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Evaluation of cases of pediatric extrapulmonary tuberculosis: a single center experience

Çocuklarda akciğer dışı tüberküloz olgularının değerlendirilmesi: tek merkez deneyimi

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Abstract

Aim: Extrapulmonary tuberculosis is observed more frequently and leads to complications with a higher rate in children compared with adults because the risk of lymphohematogen spread is higher. In this study, the clinical, laboratory, and radiologic findings and treatment outcomes were evaluated in pediatric patients who were followed up in our clinic with a diagnosis of extrapulmonary tuberculosis.

Material and Methods: Seventy patients aged 0–18 years who were followed up with a diagnosis of extrapulmonary tuberculosis between 2008 and 2017 in the Division of Pediatric Infectious Diseases in our hospital were examined retrospectively.

Results: The median age of the patients was 8,8 (range, 0,4–17) years and 47.1% were female (n=33). Twenty-seven patients (38.6%) were aged 0–4 years, 15 (21.4%) were aged 5–9 years, and 28 patients (40%) were aged 10–18 years. Forty-four patients (62.9%) were diagnosed as having extrapulmonary tuberculosis and 26 (37.1%) had pulmonary + extrapulmonary tuberculosis. The most common form of extrapulmonary tuberculosis was extrathoracic lymphadenopathy, which was found in 22 patients (31.4%). The other patients were diagnosed as having musculoskeletal system tuberculosis (n=10, 14.3%), gastrointestinal system tuberculosis (n=9, 12.9%), miliary tuberculosis (n=8, 11.4%), intrathoracic lymphadenopathy (n=7, 10%), renal tuberculosis (n=6, 8.6%), central nervous system tuberculosis (n=5, 7.1%), and pleural tuberculosis (n=3, 4.3%). Among a total of 58 patients in whom tuberculin skin test and interferon gamma release tests were studied together, tuberculin skin test positivity (n=37, 63.8%) was found with a higher rate compared with interferon gamma release test positivity (n=32, 55.2%), but the difference was not statistically significant (p=0.35). The median treatment period was 12 (range, 6–24) months. Among the patients whose treatments were terminated, improvement was observed in 52 patients (74.2%) and the development of sequela was observed in six patients (8.5%). Two patients who were diagnosed as having central nervous system tuberculosis (2.8%) died.

Conclusion: Clinical, laboratory, and radiologic data should be evaluated together when making a diagnosis of extrapulmonary tuberculosis in children. Interferon gamma release tests alone are not superior to tuberculin skin test, but should be considered to be used in combination in the diagnosis.

Keywords: Child, extrapulmonary tuberculosis, evaluation

Öz

Amaç: Çocuklarda, lenfohematojen yayılım riskinin yüksek olması nedeniyle akciğer dışı tüberküloz erişkinlere göre daha sık gözlenmekte ve daha fazla komplikasyona yol açmaktadır. Bu çalışmada, kliniğimizde akciğer dışı tüberküloz tanısı ile izlediğimiz çocuk olguların klinik, laboratuvar ve radyolojik bulguları ile tedavi sonuçları değerlendirilmiştir.

Gereç ve Yöntemler: Hastanemiz Çocuk Enfeksiyon Hastalıkları Bilim Dalı'nda 2008–2017 yılları arasında akciğer dışı tüberküloz ile izlenen 0–18 yaş arası 70 olgu geriye dönük olarak incelendi.

Bulgular: Yaş ortancası 8,8 (0,4–17) yıl olan olguların %47,1'i kız (n=33) idi. Sıfır–4 yaş arası 27 olgu (%38,6), 5–9 yaş arası 15 olgu (%21,4), 10–18 yaş arası 28 olgu (%40) vardı. Kırk dört olgu (%62,9) akciğer dışı tüberküloz, 26 olgu (%37,1) akciğer+akciğer dışı tüberküloz tanısı almıştı. Yirmi iki olguda (%31,4) en sık toraks dışı lenfadenopati saptandı. Diğer olgular sıklık sırasına göre; kas-iskelet sistemi (n=10, %14,3), gastrointestinal sistem (n=9, %12,9), miliyer (n=8, %11,4), toraks içi lenfadenopati (n=7, %10), renal (n=6, %8,6), merkezi sinir sistemi- (n=5, %7.1) ve plevra tüberkülozu (n=3,%4.3) tanıları almıştı. Tüberkülin deri testi ve interferon gamma salınım testi birlikte çalışılan toplam 58 olguda, tüberkülin deri testi pozitifliği (n=37, %63,8) interferon gamma salınım testi pozitifliğine göre (n=32, %55,2) daha fazlaydı, ancak istatiksel olarak anlamlı bulunmadı (p=0,35). Olguların ortanca tedavi süresi 12 (6–24) ay idi. Tedavisi sonlandırılan olguların 52'sinde (%74,2) iyileşme, altısında (%8,5) sekel gelişimi izlendi. Merkezi sinir sistemi tüberkülozu tanılı iki olgu (%2,8) yaşamını kaybetti.

Çıkarımlar: Çocuklarda akciğer dışı tüberküloz tanısı konulurken klinik, laboratuvar, radyolojik veriler birlikte değerlendirilmelidir. Interferon gamma salınım testleri tek başına tüberkülin deri testine üstün olmayıp, tanıda birlikte kullanılması düşünülmelidir.

Anahtar sözcükler: Akciğer dışı tüberküloz, çocuk, değerlendirme

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Introduction

Tuberculosis is the ninth leading cause of death worldwide and is the leading cause of mortality from a single infectious agent (1). According to the World Health Organization (WHO) Tuberculosis 2017 Report, children aged below 15 years constituted approximately 10% of about 10.4 million new tuberculosis cases in 2016. Around 1.3 million HIV-negative patients have died because of tuberculosis. In the same report, 66% of 12,417 new cases reported from our country were recorded as pulmonary tuberculosis. These data belong to adults and there is a limited number of reports related to children (2).

Extrapulmonary tuberculosis (EP-TBC) is observed more frequently in children compared with adults because the risk of lymphohematogen spread is high, especially in young children. Tuberculosis may affect any organ in the body including mainly lymph nodes and the central nervous system (CNS). Accompanying extrapulmonary organ involvement may be observed in patients with pulmonary tuberculosis. Attention should be paid to extrapulmonary organ involvement in patients diagnosed as having pulmonary tuberculosis because treatment should be administered for a longer period, especially in CNS tuberculosis and bone and joint tuberculosis.

In children, it is particularly difficult to make a diagnosis of tuberculosis because most signs and symptoms of tuberculosis, which is one of the most important causes of mortality in the childhood age group, are non-specific, the sensitivity of diagnostic tests is low in pediatric patients, and tuberculosis may mimic many other disease entities (3). However, the most important factor that affects morbidity and mortality rates is early initiation of treatment. Therefore, it is recommended that treatment should be initiated after the assessment of clinical and radiologic findings together when it is not possible to prove the disease through laboratory findings (4). The most important step required for making the diagnosis is a high level of suspicion. In this regard, publication of tuberculosis data in children in our country is considerably important. In this article, we aimed to contribute to our country's data by evaluating the clinical, laboratory, and radiologic findings and treatment results in our pediatric patients who were followed up with a diagnosis of EP-TBC in our clinic between 2008 and 2017.

Material and Methods

Seventy pediatric patients aged 0 to 18 years who were followed up in the Division of Pediatric Infectious Diseases in our university with a diagnosis of EP-TBC between 2008 and 2017 were included in the study. The sex, age, history of contact to tuberculosis, number of Bacillus Calmette-Guerin (BCG) scars, symptoms at the time of presentation, physical examination findings, laboratory, radiologic, and microbiologic data, and treatment regimens belonging to these patients were exaimed from the patient files.

Definition of cases

Pulmonary tuberculosis was defined as the presence of involvement of pulmonary parenchyma. Extrapulmonary tuberculosis was defined as the presence of acid-resistant bacillus (ARB) in samples obtained from extrapulmonary organs or clinical, radiologic, and histologic clinical findings. Extrapulmonary tuberculosis was classified as lymphadenitis, bone, skin, CNS, gastrointestinal system and perioneum, eye, genitourinary system, and miliary tuberculosis. In patients in whom pulmonary tuberculosis and EP-TBC existed simultaneously, it was stated that both involvements were present; the extrapulmonary organs involved were recorded (5). The diagnosis of tuberculosis meningitis was made with exploration of ARB in CSF samples and with the presence of a positive culture result and at least one radiologic finding.

Patients who had no previous tuberculosis treatment or who had received tuberculosis treatment for less than one month were defined as 'new cases.'

Patients who were previously diagnosed as having tuberculosis, completed treatment succesfully and once again developed ARB positivity and clinical and radiological findings were defined as 'recurrence cases.'

Patients whose disease was newly diagnosed and in whom the bacillus was demonstrated with smear or culture in sputum samples obtained five months or later after initiation of treatment were defined 'case coming from treatment failure' (5).

Radiologic evaluation

The radiologic imagings of all patients at baseline and at the end of treatment were evaluated by a pediatric radiologist. Pulmonary tuberculosis was screened using posteroanterior lung radiography and thoracic computed tomography and patients with EP-TBC were screened in terms of tuberculosis-specific radiologic findings by infection site.

Microbiologic evaluation

Exposure to tuberculosis bacillus was investigated through tuberculin skin tests (TST) and interferon gamma release assasys (IGRA). For the TSTs, the transverse diameter of enduration was evaluated 48–72 hours after 0.1 mL of 5TU solution was injected intradermally in the 2/3 inner surface of the forearm using a 27-gauge needle such that a 6–10–mm papule was formed ("Mantoux" method). A positive tuberculin skin response was defined as an induration size of ≥15 mm in individuals who had no risk factors and had

a BCG scar, >10 mm in individuals who had no BCG scars, and >5 mm in individuals who had risk factors (6).

Sputum, fasting gastric juice, bronchoalveolar lavage fluid, and CSF samples obtained through lumbar puncture in appropriate cases and tissue samples obtained by the organ involved, were used for microbiologic tests. In direct smears, ARB was explored and cultures were studied. Löwenstein-Jensen medium and the BACTEC-Middle-Brook test were used for culture. The diagnosis of tuberculosis was made by detecting the agent in culture and/or presence of histopathologic, clinical, and radiologic findings (6).

Ethics committee approval was obtained from Istanbul University Istanbul Medical Faculty Ethics Committee for this study (2018/581). The study was conducted in accordance with the principles of the Decleration of Helsinki. Informed conset was not required because the study was conducted retrospectively.

Statistical analysis

The Statistical Package for the Social Science (SPSS) statistical program was used for statistical analyses (Version 21, Chicago). Qualitative measurements are expressed as numbers and percentages, and quantitative measurements are expressed as mean±standard deviation (by specifying median, minimum and maximum values, when necessary). The McNemar test was used for the evaluation of dependent groups. A p value of <0.05 was considered statistically significant.

Results

Characteristics and distribution of the patients

The median age of the patients was 106 (range, 5–204) months, and 47.1% were female (n=33). Twenty-seven patients (38.6%) were aged between 0 and 4 years, 15 (214%) were aged between 5 and 9 years, and 28 patients (40%) were aged between 10 and 18 years. Forty-four patients (62.9%) were diagnosed as having EP-TBC, and 26 (31.7%) had pulmonary TBC+EP-TBC. When the distribution of the patients who had extrapulmonary tuberculosis was examined, it was found that 22 (31.4%) had extra-thoracic lymphadenopathy (LAP). The distribution of the other patients, in order of frequency, were as follows: musculoskeletal tuberculosis (n=10, 14.3%), gastrointestinal tract tuberculosis (n=9, 12.9%), miliary tuberculosis (n=8, 11.4%), intra-thoracic LAP (n=7, 10%), renal tuberculosis (n=6, 8.6%), CNS tuberculosis (n=5, 7.1%), and pleural tuberculosis (n=3, 4.3%). The patients's characteristics by diagnosis distribution is shown in Table 1.

The diagnosis of CNS tuberculosis was made through culture in one subject, radiologic findings in two patients, and with growth in culture and radiologic findings in two patients. Among the patients who were diagnosed as having gastrointestinal tract tuberculosis, one subject had biopsy findings (granulomatous inflammation) and radiologic findings (intraabdominal LAP+peritoneal thickening), one subject had positive peritoneal fluid culture, and two patients had radiologic findings compatible with tuberculosis.

Clinical findings and laboratory examinations

The most common symptom at presentation was the presence of neck swelling, which was found in 24 (34.3%) patients. Fever and night sweating were present in 11 patients (15.7%), restricted movement and pain in the extremities were present in nine (12.9%), cough was present in seven (10%), hematuria was present in seven (10%), and weight loss was present in six patients (8.6%). Blurred consciousness, vomiting, and headache were found in three patients (4.3%), vomiting was found in two patients (2.8%), and growth and developmental delay was found in one patient (1.4%).

As a result of history and family screening, the presence of contact with an individual with tuberculosis in the immediate vicinity was found in 20 patients (28.6%). BCG scar was positive in 63 patients (90%). The result was found to be positive in 39 (60%) of 65 patients who underwent TSTs. Interfero-gamma release test was found to be positive in 33 of 61 patients (54.1%). In a total of 58 patients in whom TSTs and IGRTs were performed together, the frequency of TST positivity (n=37, 63.8%) was found to be higher compared with IGRT positivity (n=32, 55.2%), but the difference was not statistically significant (p=0.35).

When the laboratory findings at the time of diagnosis were evaluated, anemia was found in 12 patients (17.1%), leukocytosis was found in three patients (4.2%), increased C-reactive protein level was found in 34 patients (48.5%), and increased erythrocyte sedimentation rate was found in 49 patients (70%). The test was found to be negative in all patients in whom anti-HIV tests were studied (36/70).

Diagnostic evaluation

Acid-resistant bacillus positivity was found as 20.6% (14/68) in various body fluids and tissue samples. *Mycobacterium tuberculosis* grew in culture with a rate of 32.6% (15/46) (Table 2). Two patients (2.8%) had isoniaside (H) resistance and two (2.8%) had rifampicin (R) resistance. Multidrug resistant tuberculosis was found in two patients (2.8%). The diagnosis was made through histopathologic examinations in 43 patients (76.2%).

Computed tomography (CT) of the lung was performed in 26 patients (37.1%), neck ultrasonography was performed in 24 (34.3%), magnetic resonance imaging (MRI) of the mus-

Table 1. Distribution of the patients

Involvement site	n (%)	Age, months median (range)	TST pos n (%)	IGRT pos n (%)	ARB pos n (%)	Culture pos n (%)	Histologic finding n (%)	Radiologic diagnostic finding n (%)	Treatment	Treatment duration, months, median (range)	Final status n (%)
Extra-thoracic LAP	22 (31.4)	84.5 (6–188)	14/21 (66.7)	10/18 (55.6)	1 (4.5)	5 (22.7)	22 (100)	–	HRZ: 20 (90.1) HRZE: (9.9)	9 (6–15)	Recovery: 19 (86.5) Lost to follow-up: 1 (4.5) Relapse: 1 (4.5) Treatment cont.: 1 (4.5)
Musculo-skeletal system	10 (14.3)	82 (7–192)	6/10 (60)	7/10 (70)	2 (20)	2 (20)	9 (90)	7 (70)	HRZE: 8 (80) HRZS: 1 (10) HRE: 1 (10)	18 (12–24)	Recovery: 5 (50) Lost to follow-up: 1 (10) Treatment cont.: 1 (10) Sequela: 3 (30)
Gastrointestinal	9 (12.9)	132 (34–204)	3/8 (37.5)	4/7 (57.1)	–	1 (11.1)	6 (66.7)	8 (88.9)	HRZ: 4 (44.4) HRZE: 4 (44.4) HRE: 1 (11.2)	12 (9–15)	Recovery: 7 (77.7) Lost to follow-up: 1 (11.1) Treatment cont.: 1 (11.1)
Miliary	8 (11.4)	146.5 (5–179)	5/7 (71.4)	3/7 (42.9)	1 (12.5)	2 (25)	2 (25)	6 (75)	HRZE: 5 (62.5) HRZS: 3 (37.5)	15 (12–24)	Recovery: 7 (87.5) Lost to follow-up: 1 (12.5)
Intra-thoracic LAP	7 (10)	28 (12–189)	4/7 (57.1)	2/7 (28.6)	1 (14.3)	1 (14.3)	1 (14.3)	6 (85.7)	HRZ: 3 (42.9) HRZE: 2 (28.6) HRZS: 1 (14.3) HRS–PAS: 1 (14.3)	9 (6–18)	Recovery: 6 (85.7) Lost to follow-up: 1 (14.3)
Renal	6 (8.6)	149.5 (53–190)	4/5 (80)	4/6 (66.7)	6 (100)	1 (16.6)	–	–	HRZ: 3 (50) HRZE: 3 (50)	9 (6–12)	Recovery: 5 (83.3) Sequela: 1 (16.7)
CNS	5 (7.1)	35 (5–202)	1/4 (25)	1/3 (33.3)	2 (40)	2 (40)	1 (20)	4 (80)	HRZE: (40) HRZS: 3 (60)	15 (12–24)	Sequela: 2 (40) Lost to follow-up: 1 (20) Mortality: 2 (40)
Pleura	3 (4.3)	170 (112–179)	2/3 (66.7)	2/3 (6.7)	1 (33.3)	1 (33.3)	2 (66.7)	2 (66.7)	HRZ: 2 (66.7) HRZE: 1 (33.3)	12 (12–18)	Recovery 3 (100)

EP-TBC: Extrapulmonary tuberculosis; ARB: Acid-resistant bacillus; E: Ethambutol; H: Izoniaside; IGRT: Interferon gamma release test; LAP: Lymphadenopathy; n: Number of patients; CNS: Central nervous system; R: Rifampicin; S: Streptomycine; Z: Pyrazinamide; cont.: Continued.

Table 2. Microbiologic data belonging to the cases of tuberculosis

Sample type	ARB positivity		Culture positivity	
	n	%	n	%
Sputum	2/8	25	1/8	12.5
FGJ	1/13	7.7	1/13	7.7
CSF	2/5	40	2/5	40
Biopsy	3/36	8.3	9/14	64.3
Urine	6/6	100	2/6	33.3
Total	14/68	20.6	15/46	32.6

FGF: Fasting gastric juice; ARB: Acid-resistant bacillus; CSF: Cerebrospinal fluid; n: Number of patients

culoskeletal system was performed in ten (14.3%), cranial MRI was performed in nine (12.9%), abdominal CT was performed in nine (12.9%), abdominal ultrasonography was performed in eight (11.5%), brain CT was performed in four (5.7%), and vertebral CT was performed in two (2.8%) patients. Bronchoscopy was performed in one patient (1.4%).

Radiologic findings related to tuberculosis disease was present in 51.6% of the patients (33/64). The pulmonary findings included hilar LAP-granuloma (n=4, 5.7%), hilar LAP-consolidation (n=3, 4.2%), endobronchial involvement (n=1, 1.4%), miliary appearance (n=8, 11.4%), and pleural thickening-effusion (n=3, 4.2%). The extrapulmonary radiologic findings included hydrocephalus (n=2, 2.8%), hydrocephalus-intracranial tuberculoma (n=2, 2.8%), intra-abdominal LAP+peritoneal thickening (n=8, 11.5%), hydronephrosis (n=1, 1.4%), and bone lesion-abscess (n=7, 10%). Ventriculoperitoneal shunt was applied in two patients because of hydrocephalus.

Treatment and final status

The median treatment period was 12 (range, 6–24) months. The most commonly used treatment regimen was HR+pyrazinamide (Z) combination, which was used in 32 patients (45.7%). Ethambutol (E)+HRZ was used in 27 patients (38.6%), HRZ+streptomycine (S) was used in eight patients (11.4%), HRE was used in two patients (2.8%), and HRS+para-aminosalicylic acid (PAS) combination was used in one patient (1.4%).

An increase in transaminase levels due to treatment was found in two patients (2.8%). Anaphylaxis developed following administration of streptomycin in one patient (1.4%).

Recovery was observed in 52 patients (74.2%) and sequela development [hydrocephalus (n=2, 2.8%), kyphosis-lordosis (n=3, 4.2%), hydronephrosis (n=1, 1.4%)] was observed in six patients (8.5%) after treatment. Recurrence was observed nine months after treatment was discontinued in one patient (1.4%). One (2.8%) of the two patients who were diagnosed as having CNS tuberculosis was lost on the 10th day and the other one who had hydrocephalus was lost at the 1st month following development of acute loss of consciousness in the follow-up. In the first one of these patients in whom herniation was considered primarily, steroid treatment could not be administered, because he presented with closed consciousness and the diagnosis was made postmortem. Steroid treatment was used in the other subject who had diffuse tuberculomas and hydrocephalus.

Discussion

In Turkey, the incidence of tuberculosis was reported as 17.2/100,000 in the Tuberculosis Control Report 2015 (7). When the distribution of the patients with tuberculosis by age groups was examined, it was found that the case rate was about 4.7/100,000 below the age of 15 years. In all cases, extrapulmonary organ involvement is found with a rate of 35.4% and both pulmonary and extrapulmonary involvement are found with a rate of 4.6%; it is noted that these rates are higher in the age group below 15 years. It is known that the risk of transformation of tuberculosis infection to morbidity and development of severe disseminated disease is increased in children, especially in the first year of life (8). In this age group, the incidence of EP-TBC increases because the risk of lymphohematogenous dissemination is high. Similarly, children aged between 0 and 4 years constituted more than one-third of our patients diagnosed as having EP-TBC in our study. In contrast to adults, the possibility of accompaniment of EP-TBC in pulmonary tuberculosis is increased in childhood. In our study, this rate was found as 37.1%. In the light of this finding, it should be emphasized that a high level of suspicion should be maintained in terms of screening extrapulmonary organ involvement when a diagnosis of pulmonary tuberculosis is made, especially in young children.

Tuberculosis lymphadenitis is generally the most common form of EP-TBC (9). In the study conducted by Coşar et al. (10) in which childhood tuberculosis was evaluated, the frequency of EP-TBC was found as 38.6% and the frequency of tuberculosis lymphadenitis was found as 11.7%. Similarly, the most common form of EP-TBC was extrathoracic lymphadenopathy (31.4%) in our study. According to the statistics of our country, pleural tuberculosis is the second most common extrapulmonary tuberculosis including children aged below 15 years. Bone-joint involvement is observed rarely and constitutes 3% of all tuberculosis cases (9). Its frequency among extrapulmonary tuberculosis cases has been reported to be about 10–35%. In our case series, the second most common extrapulmonary tuberculosis was found to be musculoskeletal tuberculosis (14.3%) in contrast to country-wide data. Pleural tuberculosis alone was the rarest form of EP-TBC. This may be related to the fact that complex cases were referred to us

because our clinic is a tertiary healthcare institution.

The most severe form of extrapulmonary tuberculosis is CNS tuberculosis and miliary tuberculosis. It has been reported that the risk of development of these two morbidities is high, especially in children aged between 6 months and 4 years (11–14). Central nervous system tuberculosis may be observed as parenchymal or meningeal tuberculosis (15). tuberculin skin tests is positive in only 30% of cases (16). Radiologically, the most common findings include hydrocephalus, basal meningeal involvement, and increased contrast uptake in the meninges (17, 18). In adults, these findings occur in 4–6 weeks, whereas they may be observed in a short period after disease onset (in 5–10 days) in pediatric cases (19). Therefore, investigation in terms of miliary tuberculosis and possible CNS tuberculosis, especially in children aged below 4 years will reduce the rates of complications and mortality.

Statistics related to the complications of tuberculosis meningitis in children show variance in the literature. In the study conducted by Anjum et al. (20) in Pakistan, the mortality rate was found as 5% in 40 children with tuberculosis meningitis, and it was reported that neurologic sequela developed in all patients who survived. In another article reported from Vietnam, the mortality rate was reported as 15% and the rate of neurologic sequala was reported as 33% in children with tuberculosis meningitis (21). In our study, the median age was found as 8,8 (range, 0,4–17) years in the patients who had CNS tuberculosis. Two patients died of herniation during the follow-up period and ventriculoperitoneal shunts were applied to two patients. In accordance with the literature data, TST and IGRT positivity rates were found to be low in our patients who had CNS tuberculosis. However, TSTs were found to be positive with a reasonably high rate (71.4%) in our patients who had miliary tuberculosis.

In a study conducted by Devrim et al. (22) in which pediatric cases of pulmonary tuberculosis and EP-TBC were evaluated, it was found that constitutional symptoms including fever, weight loss, and fatigue were found with a significantly lower rate. This may cause underdiagnosis of EP-TBC. However, it has been reported that the TST positivity rates in cases of EP-TBC are lower compared with pulmonary tuberculosis (23, 24). In cases of extrapulmonary tuberculosis, the data related to IGRT positivity rate show variance in the literature (25). In a study conducted by Azghay et al. (26), the rate of quantiferon test positivity was found to be higher in patients with tuberculosis lymphadenitis compared with the patients with pulmonary tuberculosis. However, the sensitivity of IGRT was reported to be considerably low (45%) in bone-joint tuberculosis. In our study, TST positivity (63.8%) was found to be higher compared with IGRT positivity (55.2%) in patients in whom TST and IGRT were studied together, but the difference was not statistically significant. When our study is evaluated in view of the literature, it can be stated that IGRT alone is not superior to TST in geographic areas where the incidence of tuberculosis is high and it is appropriate to evaluate patients with clinical, radiologic, and microbiologic data in combination with TST.

Treatment of extrapulmonary tuberculosis is generally similar to that of pulmonary tuberculosis; its duration may be longer according to the region involved. However, it can be stated that children generally tolerate antituberculosis drugs better than adults (27). In our study, elevated tranaminase levels were found with a rate of 2.8% and anaphylaxis was found with a rate of 1.4%. In addition, the development of complications should be closely monitored in these patients who have a high life expectancy because the possibility of extension of the disease is high. In our patient group, complications including hydrocephalus, kyphoscoliosis, and hydronephrosis were observed in six patients.

The limitations of our study include the relatively low number of patients and retrospective design. However, we think that our study is important in terms of contributing to our country's data related to pediatric tuberculosis.

In conclusion, clinical, laboratory, and radiologic data should be evaluated in combination when making a diagnosis of EP-TBC in children. Interferon gamma release tests alone are not superior to TST and they should be used in combination in the diagnosis.

Ethics Committee Approval: The study was approved by the institutional ethical review board (2018/581).

Informed Consent: As the study was a retrospective review of the laboratory data, no patient consent was obtained.

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Mali Destek: Yazarlar finalsal destek almadıklarını beyan etmişlerdir.

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