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Mycobacterial Infection in Children at the Chu Hospital Du Mali: A Series of 12 Cases

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Abstract

Introduction: Mycobacterial infections include infections with *M. tuberculosis* complex, *M. leprae*, and non-tuberculous mycobacteria. Mycobacteria can cause a wide variety of infection. Diagnosis of these infections is challenging especially in children because of low availability of clinical and laboratory services particularly in low-resource settings.

Methods: We describe a retrospective case series of mycobacteria infections in children aged 0-15 years at the pediatric department of the Hospital du Mali between January and December 2017. The diagnosis was based on clinical assessment, microbiology (microscopy, culture, PCR); histopathology findings; and radiology evidences.

Results: During the study period, 11354 children were seen in consultation among them 60 children had suspicion of Tuberculosis (TB). Mycobacteria infection was retained in 12 children. 66.7% were male and the average age was 8 years. Ten children (83.3%) were BCG vaccinated and 16.7% had history of TB contact. The most common symptoms were cough (83.3%), fever (75%), general state altered (75%) and dyspnea (50%). The locations were Lung (58.3%), miliary (16.7%), multifocal (8.3%), pericarditis (8.3%) and pleural (8.3%). The Tuberculin Skin Tests (TST) was negative in 58.3%. All children (100%) were seen more than

a month after the onset of the symptoms. Other comorbidities were malaria (25%), severe malnutrition (25%), HIV (16.7%) and hypertension (16.7%).

Conclusion: Combination of clinical, microbiological, histopathological and radiological examinations enabled us to better explore tuberculosis in children.

Keywords

Children; CHU-HDM; CICM-Mali; Mycobacteria; Tuberculosis

Introduction

Bacterial infections are major threats worldwide, causing millions of deaths each year. Tuberculosis (TB) is one of the most serious tropical diseases caused by *Mycobacterium tuberculosis* complex. It is a major public health problem affecting one third of the world's population in all age groups.

Pediatric TB represents 10 to 15% of TB cases worldwide and the diagnostic difficulty constitutes a major obstacle to the therapeutic management of the child [1,2]. In resource limited settings, most of Acid-Fast Bacilli (AFB) positive cases are treated as tuberculosis but some of these infections are caused by Non-Tuberculous Mycobacteria (NTM) [3,4]. NTM can cause a broad range of infections depending on the species and the host condition. Pulmonary disease and other clinical syndromes such as lymphadenitis, skin and soft tissue infection and disseminated disease occurs in children with underlying conditions [5,6]. There are limited data on the epidemiology, diagnosis and optimal management of tuberculosis and nontuberculous infections in children [7].

Methods

Setting

We describe 12 cases of mycobacterial infections among children at the Hopital du Mali (HDM) from January 1 to December 31, 2017. All children aged 0-15 years presenting to the hospital with clinical symptoms including long lasting cough (≥ 2 weeks), fever, night sweat, dyspnea, weight loss, history of TB contact, severe malnutrition were evaluated for TB.

Sampling

For children capable of expectorating, spontaneous expectoration was collected on two consecutive days. For younger children or in case if it was impossible to obtain spontaneous sputum, gastric tubing or induced sputum was applied. Extra pulmonary samples constituted of pus, ascite fluid, pleural fluid, cerebrospinal fluid, bronchoalveolar lavage were collected in sterile tubes with a screw cap. Pus of less abundant abscesses were collected on swabs. Samples were sent to the Rodolphe Mérieux Laboratory for testing in BSL-3 conditions. Polymicrobial samples (i.e. expectorations, pus) were digested, decontaminated with the N-acetylcysteine + 2% NaOH method and concentrated by centrifugation for 15 minutes at 3000 g at 4°C. Fluid of sterile site were used directly without pretreating. Mycobacterial microscopy after Ziehl Neelsen and auramine stain and culture using solid media (Lowenstein Jensen) and liquid media (Mycobacteria Growth Indicator Tubes) were used. Positive cultures were identified with TB Ag MPT64 (SD BIOLINE), Genotype MTBDRplus and Genotype Mycobacterium CM/AS (Hain Lifescience).

Other Methods

Tuberculin Skin Test (TST) was done using five units of standard Tuberculin during the initial visit and result read at 72 hrs. A TST ≥ 10 mm induration was considered positive.

Considering suggestive clinical features, other diagnostic tests were performed depending on the sites involved. If possible, chest X-Ray, histopathological and GeneXpert MTB/RIF assay were performed. Fine needle aspiration cytology was done for the peripheral lymph nodes.

Follow-up

After the diagnosis, children were treated as tuberculosis under the category-I regimen (new cases) for 6 months or the category-II (relapse, lost to follow-up and failure of previous TB treatment) for 8 months according to national guidelines. NTM were treated according to the clinical evaluation of the medical staff.

Results

Among 11354 children, 60 were evaluated for tuberculosis and 12 were treated for mycobacteria infection (Figure 1 and 2).

Demographics

Among the 12 children, the median age of was 8 years (range 7 months - 13 years old). Three (25%) were less or equal than 5 years old. The sex ratio was 2 (Table 1). Seven of them (58.3%) resided in rural area.

Number	Sex	Age (years/ months)	BCG vaccine	HIV	TST	Localisation
Case 1	F	8 years	Yes	Negative	Positive	Pulmonary
Case 2	F	8 years	Yes	Negative	Negative	Pulmonary
Case 3	M	3 years	Yes	Positive	Positive	Pulmonary
Case 4	M	13 years	No	Negative	Negative	Multifocal
Case 5	M	11 years	Yes	Negative	Positive	Pleural
Case 6	M	10 years	Yes	Negative	Negative	Pulmonary
Case 7	M	7 months	Yes	Negative	Negative	Miliary
Case 8	F	8 years	Yes	Negative	Negative	Miliary
Case 9	F	13 years	No	Negative	Negative	Pericarditis
Case 10	M	10 years	Yes	Negative	Positive	Pulmonary
Case 11	M	5 years	Yes	Positive	Positive	Pulmonary
Case 12	M	8 years	Yes	Negative	Negative	Pulmonary

Table 1: Epidemiologic and demographic characteristics of patients with mycobacteria infection.

Clinical Characteristics

Most children were BCG vaccinated (n=10, 83.3%) (Table 1). TST was positive in 41.6%. HIV testing was positive in 16.6% of cases (Table 2).

Number	Medical History and Risk Factors	Clinical Manifestation
Case 1	History of TB contact; malaria, severe malnutrition	Cough, alteration of general condition, fever, anorexia, chest pain
Case 2	None	Cough, alteration of general condition, fever, anorexia, chest pain, night sweats, vomiting, hemoptysis, weight loss
Case 3	HIV	Cough, fever, anorexia, bloating
Case 4	None	Cough, general state altered, fever
Case 5	History of TB contact	Cough, alteration of general condition, fever, asthenia, chest pain, dyspnea, anorexia, weight loss
Case 6	None	Cough, fever
Case 7	Severe malnutrition	Cough, fever, anorexia, diarrhea, vomiting
Case 8	High blood pressure, malaria	Cough, respiratory distress
Case 9	Severe malnutrition	Cough, general state altered, dyspnea
Case 10	Malaria	Fever, dyspnea, Hemoptysis
Case 11	HIV	Fever, dyspnea
Case 12	High blood pressure	Cough, respiratory distress, chest pain

Table 2: Clinical manifestations, underlying conditions and disease localizations in patients with mycobacteria infection.

Microbiology and Histopathology

The diagnosis was confirmed microbiologically in only five children (41.6%) (Table 3).

Number	Type of Sample	Method of Diagnosis	Confirmation	Outcome
Case 1	Sputum	microscopy/culture	<i>M. tuberculosis</i>	Dead
Case 2	Sputum	microscopy/culture	<i>M. tuberculosis</i>	Dead
Case 3	Gastric aspirate	microscopy/culture	<i>M. spp</i>	recovered

Case 4	Biopsy	microscopy/culture, and Anatomopathological	No	Relapse
Case 5	Pleural fluid	microscopy/culture	<i>M. tuberculosis</i>	Relapse
Case 6	Sputum	microscopy/culture	<i>M. phlei</i>	recovered
Case 7	Gastric aspirate	microscopy/culture	No	recovered
Case 8	Ascites fluid	Chest X-Ray	No	Dead
Case 9	Ascites and gastric fluid	Chest X-Ray	No	Loss of follow-up
Case 10	Gastric fluid	microscopy/culture	No	Dead
Case 11	Sputum	microscopy/culture	No	Loss of follow-up
Case 12	Gastric aspirate	Computed Tomography	No	Dead

Table 3: Type of sample, method of diagnosis and outcome of patients with mycobacteria infection.

Figure 1: Chest X-ray showing right pleurisy of great abundance- Case 5.

Figure 2: Microscopic examination 100x showing numerous acid-fast bacilli after Ziehl-Neelsen staining. (A) Direct examination; (B) Culture on the MGIT medium and (C) Culture on the LJ medium- Case5.

Discussions

Mycobacteria are a group of organisms characterized by their staining and identified as acid-fast bacilli. They can cause a variety of infections and the most notables are caused by *Mycobacterium tuberculosis* complex and non-tuberculous mycobacteria. Children usually gets TB infection in contact with a sputum-positive adult. They are at high risk because their immune system is less developed [8]. According to WHO, each year, at least 1 million children become ill with TB. This represent about 10-15% of all TB cases [1]. Out 60 presumptive TB cases, 12 were identified as having mycobacteria.

In our series, the diagnosis was confirmed microbiologically in only 46.1%. A controversy in childhood TB is whether bacteriological confirmation is necessary or not for the treatment [9]. Ideally, TB should be confirmed bacteriologically in order to do drug susceptibility testing. However, in children, bacteriological confirmation is challenging, as infant TB is paucibacillary, and sputum is difficult to obtain [10]. TB and NTM infections are often indistinguishable clinically or by sputum smear microscopy. This poses significant diagnostic and treatment challenges [11].

BCG Vaccination is an important way to prevent disseminated tuberculosis and tuberculosis meningitis, especially in children younger than 2 years; however, its real role has yet to be confirmed [9]. In our series, 83.3% of all children were BCG vaccinated and 100% of those with confirmed *M. tuberculosis*.

The age influences the risk of child to be exposed to TB. Older children interact more with adults in the community and are likely to be infected than younger children: In our series, the average age was 8 years.

The clinical presentation of pediatric TB varies from nonspecific symptoms to severe condition that worsen with time. The main symptoms include fatigue, loss of appetite, night sweats,

weakness, weight loss, and evening fever. For pulmonary localization, child can present chest pain and cough. Other organs can be affected (lymph nodes, kidneys, bones, meninges). In such cases, symptoms vary according to the site [12].

In our series, the most common symptoms were cough (83.3%), fever (75%), general state altered (75%) and dyspnea (50%). The locations were Lung (58.3%), miliary (16.7%), multifocal (8.3%), pericarditis (8.3%) and pleural (8.3%). Disseminated NTM infections typically occur in children with impair immune system including HIV infection. The most common NTM associated with disseminated disease is *Mycobacterium avium* complex (>90%) [13].

Other comorbidities were malaria (25%), severe malnutrition (25%), HIV (16.7%) and hypertension (16.7%).

The Tuberculin Skin Test (TST) continues to be used in high endemic TB settings as a diagnostic tool for determining Latent Mycobacterium Tuberculosis Infection (LTBI) [14]. Diagnosis of LTBI may be hampered by the non-specificity of TST, BCG vaccination, exposure to NTM, booster phenomenon, and technical issues [15]. The TST was negative in 58.3%. Because 83.3% of children were vaccinated, the high rate of TST negative might be due to the malnutrition and altered general state of most of the children.

Conclusion

Children can have TB at any age and these cases are poorly explored. There are many problems with the evaluation of pediatric tuberculosis, such as the diagnostic difficulty, the lack of resources. The proportion of pediatric TB among notified cases is lower than expected. The biological, pathological and radiological examinations make it possible to better explore tuberculosis in children. There is a need for enhanced epidemiological surveillance of adults with TB to ensure early detection and treatment to reduce the incidence of TB in children.

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