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Tuberculous meningitis in adults: MRI contribution to the diagnosis in 29 patients

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Summary
Objectives: Tuberculous meningitis (TBM) is a life-threatening disease and is difficult to diagnose. We aim to promote the role of magnetic resonance imaging (MRI) in TBM diagnosis and survey.
Design and methods: This was a retrospective study undertaken between 1996 and 2003 in which we reviewed all cases of TBM that had undergone cerebral computed tomography (CT) and MRI performed with and without contrast.
Results: We reviewed 29 patients; all had had subacute lymphocytic meningitis. Diagnosis was definite in only 11 cases and presumptive in 18 cases. MRI was performed showing one or more abnormalities in 26 cases. The use of MRI allowed the detection of CNS lesions in both brain and spine.
Conclusion: Cerebrospinal MRI performed when TBM is suspected aids in its diagnosis and is also a useful means of monitoring the course of the disease under treatment.

Introduction

Tuberculosis is still a serious international health problem, with about 8 million new cases per year and 3 million deaths.[1] Extra-pulmonary tuberculosis constitutes 15% of all tuberculous locations and includes tuberculous meningitis (TBM), which occurs in 4% of all cases.[2] Diagnosis is difficult and based on clinical and biological features, and disease progression.[3] A good prognosis depends on prompt diagnosis and treatment; hence we emphasize herein the importance of radiological findings.

Patients and methods

In this retrospective study, we reviewed all cases of patients diagnosed and treated at the department of infectious diseases in Tunis, Tunisia, between 1996 and 2003 who had undergone both injected magnetic resonance imaging (MRI) and computed tomography (CT).

CT was performed with and without contrast injection, was only cerebral, and was done in the axial plane. For MRI, a 1 Tesla-strength magnetic field was used with axial spine echo T1-weighted sequence, T2-weighted sequence, and T2 inversion—recuperation. Following gadolinium intravenous (iv) injection, a multi-planar study was performed in the echo spine T1-weighted sequence of brain and spine.

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The diagnosis of TBM was made on the basis of one of the following criteria: (i) a clinical course of subacute meningitis with low CSF glucose level and favorable response to specific anti-tuberculous treatment; (ii) a positive CSF or sputum smear for acid-fast bacilli and/or positive CSF or sputum culture for *Mycobacterium tuberculosis*; (iii) a lymphocytic subacute meningitis with radiological findings supporting TBM on cerebral MRI and/or cerebral CT.

The stage of TBM was determined by the method of Gordon and Parson:[4] at stage 1 the patient is fully conscious, at stage 2 the patient is drowsy or has focal neurological signs, and at stage 3 the patient is comatose or nearly so.

Patients were monitored with monthly clinical examination, and CSF examination was undertaken at discharge from the hospital, at one month and three months following anti-tuberculous treatment, and finally when the decision was made to stop treatment if the clinical state was satisfactory. MRI was also performed at 12 months of treatment and/or when a complication was noted.

Results

Patients

Twenty-nine patients (10 men and 19 women, age range 16—74 years (mean 42 years)) with TBM and both radiological examinations were identified. Only eleven patients were diagnosed by the second criterion (a positive CSF or sputum smear for acid-fast bacilli and/or positive CSF or sputum culture for *Mycobacterium tuberculosis*). Culture was positive in seven cases.

Clinical data

At presentation, six patients were classified as being at Gordon and Parson stage 1, and 23 at stage 2.[4] Cranial nerve palsies were noted before therapy in four cases; other focal neurological signs were noted in eight cases. Obtundation (clouded mental state, Glasgow coma scale over 12), drowsiness, or agitation, were noted in 15 cases. Neurological deterioration was noted in seven cases under treatment; all of them had experienced a treatment delay.

Treatment delay was noted in 23 cases (the stage 2 patients). Seven of them had initial neurological deterioration, three of them died early on in the treatment course at the 7th, 24th, and 47th day, and two had definite sequelae.

There was one or more tuberculous location in 19 cases: seven spinal, nine pulmonary, three pleural, three retinal, three ganglionic, one cutaneous, and one articular.

The anti-tuberculous regimen was isoniazid 5 mg/kg/day, rifampin 10 mg/kg/day, ethambutol 20 mg/kg/day, and pyrazinamide 30 mg/kg/day for two months. This was followed

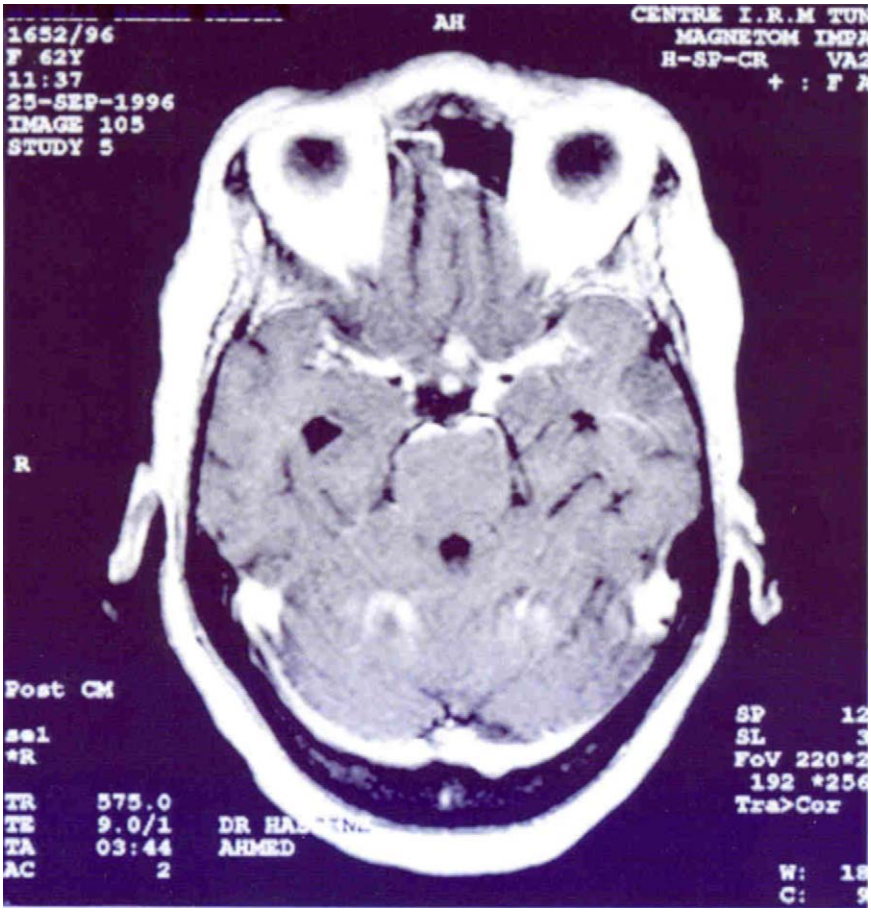

Figure 1 Axial T1-weighted MR image after administration of iv gadolinium showing basilar meningeal enhancement with tuberculomas of the olfactory bands and two cerebellar lesions.

by isoniazid—rifampin (INH—RMP) for 10 to 22 months. Corticosteroids (prednisolone) were used with stage 2 patients, at doses of 0.5—1 mg/kg/day with progressively decreasing doses for 2—3 months.

Laboratory data

The CSF was clear or xanthochromic in all cases with the total WBC count ranging from 0 to 720 $\times$ 10^6/L with a lymphocytic predominance in all cases. The CSF glucose level was low in all cases, and CSF protein level was elevated in most cases with a range of 0.17—8.28 g/L at presentation.

Radiological data

CT was normal in 19 cases, showed tuberculomas in two cases, hydrocephalus in two cases, arachnoiditis in one case, infarction in three cases, edema in one case, and an abscess in one case. Tuberculomas, arachnoiditis, and the abscess were enhanced after contrast injection.

MRI of the CNS was normal in three cases only; it showed one or more tuberculomas in 19 cases, hydrocephalus in six cases, infarction in six cases, arachnoiditis in 14 cases, external pachymeningitis in three cases, myelitis in two cases, and spondylodiscitis in five cases. Tuberculomas, arachnoiditis, external pachymeningitis, myelitis, and spondylodiscitis had a low signal in T1-weighted images, a high signal in T2, and were enhanced after gadolinium injection.

Clinical outcome

Stage 1 patients had a good outcome without any complications. Stage 2 patients improved after an initial neurological worsening in seven cases, two cases had neurological sequelae, and three patients died.

Discussion

TBM remains a life-threatening disease with the prognosis dependent on initial presentation and on treatment delay.[4,5] This is why we emphasize herein the importance of early diagnosis.

Tunisia still has an average level of tuberculosis with an incidence of 5.27/100 000 population (figure from the third trimester of 2002). AIDS is an emerging disease in our country and is a risk factor for TBM by depressing cellular immunity. However, despite the reported AIDS—TBM association, none of our patients was infected with HIV.[6—8] This can be explained by the endemicity of tuberculosis in our country.

Clinical presentation was classic: subacute course, cranial nerve palsies, hemiparesis, and impaired consciousness.[4,9] Twenty-three patients were at stage 2, indicating a slow development of symptoms, as also noted by other authors.[4,7]

Early diagnosis is important to avoid morbidity and mortality.[8,10] When a definite diagnosis relies on a CSF positive

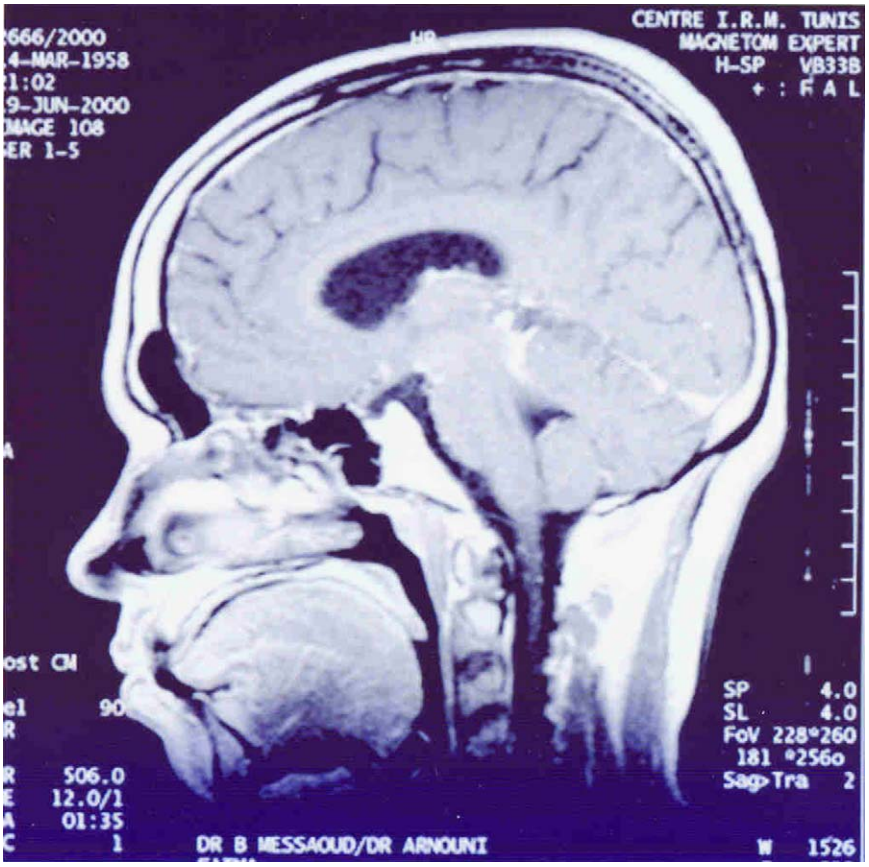

Figure 2 Sagittal T1-weighted image after administration of iv gadolinium showing peripheral and basilar meningeal enhancement with ventricular dilatation.

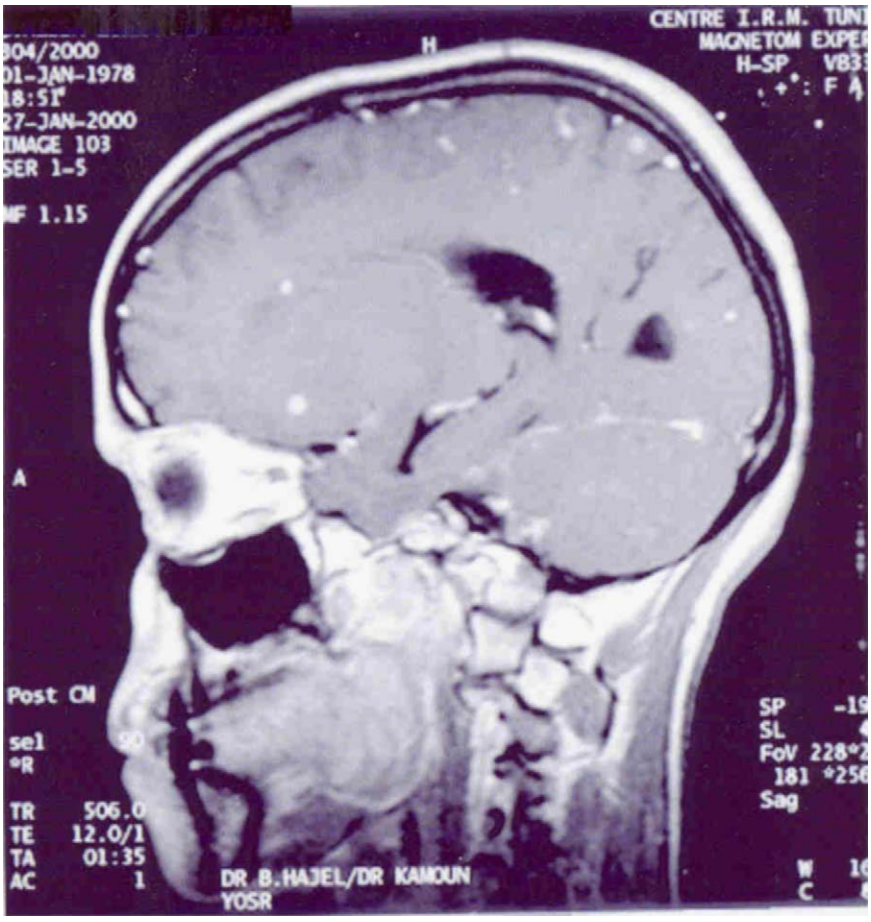

Figure 3 Sagittal T1-weighted MR image after administration of iv gadolinium showing multiple hemispheric tuberculomas with ventricular dilatation and meningeal enhancement.

culture for *Mycobacterium tuberculosis* (20—50%) or on the presence of acid-fast bacilli on CSF smear (12.5—45%), diagnosis is frequently presumptive.[3,4,9] To improve on these, and make a definite diagnosis, many methods can be used. These require specialist laboratories, incurring high costs, prohibitive to developing countries.

Dot Blot and ELISA can detect antibodies in 25—44% of patients when single antigens are used but can reach 90% of cases if a panel of antigens is used with a sensitivity of 77.27%.[1] PCR is also a promising technique that can allow a rapid diagnosis with a good sensitivity 80—91%; but its use is limited by its high expense and absence of a diagnostic test serving as an adequate 'gold standard' to evaluate it.[3] Radiological findings are not specific but when associated with clinical and biological features, they are suggestive and can be a good method of diagnosis assessment.[5]

At time of presentation, 65% of our patients had a normal CT. In other published studies, sensitivity of CT has been higher (Table 1). This can be explained by the time at which the CT was performed; early on in the course of the disease abnormalities are sub-centimetric and cannot be visualized by CT.

MRI has a better sensitivity,[11] and can show the small abnormalities in both brain and spine.[6,12] Meningeal enhancement is better visualized because of the signal contrast between the inflamed meninges and the CSF, as well as infarction.[10,11] In our study, MRI was abnormal in 89.6% of patients. It showed sub-clinical lesions in 15 cases: five cerebral and 10 spinal locations (Figures 1—3).

When a patient presents with a suspicion of TBM, MRI can be used to strengthen the diagnosis and to define all initial abnormalities of the CNS (brain and spine). MRI is also useful later on to monitor the development of abnormalities (Figures 4 and 5).[10]

When TBM is suspected, treatment should be started immediately, without waiting for a definite diagnosis.[7] In our study, treatment delay was associated with death in three cases and with neurological worsening in seven cases, two of whom had definite sequelae. Treatment duration is variable, ranging from 9 to 24 months.[2,5,13] We consider 12 months to be the minimum treatment duration for TBM due to

Table 1 CT features in other studies

	Verdon (48 cases)[6] *n*	Bossi (38 cases)[8] *N*
Normal CT	5	19
Hydrocephalus	30	10
Tuberculoma	2	12
Infarction	32	1
Arachnoiditis	28	5

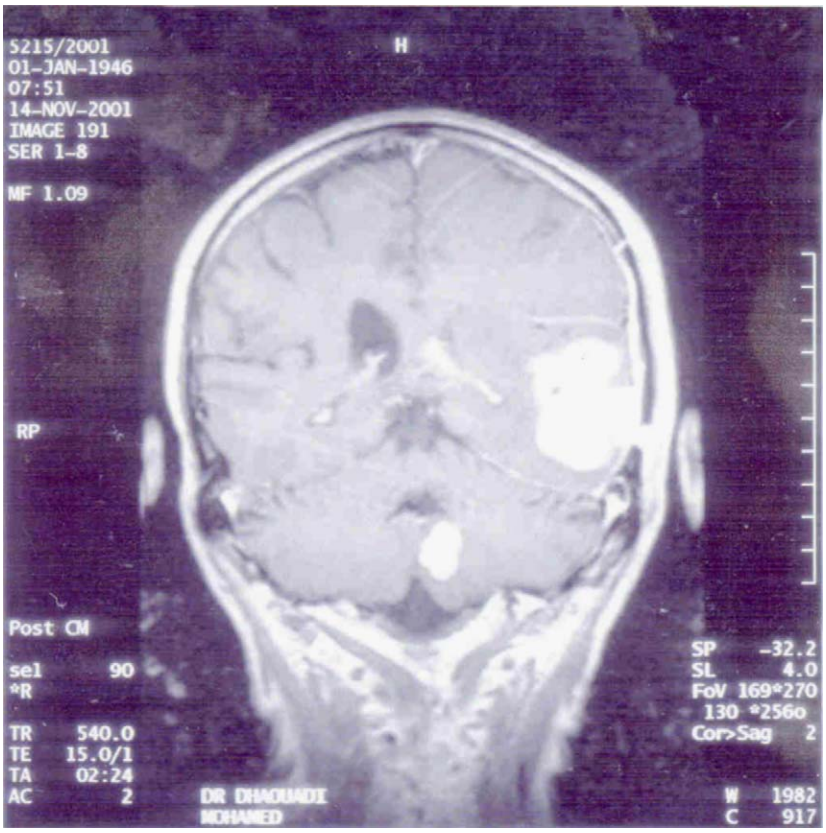

Figure 4 Coronal T1-weighted MR image after administration of iv gadolinium showing an abscess and a tuberculoma.

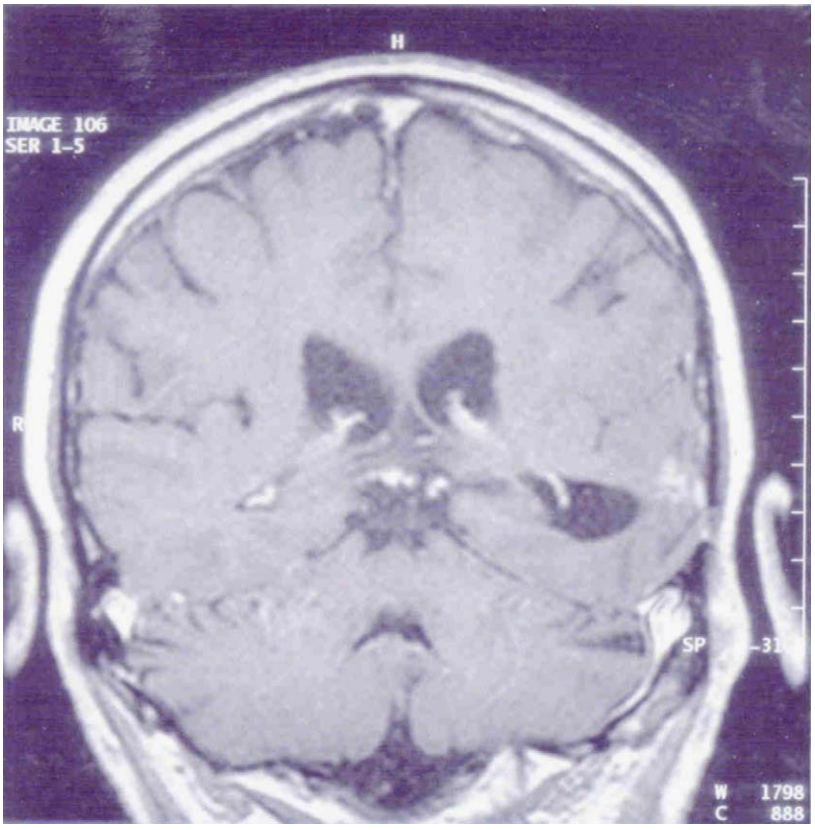

Figure 5 Coronal T1-weighted MR image after administration of iv gadolinium showing the radiological lesions disappearing under treatment.

the poor diffusion of anti-tuberculous drugs into the CSF and in tuberculomas. Corticosteroids must be used for at least six weeks, mainly in patients at Gordon and Parson stage 2, to prevent complications, to reduce duration of symptoms and frequency of sequelae, and to improve survival.[13]

Conclusion

TBM is a severe disease with high morbidity and mortality. Early diagnosis and treatment can improve patients' outcome. MRI of the CNS is a good method to strengthen diagnosis and to monitor disease progression, especially in developing countries where definite diagnosis by laboratory testing is limited. We consider that anti-tuberculous treatment should be continued for at least 12 months.

Conflict of interest: No conflict of interest to declare.

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