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ORIGINAL ARTICLE

Factors that make it difficult to diagnose cervical tuberculous lymphadenitis

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Abstract Cervical tuberculous lymphadenitis is mainly diagnosed by analyzing tissue samples obtained by fine-needle aspiration (FNA). However, some cases remain diagnostic challenges even after polymerase chain reaction analysis of FNA specimens. To delineate differences between cases that are relatively easy to diagnose and those for which diagnosis is difficult, 22 patients with cervical tuberculous lymphadenitis were studied retrospectively. FNA tissues were used to diagnose 14 cases (group A), whereas excisional biopsy was required for accurate diagnosis of 8 cases (group B). These two groups were compared with regard to results of blood examinations, ultrasound appearance, and various other procedures required to reach the final diagnosis. The results indicated that diagnosis of cervical tuberculous lymphadenitis was more difficult for patients with lower white blood cell counts, lower serum C-reactive protein levels, and absence of lymph node fusion or abscess formation on ultrasonography. The possibility of tuberculosis as a cause of cervical lymphadenopathy should always be considered, even when the presenting symptoms are not typical of this disease.

Keywords Cervical tuberculous lymphadenitis · Fine-needle aspiration · Ultrasound

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Introduction

Cervical tuberculous lymphadenitis is the most common form of extrapulmonary tuberculosis, commonly involving the jugular, posterior triangle, or supraclavicular lymph nodes [1]. A number of techniques are available for diagnosing this disease, including fine-needle aspiration (FNA) cytological analysis, analysis of tissue from excisional biopsy, isolation of mycobacteria in tissue cultures, molecular tests, and administration of the tuberculin skin test. Many authors have compared the utility of these techniques. Positivity for acid-fast bacilli (AFB) varies according to the technique used, with ranges of 0–77.8 % using Ziehl–Neelson (ZN) staining, 8–80 % using tissue cultures, and 33–94.6 % using polymerase chain reaction (PCR) analysis of tissues [2, 3]. Although the combination of FNA cytology, AFB smear, and culture may be sufficient to reach a reliable diagnosis of tuberculous lymphadenitis [2], culturing the bacilli remains the gold standard for diagnosis, and culturing may require 2–4 weeks to yield

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results [4]. In contrast to culturing, PCR is a rapid and sensitive method that requires a small sample volume, and live bacilli are not required [3, 5]. In addition, although the sensitivity of PCR is the same as that of culturing, its specificity is 100 % [2]. When cervical tuberculous lymphadenitis is suspected, we routinely perform the PCR technique. However, the PCR technique can yield false-negative results. Moreover, sometimes the possibility of tuberculosis is not suspected in the early stages of the diagnostic process.

In this retrospective study, two groups of patients—those diagnosed using FNA tissues only and those which required excisional biopsy for diagnosis—were compared with regard to laboratory data, ultrasound characteristics, and various procedures used to reach the final diagnosis of cervical tuberculosis lymphadenitis.

Materials and methods

The clinical records of 22 patients who had been diagnosed as having cervical tuberculous lymphadenitis between January 2000 and February 2013 at Himeji Red Cross Hospital, Japan, were reviewed. None of these 22 patients was suspected of having pulmonary tuberculosis on the basis of chest radiography. Patients who had any diseases other than cervical lymphadenopathy and who were under treatment were excluded from this study. Routine blood tests were performed for all patients.

To identify the location of the lymphadenopathy, cervical lymph nodes were designated as levels I–VI, according to the standard classification used for neck dissection surgery [6], as follows: I, submental and submandibular; II, between the posterior belly of the digastric muscle and the hyoid bone; III, between the hyoid bone and the cricoid; IV, below the cricoid along the jugular chain; V, posterior triangle; and VI, the central anterior neck compartment, which includes the pretracheal and paratracheal nodes.

FNA of the most representative node was carried out for all 22 patients using a 23-gauge needle attached to a 20-ml syringe. Samples were evaluated by cytological analysis. When tuberculosis was suspected, simultaneous PCR analysis of the FNA tissue was performed. The decision whether to perform an AFB smear and ZN staining or culture was left to the discretion of the attending physician. When FNA results were equivocal, excisional biopsy was performed, and again, when tuberculosis was suspected, the samples were simultaneously subjected to PCR, culture, or smear, in addition to histopathological examination.

Ultrasound evaluations were performed in 21 patients using a 10-MHz linear transducer. Ultrasonography was performed with the patient in the supine position with the neck hyperextended and a pad under the shoulders to provide optimum exposure of the neck. The shape of the cervical nodes was described using the long axis to short axis (*L*/*S*) ratio of a representative node in each case. Characteristics of the ultrasound appearance were described with special attention to irregular margins, the presence of strong echoes, fusion of nodes, presence of an internal echo, multiple nodes, presence of a lymph node hilus, posterior enhancement, and surrounding abnormal tissue [7]. The presence of fusion of lymph nodes was defined as partial or complete disappearance of a borderline echo between multiple lymph nodes. A peripheral halo was defined as strong echoes in the peripheral area of the nodes. The internal echo of lymph nodes was assessed by the presence of hyperechoic echogenicity. Tissue surrounding the suspected lymph nodes was observed to determine whether it appeared normal.

We defined patients who were diagnosed using only FNA tissue as "easy to diagnose" (group A); those for whom excisional biopsy was required were categorized as "difficult to diagnose" (group B). Statistical analysis and calculation of p values were performed using Student's *t* test and Fisher's exact probability test to delineate differences between these two groups with regard to laboratory data and ultrasound characteristics.

Results

Of the 22 patients, 6 were male and 16 female, with a mean age of 58.6 years (range, 14–86 years). No immunocompromised patients were included in this study. The clinical profiles of patients are summarized in Table 1. The location of the lymphadenopathy was left IV in 5 (22.7 %), right II in 5 (22.7 %), and right IV in 4 (18.2 %). No specific differentiating characteristic pertaining to the distribution of lymphadenopathy was noted.

FNA was performed in all 22 patients, with 14 patients diagnosed as having cervical tuberculous lymphadenitis based on analysis of tissue obtained using the FNA technique alone (group A), and the other 8 patients needing excisional biopsy for diagnosis (group B). PCR analysis of FNA tissue was not performed for 2 patients in group A, because the possibility of tuberculosis was not considered on first presentation. However, cytological analysis of tissue from these 2 cases revealed the characteristic features of tuberculosis. Of the patients in group B, 6 were suspected of having tuberculosis and underwent PCR analysis, but the PCR results were false-negatives. All 8 group B cases were diagnosed by histological examination of the excisional biopsy specimens.

Of the routine blood examination data, the white blood cell (WBC) count and level of serum C-reactive protein (CRP) were identified as predictive factors for determining