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MR of childhood tuberculous meningitis

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Summary. MR imaging was performed on 27 children with stage II-III tuberculous meningitis for the specific purpose of examining the brainstem, as well as comparison with other CT features of the disease. In addition to defining the ischemic disturbances of basal ganglia and diencephalon more clearly, MR also demonstrates the frequent occurrence of parenchymal signal abnormalities in the brainstem and adjacent temporal lobes, which are invisible or uncertain on CT. Although the presence of brainstem abnormalities on MR correlated well with clinical findings of brainstem dysfunction, clinical staging on admission remains the best prognostic indicator in advanced TBM. We also review the MR features of basal exudation, hydrocephalus and tuberculoma.

Key words: Tuberculous meningitis - MR imaging - Basal ganglia infarct - Brainstem encephalopathy - Basal exudate - Tuberculoma - Hydrocephalus

The outcome of stage II and III tuberculous meningitis (TBM) remains poor despite effective chemotherapy and the normalisation of intracranial pressure [1, 2]. A major prognostic determinant must therefore be the localisation and degree of parenchymal damage on admission, as reflected by the clinical staging of the disease. Although computed tomography (CT) will demonstrate the presence of meningovascular enhancement, basal ganglia infarction and hydrocephalus, the images do not explain the underlying pathological process responsible for the disturbance of consciousness. In particular, the brainstem dysfunction which is frequently present in stage III TBM, has no consistent radiological features [7-10], although we have noted occasional indistinct hypodense alteration in this region. In a previous clinico-pathological study [3], focal ischemic necrosis and border-zone encephalopathy were found to be present in the midbrain/pons of all patients presenting with brainstem signs, and a prospective study was therefore undertaken in an attempt to define these changes on MR.

Material and methods

MR imaging was performed on 27 patients, of whom 10 were diagnosed as stage II, and 17 stage III disease, using the British Medical Research Council criteria [4]. Ages ranged from 19 months to 8 years 6 months (mean 3 years and 5 months). Diagnosis was made on the history and typical CSF findings, together with two or more of the following: positive Mantoux test; chest radiograph of primary pulmonary disease; CT scan showing tension hydrocephalus and basal meningovascular enhancement (scans performed routinely without and with Conray 280). In 6 cases, *M. tuberculosis* was cultured from CSF or gastric aspirate. All children received anti-tuberculous drugs, and on admission, intracranial pressure was measured by a 1 hour-long continuous lumbar CSF pressure recording. This was repeated at weekly intervals thereafter, until pressure was normalised. Five ml of air were injected into the lumbar subarachnoid space at the end of the first recording, and its location on skull x-ray used to determine whether the hydro-

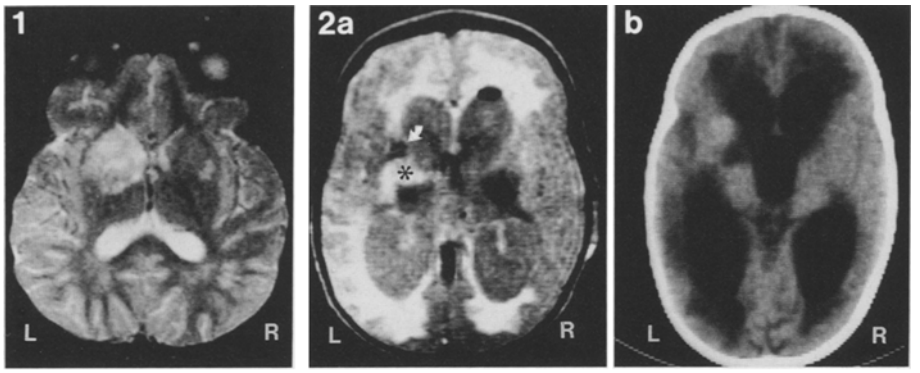

Fig. 1. Acute infarct L basal ganglia region (TR2000/TE120). Lesion is also hyperintense on the early echo but scarcely visible on the T1 image. Note smaller lesion on R

Fig. 2. **a** Focal resolved infarct with signal inhomogeneity L basal ganglia (TR2000/TE70). Anterior component of lesion (arrow) is hypointense due to mineralisation, whilst posteriorly, signal hyperintensity is compatible with spongiosis *(asterisk)*. **b** CT of same: note the hypodense abnormality cannot be easily differentiated from cavitation

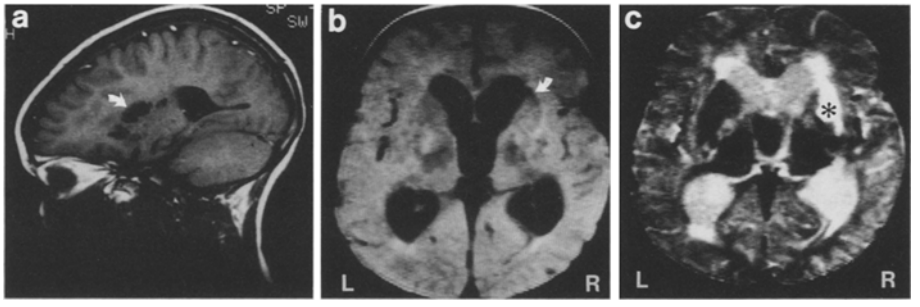

Fig. 3. **a** Resolved infarct with cavitation (TR500/TE27). Lesion *(arrow)* is CSF-isointense on all images. **b, c** Resolved infarct R basal ganglia with presumed hypertrophic gliosis (TR2000/TE27-120). Anterior component is cavitated or spongiotic (early echo, *arrow*), whilst medial part is early echo isointense, late echo hyperintense *(asterisk)*. Note the distribution of parenchymal signal abnormality characteristic of hydrostatic edema

cephalus was of communicating or non-communicating type. Eight children having a non-communication block were subjected to immediate ventriculo-peritoneal shunt. The remaining 19 children, all of whom had a lumbar CSF pressure in excess of 15 mm Hg, were included in a controlled clinical trial designed to evaluate the effect of medical treatment on raised intracranial pressure [3]. Of this group, 5 patients received oral acetazolamide and furosemide daily, whilst 3 children were given intrathecal hyaluronidase weekly. A control group of 9 patients received the prescribed anti-TB regimen only. Two children died before treatment of their raised intracranial pressure could be commenced. MR imaging was performed on a 0.5T scanner, using the spin-echo technique with TR500/TE27 ms for T1 images, and TR2000/TE27, 70, 100 and 120 ms for T2 images.

Results

Parenchymal lesions of ischemic type

Basal ganglia-diencephalon. 20 cases. In this region, lesions resembled focal infarcts, being usually homogeneous, T2-hyperintense, with sharply circumscribed edges, located predominantly in grey matter, but extending into adjacent white matter (Fig. 1). These were considered relatively acute, if there was no evidence of tissue shrinkage. In 5 cases, the lesions were inhomogeneous on the late echo, and in one instance, this was shown on CT to be partly due to mineralisation (Fig. 2 a, b). The exhibition of a CSF-isointense signal (all images) was assumed to be cavitated infarction of lacunar type or coarse spongiosis (Fig. 3 a, b). Occasionally, however, the signal was late T2-hyperintense and early-T2 isointense, an alteration only readily explained as gliosis (Fig. 3 b, c).

Brainstem-parahippocampal gyri-hypothalamus. 10 cases, all of whom had supratentorial lesions in addition. In these regions, focal or irregular-confluent T2 hyperintense signal abnormality was apparent predominantly in the parenchyma of the midbrain, with less extensive involvement of the pons (Fig. 4 c). Border zone disease was suspected by the presence of signal hyperintensity affecting the surfaces of the cerebral peduncles (Fig. 4 b). Occasionally, the pathological process involved the brainstem and adjacent temporal lobes more diffusely, with marked loss of anatomical detail, but in most of the patients in this group, there was also loss of the normal signal delineating the ambient cistern (T2 images), a change consistent with inflammatory exudation within this space (Fig. 4 d).

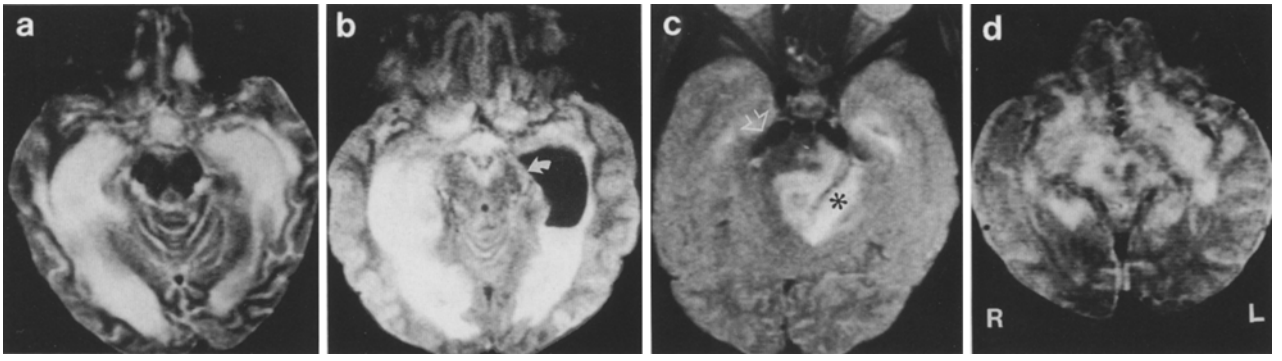

Fig. 4. **a** Normal brainstem and ambient cistern (TR2000/TE120). **b** Presumed border-zone disease, with signal hyperintensity of surfaces of cerebral peduncles *(arrow)* (TE100). **c** More diffuse abnormality of brainstem, with focal lesion in the adjacent R medial temporal lobe *(asterisk)* (TE100). Air is in prepontine cistern *(arrow)*. **d** Severe disease of brainstem and basal hemispheres with loss of normal anatomical detail (TE70)

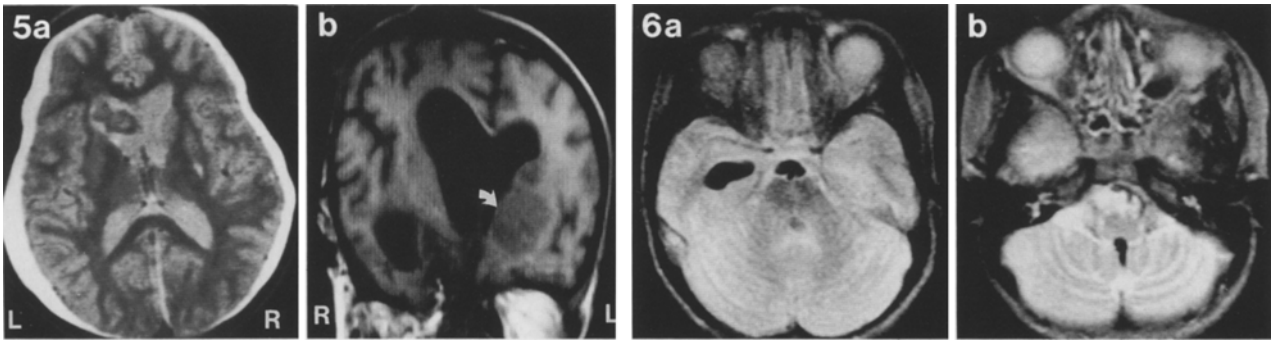

Fig. 5. **a** Tuberculoma. Wall is white-matter isointense, and hypointense relative to contents and surrounding edema (TR2000/TE120). **b** Coronal T1 image of same showing lobulation *(arrow)* and generalised hypointensity relative to white matter. Capsule is no longer visible (TR500/TE27)

Fig. 6. **a** Air sequestrated in the prepontine cistern and inferior horn. **b** Air in median foramen. Air was observed in IVth ventricle but not lateral foramina nor ambient cistern. Both images TR2000/TE100

Mass lesions

Three children exhibited one or more rounded intraparenchymal lesions of presumed granulomatous type. Masses in excess of 2 cm were characterised by a distinct T2-hypointense wall (gliomesodermal response) with inhomogeneous contents giving the faint impression of concentric lamellation (caseous necrosis) (Fig. 5 a, b). On T1 images, the wall was isointense, and the contents homogeneously hypointense. The surrounding parenchymal T2-hyperintensity was typical of interstitial edema. Smaller lesions do not show a distinct capsule, and are more uniformly T2-hypointense, with hyperintense spots. Reduction in size of the lesion with complete disappearance of surrounding edema was observed in one patient after 5 weeks of therapy. In another patient, whose brainstem was normal on admission, a pontine granuloma appeared after 7 months of therapy.

Ventricular and cisternal abnormalities

Ventricular dilatation was present in all the patients, severe in 9, and invariably accompanied by periventricular T2-hyperintensity, typical of hydrostatic edema. This signal abnormality was usually limited to the ventricular margin, but sometimes extended outwards to the cerebral cortex (Fig. 2 a). Although the degree of ventricular dilatation did not appear to correlate with the extent of periventricular edema, the latter abnormality was seen to resolve completely in 4 patients who were shunted.

Patency of the posterior fossa CSF pathway was assessed when the brainstem foramina and related cisterns could be reasonably visualised on T1 and T2 images. Of the 24 patients whose images were judged satisfactory, foramina and/or cisterns were clearly visualised in 20. Diagnostic features included a T2/T1-CSF compatible signal (Fig. 4 a) and/or the presence of air at the appropriate ana-

tomical site (Fig. 6a, b). A firm diagnosis of ambient cistern obliteration presumably due to dense exudation (Fig. 4d), could only be made in 5 patients, but in no case was air ever observed in this space. In contrast, air was frequently seen in the prepontine and cerebellomedullary cisterns as well as the median foramen.

Discussion

This MR imaging study was a prospective one, in continuation of a clinical research project designed to assess the role of raised intracranial pressure in childhood tuberculous meningitis, some of the results of which have been published elsewhere [3, 5]. One of the most important observations to emerge from that project, was that the poor prognosis associated with stage III TBM could not be ascribed solely to tension hydrocephalus. Correlation of the clinical, radiological and pathological findings in fatal cases of the disease, revealed that (when present) ischemic lesions in the basal ganglia and diencephalon as depicted on CT, were frequently associated with lesions in the brainstem which were invisible or obscure with that modality. Neuropathological studies showed such lesions to be of two types, namely ischemic and so-called 'border-zone', the latter having the features of a toxic-inflammatory encephalopathy [6].

Presumptive focal infarcts in the basal ganglia/diencephalon are sharply delineated by the MR scanner, and closely resemble the typical foci of subacute ischemic necrosis which we have regularly observed macroscopically at postmortem [3]. Cavitated infarction was inferred by T2 hyperintensity and T1 hypointensity respectively, but some lesions exhibited signal prolongation on the proton density images without concomitant T1 hypointensity, and probably reflect the acute changes of either cytotoxic edema or coagulative necrosis. There seems no reason to doubt that these lesions are due to focal ischemia occurring as a result of arteritis of the (basal) subarachnoid space vessels, with extraparenchymal occlusion of the penetrating arteries. Without the evidence of cavitation, however, we cannot tell whether some of these foci are not reversible. We also make the tentative suggestion that hypertrophic gliosis might be designated by focal late T2 hyperintensity with proton-density/T1 isointensity.

In addition to supratentorial parenchymal disease, focal signal abnormalities, punctate or confluent, were seen in the brainstem of 10 children, of whom 3 had stage II, and 7 stage III disease. All of the latter group had clinical evidence of brainstem dysfunction and of these, 3 died and 4 survived in a vegetative state. In contrast, the children with stage II TBM and intact brainstem function, recovered, 2 with residual pareses. It has to be emphasised, however, that 7 other children died in coma, without MR evidence of brainstem disturbance. The occurrence of supratentorial ischemic lesions in all patients with brainstem signal abnormalities supports the idea that most of the latter are also ischemic. Their presence in some patients without brainstem signs (stage II TBM) indicates qualitative and quantitative differences, in which cytotoxic swelling and the role of border-zone disease have to be considered. The difficulty in diagnosing the latter component of tuberculous encephalopathy, however, was ascribed to instrument resolution together with the need for sharp visual contrast between the periphery of the brainstem and adjacent cistern – an image seldom encountered.

Our material has shown that that there are no particular MR imaging attributes of the basal exudate of TBM, mainly on account of the difficulty in visualising the ambient cistern adequately, particularly when adjacent tissues are abnormal. Although lacking a satisfactory pathophysiological explanation, granulomatous meningitis is generally accepted to be associated with marked basal contrast enhancement on CT [7–10], and this was present in all the children examined. We inferred the loss of normal CSF signal on the T2 images as being indicative of subarachnoid space diesease, presumably exudative and fibrotic, although it was surprising that so few patients exhibited this abnormality. Schroth et al. [11] were also unable to detect a basal exudate. In contrast to basal meningitis, the tuberculoma appears fairly characteristic, with a crenated, T2-hypointense (white matter isointense) wall, and iso- or hypointense contents, sometimes lamellated. The structure is progressively less-defined with T1-weighting, although the presumably caseous contents are mildly hypointense relative to white matter. Surrounding edema is represented by typical late T2-hyperintensity. Although small tuberculomata (probably about 1 cm diameter) are indistinguishable from other granulomata of equivalent size, the larger lesions are not readily mimicked. Tuberculomata (including a brainstem lesion) were not considered to have had any influence on the clinical staging of the patients in this series.

The presence of increased parenchymal water in association with ventricular dilatation, was demonstrated in all the patients, although of variable extent. This contrasts with the finding of periventricu-

lar lucency in approximately 60% of patients studied with CT [8, 10]. Although children with stage III disease usually showed the severest hydrocephalus, a positive correlation between ventricular size and hydrostatic edema could not be shown. The basal lateral and/or median foramina were judged to be patent in about 80% of our patients, confirming the view of previous workers that obstruction is usually within the cisterns, the ambient cistern in particular.

In spite of effective drug therapy and the normalisation of intracranial pressure, the clinical outcome of patients with stage II-III TBM was poor, and 82% of the children in this study either died or were severely handicapped. The neurological state of the child with advanced TBM is determined by two pathogenetic processes in particular: the parenchymal changes induced by inflammation and ischemia, and the mechanical effects of raised intracranial pressure [6]. MR, in addition to much more detailed demonstration of supratentorial pathology, also reveals a brainstem encephalopathy which correlates well with clinical evidence of brainstem disease, and which we believe constitutes a specific syndrome (brainstem tuberculoma apart). However, a number of children died, whose intracranial pressure was normalised, lacking unequivocal evidence of brainstem disturbance, and in whom no parenchymal lesion could be demonstrated on MR, other than periventricular T2-hyperintensity. In this group, the only consistent imaging abnormality was CT evidence of transient meningovascular enhancement.

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