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Investigation of Japanese Encephalitis in MRI and f-MRI

Dr. Chandra Anjaiah
Department of Zoology, Osmania University, Hyderabad, Telangana, India

Abstract: *We document the fMRI features in eight patients with Japanese encephalitis. MRI was carried out on a 1.5 T system within 10±60 days of onset. In all the patients MRI revealed bilateral thalamic lesions, haemorrhagic in five. Signal changes were present in the cerebrum in four patients, the midbrain and cerebellum in three each, the pons in two and the basal ganglia in one. The lesions were haemorrhagic in three of the four patients with lesions in the cortex, two of the three with lesions in the midbrain and cerebellum, but the pontine lesions were haemorrhagic in both patients. Spinal cord involvement was seen in one of the three patients who underwent fMRI. In two patient's fMRI was repeated 3 years after the onset, showing marked reduction in ab-normal signal; and all the lesions gave low signal on both T1- and T2-weighted images. Bilateral thalamic involvement, especially haemorrhagic, may be considered characteristic of Japanese encephalitis, especially in endemic areas.*

Keywords: JE, fMRI, spinalcord, haemorrhagic.

I. INTRODUCTION

Japanese encephalitis (JE) is the commonest endemic encephalitis in southeast Asia, including India [1]. The diagnosis is commonly based on demonstrating a rising titre of antibodies against JE virus in acute and convalescent sera [2, 3]. There is a delay of at least 7 days before the diagnosis can be confirmed. In an endemic area, it is important to differentiate JE from herpes simplex encephalitis for rational therapy with acyclovir. Our initial studies on radiological and neurophysiological changes in JE revealed characteristic thalamic lesions [4] In a recent study, encephalopathy with bilateral thalamotegmental involvement was reported from Japan but the possibility of JE was not considered [5]. We report fMRI changes in seven patients with JE.

II. PATIENTS AND METHODS

We examined eight patients with JE by MRI 10±60 days after the onset of their illness. Their ages ranged between 2 and 47 years; five were male. The diagnosis was confirmed in all patients by a positive haemagglutination inhibition test, for IgM and IgG anti-bodies to JE [2]. A four-fold or greater rise in IgG was considered diagnostic. In five patients the initial titres were 1: 40 and in the remainder 1: 20. In the convalescent period a four-fold or greater rise in titres was present in all patients, between 1: 80 and 1: 320. The detailed clinical and neurophysiological findings have been reported previously [4].

fMRI of the brain and spine was carried out on a 1.5 T imager using a circularly polarised head coil and oval spinal coil, respectively. The patients were sedated if indicated. The brain was im-aged in all patients, and the spine in three only. Spin-echo pulse sequences were used to image the brain in the axial and cervical spine in the sagittal plane. T1-weighted images were obtained using repetition time (TR) 600±680 ms, echo time (TE) 15 ms, number of excitations (nex) 3, slice thickness 3±5 mm, interslice gap 0.3±0.5 mm, field of view 230±280 mm, and a 256 × 256 matrix. For proton-density and T2-weighted images, the parameters were: TR 2200±2500, TE 20/80 ms, 1 nex, slice thickness 3±5 mm, interslice gap 0.3±0.5 mm, field of view 230±280 mm and matrix 256 × 256.

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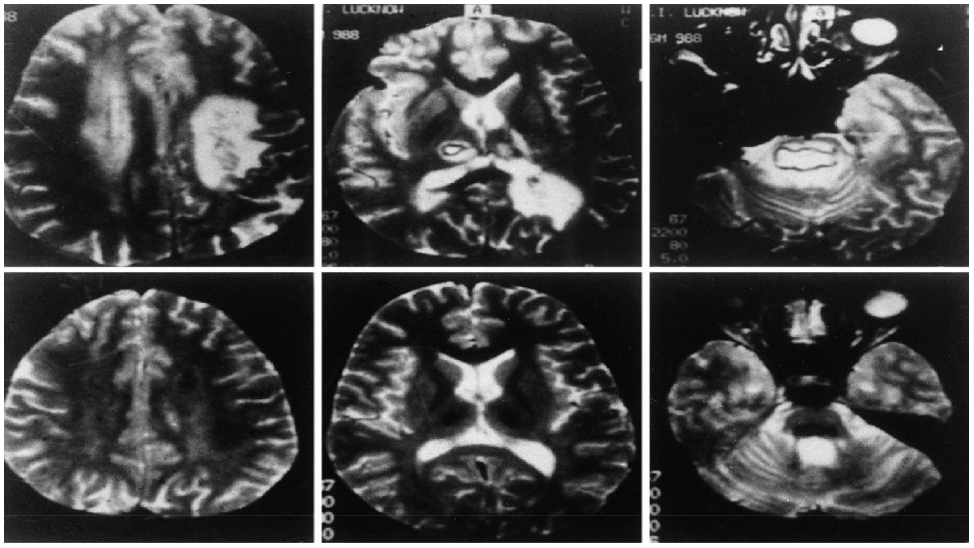
Table 1 fMRI pattern of thalamic lesions in seven patients with Japanese encephalitis (*T1W, T2W*T1-, T2-weighted,*PDW*proton density-weighted; + increased signal, ± decreased intensity, *m* mixed, * isointense)

Patient	Glasgow Coma scale	Recovery	Day of fMRI	Thalamus					
				Right			Left		
				T1w	T2w	PDW	T1w	T2w	PDW
1	4	Complete	10	+	+	+	+	+	+
2	4	partial	15	+	m	+	+	m	+
3	5	Complete	20	+	m	+	+	m	+
4	4	partial	30	+	m	+	+	m	+
5	5	partial	45	±	+	*	±	+	*
6	15	Complete	60	+	m	+	+	m	+
7	5	poor	60	±	+	+	±	+	+
8	4	poor	60	+	+	+	+	+	+

Fig:1 a,child with JE virus b, (a± b) Patient 1. Axial T2weighted images showing abnormal signal changes in acute stage (a± c) and 3 years later (d±f) There was marked reduction of signal changes in cortex thalamus and pons which were replaced by low signal at follow up (patient no. 1)

a

b



The lesions were classified as haemorrhagic or non-haemorrhagic [6].

The recovery of the patients was assessed at 3 months and classified as poor, partial or complete. Poor recovery was defined as bedridden, partial as dependence for activities of daily life, and good as complete independence. In two patients, MRI was re-peated after 3 years of illness, when the patients had

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III. RESULTS

fMRI revealed thalamic involvement in all patients. The distribution and nature of signal changes are summarised in Table 1. The lesions gave high signal on T1-weighted images in five patients, uniformly in three and with a thin high-signal rim surrounding an isointense centre in two. On T2-weighted images, these lesions had a mixed intensity pattern, the most common being a low-signal rim of varying thickness surrounding a high-signal centre (Fig. 1 b). In the other two patients, the thalamic lesions gave low signal on T1-weighted and high signal on T2-weighted images. On proton-density images, the lesions were isointense in one of these patients and gave high signal in the other.

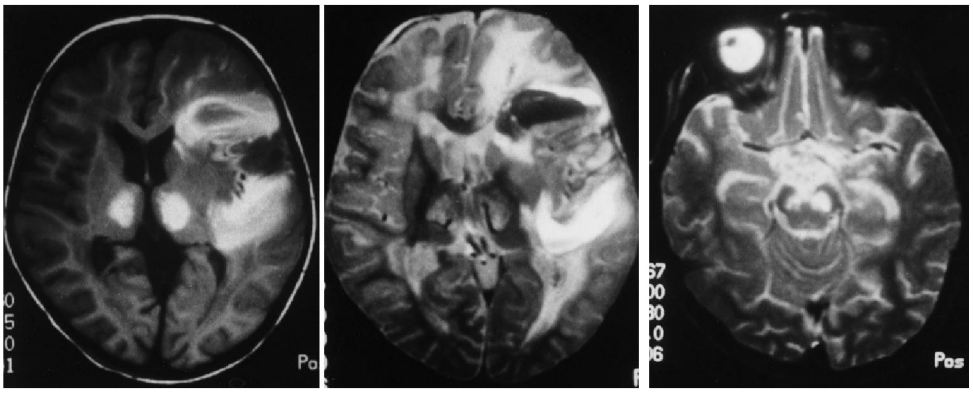

Fig. 2 a, b Patient 4. **a** T1-weighted image showing bilateral highsignal lesions in the thalamus and extensively in the left hemi-sphere. **b** T2-weighted image showing a low-signal rim surrounding high-signal lesions in the thalamus. The left frontal region gives low signal, while the temporoparietal region gives increased signal. Periventricular high signal is also seen

Fig. 3 Axial T2-weighted image showing high-signal lesions in themidbrain

Signal changes were seen in cerebral cortex in four patients and in the cerebellum in three. In three the cortical lesions (bilateral in two) gave nonspecific signal. In one patient, T1-weighted images revealed a thick high-signal rim around an isointense centre, while on T2-weighted images the periphery gave high signal with a low-signal centre in one area, and high signal on both T1- and T2-weighted images in another (Fig. 2). Cerebellar lesions were bilateral in two of the three affected patients. In one they gave high signal on T1- (Fig. 2) and low signal on T2-weighted images on both sides. In the other two, the lesions gave nonspecific signal.

The midbrain was involved in three patients, with nonspecific signal change in two of them (Fig. 3). In the third, the lesions gave high signal on both T1- and T2-weighted images. Two patients had central pontine lesions which gave high signal on T1 weighting, and had a low-signal rim around a central high-signal area on T2-weighted images (Fig. 1 c).

Lesions were seen in the basal ganglia bilaterally in one patient, giving high signal on T1-weighted images. On T2-weighting, the right-sided lesions gave low signal, while those on the left gave slightly high signal.

Cervical spinal cord involvement was present in one patient, the lesion extending over four cervical vertebrallevels. It gave high signal on T2 weighting, but was iso-intense on T1-weighted images. At least one additional site was abnormal in addition to bilateral thalamic lesions in all patients.

The lesions varied in size from 5 mm in diameter to very large areas occupying almost half a cerebral hemi-sphere. The lesions were usually rounded, but cortical lesions were irregular. White matter involvement was seen in two patients. Significant mass effect was present in only one patient. The haemorrhagic lesions displayed various stages of evolution. All but one of the patients had haemorrhagic lesions at least in one region. The haemorrhagic lesions were present on images obtained as early as 10 and as late as 60 days into the illness. However, they correlated neither with the severity of encephalitis as assessed by the Glasgow Coma Scale nor with outcome at 3 months.

fMRI in two patients after 3 years revealed marked reduction of signal changes; the residual lesions gave low signal on both T1 and T2 weighting in the thalamic and pontine areas (Fig. 1 d±f).

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IV. DISCUSSION

All our patients had bilateral haemorrhagic thalamic involvement. Other areas involved included the mid-brain, pons, cerebellum, basal ganglia, cerebral cortex and spinal cord. Our findings were consistent with the reported distribution of pathological changes [3]. In JE, diffuse meningoencephalitis affecting both grey and white matter of the cerebral hemispheres, basal ganglia, brain stem, cerebellum and thalamus has been reported in the autopsy studies [3]. Diffuse inflammatory changes are also found in the spinal cord, particularly in the lateral columns. Histology reveals cerebral oedema, con-gestion, small capillary haemorrhages and perivascular lymphocytes [3, 7]. Perivascular necrotic foci are also present. These findings however, are those of autopsy studies of patients dying of the disease.

We found a high frequency of haemorrhagic areas, especially in the thalamus [6], a finding not emphasised by other groups [8, 9]. These haemorrhagic lesions did not correlate with the severity of the illness or with the outcome. Extensive capillary haemorrhages may have been responsible for the changes we saw, which could be due to a more virulent strain of the virus. Routine CT may not reveal subacute or chronic haemorrhage, while MRI carried out within 3±4 days of the onset of disease may not reveal haemorrhagic lesions. In all our patients the initial imaging was carried out 10-60 days after the onset. In a follow-up study reported by Shoji et al. [9] MRI in three patients after 1±3 years did not reveal any haemorrhagic areas, Evidence of chronic haemorrhage can, however, persist for many years [9, 10]. In two of our patients MRI after 3 years showed marked reduction of signal changes and the lesions gave low signal on T2 weighting. These results differ from those of Shoji et al. [9], who found the lesions continued to give high signal on T2-weighted images after 1±3 years.

Haemorrhagic thalamic lesions may occur in a large number of conditions [11±14]. Tumours may be excluded on the basis of the clinical presentation. Similarly, the diagnosis of Wernicke's encephalopathy may be aided by the typical history of ethanolism with nutritional deficiency and fMRI reveals high signal on T2 weighting in the medial thalamic area [14]. Haemorrhagic thalamic infarcts have been reported in neonatal asphyxia [15, 16]. Other causes of thalamic infarcts include thrombosis of the basilar artery or its perforating branches, and deep cerebral vein thrombosis [14, 17]. Occasionally, tentorial herniation following head injury may cause thalamic infarcts [18]. Low signal in the thalamus on T2-weighted images has been reported in a variety of metabolic illnesses [19±24].

Among the viral infections involving the central nervous system, differentiation solely on imaging is difficult, with the exception of herpes simplex encephalitis with its preferential involvement of the temporal and inferior frontal lobes [25]. In mumps, demyelinated foci are scattered throughout the central nervous system

Involvement of basal ganglia along with white matter has been described in subacute sclerosing panencephalitis [27], whereas asymmetrical subcortical white matter involvement is seen in acute disseminated encephalomyelitis [28]. A periventricular white matter pattern has been described in HIV encephalitis [29].

Spinal cord involvement in JE has been reported on clinical grounds [30], histopathological changes [31] and electrophysiology [4]. In our study, only one patient had abnormal signal intensity in the spinal cord. It is possible that contrast-enhanced MRI might have revealed a greater frequency of spinal cord involvement.

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