

Tuberculosis Meningo-encephalitis in Casablanca, Morocco

Méningo-encéphalite tuberculeuse à Casablanca, Maroc

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ABSTRACT

Introduction: Neuromeningeal tuberculosis remains the most serious form of Mycobacterium tuberculosis infection. The wide clinical polymorphism and lack of specificity of radiological signs make diagnosis difficult and lead to delays in management.

Aim: To describe the epidemiological profile of confirmed Tuberculous Meningo-encephalitis.

Methods: This is a monocentric, retrospective, descriptive and analytical study of patients followed for confirmed tuberculous Meningo-encephalitis in Infectious diseases department at the Ibn Rochd University Hospital in Casablanca between January 2015 and December 2018. Analytical and multivariate logistic regression analyses were performed to identify predictors of mortality and neurological sequelae.

Results: 90 patients were included, 58% were male with an average age of 38 years. The main risk factors were low socioeconomic status (90%) and recent tuberculosis contact was observed in 13.3%. Onset of symptoms was progressive (92.2%) with average evolution of 25.4 days. Predominant clinical signs were fever (97.4%), headache (70%) and stiff neck (58%). Clinical forms were Meningo-encephalitis (59.9%) and meningitis (36.8%). Predominant Brain radiological sign was leptomeningeal contrast (35%). Cerebrospinal fluid (CSF) abnormalities: White cells mean: 128 white cells/mm³ with lymphocytic predominance (79.1%); Proteinorachia mean: 1.27g/l, Glycorrachia mean: 0.32g/l (88%). Culture on Lowenstein positive in 85% and RT- Polymerase Chain Reaction (PCR) performed in 17.7% and positive in 87.5%. All patients had received standard antituberculosis drugs combining Isoniazid, Rifampicin, Pyrazinamide and Ethambutol. Evolution was favorable with symptom resolution patient rate of 62.5%, 10% mortality, 7.8% neurological sequelae. In multivariate analysis, delayed diagnosis, hydrocephalus and Meningo-encephalitis form were independently associated with mortality or neurological sequelae.

Conclusion: Neuromeningeal tuberculosis in the form of tuberculous meningoencephalitis presents a clinical, biological and radiological polymorphism. Its prognosis depends on the earliness of the diagnosis and treatment.

Key Words: Tuberculous meningitis, Tuberculous Meningo-encephalitis, Mycobacterium tuberculosis.

RÉSUMÉ

Introduction: La tuberculose neuroméningée reste la forme la plus grave d'infection à Mycobacterium tuberculosis. Le large polymorphisme clinique et le manque de spécificité des signes radiologiques rendent le diagnostic difficile et entraînent des retards dans la prise en charge.

Objectif : Décrire le profil épidémiologique de la méningo-encéphalite tuberculeuse confirmée.

Méthodes : Il s'agit d'une étude monocentrique, rétrospective, descriptive et analytique portant sur des patients suivis pour une méningo-encéphalite tuberculeuse confirmée au service des maladies infectieuses du CHU Ibn Rochd de Casablanca entre janvier 2015 et décembre 2018. Des études analytiques et de régression logistique multivariées ont été réalisées afin d'identifier les facteurs prédictifs de mortalité et de séquelles neurologiques.

Résultats: 90 patients ont été inclus, dont 58 % étaient des hommes, avec un âge moyen de 38 ans. Les principaux facteurs de risque étaient un statut socio-économique faible (90 %) et un contact récent avec la tuberculose chez 13,3 % des patients. L'apparition des symptômes était progressive (92,2 %) avec une évolution moyenne de 25,4 jours. Les signes cliniques prédominants étaient la fièvre (97,4 %), les maux de tête (70 %) et la raideur de la nuque (58 %). Les formes cliniques étaient la méningo-encéphalite (59,9 %) et la méningite (36,8 %). Le signe radiologique cérébral prédominant était le contraste leptoméningé (35 %). Anomalies du liquide céphalo-rachidien (LCR) : moyenne des globules blancs : 128 globules blancs/mm³ avec prédominance lymphocytaire (79,1 %) ; moyenne de la protéinorachie : 1,27 g/l, moyenne de la glycorrachie : 0,32 g/l (88 %). La Culture sur milieu de Lowenstein était positive dans 85 % des cas et la réaction en chaîne par polymérase (PCR) réalisée dans 17,7 % des cas, était positive dans 87,5 % des cas. Tous les patients avaient reçu des médicaments antituberculeux standard associant l'isoniazide, la rifampicine, le pyrazinamide et l'éthambutol. L'évolution était favorable avec un taux de résolution des symptômes de 62,5 %. Le taux de mortalité était de 10 % et le taux de séquelles neurologiques était de 7,8 %. Dans l'analyse multivariée, le retard de diagnostic, l'hydrocéphalie et la forme méningo-encéphalite étaient indépendamment associés à la mortalité ou aux séquelles neurologiques.

Conclusion: La tuberculose neuroméningée en particulier la forme de méningo-encéphalite tuberculeuse présente un polymorphisme clinique, biologique et radiologique. Son pronostic dépend de la précocité du diagnostic et du traitement.

Mots clés: Méningite tuberculeuse, méningo-encéphalite tuberculeuse, Mycobacterium tuberculosis.

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INTRODUCTION

Neuromeningeal tuberculosis remains a public health problem (1). It accounts for 5-15% of extra-pulmonary tuberculosis and is considered the most serious form of *Mycobacterium tuberculosis* infection (2). Despite anti-tuberculosis treatment, death or severe neurological sequelae occur in over 50% of cases (3). In 2022, Morocco reported over 30,000 new TB cases annually, with 17% being extrapulmonary forms and global TB incidence was 133 per 100.000 population with 8.4% of HIV-positive patients. The extrapulmonary tuberculosis incidence was 17% and MDR/RR-TB incidence was 5.2 per 100.000 population (4). The great clinical polymorphism and lack of specificity of radiological signs, as well as the difficulty of identifying the bacillus biologically, make diagnosis difficult and are frequently responsible for delays in treatment.

METHODS

This is a monocentric, retrospective and descriptive study of patients followed for confirmed tuberculous Meningitis and Meningo-encephalitis in Infectious diseases department at Ibn Rochd University Hospital Center in Casablanca, Morocco from January 2015 to December 2018. Descriptive and analytical studies were carried out using Epi-info and Jamovi. Multivariate logistic regression analyses were performed to determine factors associated with mortality and neurological sequelae. The risk of error is set at 5%.

RESULTS

90 patients were included. Prevalence was 0.45%. 58% were male with sex ratio of 1.37. Average age was 38 years with age limits 19 to 79. The main risk factors were low socio-economic status (90%), recent tuberculosis contact (13.3%) and HIV infection (7.8%). The Onset of symptoms was progressive (92.2%) with mean time to diagnosis of 25.4 days. Clinical presentations: fever (97.4%), headache (70%), stiff neck (58%), unconsciousness (15.30%), vomiting (14.30%), seizures (12.40%), motor deficit (10%), cranial palsy involvement (3.30%).

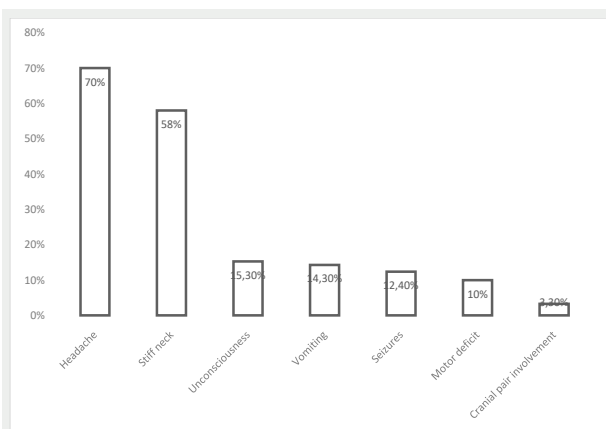


Figure 1. Neurological signs in our series

Clinical forms: Meningo-encephalitis (59.9%), Meningitis (36.8%) and Radiculomyelitis (3.3%). Lumbar puncture

was realized in 100% of cases. CSF abnormalities: clear appearance (78.8%), white cells mean was 128 white cells, Proteinorachia mean was 1.27g/l and Glycorrhachia mean was 0.32g/l. Ziehl Nielsen direct examination was positive in 0.9%, culture of *Mycobacterium tuberculosis* on Löwenstein Jensen medium was positive in 85% and 100% of cases were drug-susceptible TB. BK PCR was performed in 17.7% and were positive in 87.5% (Table 1).

Tableau 1. Cerebrospinal Fluid analysis results in our serie

Cerebrospinal fluid Analysis	Results	Percentage
Cytology (mm3)		
White cells < 500	76 cases	84,4
White cells >500	14 cases	15,6
Lymphocytes formula	71 cases	78,8
Neutrophils formula	17 cases	18,9
Mixed formula	2 cases	2,3
Mycobacterium tuberculosis search	Ziehl- Nielsen coloration positive: 1 case	1,1
	Culture on Löwenstein Jensen Medium positive : 76 cases	84.4
	DS-TB	100
	BK PCR positive : 14 cases (on 16 cases)	87,5
Proteinorachia	Mean : 1.27 g/l	
	≥1g/l : 68 cases	75.6
	] 0,3 - 1 [: 15 cases	16,6
	≤ 0,3 g/l : 7 cases	7,8
Glycorrhachia	Mean : 0.32 g/l	
	≤ 0,4 g/l : 51 cases	57
	> 0,4 g/l : 39 cases	43

Dominant Cerebral imaging abnormalities were Leptomeningeal contrast (35%), hydrocephalus (26%) and tuberculoma (16%). Chest X-rays showed abnormalities in 27.2% of cases, with sequellar lesions (11%) and tubercular miliary (10%). Fundus examination revealed 4 cases of papilledema and only 1 case of Bouchut's nodule. The blood count showed lymphopenia in 12.22% and neutrophils hyperleukocytosis in 49%. Sedimentation rate was elevated in 81%, CRP positive in 80%, and 63.9% of patients had hyponatremia. 100% had received anti-tuberculosis drugs combining Isoniazid, Rifampicin, Pyrazinamide and Ethambutol for two months, followed by isoniazid and rifampicin for seven months in 52 patients and 9 months in 48 patients. 100% received systemic corticosteroid therapy based on methylprednisolone, followed by oral prednisone. Surgery was performed in 3% of patients, with ventriculoperitoneal shunting in 10% and external shunting in 3%. The outcomes: 62.5% were cured, death in 10%, complications in 17.8% and persistent neurological sequelae in 7.8%. In multivariate analysis, delayed diagnosis over 30 days (OR: 2.9; CI: 1.2–7.0; $p=0.014$), presence of hydrocephalus (OR: 3.4; CI: 1.4–8.1; $p=0.006$), and Meningo-encephalitis presentation compared to meningitis (OR: 3.1; CI: 1.1–8.5; $p=0.028$) were independently associated with mortality or persistent neurological sequelae. HIV-positive status showed a non-significant trend towards poorer outcomes (OR: 2.7; CI: 0.8–9.2; $p=0.10$).

DISCUSSION

In our serie, confirmed tuberculous Meningitis and Meningo-encephalitis represented 0.45% of the reasons for hospitalization, in line with studies carried out in Morocco and Mali (5,6). Similar results on age and sex were reported in three studies carried in China, Morocco and France (6-8). Same risk factors were reported in a study carried out in the same department as for the mean time to treatment (7). The main clinical presentations were in line with Moroccan studies (6,7), contrary in Algeria and Vietnam where more atypical neurological presentations were reported. These divergences may reflect differences in healthcare-seeking behavior, prevalence of drug-resistant TB strains, and the burden of HIV co-infection. In Vietnam, for instance, a higher HIV prevalence in TB meningitis cases is known to modify clinical and radiological profiles and to increase disease severity (9,10). CSF abnormalities were typical, with lymphocytic predominance and elevated proteinorachia, similar to results of the study carried in the same department (7). Brain imaging abnormalities were similar to those reported in several studies (12-14) but higher than those reported in Tunisia (11). This could be due to later disease presentation in our patients or differences in imaging timing. Chest X-rays abnormalities were similar to results recorded in France, confirming that concomitant pulmonary involvement remains frequent. (8). The blood cells count results were in line with the literature and other studies (6,8). The results of Sedimentation rate, CRP and Hydro-electrolytic analysis were in line with the literature (12,15-17). Standard anti-tuberculosis treatment is recommended by the WHO (18). Studies has shown that adjuvant corticosteroid therapy improves survival rather than preventing serious sequelae, and can reduce the volume of hydrocephalus (19,20). Surgery results were similar with reported in other studies (12,21,22). Regarding outcomes, our mortality rate (10%) was lower than those reported in Vietnamese and Algerian studies (9,10), but comparable to Moroccan and French cohorts (7,8,23). Several factors as early empirical treatment initiation, systematic use of adjunctive corticosteroids, and better supportive care may explain this. Conversely, differences in TB drug resistance profiles, diagnostic delays, and comorbidity burden (particularly HIV) in Vietnam and Algeria could contribute to poorer prognoses there.

Our multivariate analysis confirmed that delayed diagnosis, hydrocephalus, and meningo-encephalitis presentation were independently associated with unfavorable outcomes, consistent with the literature (9,24-26).

Limitations:

The sample size, although relatively large for a rare condition, may still limit the generalizability of our findings.

The lack of long-term standardized follow-up limits conclusions regarding delayed neurological complications beyond the study period.

CONCLUSION

Neuromeningeal tuberculosis is a pathology with a heterogeneous clinical and radiological presentation. It is a diagnostic and therapeutic emergency, and its prognosis is closely linked to early diagnosis, rapid therapeutic management, close monitoring and regular follow-up of patients.

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