

Evaluation of Extrapulmonary Tuberculosis Cases Presenting with Different Clinical Findings

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ABSTRACT

Introduction: Extrapulmonary tuberculosis cases may display different clinical symptoms and this causes a delay in diagnosis. Nutritional deficiencies, migrations, and wars facilitate the development and the spreading speed of the disease. The aim of this article is to examine extrapulmonary tuberculosis patients with different clinical presentations.

Method: In this study, 15 extrapulmonary tuberculosis cases who were hospitalized and treated in our pediatric clinic in the last two years, has been evaluated retrospectively.

Results: The average age of our group was 11.7 ± 4.5 and six of the assessed patients were Syrian origin. The shared complaints of five patients diagnosed with peritoneal tuberculosis were abdominal pain and bloating. Abdominal ultrasonography findings of the patients in concordance with diffuse ascites. Two of these patients, Mycobacterium tuberculosis had peritoneal effusion. All of the five patients diagnosed with lymph node tuberculosis had swelling on the neck, and all had pulmonary involvement. However, only one patient's lymph node biopsy was concordant with tuberculosis. One patient bone tuberculosis patient applied to our clinic with hip and back pain symptom. Pott's abscess was observed in the patient's thorax MRI and hip MRI was concordant with tuberculous arthritis. Our patient with renal tuberculosis was diagnosed during evaluation of sterile pyuria attacks and in her urine ARB (+) was detected and M. tuberculosis grew in urine culture. One patient with central nervous system involvement applied to our clinic with clouding of consciousness and headache. The cerebrospinal fluid (CSF) findings of the patient were concordant with tuberculosis and growth was observed in the CSF culture. One case with miliary tuberculosis had hypercalcemia and pulmonary involvement. The patient's M. tuberculosis DNA PCR test was positive in bronchoalveolar lavage fluid. Another patient with pericardial tuberculosis applied due to respiratory distress and had cardiomegaly and pericardial effusion. Nine of our patients also had a contact history, 12 had purified protein derivative of tuberculin (PPD) (+), and 11 had pulmonary involvement.

Conclusion: Patients were admitted to our outpatient clinic with various clinical symptoms. After careful physical examinations were performed, detailed patient histories were taken and laboratory tests performed for differentials, patients were diagnosed with extrapulmonary tuberculosis. It was desired to emphasize that this disease may appear with different clinical presentations in endemic regions like our country.

Keywords: Child, extrapulmonary tuberculosis, pulmonary tuberculosis

ÖZ

Farklı klinik bulgularla başvuran ekstrapulmoner tüberkülozlu olguların değerlendirilmesi

Giriş: Ekstrapulmoner tüberküloz olguları değişik klinik semptomlarla bulgu verebilmekte ve tanıda gecikmelere neden olabilmektedir. Gıda yetersizliği, göçler ve savaşlar hastalığın gelişmesini ve yayılmasını kolaylaştırmaktadır. Makalemizde farklı klinik tablolarla başvuran ekstrapulmoner tüberkülozlu hastalarımız değerlendirilmiştir.

Yöntem: Son iki yılda hastanemiz Çocuk Kliniğinde yatırılarak tedavi edilen 15 ekstrapulmoner tüberküloz olgusu retrospektif olarak değerlendirilmiştir.

Bulgular: Hastalarımızın yaş ortalaması 11.7 ± 4.5 olup değerlendirilen 6 hasta Suriye kökenliydi. Periton tüberkülozu tanısı alan 5 hastamızın ortak yakınması karın şişliği ve karın ağrısıydı. Batın ultrasonografileri yaygın asit ile uyumluydu. Bu hastalarımızın ikisinde periton sıvısında Mikobakterium tüberkülozis üredi. Lenf nodu tüberkülozu tanısı alan 5 hastamızın ortak şikayeti boyunda şişlik olup, hepsinde akciğer tutulumu vardı. Bununla birlikte sadece bir hastamızın lenf nodu biyopsi sonucu tüberküloz ile uyumluydu. Kemik tüberkülozlu olgumuz kalça ve sırt ağrısı nedeniyle başvurmuştu. Hastanın toraks manyetik rezonans görüntülemesinde (MRG) Pott absesi görüldü ve kalça MRG'si tüberküloz artrit ile uyumluydu. Renal tüberkülozlu hastamız, steril piyüri atakları nedeniyle tetkik edilirken, idrarında ARB (+) ve idrar kültüründe M. tüberkülozis üremesi üzerine tanı aldı. Merkezi sinir sistemi tutulumu olan bir hasta kliniğimize bilinç bulanıklığı ve baş ağrısı ile başvurmuştu. Hastanın beyin-omurilik sıvısı (BOS) bulguları tüberkülozla uyumlu idi ve BOS kültüründe üreme gözlemlendi. Miliyer tüberkülozlu olgumuzda hiperkalsemi ve akciğer tutulumu vardı. Hastanın bronkoalveolar lavaj sıvısında M. tüberkülozis DNA polimeraz zincir reaksiyonu (PCR) testi (+) bulundu. Perikard tüberkülozlu olgumuzda BOS sıkıntısı nedeniyle başvurmuştu, kardiyomegali ve perikardiyal efüzyonu vardı. Hastalarımızın dokuzunda da ev içi temas öyküsü mevcut olup, 12'sinde tüberkülin deri testi (PPD) pozitif saptandı, 11'inde akciğer tutulumu mevcuttu.

Sonuç: Hastalarımız farklı klinik bulgularla kliniğimize başvurup, dikkatle alınan anamnez ve iyi yapılan fizik muayene ile ayırıcı tanıları yönelik yapılan tetkikler ile ekstrapulmoner tüberküloz tanısı almıştır. Ülkemiz gibi endemik bölgelerde bu hastalığın farklı klinik tablolarla ortaya çıkabileceği vurgulanmak istenmiştir.

Anahtar kelimeler: Çocuk, ekstrapulmoner tüberküloz, pulmoner tüberküloz

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Introduction

Tuberculosis (TB) is an infectious disease that causes important morbidity and mortality worldwide. Despite the measures taken, it is a health problem of which incidence is rapidly increasing in both developing and developed countries due to increased migrations. It is thought that one-third of the world's population is infected with *M. tuberculosis*, and active disease may develop at any time in 10% of them (1,2). According to the data of the World Health Organization (WHO), 650,000 (9%) of 7.5 million TB cases are pediatric patients. In developing countries, this proportion increases up to 39% (1). Turkey have some extra risk factors, since it is a neighbor to the Middle East and especially to the Syrian war zone, and migrations are common in here. Generally, the disease causes pulmonary involvement, but it may cause the clinical manifestation of extrapulmonary tuberculosis (EPTB) to appear with the involvement of all tissues and organs outside of the lung. The immune status in children, poor cellular immunity in the young age group increase the risk of turning into systemic disease and development of EPTB (3-5). Extrapulmonary tuberculosis cases can give findings with different clinical symptoms, causing difficulty in diagnosing and delay in treatment. In this article, we retrospectively evaluated the characteristics of our patients with extrapulmonary tuberculosis who had applied with different clinical presentations and had been hospitalized.

Material and Methods

15 patients, who applied to Bağcılar Training and Research Hospital Pediatric Outpatient Clinics with different symptoms between January 2016 and July 2018, diagnosed with EPTB and followed up by hospitalizing, were evaluated retrospectively. The patients' ages, complaints at admission, contact histories, imaging findings, tuberculin skin test results (TST), the results of acid-resistant bacilli research (ARB) in the fasting gastric juice, adenosine deaminase (ADA) and acid-resistant Ziehl-Neelsen (ZN) staining results of the body fluids, culture outcomes, and their responses to treatment were evaluated. According to the criteria used in our country, the TST of 5 mm and above in immunocompromised individuals, of 10 mm and above in not BCG vaccinated individuals, and of 15 mm and above in vaccinated individuals is considered to be positive (6). The approval of our study was obtained from the local ethics committee of our hospital.

Results

The average age of our patients was 11.7 ± 4.5 years, six of them were male (average age 8.3 ± 5.2), and nine of them were female (average age 11.3 ± 4.5), and six of them have of Syrian origin. Nine of our patients had close contact with active tuberculosis (TB) patients, 12 had TST (+), and 11 had pulmonary involvement. The characteristics and imaging results of the patients are presented in Table 1 and Table 2.

Table 1: Our cases' complaints at admission and demographic characteristics

Age	Gender	Nationality	TST	Involvement location	Pulmonary Involv.	Complaint	Tbc contact history
12	M	Syria	(-)	peritoneum	yes	fever, weight loss, abdominal swelling	no
14	M	Turkey	(+)	peritoneum	yes	abdominal pain, abdominal swelling	no
13	F	Turkey	(+)	peritoneum	yes	abdominal pain, abdominal swelling	no
15	M	Turkey	(+)	peritoneum	yes	abdominal pain, abdominal swelling	no
15	F	Turkey	(+)	peritoneum	yes	abdominal pain, abdominal swelling, vomiting	no
16	F	Turkey	(+)	bone	yes	swelling in the neck, hip and back pain	yes
15	F	Syria	(+)	kidney	no	abdominal pain, repetitive urinary tract infection	no
8	F	Turkey	(+)	lymph node	yes	fever, weight loss, swelling in the neck	yes
14	F	Turkey	(-)	central nervous syst.	no	headache, clouding of consciousness, vomiting	yes
13	F	Turkey	(+)	pericardium	yes	respiratory distress, fever	yes
9	F	Syria	(+)	lymph node	yes	fever, weight loss, swelling in the neck	yes
2	M	Syria	(-)	lymph node	yes	fever, weight loss, swelling in the neck	yes
16	F	Syria	(+)	miliary tbc	yes	fever, clouding of consciousness, weakness	yes
5	M	Syria	(+)	lymph node	yes	fever, weight loss, swelling in the neck	yes
8	M	Turkey	(+)	lymph node	yes	fever, weight loss, swelling in the neck	yes

Table 2: Diagnostic laboratory findings of the cases

Involvement location	Specific lab finding	Pulmonary imaging	Other radiological imaging
peritoneum	high CA, high ADA	pleural effusion in the left lung basal area	abdominal USG: Acid liquid, septa
peritoneum	high CA, high ADA, growth in the culture	lymph node in the right hilus, pleural effusion on the left	abdominal USG: Acid liquid, septa
peritoneum	high CA, high ADA	pleural effusion and hilar lymph nodes in the right lung basal area	abdominal USG: Diffuse acid
peritoneum	high CA, high ADA	bilateral pleural effusion, cavitory appearance	abdominal USG: Acid liquid, septa
peritoneum	high CA, high ADA, laparoscopic biopsy tbc, growth in the culture	calcified nodules in the right hilus, multiple nodules in the left upper lobe	abdominal USG: Diffuse acid, abdominal MRI: peritonitis carcinomatosis
bone		Gohn's complex in the right lung	thorax MR: Pott's abscess, hip MRI: tbc arthritis
kidney	AARB (+) in the urine, sterile pyuria attacks, growth in the culture	normal	abdominal CT: necrosis and a granulomatous lesion in the right kidney
lymph node		normal	superficial tissue USG: lymphadenitis, thorax CT: Mediastinal LAP
central nervous syst.	CSF findings are consistent with tbc, growth in CSF	normal	
pericardium		cavitory appearance	Thorax CT: pericardial effusion, cardiomegaly
lymph node	TBC DNA PCR (+)	bronchiectasis in both lungs, nodular lesion	Thorax CT: necrotic lymph nodes forming conglomerate in the mediastinal region
lymph node	Lymph node biopsy result TBC	normal	neck USG: lymph node in the left infra-auricular region
Miliary tbc	hypercalcemia, TBC DNA PCR (+)	interstitial infiltration,	Thorax CT: Calcified lymph nodes, cavitory lesions,
lymph node		pleural effusion and hilar lymph nodes in the left lung basal area	superficial tissue USG: lymphadenitis, thorax CT: Mediastinal LAP
lymph node		calcified nodules in the right hilus, multiple nodules in the left upper lobe	superficial tissue USG: lymphadenitis, thorax CT: Mediastinal LAP

CA: cancer antigen, ADA: adenosine deaminase, AARB: acid-alcohol resistant bacilli

The shared complaints of our five patients diagnosed with peritoneal tuberculosis were abdominal swelling and abdominal pain. It was learned from their medical histories that they had ten percent weight loss in the last 3-4 months. Since in one of these patients it resembled an ovarian tumor, malignancy was considered in the differential diagnosis. While examining in terms of ascites etiology, it was observed in the abdominal magnetic resonance imaging (MRI) that the imaging was compatible with peritonitis carcinomatosa (Figure 1). The highest Cancer antigen (CA) 125 value was 836 U/L, the laparoscopic biopsy and histopathology was consistent with tuberculosis (Figure 2). All of our patients had pulmonary

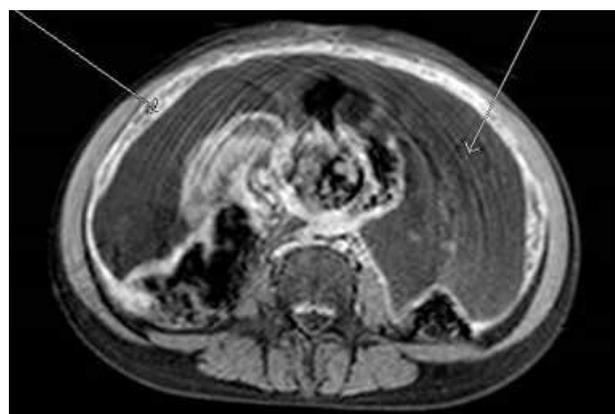


Figure 1: Peritonitis carcinomatosa

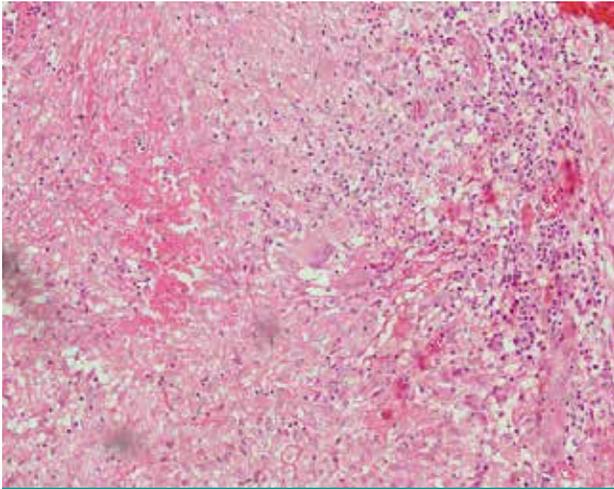


Figure 2: Peritoneal biopsy

involvement. Abdominal ultrasonography was concordant with diffuse acid. In two of these patients, *M. tuberculosis* complex grew in the peritoneal fluid.

The shared complaint of five patients with lymph node tuberculosis was swelling in the neck, and differential diagnosis for lymphadenopathy were performed to them. All of them had pulmonary involvement, and only one patient's lymph node biopsy results and histopathologic evaluation were concordant with tuberculosis.

One of our cases had bone tuberculosis, and she had both hip joint and vertebral involvement, and Pott's abscess. There was also lymphadenopathy in the neck region, in this case. Therefore, antibiotics were administered twice in the otorhinolaryngology outpatient clinics, but no improvement was observed. The patient applied to the physical therapy polyclinic due to severe hip and back pain, but she was referred to the pediatric outpatient clinics due to fail to response. Thoracic magnetic resonance imaging (MRI) confirmed the Pott's abscess involving the T8, T9, and T10 vertebrae (Figure 3) and the pelvic MRI were concordant with tuberculous arthritis. This case also had pulmonary involvement.

One of the our patients was 15 years old, Syrian origin girl with renal tuberculosis cases. The patient applied to our clinics with the complaints of abdominal pain and burning sensation during urination. She was treated with the diagnosis of urinary tract infection, and although there were abundant leucocytes in the urine, there was no growth in the culture. 15 days after discharge from the hospital, the patient applied again upon the continuance of the complaints of abdominal pain and burning



Figure 3: Pott's abscess in the vertebrae

sensation during urination. She defined persistent sterile pyuria. The patient was observed as weak and pale, and she had pain and sensitivity in the right lower quadrant. Abdominal Computed tomography (CT) showed necrosis and a calcified lesion in the right kidney (Figure 4). There was ARB positivity in the urine, and *M. tuberculosis* complex grew in the urine in the Löwenstein Jensen medium (Figure 5).

One patient with tuberculous meningitis was brought to the clinic due to a headache and clouding of consciousness. In the lumbar puncture patient, who had neck stiffness on physical examination, low glucose, high protein, and lymphocyte predominance in CSF detected. Initial cranial MR was compatible with encephalitis. The treatment of meningitis and encephalitis was initiated, but the patient's clinical manifestation did not improve. There was medial gaze defect in the left eye, and by consulting the pediatric infectious diseases department, this case was considered drug resistant disease, and quadruple antituberculosis treatment (isoniazid, rifampicin, pyrazinamide

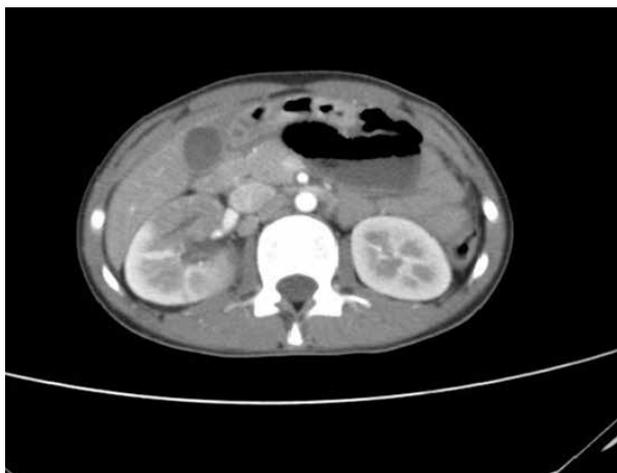


Figure 4: Renal necrosis and granulomatous lesion

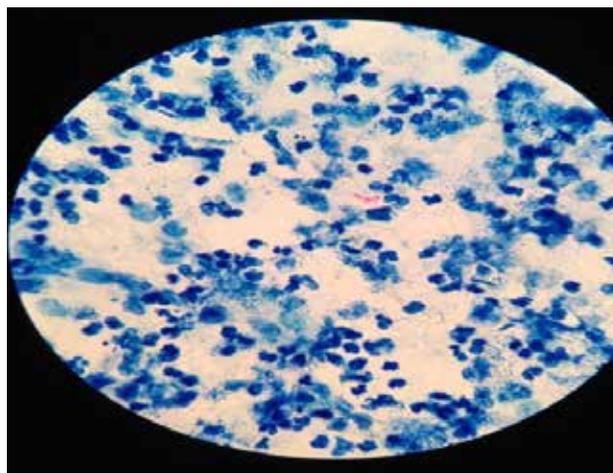


Figure 5: Mycobacterium growth in the Löwenstein Jensen medium in the urine

and ethambutol) was initiated. It was thought that the patient who started to decrease serum sodium values developed unsuitable antidiuretic hormone (ADH) syndrome. The patient's consciousness was clouded and the treatment continued in another hospital with a pediatric intensive care unit. *M. tuberculosis* complex grew in this patient's CSF culture.

Our another patient had mediastinal tuberculosis and was brought to the clinic with the complaints of intermittent rising fever and weight and intermittent coughing complaints loss for a month. In the posterior-anterior (PA) chest x-ray mediastinal expansion was detected. In the thorax CT, diffuse lymphadenopathies were detected in the mediastinum. It was difficult to distinguish malignancy in this patient. Since there was the history of tuberculosis in the family and TST was 18 mm, quadruple antituberculosis treatment was initiated, and the patient responded to the treatment.

One patient with pericardial tuberculosis was 14 years old. In the auscultation findings, the heart sounds of the patient who had applied to the hospital due to fever and coughing. In the PA chest X-ray, it was observed that the cardiothoracic ratio increased. In the echocardiography (ECHO) pericardial effusion was detected. The patient was referred to another center with a prediagnosis of pericardial tamponade. After the pericardial fluid drainage, the patient was readmitted to the service. It was learned that the patient resided in a dormitory, next to a student who had tuberculosis history. The TST and interferon gamma-induced protein 10 (IP-10) test were positive. Tuberculosis culture and ARB couldn't be performed since pericardial effusion was drained at another center.

The case with miliary tuberculosis was a 16-month-old Syrian origin patient, who applied with the complaints of fever, weakness, and lack of appetite. In the laboratory investigations of the patient who also had growth and developmental delay, hypercalcemia was detected. There were diffuse opacity and calcified lymph nodes in the pulmonary imaging of the patient. It was learned from her history that her mother had received antituberculosis therapy at the beginning of pregnancy but had not completed the treatment. In the PCR analysis the patient's tuberculosis DNA result was positive HIV result was negative.

Discussion

Tuberculosis may occur with very different clinical presentations by affecting all organs besides the lungs, which causes delayed diagnosis and treatment (7). In children, EPTB most commonly involves the lymph node, pleura, and central nervous system (8). Lymph node tuberculosis constitutes 50% of EPTB cases and occurs as a result of bacterial lymphohematogenous spread. It is observed 6-12 months after the onset of the infection. Tuberculous lymphadenopathy is usually unilateral and causes erythema and the elevated temperature on the skin (8,9). In many patients, the TST is positive, and in 30-40% of cases, tuberculosis specific findings are observed in the chest X-ray (8). The shared complaints of our five patients diagnosed with lymph node tuberculosis were swelling in the neck, and all had pulmonary involvement in consistency with the literature, and in four of them the TST was positive (+). Tuberculous lymphadenitis in endemic areas should be

considered in lymphadenopathies that are larger than 2x2 cm in size and do not respond to antibiotic treatment. Tuberculous lymphadenitis is diagnosed with excisional biopsy (8,9). The lymph node biopsy result of one of our patients was consistent with tuberculosis. One of the five patients could be diagnosed with a biopsy, while the other patients were detected when they were examined in the differential diagnosis since a response to non-specific antibiotic treatment could not be obtained. one patient with pericardial tuberculosis applied with fever and respiratory distress and had cardiomegaly. Effusion was detected in the echocardiogram. In these patients, radiological cardiomegaly (91%) is observed most commonly (10). In cases with tamponade, pericardiocentesis is diagnostic and therapeutic. Effusion usually has the characteristics of the bloody exudate. The ARB detection on direct microscopy and isolation inspecific culture rates are low. It is beneficial to examine the ADA level in the pericardial fluid for the diagnosis. It could be diagnostic if the pericardial fluid ADA level is above 35 U/L (8). The diagnosis of our patient was made with the high ADA level in the pericardial fluid, the presence of tuberculosis contact history and TST (+).

Central nervous system tuberculosis can appear as tuberculoma or meningitis, and in 10% of cases, tuberculoma and meningitis coexist. Concerning TB, it is observed in endemic countries (8,11,12). In 50% of patients, the TST is positive, and the chest x-ray is normal. In meningeal TB diagnosis, lymphocyte predominance (100-500/mm³), high protein (50-5000 mg/dl) and low glucose (20-40 mg/dl) are detected in the cerebrospinal fluid (CSF) (8). In the direct observation, in large volume (5-15 cm³) CSF, ARB is positive in 10-30% of cases (especially if the supernatant formed after centrifugation is sent as a thick smear), and in the culture in 30-70% of cases (8,13).

LP findings were consistent with tuberculous meningitis, and M. tuberculosis complex was grown in the CSF culture. The TST was positive (+), and the PA chest X-ray of our patient was normal. Hyponatremia may develop due to ADH release (11). Hyponatremia developed in our patient.

Renal and abdominal tuberculosis are rarely observed under 14 years of age because of the long incubation period (8). The age of our patient diagnosed with peritoneal tuberculosis and renal tuberculosis is high as mentioned in the literature.

Less than 50% of cases with abdominal TB can be diagnosed at the initial application, and the TST is positive in fewer than

one-third of the patients. Peritoneal tuberculosis is very rare, and it is between 0.1-3.5% in all TB cases and between 4-10% among EPTB (14). It is observed rarely and usually during adolescence, and together with pulmonary cavities. Peritoneal TB may occur in older children with the spread from the abdominal focus especially close to the mesenchymal lymph nodes, or as a result of miliary hematogenous spread (8,11). It is mainly frequently observed in the 12-14 age group (8, 14). Four of our cases were in the adolescent age group, and only one of them was young. Younger age group cases have also been reported in the literature (15,16). Initial symptoms of abdominal pain and abdominal distension are also accompanied by non-specific symptoms such as fever and weight loss (15-17). The complaints at admission in all of the five cases were abdominal pain and abdominal swelling. It was shown that the elevation of ADA in ascites has 100% sensitivity and 97% specificity. In diagnosis, paracentesis, biopsy, and culture are useful. The elevation of CA 125 levels in peritoneal TB has also been reported (18,19). The elevation of ADA and CA-125 was detected in all cases. Still another patient's biopsy result was consistent with peritoneal tuberculosis.

Renal TB is rarely observed in children, and it is regarded as a late period complication as a result of the lymphohematogenous spread of pulmonary TB. Few patients have a known TB history. The symptoms are few; fever is observed in 30% of patients. Frequent urination, dysuria, ilium pain are observed in 60-70% of patients, while the prevalence of macroscopic hematuria is 30% (8,11). Granulomatous lesions are frequently observed on imaging (75-80%). The TST is usually positive. The chest X-ray is pathological in 50% of patients with renal TB. The most frequent urinary findings are sterile pyuria and microscopic hematuria. Bacterial agents and superinfection are observed in 12-50% of cases. Urine ARB cultures are positive in 50-90%, and PCR in urine samples is 50% sensitive (8). Our case was treated by hospitalizing with urinary tract infection diagnosis. Later, while performing examinations due to repetitive sterile pyuria attacks, the diagnosis was made. There was no tuberculosis contact in the history, and also no pulmonary involvement was detected. The TST was positive (+) and ARB was positive (+) in the urine, and mycobacterium grew in the urine in the Löwenstein Jensen medium.

Bone tuberculosis can occur in 1-2% of all TB, with the lymphohematogenous spread from the adjacent regional lymph

node or infected adjacent bone tissue. After primary infection, symptoms begin in an average of 1-3 years, and the diagnosis is delayed due to the complete absence of TB contact history and the late appearance of clinical findings (8). The most common bone TBs are spondylitis, arthritis, and osteomyelitis, respectively. The spinal bone comprises 50% of TB cases, and it is divided into three according to the involvement of the vertebra: one or more involvements from the anterior (most common), paradiscal and central (8,11,20,21) vertebrae can be observed. The lower thoracic and lumbar regions are most commonly involved, and the anterior corpus of the vertebrae is firstly involved, in the late period the intervertebral disc is involved, and Pott's abscess occurs with the paraspinal tissues and subligamentous spread. In Pott's disease in children, a low-grade fever, restlessness, back pain (usually without significant sensitivity), and abnormal posture may be observed; the child does not want to walk. Involuntary immobilization and rigidity of the spine due to muscle spasm can occur (8,21). Tuberculous arthritis cases usually involve monoarthritis, painless and large joints; 30% of all bone TB cases are accompanied by hip or knee involvement (8,20). In our case, there was vertebral involvement and hip tuberculosis. There was also lymphadenopathy in the neck region. This patient was examined and treated for a long time by the otorhinolaryngology clinic and physical therapy clinic, but then directed to us. The diagnosis was made, as a result of assessing the patient as a whole, questioning the family history, and determining that the findings of MRI imaging were consistent with tuberculosis.

Currently, two different methods are used in the diagnosis of tuberculosis: the TST for a hundred years, and Interferon Gamma Release Assays (IGRAs) for the last ten years. Both methods are indirect diagnostic tools to investigate whether the host has cellular immunity against the TB antigens (memory T-cell response), and none can differentiate latent TB and active TB disease from each other (22). These tests could not be sent from our patients because IGRAs cannot be studied in our hospital but can be studied in private laboratories, but from one of our patients, an interferon gamma-induced protein 10 (IP-10) test could be studied. It has been suggested by the WHO that IGRAs should not be used instead of the TST in low- and middle-income countries, since in the literature most of the IGRA studies have been carried out in high-income countries,

and only estimations have been made for low and middle-income regions with high infection rates (23).

Examination of clinical specimens in the bacteriological diagnosis of TB is very important to confirm the diagnosis. The bacteriological examination is the direct detection of *M. tuberculosis* by sample collection and preparation, microscopic examination of the presence of acid resistant bacilli (ARB), culture and identification, and nucleic acid amplification (NAA) from clinical specimens. In extrapulmonary TB (according to anatomic localization, with or without pulmonary TB): urine, blood, abscess material, cerebrospinal fluid, biopsy material, pleural fluid and other body fluids, synovial fluid, bone marrow and tissue biopsies (24-28). Bacteriological studies have also been observed to be very useful in the diagnosis of our cases.

In HIV-infected children, the risk of transformation from infection to disease, reinfection or reactivation is high. It is under risk concerning atypical pulmonary findings and EPTB, and it accounts for 60% of TB cases in this population. HIV-positive children with TB have higher mortality than those who are HIV-negative (29,30). In our cases, HIV (+) was not detected.

Our cases were presented to emphasize the fact that EPTB can be observed with different clinical presentations and it takes time to diagnose it. Due to its location, Turkey gets a massive migration from countries experiencing war conditions. Low socioeconomic conditions and difficult living conditions facilitate the development of tuberculosis and EPTB. EPTB is also a disease which should be considered in the differential diagnosis of infectious diseases and malignancy in childhood.

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Informed Consent: Written informed consent was obtained from the patient.

Ethics Committee Approval: Ethics Committee approval was obtained from the local ethics committee.

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