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CASE REPORT

An unusual combination of extrapulmonary manifestations of tuberculosis in a child

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Summary We report the case of a 10-year-old girl who presented to the emergency department with acute abdominal pain. She was diagnosed as having extrapulmonary tuberculosis (TB) with multifocal osteomyelitis of the spine and ribs, peritonitis and intestinal involvement. We describe the clinical presentation of this unusual constellation of the disease in the absence of pulmonary involvement in a child and discuss the diagnostic challenges and treatment of these rare forms of TB.

Introduction

Tuberculosis (TB) is a serious global problem. The World Health Organization (WHO) 2010 report on global control of TB stated that there were 9.4 million new cases in 2009; of these, 1.7 million people died from TB (4700 deaths a day). Since 1995, 41 million people with TB have been successfully treated and up to 6 million lives saved through directly observed therapy (DOT) and the Stop TB Strategy [1]. However, despite the launch of successful strategies to combat the disease, TB is still a major health problem in many countries. We present the case of an unusual combination of extrapulmonary manifestations of TB to increase the awareness of uncommon types of TB, their manifestations and the related management in children.

Case report

A previously healthy 10-year-old girl was referred from a primary health care clinic to a tertiary-care hospital in Riyadh, Saudi Arabia, for the urgent

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surgical evaluation of acute abdominal pain. Her pain had started suddenly, was moderately severe and was generalized with no radiation. She had suffered from a low-grade fever associated with night sweats for the last month and presented with a two-kilogram weight loss. There was no history of cough, vomiting, stool abnormalities, rash or bone pain. Family history revealed that three relatives who were visiting the family for a short period were later diagnosed to have pulmonary TB. The child was exposed to these relatives before they received antituberculous treatment. The patient had been immunized at birth with the Bacillus Calmette-Guérin (BCG) vaccine.

On physical examination, the child looked unwell and emaciated. Her temperature was 38.3 °C. Her other vital signs were normal. Her weight was 20 kg, and height was 121 cm, both of which were below the 5th percentile for her age. The abdomen was distended with generalized tenderness. There was tenderness over the lower spine. The neurological exam showed power, tone, and reflexes to be normal. There was no jaundice, lymphadenopathy, joint swelling or tenderness, or skin rash.

Initial laboratory investigations showed a hemoglobin level of 108 g/L, white blood cell count of 5.7×10^9/L with normal differential, and erythrocyte sedimentation rate of 10 mm/h. Liver function tests were normal. Abdominal ultrasound showed diffuse omental mesenteric thickening and nodularity, multiple mesenteric lymph nodes, thickening and edema of the small intestinal wall and small amount of free peritoneal fluid with multiple internal septations. A computed tomography (CT) scan of the abdomen confirmed these findings. In addition, there was an increased bone density of the second lumbar vertebral body with osteolytic lesion seen in the right side anteriorly associated with small adjacent soft tissue swelling suggestive of osteomyelitis of the L2 vertebral body. Chest radiography showed thinning and a periosteal reaction involving the first and second left ribs with destruction of the first rib. The lung parenchyma and pleura were normal, and there was no mediastinal lymphadenopathy. A CT scan of the neck and chest showed destruction of the left first rib with extraosseous extension and an adjacent soft-tissue swelling measuring approximately 9 cm vertically. Whole-spine magnetic resonance imaging (MRI) showed abnormal bone marrow signals with abnormal enhancement involving the cervical (C1, C7), thoracic (T1), lumbar (L2) and sacral (S3) vertebral bodies with mild compression of the C7 vertebra and vertebral destruction involving the right lateral corner of L2. MRI also revealed destruction of the left first rib with a well-defined soft-tissue mass adjacent to it. The spinal cord was normal with no compression or focal lesions. The MRI findings were in keeping with multifocal areas of osteomyelitis. A Mantoux test resulted in an 18 mm wheal at 72 h. The results from the Interferon-Gamma Release Assay (IGRA) using the QuantiFERON®-TB Gold In-Tube test were also positive. Human immunodeficiency virus (HIV) testing was negative. The mass adjacent to the first rib was aspirated using ultrasound guidance, and thick pus was observed. The acid-fast bacilli (AFB) stain on the specimen was positive, and cultures grew *Mycobacterium tuberculosis*.

The patient was given a final diagnosis of extrapulmonary TB that manifested as multifocal osteomyelitis and abdominal involvement with peritonitis. She was started on antituberculous therapy with rifampin, isoniazid, pyrazinamide and ethambutol. Within a week of starting treatment, the patient's health improved with the resolution of fever and decreased abdominal pain and distension. The patient was also given back-support braces and followed up by orthopedics.

Discussion

The diagnosis of TB in children is often challenging because of the paucibacillary nature of the disease and relatively lower culture yields. Furthermore, TB can mimic a wide variety of diseases, ranging from benign common illnesses to malignancy. In general, the diagnosis of TB is made based on epidemiological risk factors, clinical features and imaging studies in addition to a positive tuberculin skin test and/or IGRA. The spectrum and severity of the disease are influenced by host factors such as age and immunological status. Pulmonary parenchymal disease and associated mediastinal lymphadenopathy are the most common clinical manifestations of TB in children and account for 60—80% of all cases. The most common extrapulmonary manifestation is lymphadenopathy (67%). Other extrapulmonary manifestations include miliary/disseminated disease and central nervous system, pleural, skeletal, abdominal, cutaneous and renal involvement [2]. Abdominal TB is uncommon in children [3—5]. It results from lymphohematogenous dissemination from a primary lesion or the ingestion of infected sputum or unpasteurized milk products infected with *Mycobacterium bovis*. Abdominal TB usually presents with chronic abdominal pain, weight loss,

fever, anorexia, abdominal masses and distension. An acute presentation mimicking surgical abdomen, though rare, can occur in children [3]. Peritonitis and nodal disease, which were present in our patient, are the most common forms of abdominal TB in children [3,4]. The CT scan is the imaging modality of choice, as it allows for the evaluation of intestinal wall thickness, ascites, involvement of the abdominal viscera and lymphadenopathy [2]. Barium studies and endoscopy can also help diagnose intestinal disease [3]. The evaluation of ascitic fluid revealed the presence of a lymphocytic exudate. AFB stain and culture are positive in one-third of patients [2]. In some cases, laparoscopy is necessary for obtaining tissue specimens. The response to antituberculous therapy may indirectly prove the clinical diagnosis of abdominal TB when laboratory confirmation is lacking, especially in endemic areas [3]. Recent studies demonstrated the success of long-duration (12-month) antituberculous treatment without the need for adjunctive corticosteroids [3,4]. Skeletal TB is another uncommon form of TB that is observed in 1—2% of children with TB because of hematogenous spread. TB spondylitis (Pott's disease) is the most frequent manifestation and occurs in 50% of children with skeletal TB [2]. The subligamentous spread of the infection may lead to multiple levels of contiguous involvement or leave the vertebral body unaffected. Extension of the infection into the adjacent soft tissue and the consequent formation of paravertebral or epidural masses are common. MRI detects spinal tuberculosis 4—6 months earlier than conventional methods, such as plain radiographs. MRI is also the modality of choice for determining the extent of soft-tissue involvement and for assessing the response to treatment [6]. The diagnosis of Pott's disease is made based on classical clinical and radiological findings; otherwise, tissue-based diagnosis is necessary [7]. TB osteomyelitis comprises 10% of microbial skeletal osteomyelitis cases. Clinically, local signs of infection, such as tenderness to palpation, swelling and diminished range of motion, are found [2]. On imaging, TB osteomyelitis may appear as cystic, well-defined lesions, infiltrative lesions or spina ventosa, which indicates the presence of underlying bone destruction, an overlying periosteal reaction and fusiform expansion of the bone resulting in cyst-like cavities with diaphyseal expansion [6]. TB osteomyelitis of the rib is a rare entity that responds well to medical treatment. Surgery may help in establishing the diagnosis or treating complications [8]. In a series of seven children with TB osteomyelitis of the rib, surgery was indicated, as all presented with a discharging sinus on the chest wall [9]. The revised WHO guidelines for the treatment of TB in children recommend that osteoarticular TB should be treated with a four-drug regimen (rifampin, isoniazid, pyrazinamide and ethambutol) for 2 months followed by a 2-drug regimen (isoniazid and rifampin) for 10 months [10].

Although our patient had no history suggesting recurrent infections with intracellular organisms, Mendelian susceptibility to mycobacterial disease (MSMD) is a possibility. The recently described mutation of the interleukin-12 receptor-β1 chain may have been involved [11]. Our patient has been referred to the immunology service for further work-up to identify any underlying state of immunodeficiency.

In conclusion, TB can present in a variety of ways, with either acute or chronic symptoms and with or without pulmonary involvement. A high index of suspicion is required for early diagnosis of these unusual and serious forms of TB even in areas where TB is endemic. With the world becoming a global village, such patients may also present to health care institutions in countries where TB is not traditionally observed.

Conflict of interest

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