

Neuromeningeal Tuberculosis (TNM): Study of 24 Cases Covering Clinical, Paraclinical, Therapeutic and Progressive Aspects

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Abstract

Original Research Article

This study aims to analyse the epidemiological, clinical, paraclinical, therapeutic and evolving aspects of neuromeningeal tuberculosis (TNM) through a retrospective study of 21 patients hospitalized between January 2019 and December 2023 in the infectious diseases department of the Rabat military hospital. The average age at diagnosis was 49.5 years, with a predominance in the age group of 20 to 40 years (47.61%). The average time to diagnosis was 25 days. Initial symptoms were generally general signs (100%), followed by headache (61.90%), vomiting (47.61%) and motor deficits (33.33%). All patients underwent lumbar puncture and brain CT scan. Anti-bacillary treatment and corticosteroid therapy were administered to all participants. The outcome was favorable in 61.90% of cases, fatal in 9.52%, and marked by neurological sequelae in 28.57%.

Keyword: TNM.

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INTRODUCTION

Neuromeningeal tuberculosis (TNM) represents 5 to 15% of extrapulmonary locations and constitutes the most serious form of infection by *Mycobacterium tuberculosis*. It is responsible for death and serious neurological sequelae in more than 50% of cases despite antibacillary treatment [1, 2]. This prognosis is closely linked to the early diagnosis and the quality of treatment [1]. The great clinical polymorphism and the lack of specificity of the radiological and biological signs apart from the identification of Koch's bacillus (BK) by the polymerase chain reaction (PCR) in the cerebrospinal fluid (CSF), makes the diagnosis difficult and are frequently responsible for a delay in treatment.

OBJECTIVE

The main objective of this study was to explore in depth the different dimensions of neuromeningeal tuberculosis in these patients, emphasizing its epidemiological, clinical, paraclinical, therapeutic and progressive profile.

METHODES

This retrospective study included 21 patients hospitalized for neuromeningeal tuberculosis between

January 2019 and December 2023 in the infectious diseases department of the MOHAMED V military hospital in Rabat. The inclusion criteria were defined, with particular attention to clinical, paraclinical and therapeutic aspects.

Study Population

The study reports all files classified as TNM in hospitalization registers. Only files meeting our inclusion criteria were retained. At least two of the following criteria: a suggestive meningeal or febrile and subacute confusional clinical syndrome. The presence of lymphocytic meningitis on lumbar puncture, brain imaging suggestive of tuberculosis lesions, identification of BK by PCR or direct examination and histological confirmation after brain biopsy.

The sources of the various data collected on the operating sheets were clinical observations, letters from general practitioners or specialists, the results of paraclinical explorations and the follow-up noted by the department's doctors on the medical file during external consultations.

RESULTS

The mean age at diagnosis was 49.5 years, with a range from 17 to 82 years. The most represented age

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group was 20 to 40 years old, constituting 47.61% of cases, followed by the age group 40 to 60 years old with 28.57%. Patients under the age of 20 accounted for 4.76%, while those over the age of 60 accounted for 19.04%.

The median diagnostic time between the first revealing sign and the actual diagnosis of the disease (date of the first lumbar puncture) was approximately 25 days. A slight female predominance was observed, with a sex ratio of 0.9. The mode of onset of the disease was subacute in 71.4% of cases and progressive in 28.6% of cases. The telltale functional signs and clinical examination signs are summarized in Figures (1) and (2), as well as in Table 1.

All patients underwent chest radiography. It was interpreted as pathological in 28.5% of patients, presenting lesions suggestive of miliary tuberculosis in 23.8% and sequelae of pulmonary tuberculosis in 4.76%. It was normal in 71.5% of patients.

Testing for Koch bacilli (BK) in sputum was negative in all cases (100%).

Brain computed tomography (CT) was performed in 90% of patients, returning normal in 23.81% and showing lesions suggestive of neuromeningeal tuberculosis in 66.66%. The CT signs were dominated by signs of leptomeningitis and tuberculomas (Figure 3A).

Ten patients underwent brain magnetic resonance imaging (MRI), revealing pathological findings in 70% of them. Tuberculomas were the most common abnormality, observed in 43%. One patient presented with multiple brain abscesses, and two others presented with deep sylvian infarcts (Figure 3B).

Spinal MRI was performed in 3 patients, revealing images of spinal arachnoiditis in 2 cases, while it was normal in 1 case.

All patients initially underwent lumbar puncture, and the results of this are detailed in Table 2.

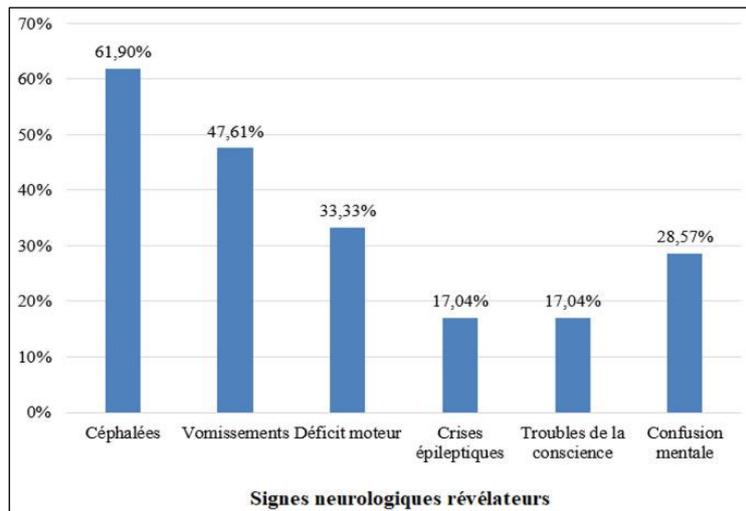


Figure 1

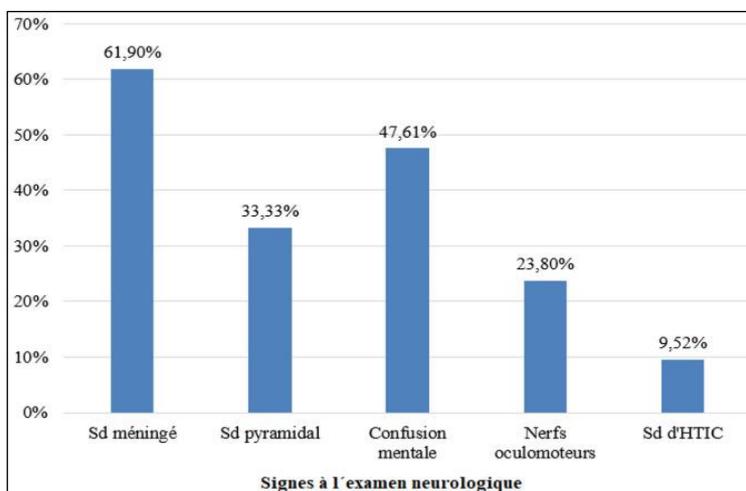


Figure 2

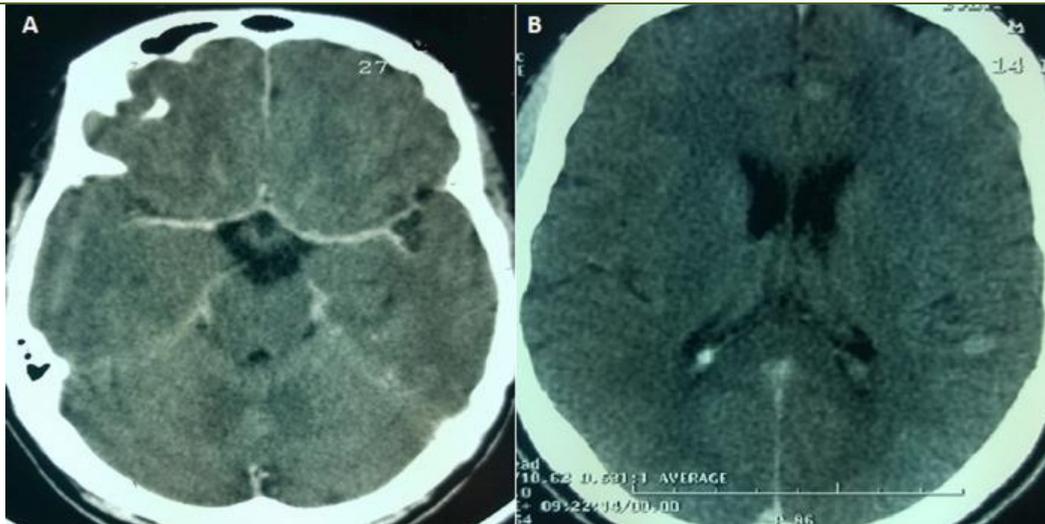


Figure 3: A) axial section of a brain CT showing leptomeningitis; B) axial section of a brain CT showing left hemispherical tuberculomas

Table 1: Results of CSF analysis

Analyse du LCR	Résultats (cas)
Aspect macroscopique	Clair dans 95% (20 cas)
Cytologie	≥ 5 Go/mm ³ : 95 % (20 cas)
Formules	Prédominance lymphocytaire : 90% (18 cas)
Protéïnorrhée	≤ 0,3g/l : 20% (4 cas)
	≥ 1g/l : 70% (14cas)
Glycorachie	≥ 0,5g/l : 14,3% (3cas)
	≤ 0,5 g/l : 85,7% (18 cas)
Recherche de BK	Examen direct : positif dans un cas
	Culture : positif 1 cas
	PCR : positif 24 cas

Anti-tuberculosis treatment was administered early to all patients, with an average start time of 5 days.

- The treatment involved the combination of 4 RHZE anti-bacillary drugs (ERIP K4) in 15 cases and RHZS in 6 cases, for 2 months, followed by 2 RH anti-bacillary drugs for 7 to 9 months.
- Systemic corticosteroid therapy based on intravenous methylprednisolone at the beginning, followed by an oral relay with prednisone, was administered to all patients. The average dose of this corticosteroid therapy was 50 mg/day, and its total duration was 3 months, with a gradual reduction in doses from the 6th week.
- Two patients underwent neurosurgical treatment, including ventriculoperitoneal diversion for hydrocephalus and surgical drainage of a brain abscess.
- The evolution was favorable in 13 patients, or in 61.9% of cases.
- It was fatal in 2 patients, representing 9.52% of cases.
- Six patients retained neurological sequelae, or 28.57% of cases.

DISCUSSION

Tuberculosis is a serious infectious disease, with an incidence of 8 million new cases and one million deaths per year [1]. TNM represents 10 to 30% of intracranial expansive lesions in developing countries [3]. It is rare in industrialized countries, but increasingly common since the human immunodeficiency virus (HIV) pandemic.

2 to 5% of patients with tuberculosis have an associated cerebromeningeal localization, and the frequency rises to 10% in HIV-positive patients [3]. In our series, the mean age at diagnosis in this study was 49.5 years, with variability ranging from 17 to 82 years and a median diagnosis time of 25 days. The distribution

of TNM according to sex is differently appreciated in the literature. For the majority of authors it is predominantly male [5, 4]. TNM mainly affects young people with an average age varying between 27 and 65 years.

In our study, the sex ratio is 0.9. Meningoencephalitis was the most frequent clinical form at the time of diagnosis (57.14%), followed by basilar meningitis (33.33%) and one case of radiculomyelitis and one case of meningoencephalitis. radiculo-myelitis. These results are generally consistent with those of other series in the literature [6-9].

The scan images were represented by meningeal contrast enhancement, tuberculomas,

hydrocephalus, ischemic lesions and abscesses. meningeal contrast enhancement is the most common anomaly (42.9%), exceeding the rates reported in the literature. 22% for Bakhella *et al.*, 23% for Chelaïfa *et al.*, 20.8% for Marx *et al.*, and 20% for Gunawardhana *et al.*, [6, 7, 10, 11]. Tuberculomas occupy second place in our study, i.e. 28.6% of cases. This frequency matches that of the series by Gunawardhana *et al.*, [11].

MRI has been shown to be more sensitive than CT in detecting small tuberculomas, particularly in the brainstem [12], cerebellum and spinal cord [13]. Indeed, MRI identified tuberculoma lesions in 42.8% of cases, while CT revealed tuberculomas only in 28.6% of cases. The culture was positive in only one patient (4.8%), highlighting the complexity of bacteriological confirmation [14, 23].

The treatment of the patients followed the schedule recommended by the Moroccan Ministry of Public Health. Corticosteroid therapy, as an adjuvant treatment for TNM, was administered in accordance with practices established for several decades [22] and the American Thoracic Society [21] and for 7 to 10 months for the Superior Council of Public Hygiene of France. [21]. Standard anti-tuberculosis treatment combines the four major anti-tuberculosis drugs: H, R, E and Z for 2 months, then H and R for 7 months according to the recommendations of the French Society of Pneumology [19]. In our series, PCR was performed in 9 patients, with a positivity of 66.67%, demonstrating its usefulness in early diagnosis. This result is lower than that of Ouhabi [18]. Its sensitivity is around 60%, while the precision is around 90% [17]. More recently, the diagnosis of neuromeningeal tuberculosis (TNM) depends on the contribution of gene amplification techniques. Indeed, PCR allows early and rapid diagnosis within 24 hours.

The British Infection Society recommends, based on several studies and meta-analyses, the initiation of corticosteroid therapy for all patients with tuberculous meningitis at a dose of 0.4 mg/Kg/d, with a reduction in doses. 6 to 8 weeks. The prescribed dosage and taper duration differ for the Royal College of Physicians (RCP) and the National Health Service (NHS). The first recommends a reduction in doses of corticosteroids after 2 to 4 weeks of treatment at full doses, while that the second recommends tapering within 2 to 3 weeks following the start of corticosteroid therapy [24]. In our series, all patients received systemic corticosteroid therapy based on methylprednisolone followed by oral prednisone at a dose of 0.5 to 1 mg/kg/day. Corticosteroid therapy would also find its place alongside anti-tuberculosis antibiotics in certain circumstances. It reduces mortality and neurological after-effects in patients presenting with an average severity (confusion, signs of focalization), other authors demonstrate a benefit in serious cases such as coma.

Finally, corticosteroid therapy would also reduce the volume of hydrocephalus [25]. TNM remains a severe infection with a sometimes poor prognosis (mortality between 15 and 40%) [26]. The mortality in this study being 9.52%. The importance of early diagnosis and rapid treatment is emphasized, and the use of standardized diagnostic criteria could improve patient care.

CONCLUSION

TNM remains a severe, highly polymorphic infection that can be life-threatening. Diagnosis has long relied on the contribution of medical imaging, notably CT and MRI. Its bacteriological confirmation is not always easy and when it exists, it is often late. Only early diagnosis and treatment initiated early enough guarantee a good prognosis. Finally, patient care could be improved by the adoption of a universal diagnostic consensus based on standardized diagnostic criteria.

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