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Multifocal Tuberculosis in Immunocompetent Children, Still A Current Problem: About 13 Cases

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Abstract **Original Research Article**

Multifocal tuberculosis corresponds to involvement of at least two extra-pulmonary sites associated or not with pulmonary involvement. ***Material and Method***: This is a retroprospective descriptive study of patients diagnosed with tuberculosis between 2018 and 2022, in the pediatric infectious diseases department at the Rabat children's hospital. Clinical, paraclinical, therapeutic and evolutionary data were collected on a pre-established information sheet. ***Results***: 13 cases were collected in this study, the patients were all correctly vaccinated with BCG, with notion of tuberculosis contagion in 6 cases which were not screened, the localizations found in this series, pulmonary, peritoneal, spinal, cerebral, meningeal and lymph node, the evolution under treatment started early is favorable**.** ***Discussion***: Multifocal tuberculosis poses a diagnostic problem given its clinical polymorphism, which causes delay in diagnosis. Several localizations are found, the most frequent being meningocerebral in this series and lymph node in the literature. A genetic predisposition to the disease has been suggested in immunocompetent patients.

Keywords: Multifocal tuberculosis, pulmonary involvement, retroprospective descriptive study, tuberculosis contagion.

INTRODUCTION

Due to its high incidence, tuberculosis (TB) is a major public health problem in developing countries, particularly in Morocco. An estimated 7 to 8 million new cases of TB are diagnosed each year [2], Multifocal tuberculosis corresponds to involvement of at least two extra-pulmonary sites, with or without pulmonary involvement. Multifocal forms are rare: 9-10% of extra-pulmonary localizations. Multifocal tuberculosis usually occurs in immunocompromised patients, but can also affect immunocompetent patients [1], and this study aims to describe the different clinical and evolutionary features of this clinical form of tuberculosis in children.

MATERIAL AND METHOD

This is a retroprospective descriptive study of patients diagnosed with tuberculosis, covering a period between 2018-2022, in the pediatric infectious diseases department at the RABAT children's hospital. Clinical, paraclinical, therapeutic and evolutionary data were collected on a pre-established information sheet reported on an Excel file, based on inclusion and exclusion criteria.

***Inclusion Criteria:**

1. Child aged 3 months to 15 years.
2. Diagnosis of tuberculosis based on presumptive criteria (contact, signs of impregnation, imaging and/or bacteriology, GeneXpert MTB, BK or culture).
3. At least 2 tuberculosis sites.
4. Immunocompetent terrain.

***Exclusion Criteria:**

1. Immunodeficiency (HIV or other).
2. Infant less than 3 months old.

RESULT

13 cases were collected in our study, all patients were correctly vaccinated with BCG, tuberculosis contagion was found in 6 cases which were not screened, in this study tuberculosis concerned 7 localizations, pulmonary found in all patients, peritoneal in 6 cases as well as cerebral localization, meningeal localization in 4 cases, cutaneous involvement in only 1 case and one case with a spinal localization such as spondylodiscitis and another with lymph node localization. In 8 cases, the diagnosis of tuberculosis was made on the basis of

clinical and radiological findings, in 1 case the diagnosis was made by histological study, and in 4 cases the diagnosis was confirmed by bacteriological study. Time to diagnosis varied, with an average of 5 months. The patients included in this study received nine months' anti-tuberculosis treatment combined with 2 months' oral corticosteroid therapy, with a good clinical, biological and radiological evolution in 85% of our series, with a single death after 8 months of evolution, and an infant who progressed to chronic respiratory failure.

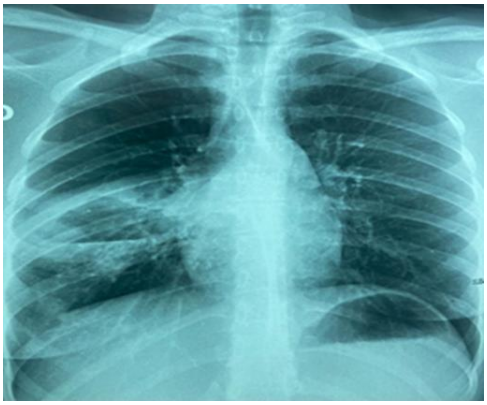

Figure 1: Image of a tubercular cavern (starting point for multifocal TB)

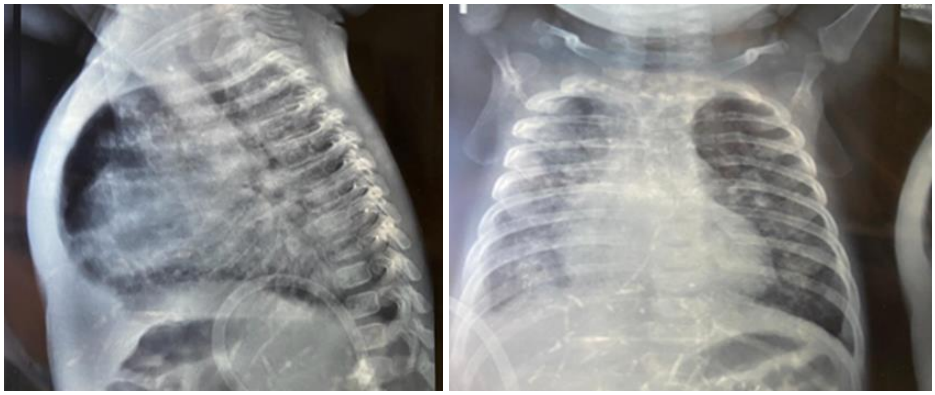

Figure 2: Chest X-ray image of tuberculous miliaria, front and side

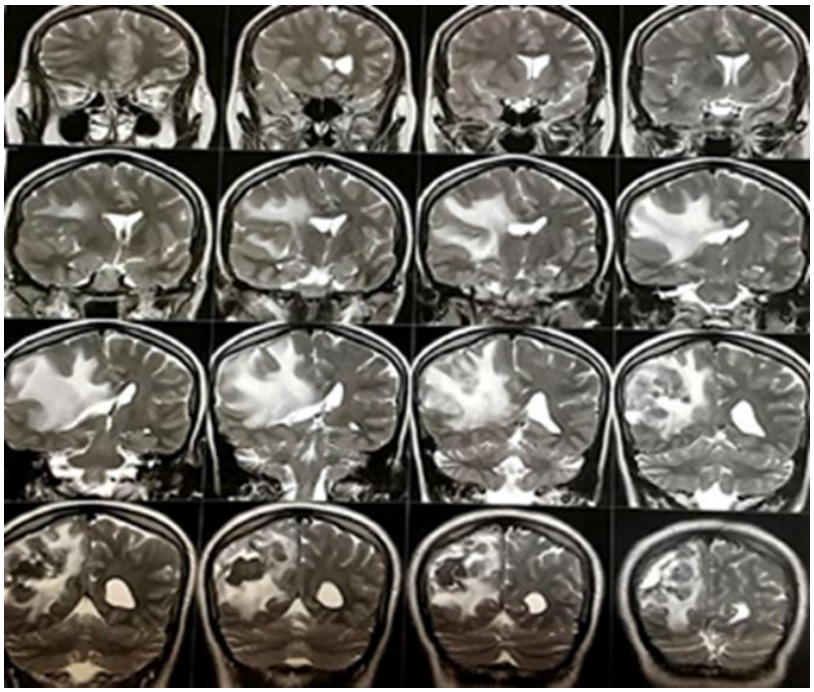

Figure 3: Brain IRM showing an image of a cerebral tuberculoma

DISCUSSION

Tuberculosis (TB) remains a major health problem, and the World Health Organization (WHO) has declared a global emergency [3], Tuberculosis can mimic other diseases and present in an atypical clinical scenario. Although tuberculosis can be taken into account in the differential diagnosis of a young patient presenting with multifocal disease,

Disseminated or multifocal tuberculosis is characterized by the presence of multifocal tuberculous areas in different organs. Disseminated hematogenous tuberculosis, on the other hand, is characterized by the presence of a large number of tubercle bacilli in all sites of the body. The disease may be activated years later in one or more sites, leading to the development of multifocal disease. In contrast, miliary tuberculosis describes any progressive hematogenous disseminated tuberculosis [4]. Miliary tuberculosis develops when numerous organisms simultaneously gain access to pulmonary or systemic veins. Multifocal forms most often occur in immunocompromised patients, but there is currently a marked resurgence in immunocompetent patients.

This form of tuberculosis poses a real diagnostic problem, given its clinical polymorphism and the associated economic and cultural problems, which are at the root of the delay in diagnosis.

Several hypotheses have been put forward to explain the occurrence of this severe form of the disease, such as the prevalence in Morocco, which suggests a genetic predisposition. Studies have evoked and described the Mendelian susceptibility syndrome to mycobacterial infections, a genetic syndrome linked to an alteration in antimycibacterial immunity mediated by the interleukin 12-interferon gamma [5, 6] axis, and nine genes have been identified as responsible [7].

In this study, the localization was double or triple, in the absence of any immune deficiency, and was most often secondary to hematogenous dissemination of M. tuberculosis, most often from a pulmonary focus (100% in this series), sometimes from a lymph node, liver or spinal location [8]. Tuberculous meningitis and intracranial tuberculoma are the forms most frequently observed in this case series and in the literature. The full clinical picture of meningitis is rarely found. The symptomatology is that of febrile meningitis, sometimes associated with neurological localization, with progressive onset and classic CSF findings, notably hypoglycorachia and hyperproteinorachia [9]. Tuberculomas present with focal, progressive onset, associated with meningeal signs [10].

Node location was diagnosed in one case in our series; on the contrary, they are the most frequent in the various series in the literature, contributing easily to the diagnosis through their accessibility to anatomopathological examination.

Osteoarticular localization occurs in 1 to 5% of cases, depending on the series. This location is often under-diagnosed, especially if it is the first to appear, which sometimes explains the delay in diagnosis. It is often spondylodiscitis, more rarely peripheral arthritis [11].

Peritoneal localization is the most common in this series; in the literature, it is described as relatively frequent, representing 5 to 10% of extra-pulmonary localizations [12]. It is evoked by an abdominal pain syndrome and transit disorders, complemented by imaging in favor of necrotic adenopathies, a biopsy with anatomopathological study and PCR (genexpert) of the sample to retain the diagnosis of tuberculosis [13].

Bacteriological confirmation is always disappointing, as the disease is most often extra-pulmonary, and even molecular biology has not made the diagnosis easier. Treatment of multifocal tuberculosis is similar to that of pulmonary tuberculosis. However, prolonged treatment of 9 to 12 months is recommended in cases of central nervous system involvement. The addition of corticosteroids is strongly recommended in cases of pericarditis and meningeal tuberculosis [15]. Progression with treatment, started as early as possible, is often favourable, enabling sequelae to be avoided. In our series, only one death occurred after 8 months, and one infant progressed to chronic respiratory failure.

CONCLUSION

Multifocal tuberculosis is a serious form of the disease. However, it can affect immunocompetent subjects, and diagnostic hypotheses, notably genetic, have been put forward to explain this serious form occurring in immunocompetent subjects. It is therefore essential to systematically check for dissemination of the tuberculosis germ, for better management. The prognosis is often favorable, depending on the type of involvement and the early initiation of anti-tuberculosis drugs.

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