Cervical Tuberculous Lymphadenitis in a Frequent Traveler to Endemic Areas of Tuberculosis

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Scrofula or cervical tuberculous lymphadenitis (CTBL) should be suspected in patients with a history of potential exposure to tuberculosis present with cervical lymphadenopathy. A 55 year-old frequent traveler to Philippine and Thailand developed swelling of the bilateral cervical lymph nodes, and positive conversion of purified protein derivative of tuberculin (PPD) without pulmonary manifestations. The excisional biopsy of the cervical lymph nodes was useful for prompt diagnosis of CTBL, and the patient was successfully treated with isoniazid (INH) and rifampicin (RFP).

(Internal Medicine 36: 211–213, 1997)

Key words: scrofula, extrapulmonary tuberculosis, lymphadenopathy

Introduction

The incidence rates of tuberculosis in some Asian countries (Thailand, Viet Nam, India, and Philippine) and in Japan, 50–275 and 35.7 per 100,000 persons per year respectively, are still higher than those in Western countries (1, 2). In addition to traditional intrafamilial and nosocomial infection, new modes of transmission of tuberculosis should be considered in this era of developed transportation. Transmission of tuberculosis from a passenger to the others during a long airplane flight is known to occur (3). Some cases with peripheral tuberculous lymphadenopathy without pulmonary manifestation are reported to be associated with a history of travel to areas where tuberculosis is endemic (4).

Case Report

A 55 year-old Japanese male who had been a frequent traveler to Philippine and Thailand, presented with bilateral cervical lymphadenopathy of 1-month duration. There was no significant past medical history or family history of tuberculosis or malignant diseases. There was no history of intravenous drug abuse or irradiation to the neck in the past. The typical clinical symptoms of tuberculosis such as fever, night sweats, body weight loss, productive cough were absent. On physical examination, 8 to 10 conglomerated, elastic hard, painless, nonfluctuant, soy-bean sized lymph nodes were palpable in the posterior cervical triangle on each side. The oral cavity and

nasopharynx were normal. Chest was clear to auscultation. Liver and spleen were not palpable. Laboratory data was essentially normal except for slightly increased erythrocyte sedimentation rate and positive conversion of purified protein derivative of tuberculin (PPD) reaction with vesicular formation which had been negative 5 years prior to this episode. White cell count was normal with a normal differential. Atypical lymphocytes were not noted. Angiotensin converting enzyme was normal. Although lymphadenopathy due to human immunodeficiency virus (HIV) infection was suspected from a history of unprotected sexual relations with prostitutes overseas, anti-HIV antibody was negative (Table 1). Sputum examinations including mycobacterial DNA, culture, and smear were all negative. Ultrasonogram of the neck, although not diagnostic, showed conglomerated hypoechoic masses in the bilateral posterior cervical triangle. Computed tomography (CT) scan of the neck was not performed. Chest X-ray was normal. There was no hilar lymph node enlargement. Lymphadenopathy was not found in abdominal ultrasonogram and chest CT.

Differential diagnosis of cervical lymphadenopathy in this patient included lymphoma, metastatic lymphadenopathy, infectious mononucleosis, sarcoidosis, histiocytic necrotizing lymphadenitis (5), eosinophilic necrotizing lymphadenitis (6), and cervical tuberculous lymphadenitis (CTBL). Excisional biopsy of the cervical lymph node was performed. Caseous necrosis and Langhans' giant cells were observed by HE stain (Fig. 1), and acid fast bacilli (AFB) stain-positive bacteria were noted. Mycobacterial culture from the lymph nodes was not

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Received for publication July 29, 1996; Accepted for publication December 9, 1996

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performed. The diagnosis of CTBL was made in view of clinical and pathological findings. Admission and isolation were thought to be unnecessary based on physical findings and laboratory

data. The antituberculous regimen consisted of isoniazid (INH) 300 mg/day and rifampicin (RFP) 450 mg/day was administered for 6 months on an out-patient-basis. Lymphadenopathy disappeared gradually without side effects of antituberculous medications. Erythrocyte sedimentation rate also became normal. There was no recurrence of cervical lymphadenopathy or emergence of pulmonary lesions. Physical examination, PPD, chest X-ray, and erythrocyte sedimentation rate of the other members of the patient's family were not significant.

Table 1. Laboratory Data

Leukocytes	3,800/ μ l
Neutrophils	49%
Monocytes	1.0%
Eosinophils	2.0%
Basophils	2.0%
Lymphocytes	46%
Red blood cells	465×10^4 / μ l
Hemoglobin	15 g/dl
Hematocrit	41.2%
Platelets	26.4×10^4 / μ l
Aspartate aminotransferase (AST)	27 U/l
Alanine aminotransferase (ALT)	24 U/l
Amylase	110 U/l
Creatinine	1.0 mg/dl
Glucose	80 mg/dl
HBs antigen	(-)
anti HCV antibody	(-)
anti HIV antibody	(-)
C-reactive protein	1.0 mg/dl
Erythrocyte sedimentation rate	23 mm/h
Urinalysis	glucose (-) protein (-) occult blood (-)
PPD	$10 \times 10/30 \times 28$ mm
Angiotensin converting enzyme	15.9 U/l
TPHA (-) STS (-)	
Carcinoembryonic antigen (CEA)	1.8 ng/ml
Ferritin	192.1 ng/ml

Discussion

Mycobacterial cervical tuberculosis, or scrofula, may be caused by mycobacterium tuberculosis or by atypical mycobacteria. It is important to distinguish these two entities, as the medical and surgical treatments of these entities differ (7). As the present patient had positive conversion of PPD reaction, CTBL associated with initial infection with mycobacterium tuberculosis was more likely than reactivation of tuberculosis or atypical mycobacterial cervical lymphadenitis which is predominantly a disease of childhood (8).

Diagnosis of CTBL is made by excisional lymph node biopsy followed by Ziehl-Neelsen staining, culture, and DNA probe method. Fine needle aspiration with ultrasonogram (9, 10), PPD, CT scan are also useful. Excisional biopsy is reported to be the most reliable diagnostic test for CTBL (11). Noninvasive diagnostic methods have also been pursued to minimize unnecessary lymph node resection. Winkelbauer et al (12) reported that the sonographic features typical of CTBL are multiple, enlarged, conglomerating roundish and oval lymph nodes. These lymph nodes are hypoechoic, exhibit posterior echo

Figure 1. Microscopic findings of the biopsied cervical lymph node. Langhans' giant cells, epithelioid cells and caseous necrosis are seen ($\times 100$).

enhancement and have sharp margins. With caseation, however, there are blurred borders. In cold abscesses an inhomogeneous texture with inhomogeneous shadows is found. A tentative diagnosis of CTBL may be made due to the polymorphous sonographic pattern if history and clinical findings are taken into account. A proper histological and microbiological work-up is still essential for confirmation of the sonographic diagnosis (12). For CT findings, Lee et al (13) reported that CTBL usually shows a central low density and peripheral rim enhancement that tends to be thick and irregular compared with a malignant lymphadenopathy. Multilocular low densities with peripheral enhancement and a large confluent low density with a lesser degree of fat plane obliteration than a pyogenic abscess are suggestive features of advanced CTBL (13). Kim et al (14) reported that the following are suggestive of tuberculous lymphadenitis: the presence of conglomerated nodal masses with central lucency, thick irregular rim of contrast enhancement and inner nodularity, varying degree of homogeneous enhancement in smaller nodes, dermal and subcutaneous manifestations of inflammation such as thickening of the overlying skin, engorgement of the lymphatics and thickening of adjacent muscles, and a diffusely effaced fascial plane. However, common CT patterns of tuberculous adenitis may also be seen in nonspecific abscess-forming lymphadenitis, lymphoma and metastatic lymphadenopathy (14).

CTBL in patients with lymphoma has also been reported (15). Empirical use of antituberculous medications without histological diagnosis resulted in delay in diagnosis of malignancy (16). The physician must keep in mind that cervical scrofula should be included in the differential diagnosis of any neck masses, and malignant neck tumors particularly should be differentiated from scrofula. Recommended therapy for scrofula with pocket formation is selective neck dissection followed by antituberculous chemotherapy, which can shorten the period of treatment (17). Scrofula without pocket formation is treated with two or three antituberculous medications (18, 19). Irradiation was utilized for the treatment of CTBL in the past, and secondary neoplasms occurred in some cases. Radiation-induced malignant neoplasms are reported to be not so radioreistant (20). As extrapulmonary manifestation is a common form of tuberculosis in the immunocompromized host, HIV test and/or CD4 count should be checked, if the patient has risk factors for acquired immunodeficiency syndrome (AIDS) including intravenous drug abuse, homosexual maleness, or unprotected promiscuous sexual behavior.

In the present patient, CT scan of the neck was not performed and the findings of ultrasonogram of the neck were not diagnostic. Excisional biopsy of the cervical lymph nodes, however, was useful for a prompt diagnosis. When we see patients with cervical lymphadenopathy, evaluation of the history of potential exposure to tuberculosis is important. Although imaging

studies are helpful in the diagnosis, biopsy of the lymph nodes should be performed promptly in patients with suspected tuberculosis or malignancy.

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