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Tuberculous meningitis-related ischemic stroke: A retrospective study from a tertiary care hospital

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ABSTRACT

Background: Patients with tuberculous meningitis (TBM) are at high risk of ischemic stroke, and stroke is a poor prognosticator of TBM. However, reports regarding the predictors of stroke in TBM patients are scanty. The aim of this study was to investigate the clinical characteristics and predictors of tuberculous meningitis-related ischemic stroke (TBMRIS).

Methods: This retrospective study was conducted among TBM patients without traditional vascular risk factors from a tertiary care hospital between January 2017 and November 2022. Patients were divided into TBMRIS group and TBM-only group according to presence of stroke. Clinical, laboratory and radiological variables were compared between the two groups. Predictors of stroke were identified using binary logistic regression analysis.

Results: A total of 176 TBM patients were included in the study. Forty-nine patients with stroke were classified as TBMRIS group and 127 patients without stroke were classified as TBM-only group. In TBMRIS group, 41 (83.7 %) patients experienced stroke within 3 months after the onset of meningitis symptoms and 10 (20.4 %) patients presented silent stroke. Stroke occurred in basal ganglia in 57.1 % of patients. About 73.5 % of patients showed multiple stroke lesions and 38.8 % of patients had stroke involving multiple vascular territories. There were significant differences in focal neurological deficit, stage of meningitis, short-term outcome, serum sodium, cerebrospinal fluid (CSF) white cell count, CSF adenosine deaminase (ADA), CSF protein, leptomeningeal enhancement, tuberculoma between TBMRIS group and TBM-only group. Binary logistic regression analysis revealed that focal neurological deficit, CSF white cell count and leptomeningeal enhancement were the independent risk factors for stroke, and tuberculoma was negatively correlated with stroke.

Conclusion: Most of TBMRIS develop within 3 months after the onset of meningitis symptoms and basal ganglia is the most frequent site. Multiple stroke lesions and involvement of multiple vascular territories are commonly observed. Focal neurological deficit, CSF white cell count and leptomeningeal enhancement are the predictors of stroke in patients with TBM.

1. Introduction

Tuberculous meningitis (TBM) is accounted as the most serious manifestation of tuberculosis (TB), leading to substantial mortality and severe neurologic deficits in children and adults despite availability of progressive chemotherapy [1]. The severe complications following TBM include hydrocephalus, tuberculoma and ischemic stroke [2,3], and the incidence of ischemic stroke in all TBM cases is 13–57 % [2]. TBM ever became an important etiology of stroke in young people in some developing countries, and presence of stroke was considered to be a significant predictor of poor prognosis in TBM patients [4]. Clinicians face great challenges in the diagnosis and management of TBM and prevention of subsequent stroke.

The association between TBM and ischemic stroke has long been studied. Previous studies have indicated that TBM could directly lead to ischemic stroke through a variety of known and unknown mechanisms, namely tuberculous meningitis-related ischemic stroke (TBMRIS). However, there are few studies that successfully eliminate the impact of traditional cerebrovascular risk factors (hypertension, diabetes mellitus, smoking and atrial fibrillation, etc) which are the main causes of atherosclerotic infarction and cardiogenic embolism. The pathophysiology of stroke may differ among patients with and without these risk

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factors. Therefore, it is necessary to fully investigate these strokes occurring in TBM patients without traditional vascular risk factors. Moreover, some studies were based on cranial computed tomography (CT) rather than magnetic resonance imaging (MRI). Compared to CT, MRI has a much higher value in discriminating infectious diseases in central nervous system and ischemic cerebrovascular diseases.

We performed the present study which was based on participants without any conventional risk factors and cranial MRI to better elucidate the clinical characteristics and independent predictors of TBMRIS by reviewing a retrospectively collected database.

2. Methods

2.1. Study population and grouping

Ethical approval was granted by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University. Patients admitted with TBM to the tuberculosis wards of the Fourth People's Hospital of Nanning City, a tertiary referral centre for patients with infectious diseases, between January 2017 and November 2022 were recruited in the study. Patients who met the following criteria were included: (1) Age ≥ 18 years; (2) Diagnosed as TBM. Exclusion criteria included: (1) Presence of traditional vascular risk factors including hypertension, diabetes mellitus, smoking, atrial fibrillation, hyperlipidemia, coronary artery disease, and history of ischemic and hemorrhagic stroke; (2) Conditions which were prone to thromboembolic stroke, such as recent surgical history, patent foramen ovale, rheumatic valvular heart disease and malignancy; (3) Concomitant diagnosis of other intracranial infectious diseases, such as cryptococcal meningitis and toxoplasma encephalopathy; (4) Intracranial hemorrhage diseases; (5) Primary hematological diseases; (6) Severe cardiac, hepatic, renal dysfunction; (7) Unavailability of cerebrospinal fluid (CSF) and brain MRI data; and (8) Presence of chronic stroke lesions on MRI.

The diagnosis of TBM was based on the standardised clinical case definition by Marais et al [5]. Definite TBM was defined as suggestive clinical presentation plus one or more of the following: positive acid-fast bacilli smear in the CSF; positive mycobacterium tuberculosis (MTB) culture from CSF; or a CSF positive commercial nucleic acid amplification test (NAAT). Probable TBM was defined as suggestive clinical presentation plus a total diagnostic score ≥12 (At least 2 points either come from CSF or cerebral imaging criteria) plus exclusion of alternative diagnoses. Possible TBM was defined as suggestive clinical presentation plus a total diagnostic score of 6–11 plus exclusion of alternative diagnoses.

Considering the difficulty of accurate diagnosis of TBMRIS, in this study TBMRIS was defined as ischemic stroke occuring in TBM patients without any traditional vascular risk factors by referring to the conception of cancer-related ischemic stroke [6,7]. The enrolled TBM patients were divided into two groups, TBMRIS group and TBM-only group according to presence of stroke (Fig. 1).

2.2. Clinical management and data acquisition

General demographics and clinical characteristics such as age, gender, diagnosis of pulmonary TB, time between meningitis onset and stroke diagnosis, clinical symptoms and signs on admission including headache, vomiting, fever, neck stiffness, seizure, focal neurological deficit, altered consciousness, cranial nerve palsy were collected. According to the modified British Medical Research Council clinical criteria, TBM severity was classified into three stages: Stage I, alert and oriented without focal neurological deficit; Stage II, Glasgow Coma Scale (GCS) 10–14 with or without focal neurological deficit or GCS 15 with focal neurological deficit; Stage III, GCS less than 10 with or without focal neurological deficit [8]. Complete blood cell count, coagulation indices, human immunodeficiency virus (HIV) serology were documented. CSF findings including white cell count, lymphocyte percentage, adenosine deaminase (ADA), protein, glucose, chloride, acid-fast bacilli smear, pathogenic culture, NAAT were obtained.

The brain MRI films of the patients were co-reviewed by an experienced neuroradiologist and a neurologist. Abnormal radiological findings including leptomeningeal enhancement, hydrocephalus, tuberculoma, ischemic stroke (location and vascular distribution) and angiographic abnormalities were identified in consensus (Fig. 2). The presence of more than one stroke lesion was considered as multiple. According to vascular distribution, affected vascular territory were classified into single territory which was defined as unilateral anterior circulation or posterior circulation, and multiple territories which was defined as bilateral anterior circulations, or anterior and posterior circulations, simultaneously. Referring to previous studies [2,9], acute ischemic stroke was diagnosed when MRI films showed diffusion weighted imaging (DWI) hyperintensity and corresponding hypointensity on apparent diffusion coefficient (ADC), no matter whether or not

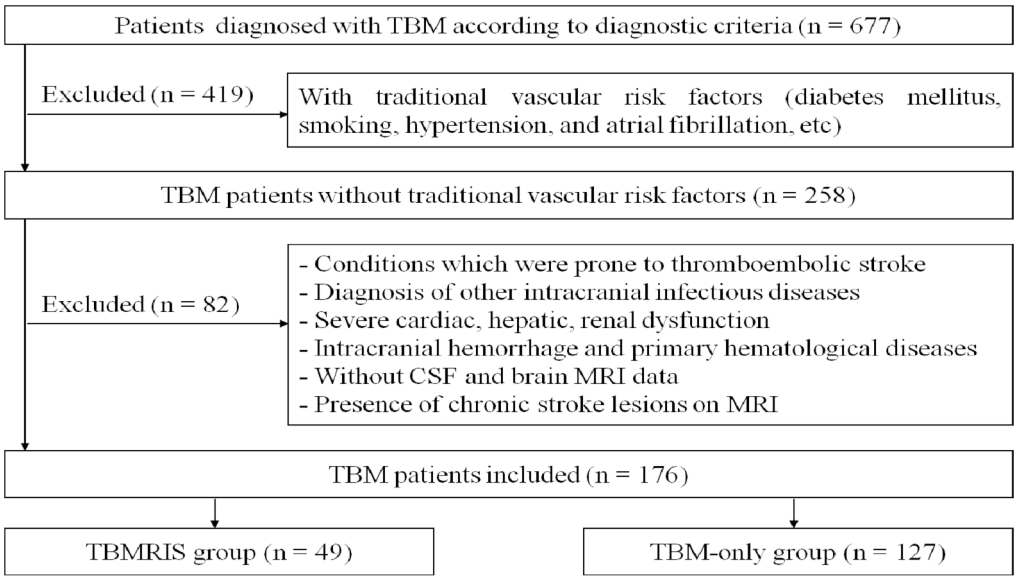

Fig. 1. Patient enrollment flowchart. TBM, tuberculous meningitis; TBMRIS, tuberculous meningitis-related ischemic stroke; CSF, cerebrospinal fluid; MRI, magnetic resonance imaging.

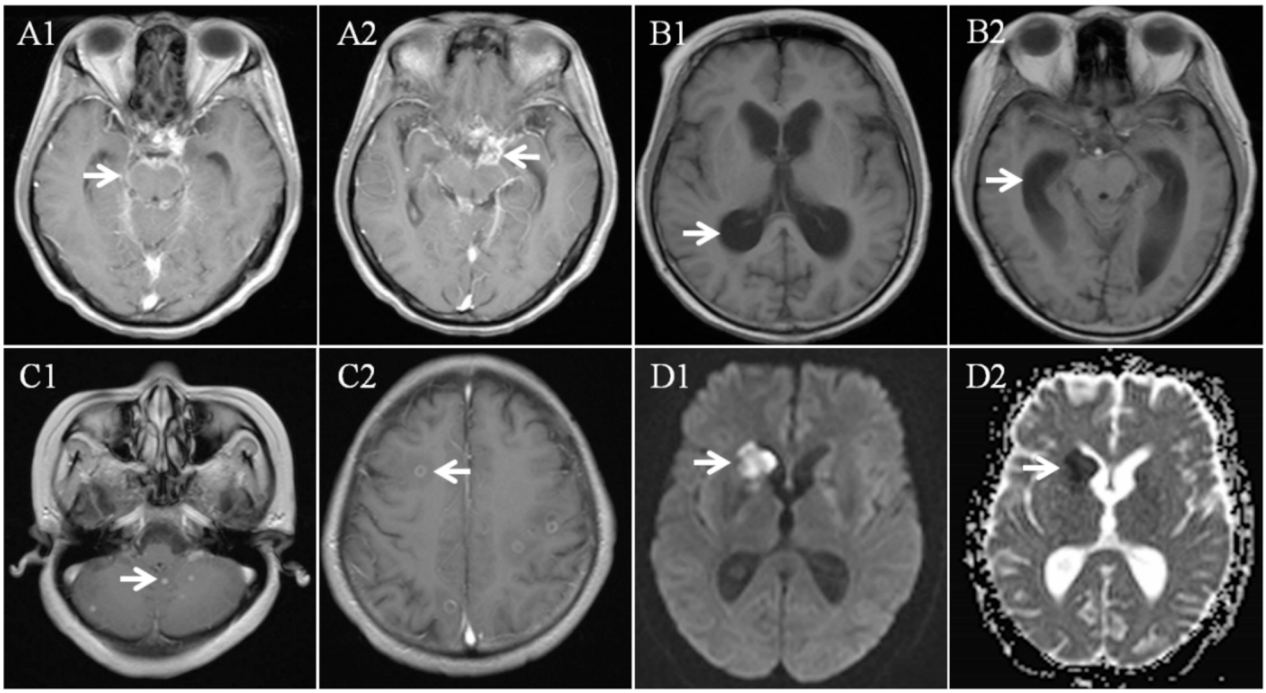

Fig. 2. Abnormal radiological findings in patients with TBM. (A1-A2) Basal meningeal enhancement (arrow); (B1-B2) Hydrocephalus (arrow); (C1-C2) Multiple tuberculomas (arrow); (D1-D2) Acute ischemic stroke in basal ganglia (arrow).

the patient had obvious stroke symptoms.

According to the recommendations of the World Health Organization, all patients in both TBMRIS group and TBM-only group received standard antituberculosis treatment. Patients in TBMRIS group were treated with aspirin after diagnosis of stroke according to the guideline for acute ischemic stroke from the American Heart/Stroke Association [10]. Neurological disabilities were measured at discharge. Short-term outcome was evaluated with a modified Rankin Scale (mRS), and classified as good (mRS score 0–2) or poor outcome (mRS score 3–6) [11].

2.3. Statistical analysis

All statistical analyses were performed with IBM SPSS Statistics version 26.0. Continuous variables were presented as mean ± standard deviation (SD) and categorical variables were presented as frequency and percentage. Student's *t*-test (or Mann-Whitney *U* test) was used to compare continuous variables, while Chi-square test (or Fisher exact test) was for categorical variables. Univariate analysis was performed between TBMRIS group and TBM-only group. Two-tailed p value < 0.05 was considered to be statistically significant. Binary logistic regression analysis was undertaken to assess the predictors of stroke in TBM patients.

3. Results

3.1. Clinical, laboratory and radiological variables between groups

Finally, 176 TBM patients fulfilled our inclusion criteria and were included in the study. Among them, 124 (70.5 %) were males and 52 (29.5 %) were females, with an average age of 39.1 ± 14.5 years. Seventy-seven (43.8 %), 63 (35.8 %) and 36 (20.4 %) patients were diagnosed with definite, probable and possible TBM, respectively. There was no difference in the incidence of stroke among these three categories of TBM. Forty-nine patients suffered from ischemic stroke and were classified as TBMRIS group, while 127 patients without stroke were classified as TBM-only group. There were no significant differences in age, gender, pulmonary TB and HIV infection between groups. Compared with TBM-only group, TBMRIS group had a higher frequency of focal neurological deficit, while other clinical symptoms and signs such as fever, headache, vomiting, neck stiffness were not found to be significantly different between groups (Table 1). The differences in stage of meningitis between groups was remarkable. Fifteen (30.6 %) patients in TBMRIS group and 21 (16.5 %) patients in TBM-only group had a poor short-term outcome, and the difference was significant ($p = 0.038$).

TBMRIS group had a lower level of serum sodium than TBM-only group (130.7 ± 5.3 vs. 133.0 ± 6.0, $p = 0.018$), while no significant differences in leukocytes, hemoglobin, platelet counts, FIB, INR, PT, APTT, albumin, D-dimer were observed. CSF examination showed that TBMRIS group had more white cell counts (207.1 ± 202.9 vs. 143.2 ± 175.8, $p = 0.006$), higher level of ADA and protein (19.4 ± 18.3 vs. 15.7 ± 15.2, $p = 0.017$, 2062.0 ± 1537.4 vs. 1603.1 ± 1033.1, $p = 0.011$, respectively).

Radiological findings revealed significantly higher incidence of leptomeningeal enhancement (61.2 % vs. 38.6 %, $p = 0.007$) and lower incidence of tuberculoma in TBMRIS group (40.8 % vs. 59.1 %, $p = 0.030$) (Table 1). Both groups had similar frequency of hydrocephalus. Cerebral magnetic resonance angiography (MRA) data were available in part of patients in both groups, and showed abnormality in 6 out of 13 (46.2 %) patients in TBMRIS group and 4 out of 20 (20 %) patients in TBM-only group ($p = 0.226$).

3.2. Characteristics of stroke in TBMRIS group

Of the 49 patients in TBMRIS group, 41 (83.7 %), 5 (10.2 %) and 3 (6.1 %) patients experienced stroke within 3 months, 3 to 6 months and more than 6 months after the onset of meningitis symptoms, respectively (Table 2). Thirty-nine (79.6 %) patients present symptomatic stroke and 10 (20.4 %) patients present silent stroke. Twenty-eight (57.1 %) patients had stroke in basal ganglia, followed by thalamus, cortical, subcortical white matter, brainstem and cerebellum. Thirteen (26.5 %) patients showed a single stroke lesion in a single vascular territory, and 36 (73.5 %) patients showed multiple stroke lesions in a single vascular territory or multiple vascular territories. Stroke occurred in multiple vascular territories in 19 (38.8 %) patients, including bilateral anterior

Table 1
Characteristics of TBMRIS group and TBM-only group.

	TBMRIS group (n = 49)	TBM-only group (n = 127)	p-value
Age, years, Mean ± SD	40.7 ± 14.3	38.5 ± 14.5	0.351
Male, n (%)	35 (71.4)	89 (70.1)	0.860
Pulmonary TB, n (%)	23 (46.9)	55 (43.3)	0.664
HIV infection, n (%)	4 (8.2)	13 (10.2)	0.894
Clinical symptoms and signs, n (%)			
Fever	40 (81.6)	102 (80.3)	0.843
Headache	35 (71.4)	86 (67.7)	0.634
Vomiting	17 (34.7)	40 (31.5)	0.684
Neck stiffness	25 (51.0)	55 (43.3)	0.357
Altered consciousness	20 (40.8)	41 (32.3)	0.286
Focal neurological deficit	37 (75.5)	19 (15.0)	< 0.001
Seizure	5 (10.2)	18 (14.2)	0.484
Cranial nerve palsy	7 (14.3)	13 (10.2)	0.448
Stage of TBM, n (%)			
Stage I	7 (14.3)	76 (59.8)	
stage II	36 (73.5)	41 (32.3)	
stage III	6 (12.2)	10 (7.9)	< 0.001
Short-term outcome, n (%)			
good (mRS score 0–2)	34 (69.4)	106 (83.5)	
poor (mRS score 3–6)	15 (30.6)	21 (16.5)	0.038
Laboratory findings, Mean ± SD			
Leukocytes, 10^9/L	8.05 ± 2.28	7.85 ± 2.82	0.663
Hemoglobin, g/L	112.5 ± 17.7	116.4 ± 19.7	0.128
Platelet counts, 10^9/L	275.8 ± 82.2	291.0 ± 104.9	0.362
FIB, g/L	3.85 ± 0.95	3.73 ± 1.17	0.522
INR, ratio	1.03 ± 0.11	1.02 ± 0.11	0.698
PT, second	13.2 ± 1.4	11.9 ± 1.3	0.197
APTT, second	33.7 ± 4.7	33.1 ± 9.2	0.685
Albumin, g/L	33.9 ± 5.7	35.8 ± 6.2	0.092
D-dimer, μg/ml	1.93 ± 1.51	1.83 ± 1.75	0.786
Serum sodium, mmol/L	130.7 ± 5.3	133.0 ± 6.0	0.018
CSF findings, Mean ± SD			
White cell count, cell/mm^3	207.1 ± 202.9	143.2 ± 175.8	0.006
Lymphocyte percentage, %	67.3 ± 27.8	66.3 ± 27.2	0.838
ADA, U/L	19.4 ± 18.3	15.7 ± 15.2	0.017
Protein, mg/L	2062.0 ± 1537.4	1603.1 ± 1033.1	0.011
Glucose, mmol/L	1.94 ± 0.66	2.13 ± 0.85	0.143
Chloride, mmol/L	111.0 ± 7.3	113.2 ± 9.4	0.138
Radiological findings, n (%)			
Leptomeningeal enhancement	30 (61.2)	49 (38.6)	0.007
Hydrocephalus	8 (16.3)	18 (14.2)	0.718
Tuberculoma	20 (40.8)	75 (59.1)	0.030
MRA abnormality	6/13 (46.2)	4/20 (20)	0.226

TBM, tuberculous meningitis; TBMRIS, tuberculous meningitis-related ischemic stroke; SD, standard deviation; HIV, human immunodeficiency virus; FIB, fibrinogen; INR, international normalized ratio; PT, prothrombin time; APTT, activated partial thromboplastin time; CSF, cerebrospinal fluid; ADA, adenosine deaminase; MRA, magnetic resonance angiography.

circulation in 11 (22.4 %) patients, and anterior and posterior circulation in 8 (16.3 %) patients. Of the 19 patients with multiple territories involvement, stroke lesions were located in two vascular territories in 15 (30.6 %) patients and three vascular territories in 4 (8.2 %) patients (Figs. 3 and 4).

3.3. Predictors of stroke in TBM patients

Variables with a p value < 0.05 in univariate analyses including focal neurological deficit, stage of meningitis, serum sodium, CSF white cell count, ADA in CSF, CSF protein, leptomeningeal enhancement, tuberculoma were included in binary logistic regression analysis. The result showed that focal neurological deficit (OR 23.724; 95 % CI 9.103–61.826; p < 0.001), CSF white cell count (OR 1.003; 95 % CI 1.000–1.005; p < 0.05) and leptomeningeal enhancement (OR 2.442; 95 % CI 0.992–6.010; p < 0.05) were independent risk factors for stroke. Tuberculoma (OR 0.328; 95 % CI 0.126–0.857; p < 0.05) was negative related with stroke (Table 3).

Table 2
Characteristics of stroke in TBMRIS group.

Features	n (%)
Time between meningitis onset and stroke diagnosis	
< 3 months	41 (83.7)
3–6 months	5 (10.2)
> 6 months	3 (6.1)
Stroke form	
Symptomatic	39 (79.6)
Silent	10 (20.4)
Location of stroke	
Cortical	9 (18.4)
Subcortical white matter	9 (18.4)
Basal ganglia	28 (57.1)
Thalamus	11 (22.4)
Brainstem	8 (16.3)
Cerebellum	4 (8.2)
Affected vascular territory	
Single territory	30 (61.2)
Single lesion	13 (26.5)
Multiple lesions	17 (34.7)
Multiple territories	19 (38.8)
Lesions in bilateral anterior circulation	11 (22.4)
Lesions in anterior and Posterior circulation	8 (16.3)
Lesions in two territories	15 (30.6)
Lesions in three territories	4 (8.2)

TBMRIS, tuberculous meningitis-related ischemic stroke.

4. Discussion

Ischemic stroke as a complication of TBM is not uncommon, with an incidence of 13–57 % in clinical study and up to 22–72 % in autopsy [2]. In the present study, 27.8 % of TBM patients were found to have stroke, which showed a relatively high morbidity of this complication in local patients with TBM. In the TBMRIS group, most patients (41/49, 83.7 %) experienced stroke within 3 months after the onset of meningitis symptoms, suggesting that TBMRIS was most likely to occur during the intensive inflammatory response period in patients with active TBM. Ischemic stroke in TBM patients may present in symptomatic or silent form on admission or during hospitalisation [9]. About 20.4 % of patients in TBMRIS group in our study displayed silent stroke, reminding us of the necessity for constant vigilance to this form of stroke. Fever and headache were the most commonly seen symptoms in both TBMRIS group and TBM-only group, while focal neurological deficit was more prevailing in TBMRIS group, which was comparable to previous studies by Sheu et al and Chen et al [9,12].

Current evidence suggest that several mechanisms may contribute to TBMRIS. Fibrinocellular exudates secondary to intense inflammatory reaction wrap the cerebral arteries, resulting in three most common vascular pathologies involving infiltrative, proliferative and necrotising processes, either in isolation or in combinations [13]. These pathological changes may cause arteritis, vasospasm, stenosis and subsequently stroke [14]. Furthermore, inflammatory exudates may obstruct CSF circulation and lead to hydrocephalus, which may cause stretching of blood vessels and decreased cerebral blood flow [3]. Moreover, cerebral salt wasting syndrome may play a role in the pathophysiology of TBMRIS as it can lead to hyponatremia, hypovolemia and hypoperfusion [3]. Inadequate dietary intake and inappropriate use of dehydrating - agents may aggravate cerebral vascular hypoperfusion. Luminal thrombosis is the main mechanism of atherosclerotic infarction which is the main type of stroke in the elderly. However, its role in TBMRIS remains controversial since previous autopsy studies revealed that evidence of arterial thrombosis could not be found or was uncommon [4]. We had excluded patients with conventional vascular risk factors from our study to minimize the impact of atherosclerosis and embolism. Also worthy of note was the significantly elevated level of plasma D-dimer in TBM patients in our study, although no significant difference in D-dimer

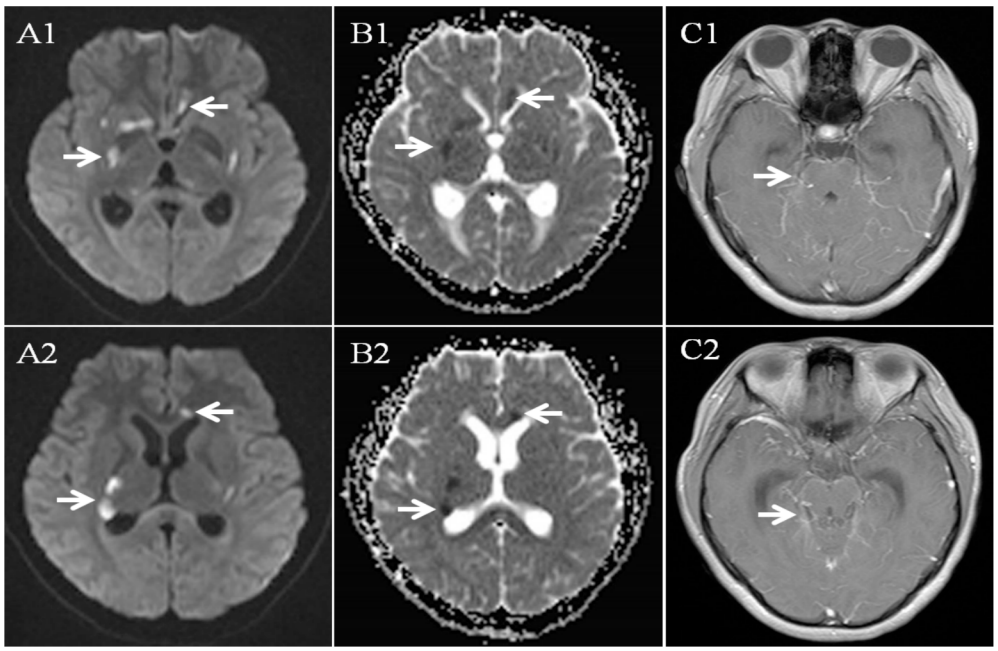

Fig. 3. A 18-year-old female with TBM. (A1-A2) Axial diffusion-weighted imaging (DWI) and (B1-B2) apparent diffusion coefficient (ADC) showed multiple stroke lesions involving bilateral anterior circulation (arrow). (C1-C2) Axial enhanced magnetic resonance imaging (MRI) showed basal meningeal enhancement (arrow).

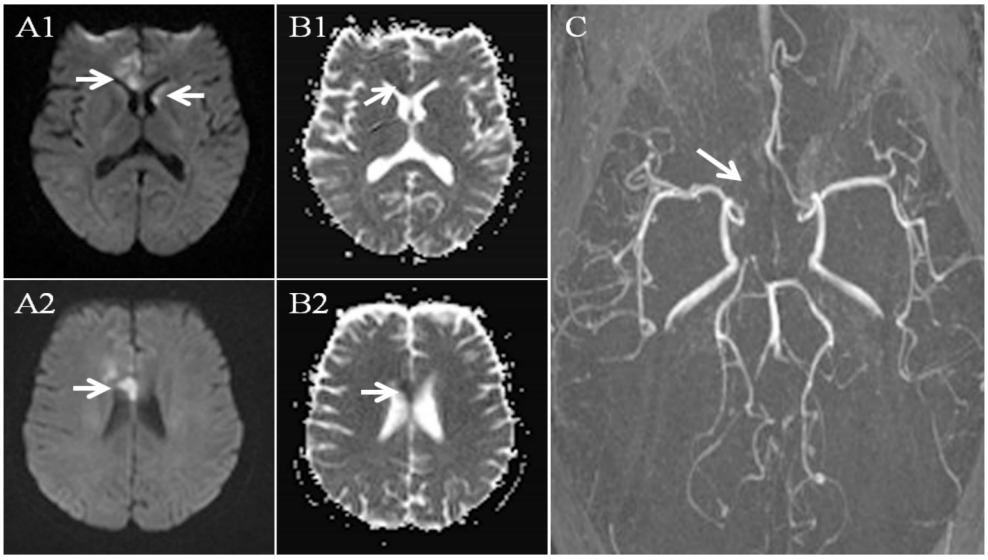

Fig. 4. A 45-year-old female with TBM. (A1-A2) Axial diffusion-weighted imaging (DWI) and (B1-B2) apparent diffusion coefficient (ADC) showed multiple stroke lesions involving bilateral anterior circulation (arrow). (C) Magnetic resonance angiography (MRA) showed occlusion of right anterior cerebral artery (arrow).

Table 3
Predictors of stroke in TBM.

	β	OR	95 % CI	p-value
Focal neurological deficit	3.166	23.724	9.103–61.826	< 0.001
CSF white cell count	0.003	1.003	1.000–1.005	0.027
Leptomeningeal enhancement	0.893	2.442	0.992–6.010	0.049
Tuberculoma	−1.114	0.328	0.126–0.857	0.023
Constant	−2.718	0.066		< 0.001

TBM, tuberculous meningitis; CSF, cerebrospinal fluid; OR, odds ratio; CI, confidence interval.

level was found between groups. D-dimer is a degradation product of fibrin monomer and a sensitive marker of hypercoagulability. A hypercoagulable state in TBM patients has been reported and may further increase the risk for stroke [15]. Dalal et al concluded in 1979 that hemodynamic hypoperfusion due to a variable combination of vasospasm, intimal proliferation and thrombosis might be the main pathogenesis of stroke in TBM patients [16], which is still widely supported by others today. The pathogenesis of TBMRIS is complex and has not been fully elucidated, more researches are needed.

In the present study, basal ganglia was the most frequent site of stroke, found in 57.1 % of our patients, and this was in agreement with previous studies by Zhang et al (50 %), Kumar et al (54.3 %) and Kalita et al (54 %) [2,3,17]. Multiple stroke lesions and involvement of multiple vascular territories were commonly observed in our study, which was comparable to previous report by Tai et al [14]. These may be attributed to the uneven distribution of inflammatory exudates. The blood vessels most affected by exudates are on the base of the brain and

in the Sylvian fissures, where the exudates are most abundant and the vessels of the circle of Willis are located [13]. Blood vessels supplying the basal ganglia are most frequently involved, causing the basal ganglia to be the most vulnerable stroke area [15]. Hsieh et al found that strokes were most likely to occurr in the "TB zone", which consisted of the head of the caudate nucleus, the anteriomedial thalami and the anterior and genu limb of the internal capsule [18]. However, Tai et al revealed that stroke in TBM involved mainly the perforators and terminal cortical branches, and suggested that vascular supply classification was more accurate than the classification of "TB zone" versus "ischaemic zone" [14].

More white cell counts in CSF, higher level of CSF protein and ADA, more common leptomeningeal enhancement and less common tuberculoma were observed in TBMRIS group, which might suggest different inflammatory processes in the meninges between TBMRIS group and TBM-only group. CSF white cell, CSF protein, ADA level in CSF, and meningeal enhancement are often used to assess the inflammatory intensity of meningitis and therapeutic effect in clinic, and increased values of these indicators in TBMRIS group might indicate stronger inflammatory reaction than TBM-only group. The association between tuberculoma and stroke is still not well known. Some studies reported a similar frequency of tuberculoma in TBM patients with and without stroke [3,9,12]; on the contrary, other studies showed a higher incidence of tuberculoma in non-stoke patients [2,19,20]. Multiple reasons might account for the inconsistent results, such as regional difference, different sample size and inclusion criteria. In this study, tuberculoma was more frequently noted in TBM-only group, and was negatively correlated with stroke in logistic regression analysis. The formation of tuberculoma is most likely because of an immunological response to brain parenchyma infection [2,19,21], which may restrict the propagation of MTB. More studies are needed to clarify the underlying mechanisms between tuberculoma and stroke.

Our study showed that focal neurological deficit, CSF white cell count and leptomeningeal enhancement were the independent risk factors for stroke in TBM. A prospective study also indicated that CSF white cell count and leptomeningeal enhancement were predictors of stroke in TBM patients [2]. Focal neurological deficit was also been found to be a predictor of stroke in a retrospective study [22]. In our study, serum sodium, stage of meningitis, CSF protein and ADA level were found significantly different between groups in univariate analysis, but were not the independent risk factors for stroke in logistic regression analysis.

MRA abnormality has been reported in 43.2–50.7 % of TBM patients [10,23,24], and may be associated with stroke and poor outcome [23]. The proportion may rise to 65.2 % in patients with stroke [3]. Only a few patients in our study underwent MRA and the difference in MRA abnormality was not significant between TBMRIS group and TBM-only group, so increasing the sample size was necessary.

Despite the fact that effective antituberculosis treatment is available, TBM still remains a serious life-threatening disease. The presence of stroke may complicate a variable proportion of TBM cases and further aggravate their prognosis, especially in later stage of meningitis. Adjunctive dexamethasone might act to improve outcome from TBM by reducing hydrocephalus and preventing stroke [25]. A systematic review indicated that aspirin could reduce the risk of stroke in patients with TBM, but did not affect mortality [26]. A randomised double blind phase 2 trial showed that aspirin might be beneficial in preventing stroke and reducing mortality in patients with TBM [27]. Therefore, adjunctive dexamethasone and aspirin are revealed beneficial to TBM patients with stroke in some studies, and warrant further investigation.

There are several limitations in our study. Firstly, it is a retrospective and single-center study, so selection bias may exist. Secondly, our sample size was relatively small, especially TBMRIS group, since we excluded TBM patients with vascular risk factors who accounted for the majority of TBM cases. Furthermore, we could't evaluate their long-term prognosis as a sound and effective follow-up mechanism was not established.

5. Conclusion

In conclusion, TBMRIS most likely occurs in basal ganglia within 3 months after the onset of meningitis symptoms and may present in silent form. Multiple stroke lesions and involvement of multiple vascular territories are common. Focal neurological deficit, CSF white cell count, leptomeningeal enhancement are the predictors of stroke in patients with TBM. Large series of prospective studies are warranted to validate these findings in the future.

Ethics approval and consent to participate

Ethical approval was granted by the Guangxi Medical University Review Board. Study participants have given their full consent for publication.

CRediT authorship contribution statement

Xuhui Deng: Writing – original draft, Methodology, Data curation, Conceptualization. **Qiuhui Huang:** Supervision, Formal analysis, Data curation. **Hua Huang:** Validation, Methodology, Data curation. **Shengri Chen:** Validation, Methodology, Data curation. **Xue Wang:** Validation, Project administration. **Zhijian Liang:** Writing – review & editing, Funding acquisition, Conceptualization.

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Data availability

The data are available from the corresponding author on reasonable request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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