

## Extrapulmonary tuberculosis with recurrent multiple lymphadenopathy in a pediatric patient

Ezgi Hasbek<sup>1</sup>, Emine Kübra Dindar Demiray<sup>2</sup>, Sevil Alkan Çeviker<sup>3</sup>, Mehmet Hüseyin Metineren<sup>4</sup>

<sup>1</sup>Department of Child Health and Diseases, Bitlis State Hospital, Bitlis, Turkey

<sup>2</sup>Department of Infectious Diseases and Clinical Microbiology, Bitlis State Hospital, Bitlis, Turkey

<sup>3</sup>Department of Infectious Diseases and Clinical Microbiology, Çanakkale 18 Mart University Faculty of Medicine, Çanakkale, Turkey

<sup>4</sup>Department of Pathology, Kütahya Health Sciences University, Evliya Çelebi Training and Research Hospital, Kütahya, Turkey

### ABSTRACT

Although tuberculosis is a disease that can be prevented and treated, it remains a significant health problem in developing countries, such as our country. Tuberculosis is an important public health problem in children as well as in adults in our country. Both pulmonary and extrapulmonary tuberculosis can be seen in children. In children, the most common form of extrapulmonary tuberculosis is tuberculous lymphadenitis. Although viral factors are more common in pediatric patients presenting with lymphadenopathy, tuberculosis is also an important disease to be considered in the etiology of lymphadenopathy in children. In this case report, we aimed to emphasize the importance of tuberculosis in terms of etiologic approach in a patient who presented to the pediatrics outpatient clinic with multiple lymphadenopathies.

**Keywords:** Extrapulmonary tuberculosis, multiple lymphadenopathy, pediatric patient, tuberculous lymphadenitis.

Although tuberculosis is a preventable and treatable disease, it still remains a significant health problem worldwide, especially in developed and developing countries. The rate of infectiousness in children is low, however, its diagnosis and treatment in childhood is fundamental, as it is a source of transmission and reactivation tuberculosis in adulthood.<sup>[1]</sup> According to the 2018 data of the World Health Organization, 11% of cases infected with tuberculosis are children under 15 years of age.<sup>[2]</sup> The most common form of extrapulmonary tuberculosis in children is tuberculous lymphadenopathy (LAP).<sup>[3]</sup>

Viral and bacterial infectious agents are the most common causes of LAPs. In the etiology of chronic recurrent LAPs, granulomatous diseases such as malignancy and tuberculosis should also

be considered.<sup>[4]</sup> In this case report, we present a patient who was hospitalized and treated for multiple LAPs several times due to chronic recurrent LAPs, which is significant in terms of diagnosing tuberculosis.

### CASE REPORT

A 14-year-old female patient presented to the pediatric outpatient clinic with complaints of fever, and pain and swelling in the left side of the neck. In addition to these complaints, the patient also stated long-term fatigue, fever, and mild weight loss. The patient's story revealed she was followed up at an external center for about three years due to short stature and received growth hormone treatment, underwent operation for retropharyngeal abscess about 1.5 years

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**Correspondence:** Ezgi Hasbek, MD. Bitlis Devlet Hastanesi, Çocuk Sağlığı ve Hastalıkları Kliniği, 13000 Bitlis, Türkiye.  
Tel: +90 506 - 687 37 68 e-mail: mdezgihasbek@gmail.com

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ago, and was previously hospitalized a few times due to diagnosis of LAP of the neck. It was determined that the patient's vaccines were all applied on schedule, there was no evidence to suggest immunodeficiency after vaccination, and PPD (purified protein derivative) test was applied during the previously operated period and the result was negative. The patient was not regularly taking any drugs.

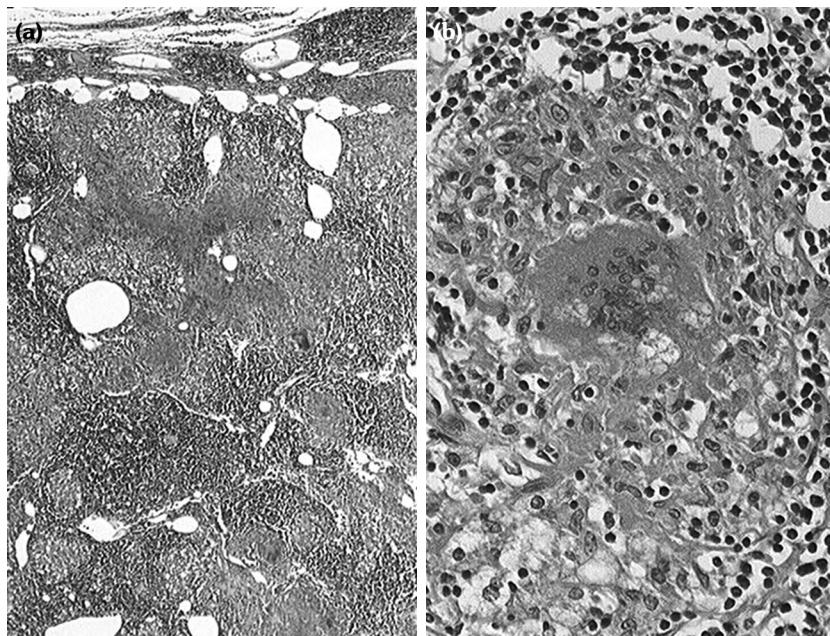
Physical examination revealed the patient was in moderate general condition, conscious, and fatigued. Body temperature was 38.6°C, pulse 100/min, and arterial blood pressure 120/70 mmHg. Conglomerate LAP, the largest diameter of which was 2×2 cm, was determined with palpation in the left submandibular region. Except for the submandibular region, the patient did not have LAP or organomegaly in the supraclavicular, axillary, inguinal, or epitrochlear regions. Other systemic examinations were normal.

Laboratory analysis revealed white blood cell (WBC) count 10,060/mm<sup>3</sup>, Hemoglobin 12.2 g/dL, platelet count 170,000/mm<sup>3</sup>, hematocrit 38.2%, mean corpuscular volume (MCV) 83.6 fL, and C-reactive protein (CRP) 9.9 mg/L. Glucose, liver and kidney function tests, and serum electrolytes were in normal range.

Hilar LAP was not detected in the posteroanterior and lateral chest radiographs. Neck ultrasound revealed reactive LAP in the left and right submandibular, posterior cervical, and jugular chain, the largest of which was 24×9 mm in diameter, and slightly enlarged thyroid gland with pseudo-nodular appearance in the posterior subcapsular region that was reported as compatible with Hashimoto's disease, though results of thyroid function tests and antibody tests were normal.

The patient was hospitalized at the pediatric ward for investigation and treatment of LAP etiology. The patient was consulted to the department of infectious diseases due to history of chronic recurrent LAP, fever, and unexplained weight loss. The patient's blood culture was taken. Serology tests for Toxoplasma, Rubella, Cytomegalovirus (CMV), Epstein-Barr virus (EBV), and Brucella serology tests for LAP etiology were requested due to being endemic in the region. Viral serology and Brucella tests were negative. Peripheral smear was analyzed and

there were no findings in favor of malignancy. Fasting gastric fluid was collected for three days. Ampicillin sulbactam at a dose of 100 mg/kg/day and ibuprofen at a dose of 10 mg/kg were initiated as empiric treatment. However, on the third day of the treatment, the patient, whose fever and acute phase values did not regress, was consulted to the ear, nose and throat department in terms of deep neck infection, and contrast-enhanced magnetic resonance imaging (MRI) of the neck was performed. Deep neck infection was not considered. However, the current treatment was extended; ampicillin sulbactam was discontinued and the treatment was switched to meropenem and vancomycin. The first dose of vancomycin caused urticarial allergic reaction; vancomycin was discontinued. The treatment was switched to meropenem and clindamycin and the allergic reaction regressed throughout follow-up. The patient's lymph node was excised and sent to pathologic analysis (Figure 1). After 10 days of treatment, the patient's fever was responsive and enlarged lymph nodes regressed in size. The patient was discharged and followed up as an outpatient. During outpatient follow-up, fasting gastric fluid stained with Ehrlich-Ziehl-Neelsen (EZN) and the culture tested positive, and the patient was referred to the Tuberculosis Control Dispensary for tuberculosis treatment. Antituberculosis treatment was initiated and the other members of the patient's family were also referred to the Tuberculosis Control Dispensary. The patient received 4-drug antituberculosis treatment (isoniazid, rifampin, pyrazinamide, and ethambutol) for the first two months, and 2-drug antituberculosis (isoniazid and rifampin) treatment for four months. The patient was called in for routine outpatient follow-ups and was examined and tested in terms of adverse side effects of the treatment. After a total of six months of antituberculosis treatment, the patient was hospitalized and fasting gastric fluid collected for three consecutive days was sent to the external laboratory for EZN staining and culture. The patient, whose results were found to be negative, did not have complaints of recurrent LAP or fever during follow-up. The other members of the patient's family also completed treatment. The patient was educated regarding tuberculosis disease and prevention, and was discharged with recommendation of reapplying to the pediatrics outpatient clinic if symptoms were to recur.



**Figure 1.** (a) Multiple granulomas in lymph nodes, (b) further enlargement, epithelial cells, and giant cells (H-E,  $\times 200$ ).

## DISCUSSION

Tuberculosis ranks as the leading cause of death from a single infectious agent, and is the ninth leading cause of death worldwide.<sup>[5]</sup> According to the 2018 data of the World Health Organization, children under 15 years of age account for 11% of infected individuals.<sup>[2]</sup> In our country, incidence of TB in children under 15 years of age is about 4.7 per 100,000.<sup>[6]</sup> In the pediatric age group, the lymphohematogenous spread is higher and extrapulmonary tuberculosis (EPTB) is more common. Clinical history, physical examination, and clinical and laboratory findings are helpful in the diagnosis of EPTB, however diagnosis and treatment may be delayed since they are less frequent than in pulmonary tuberculosis and may mimic several manifestations from malignancy to benign diseases seen in childhood (meningitis, sarcoidosis, fungus, sterile pyuria, Crohn's disease, dermatological pathologies, non-tuberculosis mycobacteria, acute abdomen, etc.).<sup>[7]</sup>

In our patient's previous hospital admissions, LAP was thought to have developed secondary to upper respiratory tract infections. When questioned, pre-diagnoses of malignancy or immunodeficiency were considered because of the

patient's previous drainage due to retropharyngeal abscess and frequent LAP. However, the absence of LAP in other peripheral ultrasound examinations, negative viral and Brucella tests, lack of atypical cells in peripheral smear, skin infections that suggested immunodeficiency, and no recurrent systemic infections excluded us from these diagnoses. Granulomatous infections are frequently the cause of chronic LAP. Therefore, tuberculosis was considered in our patient, fasting gastric fluid was collected and material was sent to the Tuberculosis Dispensary; results of EZN staining and culture results were positive and the patient was diagnosed with LAP. Antituberculosis treatment lasted six months and the patient was called for regular follow-up.

In conclusion, our case was a pediatric patient who was diagnosed with tuberculous LAP and was started treatment for chronic LAP. Although infectiousness rates are low in pediatric patients, early treatment carries great importance due to the fact that it is a source of infection and reactivation tuberculosis in adulthood.<sup>[8]</sup> Tuberculous lymphadenopathy is the most common form of extrapulmonary tuberculosis and it should be kept in mind when considering chronic LAP etiology in children.

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