CASE REPORT OF TUBERCULOSIS IN A CHILD WITH UNCLEAR VACCINATION HISTORY: DIAGNOSTIC AND THERAPEUTIC CHALLENGES

Przypadek gruźlicy u dziecka z wątpliwą historią szczepienia: wyzwania diagnostyczne i terapeutyczne

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Abstract

Tuberculosis is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*, which often affects the lungs, but can also invade other organs. Despite the obligation of universal vaccination against tuberculosis, there are sill cases of disease, especially in unvaccinated children. This article describes a clinical case of a 17-year-old girl who was admitted to the hospital with symptoms of pulmonary tuberculosis. The girl presented with cough, fever, and weakness. A chest X-ray confirmed characteristic lesions indicative of tuberculosis. Thorough clinical evaluation and laboratory tests confirmed the diagnosis. The patient had a questionable history of tuberculosis vaccination, which posed a risk factor for infection. Treatment with anti-tuberculosis antibiotics was initiated, and after several months, an improvement in the girl's health status was observed. Follow-up examinations showed regression of lung lesions, confirming therapeutic effectiveness. This case underscores the importance of tuberculosis vaccination and the necessity of monitoring unvaccinated children for prompt detection and treatment of the disease.

Streszczenie

Gruźlica jest chorobą zakaźną, wywoływaną przez bakterię *Mycobacterium tuberculosis*. Może dotyczyć każdego narządu, ale najczęstszą postacią jest gruźlica płuc. Pomimo obowiązku powszechnych szczepień przeciwko gruźlicy zdarzają się przypadki zachorowań, zwłaszcza u nieszczepionych dzieci. W niniejszym artykule opisano przypadek 17-letniej pacjentki, która została przyjęta do szpitala z objawami zapalenia płuc. Dziewczynka zgłosiła się z kaszlem, gorączką i osłabieniem. Wykonano badanie radiologiczne klatki piersiowej, które wykazało zmiany charakterystyczne dla gruźlicy płuc. Wnikliwa ocena kliniczna oraz badania dodatkowe potwierdziły rozpoznanie. Pacjentka miała wątpliwą historię szczepienia przeciwko gruźlicy, co stanowiło czynnik ryzyka zachorowania. Rozpoczęto leczenie przeciwprątkowe i po kilku miesiącach obserwowano poprawę stanu jej zdrowia. Badania kontrolne wykazały regresję zmian w płucach, co potwierdziło skuteczność terapii. Przypadek ten podkreśla sens szczepień przeciwko gruźlicy oraz konieczność monitorowania dzieci nieszczepionych w celu szybkiego wykrycia i leczenia choroby.

Keywords: vaccination, tuberculosis, immigrants, *Mycobacterium tuberculosis*

Słowa kluczowe: szczepienia, gruźlica, imigranci, *Mycobacterium tuberculosis*

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Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* (MTB). Although the lung is the predominant site of TB, other organs may be also involved. TB is a significant health challenge worldwide, especially in developing countries, where access to healthcare is limited. It is estimated that one-third of the world's population is infected with MTB, with 5–10% of those infected eventually developing the disease [1].

Despite advances in diagnosis and treatment, TB remains a diagnostic and therapeutic challenge, particularly in children with uncertain vaccination status. Paediatric patients have a higher risk of developing active TB, especially those infected before the age of 5 years [2]. Consequently, identifying children with latent infection and providing them with preventive treatment are key to controlling and eliminating TB [3].

The diagnosis of TB in children can be particularly challenging due to non-specific symptoms and the difficulty in obtaining microbiological confirmation. The lack of reliable vaccination data makes the diagnostic process even more complicated. When TB is suspected in a child with an uncertain vaccination history, accurate diagnosis and prompt treatment are essential to prevent disease progression and transmission.

In countries with low rates of TB, symptoms are significantly more likely to occur in immigrants than in the resident population. This epidemiological situation persists during the first years of residence in the host country [4]. In fact, the majority of new TB cases in the Western paediatric population occur in children born to immigrant families [5].

In the case presented below, we highlight the importance of a thorough clinical assessment, including a detailed medical history and appropriate diagnostic investigations.

Case report

A 17-year-old female patient of Ukrainian origin was admitted to the Department of Paediatrics, Nephrology and Paediatric Allergology due to epigastric pain occurring for 3 days, episodes of fever up to 38°C, and cough persisting for about a month. The girl had been diagnosed with bronchitis two weeks before. Amoxicillin with clavulanic acid was used for treatment, without significant improvement.

On admission, the patient was in a relatively good general condition. Significant abnormalities included yellowing of the skin, isolated crackles in the middle field of the left lung on auscultation over the lung fields, epigastric pain on palpation and a weakly positive Chelmonski sign.

Laboratory workup revealed moderately elevated inflammatory markers (CRP 3.2 mg/dL; normal <0.5 mg/dL), with high ESR (95 mm), elevated total bilirubin (2.3 mg/dL; normal 0.0–1.2 mg/dL) and conjugated bilirubin (1.0 mg/dL; normal 0.0–0.2 mg/dL), with normal aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transpeptidase and amylase. Peripheral blood count showed normocytic anaemia (haemoglobin 9.8 g/dL), thrombocytosis (482 × 10^9/L; normal 150–350 × 10^9/L;), elevated red cell volume distribution (70.20 fL; normal 37.1–44.2 fL), high reticulocyte concentration (12.74%; normal 0.90–1.49%) and reduced haptoglobin (<8 mg/dL; normal 30–200 mg/dL).

The peripheral blood count and elevated bilirubin prompted the attending physician to include autoimmune haemolytic anaemias in the differential diagnosis. Microscopic peripheral blood smear showed erythroblasts, marked anisocytosis, numerous polychromatophilic RBCs and few spherocytes. Urinalysis showed no signs of infection; trace urobilinogen was detected.

An abdominal ultrasound was performed due to suspected cholecystitis or cholangitis, which showed only a slightly enlarged spleen (137 mm in length). The other abdominal organs appeared unremarkable.

A chest radiograph was taken to search for the source of the infection, which showed interstitial densities in the upper and partially mediastinal fields of the left lung, with an area of consolidation mainly increased in the perihilar region, and discrete interstitial densities in the mediastinal part of the right lung (fig. 1).

Clarithromycin was empirically included.

Due to the rather extensive inflammatory changes in the lung parenchyma and an enlarged spleen, it was decided to extend the diagnosis with a CT scan of the chest and abdomen. Chest CT showed parenchymal thickening, with air bronchogram in segments 1, 2, 3, 6, and with focal parenchymal destruction and cavities in segment 3 (the largest measuring 14 × 13 mm) (fig. 2). Tree-in-bud lesions were found in the lingula of left lung. Lesions of similar morphology, as well as peribronchial cuffing in

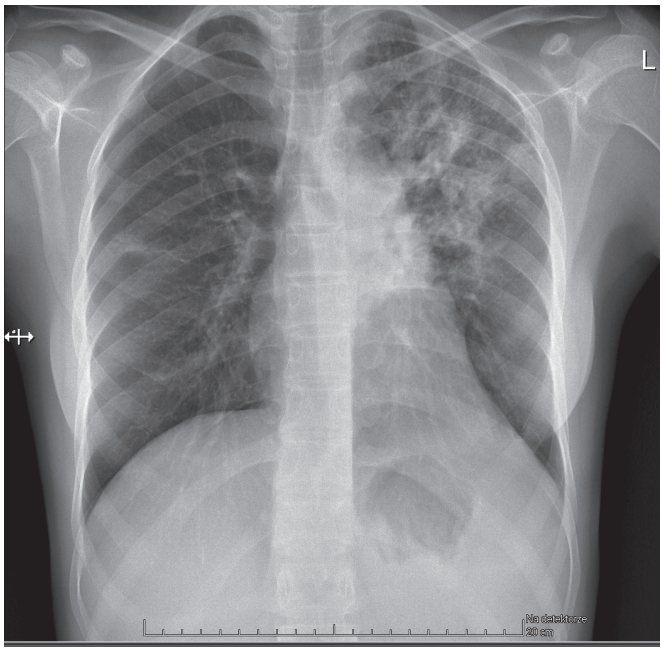

Figure 1. Chest X-ray in the patient before treatment onset

segment 3 were described in the right lung. Parenchymal changes were also visualised in the apices of both lungs. The radiological findings suggested that TB should be considered in the differential diagnosis.

An abdominal CT scan showed an enlarged spleen (up to 140 × 105 mm).

An extended family history revealed that the girl's father had contracted tuberculosis 3 years before.

No Bacille Calmette-Guérin (BCG) vaccination scar was found on physical examination of the girl, despite parental assurances that the child had been vaccinated in accordance with the Ukrainian vaccination programme.

The patient underwent the Quantiferon TB Gold test, which was positive, and the GeneXpert MTB/RIF polymerase chain reaction (PCR) test, which identified the genetic material of *Mycobacterium tuberculosis*, without *RpoB* mutation-associated resistance to rifampicin.

Based on the entire clinical picture, as well as laboratory and imaging findings, pulmonary tuberculosis was diagnosed and hereditary spherocytosis was suspected.

The patient was transported to the Mazovian Centre for Treatment of Lung Diseases and Tuberculosis in Otwock for further diagnosis and treatment. Here, investigations were performed to confirm the presence of TB, i.e. BD MAX genetic testing of sputum and stool, bacterioscopy of sputum and gastric lavage, and conventional culture from the collected material, in which acid fast bacilli were cultured after 3 weeks on sterile media. Once drug susceptibility was confirmed, therapy based on rifampicin, isoniazid, ethambutol and pyrazinamide was administered for two months. An ophthalmological consultation was sought prior to treatment onset to exclude any ophthalmic contraindications. Initially, rifampicin, isoniazid and ethambutol were included, and after two days of good tolerance, pyrazinamide was added.

Three weeks after treatment onset, regression of symptoms such as cough and auscultatory changes over the lung fields was observed. The patient also reported improved well-being and appetite.

A follow-up bacteriological evaluation of gastric lavage one month after treatment onset detected no mycobacteria. It was decided to continue anti-TB treatment with rifampicin/ isoniazid for another 9 months due to the presence of a newborn at home.

After another moth, a follow-up bacteriological analysis was performed, showing no mycobacteria in the smear.

Chest radiography performed in the last days of the quadruple therapy showed almost complete regression of parenchymal and interstitial thickening in the right lung and a significant reduction of inflammatory changes in the left lung.

The patient was discharged home in good condition, with the recommendation to continue the above-mentioned

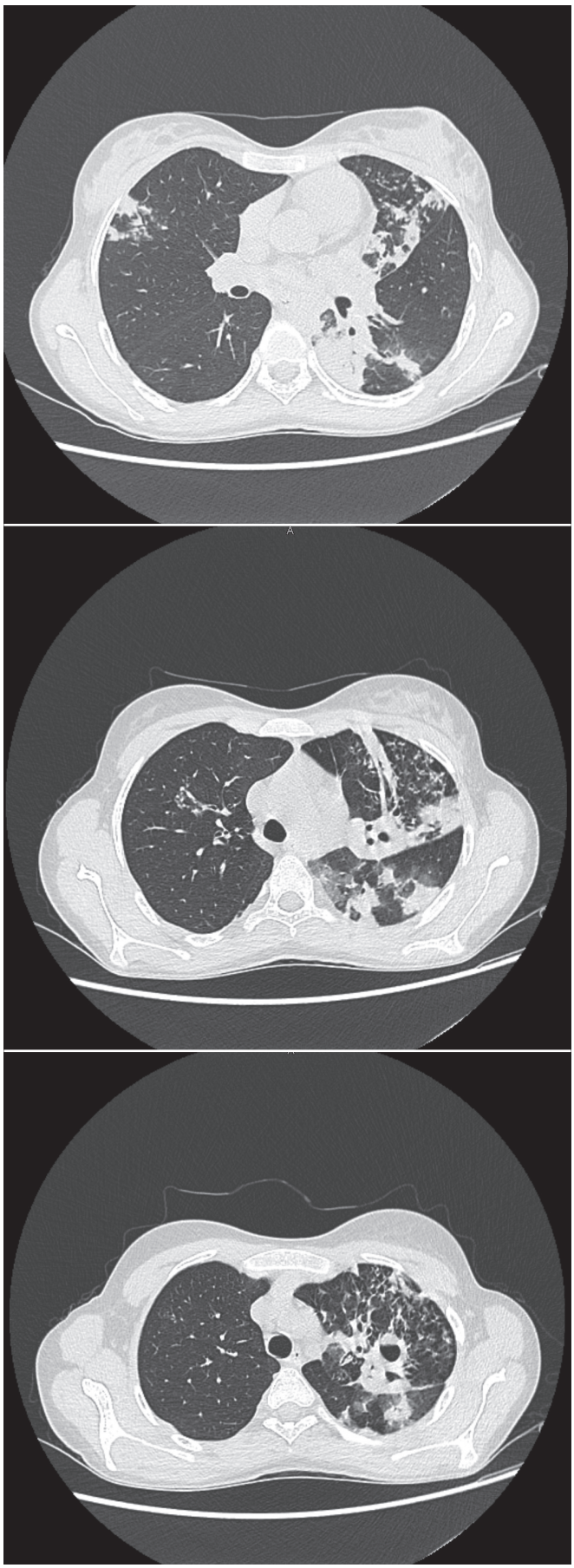

Figure 2. Chest CT before treatment onset. Images taken at different chest levels

medications and to report for a scheduled haematological diagnosis to confirm spherocytosis.

Diagnostic procedures to detect infection in immediate family members confirmed asymptomatic mycobacterial infection in the patient's 5-year-old niece.

Discussion

Every year, tens of millions of children are exposed to *Mycobacterium tuberculosis* infection, with TB remaining a significant infectious cause of mortality in the paediatric population [6]. Children aged 2 to 5 years, closely followed by adolescents (10–18 years), are most likely to be infected [7]. MT is spread through air, mainly by patients with active pulmonary or laryngeal tuberculosis. It is characterised by slow replication and is capable of transitioning to a 'latent' state. Due to young age and, sometimes, immune deficiencies, latent TB may progress to active disease up to many years after the initial infection and despite having received BCG vaccination.

The diagnosis and confirmation of tuberculosis in children is often challenging, even with advanced medical technology. Molecular microbiological methods may fail due to their low sensitivity, especially in the paediatric population. Immunodiagnostic tools are more sensitive, but some of them have low specificity. They also fail to distinguish between active and latent TB, which however can be achieved with tuberculin skin test (TST) and interferon gamma release assay (IGRA).

Studies have shown that IGRA has a higher specificity than TST in detecting TB infection, particularly in low TB incidence countries and among vaccinated children. Based on a meta-analysis conducted between 2000 and 2011, the specificity of IGRA in TB-vaccinated individuals was estimated at 85–95% vs. 45–60% for TST [8]. The lack of data on the efficacy of IGRAs in children <5 years of age means that these tests are rarely used in this age group [9]. In contrast, TST is used routinely in children as young as 4 to 6 months of age [10]. It is recommended that sputum and gastric lavage be collected for testing in older and younger children, respectively.

Available PCR methods can confirm the presence of mycobacterial genetic material within a few days. However, it should be emphasised that these tests are only complementary to mycobacterial culture. Mycobacterial culture on Löwenstein-Jensen medium allows not only the identification of mycobacteria, but also the assessment of their sensitivity to treatment. Since the sensitivity of mycobacterial detection in the paediatric population using this method is much lower than in adults, the decision to initiate TB treatment should be made before microbiological confirmation. Less than 40% of cases of TB in children are usually confirmed by culture [11].

Latent MT infection is usually diagnosed in the absence of any clinical or radiological signs of tuberculosis. It is recommended that IGRA or TST be performed mainly in children exposed to patients with pulmonary TB, transplant recipients, patients intended to receive TNF-alpha antagonist therapy and immigrants from high TB incidence countries. According to the experts from the Centres for Disease Control and Prevention, planned long-term glucocorticoid therapy is also an indication for diagnosis of latent infection [12]. Before performing the above-mentioned investigations, it is reasonable to exclude possible symptoms of active TB, such as chronic cough or subfebrile state, growth and weight gain disorders, and haemoptysis.

Age <5 years, diabetes mellitus, congenital or acquired immune disorders and steroid therapy are factors that increase the risk of developing active TB. After reaching the diagnosis of pulmonary TB, a therapy combining four drugs, each with a different function, is recommended: rifampicin and isoniazid act as bactericides, eliminating bacteria in the replicative phase, while pyrazinamide and ethambutol, which are sterilising drugs, act on the low-metabolism bacterial population. This treatment regimen is prescribed initially for 2 months, followed by rifampicin and isoniazid alone for further 4 months. Transaminases and bilirubin should be measured before treatment onset, especially in patients with liver disease.

If there is a pleural effusion, drainage is required. Treatment of latent tuberculosis can last 6 months and involves regular intake of one anti-TB drug per day, or 3 months with two different anti-TB agents. In some cases, glucocorticoids and pyridoxine may be added to the therapy.

Drug-resistant TB poses one of the biggest challenges in the treatment of MT infection. Multidrug-resistant TB refers to the presence of resistance to at least isoniazid and rifampicin, two of the four key first-line drugs used in standard anti-tuberculosis therapies. Highly drug-resistant TB shows additional resistance to any fluoroquinolone and at least one of three second-line drugs: amikacin, kanamycin or capreomycin. A recent meta-analysis estimated that approximately 3.1% of new TB cases diagnosed in children in 2010 were drug-resistant [13].

Individuals exposed to a patient with an active TB disease are placed under epidemiological surveillance and undergo diagnosis to detect active TB or mycobacterial infection. Isoniazid preventive therapy may be used if necessary. Each confirmed case of the disease must be reported to the Provincial Sanitary and Epidemiological Station.

Research has shown that vaccination significantly reduces the risk of severe forms of TB, such as meningitis and miliary TB, which can be life-threatening in infants. The BCG vaccine is effective in protecting against pulmonary TB in children, but unfortunately its efficacy decreases 10–20 years after vaccination and it no longer provides good protection for adolescents and adults [14]. Work is currently underway to develop a new, more effective vaccine that also protects adolescent patients and produces a long-lasting immune response. Research on the combination of BCG and a subunit vaccine may provide a new immunisation strategy, which could significantly reduce TB morbidity and mortality by 90% and 95%, respectively, by 2035 [15].

Treatment of latent MT infection considerably reduces the risk of developing active disease. Effective treatment of both latent and clinically overt TB may reduce morbidity and mortality in children.

Conclusions

Other possible causes than those currently prevalent in Poland should also be considered when diagnosing infections in immigrants [16]. Differences in clinical manifestations of the disease, as well as language and cultural barriers that may complicate accurate diagnosis and treatment should also be taken into account [17]. The diagnostic and therapeutic process in suspected TB cases requires the use of a wide panel of laboratory and imaging methods and careful analysis of their results. Early identification and precise verification of the pathogen are key to implementing appropriate treatment. d paediatricians, infectious disease specialists and pulmonologists is essential to ensure optimal treatment and control of TB in children. Preventive management and the use of appropriate therapy, in line with current standards, help reduce the spread of TB.

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