not show any lymphoadenopathy. Second, there are a few reports demonstrating that plasma interleukin-6 levels are increased in patients with pheochromocytoma who have a febrile condition [7, 8]. However, biochemical studies did not show any elevation of plasma catecholamines and any urinary excretion of them. Third, it is well known that the adrenal gland is an organ receiving metastasis of malignant tumor. Among the above possibilities, we speculated that malignant lymphoma was the most likely possibility, and the patient was operated on to remove the right adrenal gland. However, adrenal biopsy is generally restricted to the few instances for which it is indicated. When only the adrenal mass is enlarged with febrile condition, adrenal biopsy might have been the ideal diagnostic approach for this patient.

The development of computer imaging has enabled us to easily find an adrenal mass. Adrenal incidentomas are not infrequently discovered by abdominal CT scan and echogram when patients are examined for other symptoms and signs in abdomen. In the present study right adrenal mass appeared as a low density, well-encapsulated, homogenous mass on abdominal CT scan. It became weakly and heterogeneously enhanced after administering iodine. Functioning adrenal tumors are, generally, not enhanced by iodine on abdominal CT scan [9, 10]. There was a difference in the appearance on CT scan between adrenal tumor and the present mass. After the adrenalectomy, histological study diagnosed as adrenal tuberculosis. A few reports have indicated the appearance of adrenal tuberculosis on CT scan [11, 12]. Infectious adrenal mass has to be characterized on computer imaging.
thus providing a diagnostic value.

In the present study it was hard to diagnose the case as adrenal tuberculosis, because specific examinations for tuberculosis were all negative as mentioned above. It is well-known that bilateral adrenal tuberculosis is the cause of adrenal insufficiency [13]. Patients have been diagnosed as adrenal insufficiency: their pathological cause is investigated, and thereafter an old tuberculosis infection is clarified. Abdominal X-ray film shows calcification of bilateral adrenal glands. Abdominal CT scan depicts bilateral enlargement of adrenal glands [11, 12]. In contrast, in the present patient adrenal tuberculosis was quite atypical. It was active inflammation in only the right adrenal gland in the absence of any other infected organ. We should note that diabetes mellitus may suppress the immune system and affect the incidence and clinical course of adrenal tuberculosis. There is a report discussing active adrenal tuberculosis [6]. Adrenal tuberculosis was seen in 52 of the 871 patients with active tuberculosis at autopsy, and in only 3 patients at adrenalectomy. The adrenal gland was the only organ involved by active tuberculosis in 14 of these 55 patients at autopsy. The study clarified that no patient with active adrenal tuberculosis was reported without histological examination. The present study strongly indicates that acute adrenal tuberculosis has to be characterized by its clinical features, and that it is very important to apply appropriate diagnostic procedures in future.

References