Ischemic Infarction in 25 Children With Tuberculous Meningitis

Ramón Leiguarda, MD, Marcelo Berthier, MD, Sergio Starkstein, MD, Martín Nogués, MD, and Pedro Lylyk, MD

Twenty-five cases (38%) of ischemic infarction occurred among 65 cases of tuberculous meningitis in patients <14 years of age. The male : female ratio was 1.3:1. The most frequent clinical findings were meningeal signs, fever, alteration of consciousness, cranial nerve involvement, seizures, and focal neurologic deficit. Twenty-three patients had anterior circulation infarcts, and two more had infarcts in the verteobasilar territories. Distribution of infarcts in the anterior circulation was shown by computed tomography in the territories of the following arteries: lenticulostriate, 10 cases unilateral and 6 bilateral; middle cerebral, 3 cases; internal carotid, 1 case; multiple areas, 3 cases. Of the 25 ischemic infarction cases, 23 (92%) had hydrocephalus, 19 (76%) basal exudates, and 2 (8%) tuberculomas. Outcome was poor since no patient with infarction recovered completely. Six died and bilateral subcortical infaracts led to a considerably higher mortality than unilateral ones, whether cortical or subcortical. (Stroke 1988;19:200-204)

Ischemic infarctions secondary to panarteritis are a common finding in tuberculous meningitis (TBM). Dastur et al1 in a review of 100 brains found infarction in 41%, whereas Bhargava et al2 in a computed tomography (CT) study observed infarcts in 28.1% of their series. However, there are certain features peculiar to these lesions that have not been fully appreciated.

The present work was undertaken to study 1) the arterial distribution of the ischemic infarctions, 2) the influence of ischemic lesions on the clinical picture, 3) the association between ischemic infarction and other tuberculous lesions such as hydrocephalus, basal exudates, or tuberculomas, and 4) the significance of these lesions in the prognosis of the disease.

Subjects and Methods

Sixty-five patients <14 years of age with the diagnosis of TBM were selected for study. The diagnostic criteria for TBM were based on epidemiologic and clinical data, cerebrospinal fluid (CSF) findings, and a response to antituberculous therapy.3-4 CSF findings included either positive identification of tubercle bacilli or, when this was lacking, an abnormal CSF compatible with TBM, that is, a moderate degree of lymphocyte pleocytosis, increased protein, and reduced sugar. Other causes of basal meningitis, whether neoplastic or fungal, were excluded. Patients were divided into two groups according to the presence or absence of infarctions as determined by CT. Group I consisted of 25 patients with infarctions; Group II had 40 patients with no evidence of infarction. The vascular distribution of infarcts on CT was assessed according to Damasio's guidelines.5 In a few cases, angiography was also performed.

Analysis of the results of the two groups of patients was made with regard to clinical features, CSF profile, CT scan findings, and prognosis.

All patients received the following therapeutic regimen: 15–20 mg isoniazid/kg/day, 10 mg rifampin/kg/day, 15–25 mg ethambutol/kg/day, and 20–25 mg streptomycin/kg/day. A ventriculoperitoneal shunt was placed in 18 patients of Group I and in 13 of Group II because of hydrocephalus. The χ² test was used for statistical analysis.

Results

Table 1 shows the clinical findings for both groups of patients. There was no significant difference in age distribution between Groups I and II (mean age 3.5 and 4.1 years, respectively). Sex distribution in each group was roughly equal.

Stupor, coma, and signs of increased intracranial pressure were more common in Group I than in Group II (p<0.05). Cranial nerve palsies, mainly affecting oculomotor and facial nerves, were more often seen in Group I patients, although group differences were not significant. Both generalized and focal seizures were observed often in both groups. As expected, focal motor deficits were found much more frequently in Group I patients (p<0.05) and correlated well with CT lesion location. All Group I patients who developed unilateral choreoathetoid movements had an infarction involving the contralateral caudate nucleus.

In the CSF profile (Table 2) the only contrasting finding was the CSF opening pressure, which was higher in Group I. However, this parameter failed to correlate with the degree of hydrocephalus, which was similar in patients from both groups.


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glucose content as well as cell count proved similar in both groups. Tubercle bacilli were demonstrated by smear and/or culture in the CSF of 28% of the patients from Group I and in 32% from Group II.

Table 3 shows infarction location for Group I as depicted by CT scan. Twenty-three patients (92%) had anterior circulation infarctions, whereas only two (8%) had lesions in the vertebrobasilar territory. Of the 23 with anterior circulation infarctions, in 16 the lesions were distributed in the territory of the lenticulostriate arteries (either unilateral or bilateral) whereas in the other 7 patients, more extensive areas were affected. One patient had an extensive infarction of the internal carotid artery (ICA), and the angiogram showed severe segmental narrowing of the supraclinoid portion of the carotid artery (Figure 1). Of the two vertebrobasilar cases, one developed bilateral occipital infarctions, whereas the other had a unilateral mesencephalon-subthalamic lesion. In the latter case the angiogram (Figure 2) demonstrated irregular narrowing of the basilar system and an aneurysm in the right middle cerebral artery (MCA).

Other pathological lesions visualized on CT (Table 4) included hydrocephalus and pathological enhancement of the basal cisterns. These were slightly more frequent in Group I than in Group II, although the difference failed to reach significance. On the other hand, tuberculomas were five times as common in Group II (p<0.05).

Prognosis in Group I was poorer than in Group II (Table 5) since no patient in the former recovered completely and 24% died; mortality was three times that for Group II (p<0.05). Bilateral subcortical infarction led to higher mortality (66%) than unilateral, whether cortical or subcortical (13%).

Discussion

Ischemic infarctions are a common severe complication of TBM. Their incidence in our series was 38%, which is in agreement with previous reports.1,2 Meningeal inflammatory exudate is known to involve the adventitia and to progressively spread, affecting the entire vessel wall, leading to necrotizing panarteritis with secondary thrombosis and occlusion. Panarteritis mainly involves the small and medium-sized arteries, although the capillaries and veins may also be affected. Larger arteries mostly show periarteritis alone. Circumscribed tubercles are found in the adventitia extending at times to the media and intima, whereas well developed tuberculomas or a complete caseous necrosis can rarely be seen. In treated cases, fibrous endoarteritis, rather than necrotizing...
panarteritis, is a characteristic vascular finding.6,7 The perforating vessels at the base of the brain, particularly at the origin of the lenticulostriate arteries, are predominantly involved. This agrees with the most usual and severe distribution of exudate within the subarachnoid cisterns and explains the basal ganglia infarctions so often seen on CT.2 The dilated ventricles stretching the already-compromised vessels may also favor the development of infarctions in such locations.8

The stem and/or cortical branches of the MCA in the sylvian fissure and the supraclinoid portion of the ICA may also be damaged. Involvement of the vertebrobasilar system is uncommon, although occasionally extensive infarctions in the distribution of both posterior cerebral arteries or small brainstem lesions may be observed.8

The clinical features of TBM have been the subject of lengthy reviews,6-9 but only a few aspects relevant to the associated ischemic lesions deserve consideration here.

Alteration of consciousness and signs of increased intracranial pressure were found more frequently in Group I. This finding was more attributable to the severity of the inflammatory process than to the degree of hydrocephalus, which proved similar in both groups. Cranial nerve involvement is seen in 17.4-45.2% of patients with TBM, and according to various series10-12 the III, IV, and VII cranial nerves are the most commonly affected. Although group differences were hardly significant, the incidence of cranial nerve palsies among our Group I patients was higher than in Group II. We believe that this finding, together with the prevalence of meningeal signs in Group I, demonstrated meningeal involvement more patently than the basal exudate seen on CT scanning. On the other hand, the severity of meningeal involvement was apparently not reflected by the degree of CSF abnormalities since changes were similar in both groups except for opening pressure. These findings are in agreement with those of Mathew et al12 and Wadia and Singhal,13 who also reported lack of correlation between arterial lesions seen on angiography and CSF abnormalities.

Seizures, whether focal or generalized, were commonly observed in both groups, with an incidence similar to previous studies.9,14 As expected, focal neurologic deficits were much more frequent in Group I patients and correlated with the site of lesions visible on CT. The incidence of focal motor deficit in Group I was higher than previously reported.9,11,14 Some patients in Group II had either focal motor deficit or unilateral abnormal involuntary movements in spite of the lack of demonstrable lesion on CT scan. We believe that small, unrevealed ischemic infarctions may well account for these clinical manifestations.

Twenty-four percent of Group I patients had unilateral choreoathetoid movements. Abnormal involuntary

![Figure 1. Angiogram showing severe segmental narrowing of supraclinoid portion of left internal carotid artery (arrow).](http://stroke.ahajournals.org/)

**Table 3. Locations of Infarctions by Computed Tomography in 25 Children With Tuberculous Meningitis**

<table>
<thead>
<tr>
<th>Location</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid system</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal carotid artery stem</td>
<td>23</td>
<td>92</td>
<td>1</td>
<td>4</td>
<td>16</td>
<td>64</td>
<td>10</td>
</tr>
<tr>
<td>Middle cerebral artery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lenticulostriate arteries</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical branches</td>
<td>19</td>
<td>76</td>
<td>2</td>
<td>8</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Middle cerebral artery stem</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical and subcortical arteries</td>
<td>3</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vertebrobasilar system</td>
<td>2</td>
<td>8</td>
<td>1</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior cerebral artery (bilateral)</td>
<td>1</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterioriomedial choroid system</td>
<td>1</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
movements are more frequently seen in children than in adults with TBM but are relatively unusual even though in exceptional cases such movements may be the predominant clinical feature of the disease. All of our patients with unilateral choreoathetoid movements had an infarction involving the contralateral caudate nucleus. In most of them, the anterior limb of the internal capsule and part of the putamen were also affected.

Contralateral hemichorea has been described with infarction affecting primarily the caudate nucleus and the putamen. Saris' review of 11 cases of hemichorea showed that in nine the caudate nucleus was predominantly involved, and in six the putamen was also affected. Recently, Kase et al. reported an adult case of hemichorea and hemiballismus caused by a lacunar infarction involving the anterior putamen, anterior limb of the internal capsule, and head of the caudate nucleus, a lesion location almost identical to that of our patients with involuntary movements. Other movement disorders observed in our series, such as generalized myoclonus and tremor, seemed unrelated to vascular lesions.

Angiographic features of TBM have already been widely described and consist of a triad that includes evidence of hydrocephalus, narrowing of the arteries at the base of the brain, and narrowed or occluded small and medium-sized arteries, sometimes with early draining veins. Several different types of collateral circulation have also been observed. In addition to these features, we found a patient who developed an aneurysm of the horizontal portion of the MCA, which we believe was a bacterial aneurysm of the extravascular type since it was located in a portion of the artery that was bathed in a thick inflammatory exudate and that showed areas of segmental narrowing. The aneurysm ruptured, causing fatal hemorrhage during the active phase of the disease.

Bacterial aneurysms make up 2.5–6.2% of all intracranial aneurysms and include those of embolic origin secondary to bacterial endocarditis, which are the most common; the so-called primary or cryptogenic aneurysms, in which no inflammatory focus can be demonstrated; and those of extravascular origin, formed as a result of infection extending from a neighboring focus (e.g., cavernous sinus thrombophlebitis, skull osteomyelitis, and meningitis). In these cases, the infection probably spreads from the adventitia toward the internal elastic lamina, weakening the vessel wall, with subsequent formation of an infectious aneurysm.

Bacterial aneurysms of the extravascular type are extremely rare in TBM, and we were able to find only two previous cases. Suwanwela et al. reported post-mortem findings in a patient with multiple calcified aneurysms, one fusiform involving the anterior cerebral artery and three of a saccular type located in the middle, anterior, and posterior cerebral arteries. All originated at sites in which basal exudates were plentiful. Another case was described by Brown in a patient with an aneurysm in the basal and upper cerebellar arteries adjacent to a tuberculoma. Since angiography is not performed routinely in TBM patients, it is likely that such lesions are not being detected.

### Table 4. Other Pathological Lesions Visualized on Computed Tomography in 65 Children With Tuberculous Meningitis

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Group I (n = 25)</th>
<th>Group II (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocephalus</td>
<td>23</td>
<td>35</td>
</tr>
<tr>
<td>Basal exudates</td>
<td>19</td>
<td>26</td>
</tr>
<tr>
<td>Tuberculomas</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Tuberculous abscess</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Group I, with cerebral infarction determined by computed tomography; Group II, no evidence of infarction.
TABLE 5. Prognosis in 65 Children With Tuberculous Meningitis

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 25)</th>
<th>Group II (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dead</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Dead</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Vegetative state</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Sequelae</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>Full recovery</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Group I, with cerebral infarction determined by computed tomography; Group II, no evidence of infarction.

patients due to well-known complications, we cannot estimate the true incidence of aneurysms in our series.

Infarcts were accompanied by other pathological lesions on CT scan. Hydrocephalus and basal exudate were present in 92 and 76% of the Group I cases, respectively. However, contrary to expectations, Group II patients also showed a high incidence of hydrocephalus of similar severity and basal exudate of almost equal density. Tuberculomas were seen much more frequently in Group II patients, probably implying different pathophysiological mechanisms.

Except for the increased frequency of tuberculomas in Group II patients, the two groups were treated similarly and had no other distinguishing features except for the chosen distinction of presence or absence of infarctions. We believe that this distinction determined prognosis, with Group I showing a far worse outcome due to the presence of infarctions. No patient in Group I recovered completely, and overall mortality was three times that of Group II. Our findings confirm and extend those reported by Wadia and Singhal, who also observed that patients with TBM and vascular lesions demonstrable by angiography have a poorer prognosis and more permanent neurologic deficits compared with the other cases in their series.

References


Key Words • tuberculosis, meningeal • cerebral ischemia • child
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