COMPLICATED TUBERCULOSIS MENINGITIS: A CASE REPORT

MENINGITE TUBERCULEUSE COMPLIQUEE CHEZ UN ENFANT TUNISIEN

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Abstract

Background: Tuberculous meningitis (TBM) may occur with tuberculosis infection, and young children are more prone to this disease .It is associated with significant complications of central nervous system. The clinical manifestations, time course, and treatment of TBM are unlike those of other types of meningitis.
Observation: This case study highlights the typical presentation, course, and management of TBM in a 5-year-old Tunisian boy and provides an overview of this devastating disease. The patient developedactive quadriventricular hydrocephalus requiring external ventricular drainage and then ventriculo-peritoneal shunt.He had an uneventful recovery and was followed up for the past three year.
Conclusion: TBM presents unique challenges for nurses caring for patients. We focused on the significance of early diagnosis and prompt treatment.

Key - words: Tuberculosis meningitis; Children; Hydrocephalus.

Résumé

Introduction: la méningite tuberculeuse peut être associée à des complications importantes du système nerveux central. Les jeunes enfants sont plus à risque.
Observation : cette présentation de cas met en évidence les particularités cliniques et de prise en charge de la méningite tuberculeuse chez un garçon de 5 ans et donne un aperçu de cette maladie dévastatrice. Le patient a développé une hydrocéphalie active nécessitant une dérivation ventriculo-péritonéale. L'évolution était favorable tout au long du suivi pendant 3 ans.
Conclusion : la méningite tuberculeuse est de diagnostic souvent difficile. Il faut savoir y penser pour la rechercher et la traiter précocement. Seul le délai diagnostic et de prise en charge conditionne le pronostic.

Mots -clés : Méningite tuberculeuse ; Enfant ; Hydrocéphalie.

ملخص

مقدمة: يمكن أن يترافق التهاب السحايا السلي مع مضاعفات خطيرة في الجهاز العصبي المركزي. يعتبر الأطفال الصغار أكثر عرضة للخطر.
الملاحظة: سلطنا الضوء على السمات السريرية والعلاجية لحالة صبي يبلغ من العمر 5 سنوات و الذي يحمل التهاب السحايا السلي مما قدم لنا لمحة عامة عن هذا المرض المدمر. تطورت سلبا حالة المريض بظهور استسقاء الرأس النشط والذي استوجب اشتقاق بطينية صفاقي. كانت النتيجة مواتية طوال 3 سنوات من المتابعة.
الخلاصة: غالبًا ما يصعب تشخيص التهاب السحايا السلي. علينا أن نعرف كيف نفكر في الأمر لكشفه ومعالجته مبكرًا. فقط التبكير في التشخيص والعلاج هو الذي يحدد الإنذار.

الكلمات المفاتيح : التهاب السحايا السلي ; الطفل ; استسقاء الرأس.

INTRODUCTION

Despite the global program of vaccination, Tuberculosis (TB) is still a major public health problem worldwide. According to current estimates of the World Health Organization (WHO) in 2018, one million children suffered from TB around the world; and 0.14 million children died because of it [1].

TBM is the most severe form of tuberculosis associated with significant morbidity including severe and irreversible neurologic sequelae and mortality [2].Meningitis occurs when infection spreads into the subarachnoid space, resulting in an exudative inflammatory response that can be complicated by obstruction of cerebrospinal fluid (CSF) flow and vascular compression and occlusion, with occasional involvement of the cranial nerves in the brain stem.[2,3].

We present a case of achild with TBM who was hospitalized inthe pediatric emergency and resuscitation department at the Hedi Chaker University Hospital, Sfax, Tunisia.

OBSERVATION

A 5 -year-old boy with no significant personal medical history presented to the pediatric department with vomiting, fever and headache. He had received the Bacillus Calmette Guerin (BCG) vaccine at birth. For fifteen days, he had febrile attacks, headache, asthenia, weight loss, abdominal pain, night sweats and vomiting, treated with azithromycin and amoxicillin without amelioration. Thus he was hospitalized.

On admission, the child was tired with high grade fever but vitally stable. He was conscious and alert, his cranial nerves were intact. Signs of meningeal irritation were not present; his sensory and motor examination was completely normal. Investigations showed normal hemogram, negative C-reactive protein. His chest x-ray did not show any abnormality and urine was sterile.

The evolution was characterized by the occurrence of somnolence and hallucinations on the second day of hospitalization. The brain scan was normal. The cerebrospinal fluid was clear, containing 235 leucocytes / mm3 with 85% lymphocytic preponderance; protein: 0.69 g / L, glucose: 2.06 g / L, chlorine: 108 mmol/l and no germ on direct examination.

The clinical and biological picture suggested viral meningo encephalitis, decapitated bacterial meningitis or a TBM. At the resumption of the interview, the parents indicated that the father was treated, 20 years agofor pulmonary tuberculosis. The child was treated with acyclovir, cefotaxime and vancomycine. Polymerase chain reaction *(*PCR) to detect herpes simplex virus *(HSV)* was negative. Cerebral magnetic resonance imaging (MRI) realized on the fourth day of hospitalization showed a diffuse and bilateral lepto-meningeal enhancement, predominant at basal cisterns and the left Sylvian valley. The fundus examination showed a papillary edema. A second lumbar puncture was realized on the fifth day of hospitalization and it showed 320 leucocytes / mm3 (75% lymphocytes), protein: 0.69 g / L, glucose: 1.8 g / L, CSF to random blood sugar (RBS) ratio : 0.66. No germ on culture and the search for mycobacterium tuberculosis (Mtb) by PCR was negative. The search of acid-fast bacilli on sputum was negative. Quantiferon test was positive. Antituberculosis treatment was started, including oral isoniazid, rifampicin, pyrazinamide and ethambutol with intravenous dexamethasone.

On the fifteenth day of hospitalization, the patient presented blindness with a generalized seizure. The control brain scan showed left lenticulo-capsulo-caudate ischemia and active quadric ventricular hydrocephalus (**Figure 1**). There for he was external ventricular drains were inserted under anesthesia.

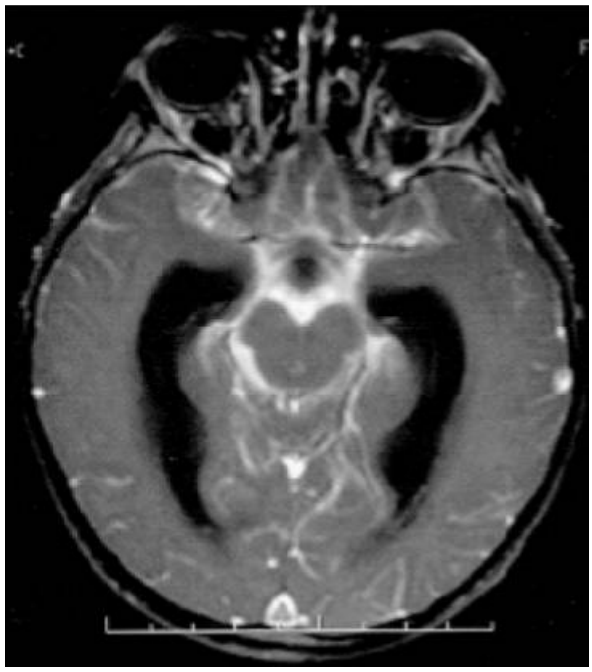

Figure 1: Axial T1-weighted MRI image with Gadolinium showing extensive meningeal enhancement and hydrocephalus secondary to tuberculous meningitis.

The evolution was marked by the occurrence of bacterial meningitis on external ventricular drains and the patient received one month of nosocomial antibiotic therapy. Then, the patient benefited from a ventriculo-peritoneal shunt. The subsequent evolution was favorable. Brain MRI performed a year after the diagnosis, showed an important regression of the lepto-meningeal enhancement with a slight dilatation of the third ventricle and the two lateral ventricles. The child received 12 months of antituberculosis treatment. Currently, after 2 years of decline, the child is doing well, without any neurological disability and with good school results.

DISCUSSION

Tuberculosis is still a public health problem despite the program of the WHO for vaccination and prevention. It remains an important and potentially preventable cause of childhood illness and death, in developing countries due to poverty, social disruption, malnutrition, different causes of immune suppression**.** Various clinical forms can be revealing [4].TBM represents roughly 1% of all cases of TB and is associated with high mortality and residual neurologic sequelae, even with adequate treatment. In endemic countries the highest incidence of TBM is reported in children aged 2–4 years [5].

The rapid diagnosis is crucial for a successful disease management: early diagnosis and treatment of TBM is the single most important factor determining outcome [6].In practice, TBM is difficult to diagnose in its early stages with a consequent delay in the initiation of therapy because of difficulties of access to health care in poor countries and the low incidence of the disease in Western countries [7].TBM remains the most lethal form of TB. The clinical diagnosis of TBM is also difficult because of unspecific symptoms and signs. It causes various clinical manifestations which overlap with other non-tuberculosis etiologies. The microbiological diagnosis is also difficult, due to the low sensitivity of culture for Mtb and of the microscopy for acid-fast bacilli in cerebrospinal fluid (CSF) [6].The gold standard in diagnosing TBM is positive culture of Mtb from CSF. The polymerase chain reaction (GeneXpert test) allows for a rapid and specific diagnosis of TBM.

TBM could be classified as “definite” when CSF demonstrates acid-fast bacilli on microscopy, a positive Mtb culture and/or a positive CSF Mtb commercial nucleic acid amplification test, in an individual with symptoms or signs suggestive of the disease. We used a Pakistan Pediatric Association (**PPA)**scoring chart for the probable diagnosis of tuberculosis adopted internationally as well as by the WHO to diagnose tuberculosis in childhood. This scoring system is based on clinical history, CSF examination results and neuro imaging findings as well as evidence of extra neural TB. A prospective study was conducted in India; the goal was to find simple clinical and biological criteria predicting a tuberculous cause in the presence of meningitis. This investigation studied 232 children with meningitis, including 110 tuberculosis patients. Five criteria were found to be predictive: clinical prodromes of more than seven days (including fever), optic atrophy of the fundus, focal neurological deficit, existence of extrapyramidal movements and less than 50% of neutrophils in the cerebrospinal fluid. The presence of at least three of these five criteria had a sensitivity and specificity greater than 98% [8].

In Dakar, in a recent study published in 2016, of 23 children with TBM, 9 died and 11 had sequelae[9]. Another large childhood study documented neurological disability in about 75% of survivors,despite an exceptionally low mortality rate of only13% and a treatment with antituberculosis chemotherapy [10].In a French series of 32 children with TBM, observed at St. Vincent de Paul Hospital, another diagnosis was initially considered in 23 cases (72%), ten children died (31%) and six had sequelae (19%). In the United States, in another retrospective series of 31 children with TBM, the death rate was 18% and the rate of sequelae 29%; the occurrence of these complications was directly related to the clinical neurological status at the time of admission and time to start treatment[11].

According to the**UKMedical Research Council guidelines**[5] the clinical severity of TBM is characterized into three stages:

Stage 1 is characterized by the non-specific symptoms such as fever, headache, irritability, drowsiness and malaise.

Stage 2 is characterized by the low Glasgow Coma Scale (GCS) of 11-14, with or without focal neurological deficit or GCS 15 with neurological deficit.

Stage 3 is characterized by GCS of 10 or less than10, with or without a focal neurological deficit.

TBM of the child is most often primary tuberculosis; contrary to the adult where it is frequently the reactivation of old tuberculosis

remained latent. This implies the search for a contaminating subject in the close circle[12].The prognosis very much correlates with the clinical stages of tuberculous meningitis. The patients who survived suffer severe neurological disability, including motor deficits, cognition decline, seizures, cranial nerve palsies and hydrocephalus. The inflammatory basal exudate causes obstruction to the CSF flow resulting in a communicating type of hydrocephalus in about 80% of the cases. Hydrocephalus, either communicating or obstructive occurs in 60% to 90% at presentation. It is a se que la or complication of TBM[13].

Treatment (four oral anti-TB drugs) must be instituted early, usually before bacteriological certainty and the drug doses are similar to pulmonary TB. While WHO recommends a standard four-drug treatment regimen comprising isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) for two months (the intensive phase) followed by 10 months of continuation phase treatment with H and R, at country levels, different regimens are used : the therapy can be prolonged for 18 months[14,15].This is largely because of the paucity of clinical trials regarding the treatment of pediatric TBM. In one meta-analysis assessing pediatric TBM outcomes in multiple international settings, almost 27 different regimens were used with varied dosage and duration [16]. Isoniazid and pyrazinamide have excellent cerebrospinal fluid penetration, with lesser penetration for ethambutol. Children can be given prednisolone 4 mg/kg/24 h (or equivalent dose dexamethasone 0.6 mg/kg/24 h) for 4 weeks, followed by a tapering course over 4 weeks [17,18]. The latest Cochrane reviews [19]showed a large effect of corticosteroids on mortality, but there was insufficient data to understand their effect on disability among survivors. Thiongane [9] even advocates treating meningitis with basilar location, cranial nerve palsy or hydrocephalus as tubercular and instituting treatment empirically. Imaging is often of great help: it can highlight meningeal enhancement in the basal brain and communicating hydrocephalus which are the most common radiographic findings in patients with tuberculous meningitis. Infarctions often occur despite anti-tuberculosis treatment, with the basal ganglia and internal capsule being most affected. Indications for surgery include persistent hydrocephalus, in which a ventricular peritoneal shunt is placed to alleviate the increased intracranial pressure. The complications of shunt surgery include shunt infection and shunt blockage requiring one or multiple revisions[17,18].

Tuberculosis is a preventable disease.BCG vaccination has shown some efficacy in the prevention of tuberculous meningitis-associated mortality. It is recommended at birth in resource-poor countries and the development of more effective vaccines is underway. The occurrence of tuberculous meningitis in a child vaccinated with BCG does not call into question the validity of this vaccination: in the absence of routine vaccination, the expected annual number of tuberculous meningitis in children under five in France is eight instead of the two cases observed. Moreover, in the United States, where vaccination is not compulsory, the incidence of tuberculous meningitis in children is forty times higher than in France [12].In India, a recent study that compared TBM in vaccinated and unvaccinated children showed that although BCG vaccination cannot prevent occurrence of TBM, vaccinated children appear to maintain better mentation and ultimately have a better result than unvaccinated children. Investigation of children in contact with tuberculosis infectious index cases and prophylactic therapy should also be used to prevent childhood tuberculosis.

CONCLUSION

More work is needed to understand the total burden of tuberculous meningitis in high-incidence settings, with particular attention to the consequences of permanent disabilities among childhood survivors of this disease. In-depth, history taking should be considered as well as prevention campaigns.

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