HERPES ENCEPHALITIS IN CHILDREN*

MRI Assessment

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SUMMARY: Çakmakçı H, Kovanlıkaya A, Obuz F, Kovanlıkaya İ, Pırnar T. (Department of Radiology, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey). Herpes encephalitis in children: MRI assessment. Turk J Pediatr 1998; 40: 559-566.

The magnetic resonance imaging (MRI) findings in 14 patients with biopsy or polymerase chain reaction proven herpes simplex encephalitis were retrospectively reviewed to evaluate the diagnostic value of MRI in the early diagnosis of herpes simplex encephalitis in children. In addition to the early findings, follow-up MRI scans were obtained in four patients. Typical limbic system involvement was seen in 78 percent of the cases. Contrast-enhanced MRI was found to be superior to routine MRI sequences and computerized tomography (CT) in the early detection of inflammation. Follow-up MR images in four patients demonstrated the volume loss and late petechial hemorrhage in the involved regions. Magnetic resonance imaging is the method of choice in the diagnosis and follow-up of herpes simplex encephalitis. *Key words: magnetic resonance imaging, herpes simplex encephalitis, brain, computerized tomography.*

Herpes simplex encephalitis (HSE) is the most common cause of sporadic encephalitis in children[1,2]. In neonates, it tends to be part of a disseminated infection and can be due to either herpes simplex virus (HSV) type 1 or 2. Older infants, children, and adults get the disease localized to the CNS (central nervous system), which is almost exclusively HSV 1[2,3]. Herpes simplex virus encephalitis is characterized by a fulminant necrotizing encephalitis with petechial hemorrhage and early involvement of the medial temporal regions[4,5]. Mortality is high, approaching 70 percent. The success of antiviral treatment depends on early diagnosis and prompt institution of therapy[6]. This study aims to assess the role of magnetic resonance imaging (MRI) in the early diagnosis of this disease.

Material and Methods

Computerized tomography (CT) and magnetic resonance imaging (MRI) studies of 14 patients (8 females, 6 males) were retrospectively reviewed. The ages of the patients ranged from seven to 15 years with a mean age of 10.2 years. The most common clinical presentation was altered mental status. All patients had a MRI study within five to 10 hours of the initial clinical symptomatology. All 14 patients also had CT scans. All CT scans were performed with a GE 9800 HLA

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scanner in the axial plane with a 10 mm slice thickness. Both pre-and post-contrast images were obtained. Magnetic resonance imaging studies were done on a 1.0T Siemens magnet. Spin echo (SE) T2 weighted (TR msec/TEmsec: 2000/90) axial and pre-and post-gadolinium SE T1 weighted (TR/TE: 600/15) images in the axial and coronal planes were obtained. Four patients had follow-up MRI scans done 10 days after the onset of symptoms. Both MR and CT images were reviewed for the location, intensity/density, enhancement patterns of the lesions and the presence of hemorrhage.

Results

Unilateral temporal lobe involvement was detected in 10 of 14 patients. Bilateral temporal lobe involvement was seen in two patients and bilateral parietooccipital lobe involvement was present in two other patients. Temporal lobe dominance was 78 percent. One patient had isolated basal ganglia lesions. Computerized tomography was able to demonstrate the pathology in only eight of 14 patients (57%) (Fig. 1a). A Summary of CT and MRI findings is given in Table I. On MRI, lesions appeared hypointense on T1 weighted images and hyperintense on T2 weighted images (Fig. 1b). While no signal abnormalities were detected on the T2 weighted and non-contrast T1 weighted images of a patient (Case 11) (Fig. 2a), post-gadolinium T1 weighted images revealed impairment of the blood-brain barrier in the left parietooccipital region (Fig. 2b). Four of 14 patients had evidence of early hemorrhage on T1 weighted images (29%) (Fig. 1c). Contrast

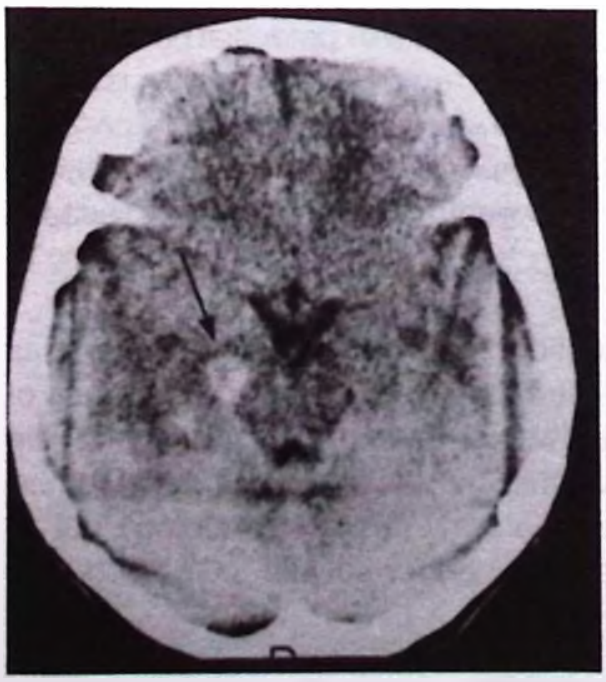

Fig. 1a

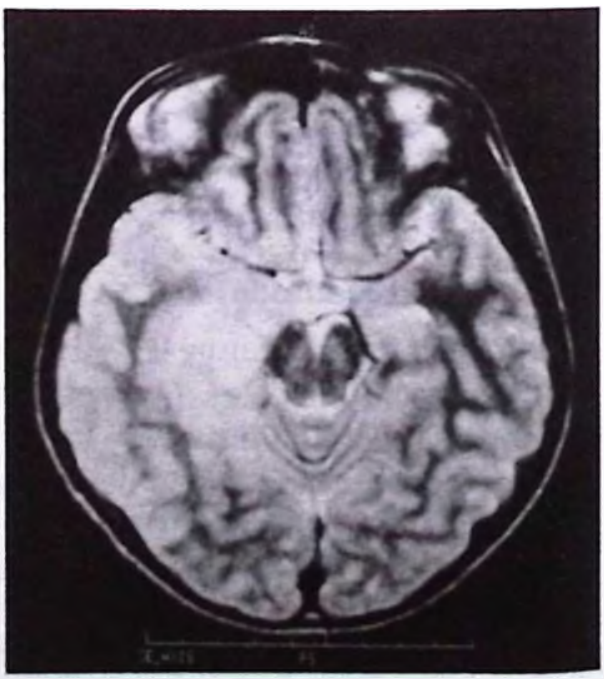

Fig. 1b

Tablo I: CT and MRI Findings of the Patient

Patient No.	Age/Sex	CT	MRI					
			Location	Intensity on T2 W1	Intensity on T1W1	Early hemorrhage	Contrast enhancement	Other
1	8/F	Normal	Right temporal	hyperintense	hypointense	–	+	
2	9/M	Pathologic	Right temporoparietal	hyperintense	hypointense	+	+	late hemorrhage
3	12/F	Normal	Left temporal	hyperintense	hypointense	–	+	
4	10/F	Pathologic	Right temporal	hyperintense	hypointense	+	+	late hemorrhage
5	7/F	Normal	Bilateral parietooccipital	hyperintense	hypointense	–	+	
6	12/M	Pathologic	Right temporal	hyperintense	hypointense	–	+	late hemorrhage
7	6/M	Pathologic	Bilateral temporal	hyperintense	hypointense	–	+	
8	15/F	Pathologic	Letf temporal	hyperintense	hypointense	+	+	
9	7/F	Normal	Left temporal	hyperintense	hypointense	+	+	late hemorrhage
10	11/F	Pathologic	Right temporal	hyperintense	hypointense	–	+	
11	10/M	Normal	Left parietooccipital	isointense	isointense	–	+	
12	13/M	Pathologic	Right temporal	hyperintense	hypointense	–	+	
13	11/M	Normal	Right basal ganglia	hyperintense	hypointense	–	+	
14	12/F	Pathologic	Right temporal	hyperintense	hypointense	–	+	

CT. computerized tomography, MRI: magnetic resonance imaging, WI: weighted image.

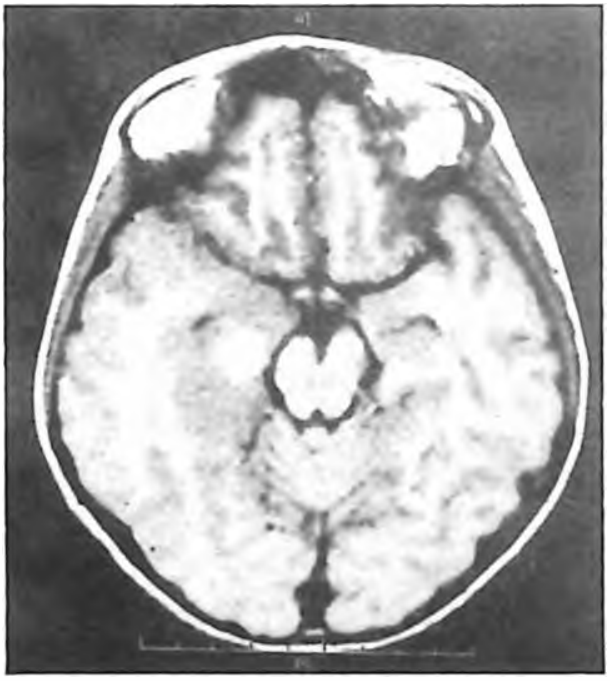

Fig. 1c

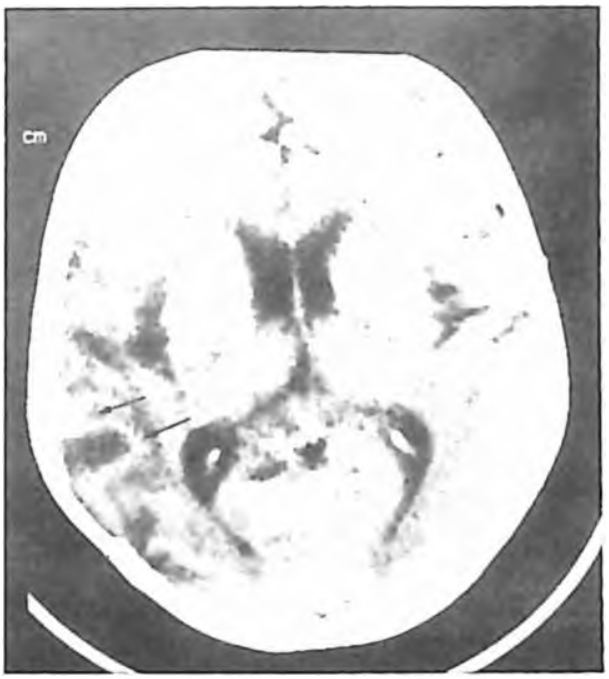

Fig. 1d

enhancement was seen in all patients. The pattern of enhancement was gyral in eight patients (Fig. 1g) and nodular in six patients. Follow-up MRI scans of the four patients demonstrated cortical atrophy and gyral hemorrhage (Figs. 1d-f). In addition to the gyral hemorrhage one patient also had hemorrhage involving the basal ganglia.

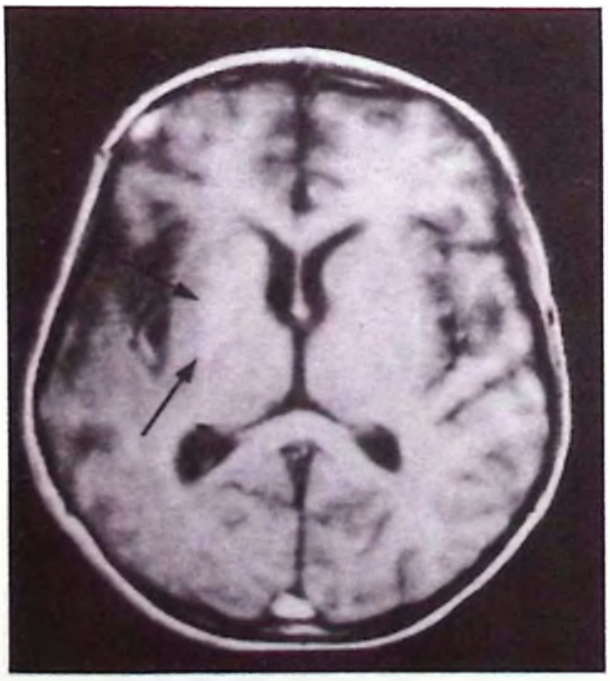

Fig. 1e

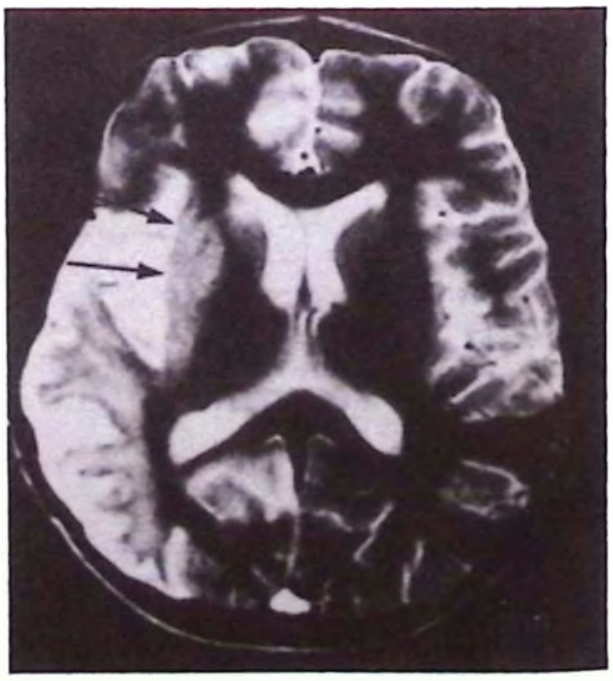

Fig. 1f

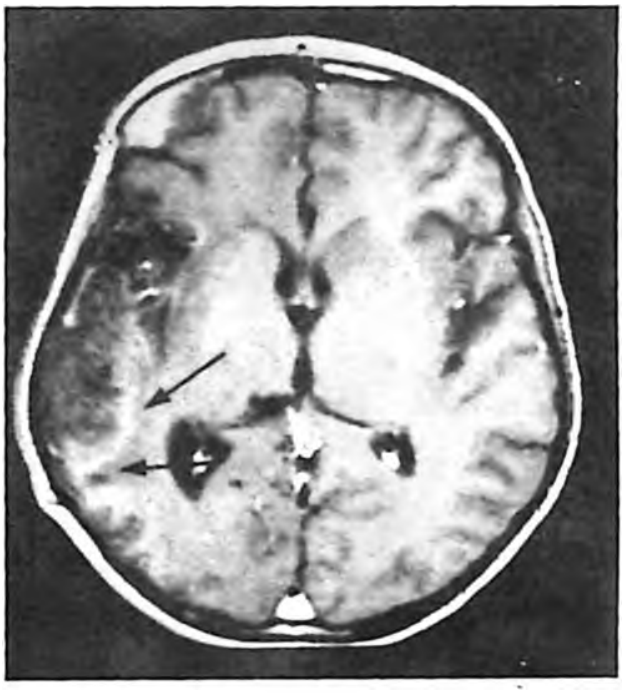

Fig. 1g

Figure 1: Case 2. Herpes virus encephalitis involving right temporoparietal lobe.
a: unenhanced axial CT scan showing early hemorrhage in the right limbic system (arrow).
b: T2 weighted axial MR image showing increased signal in the same region.
c: unenhanced T1 weighted MR image shows focal hemorrhage and sulcal effacement.
d: late follow-up unenhanced CT scan showing gyral hemorrhage in the parietal lobe (arrows).
e: late unenhanced T1 weighted MR image. f: T2 weighted MR images show basal ganglia hemorrhage (arrow) as well as postnecrotic atrophic changes within the right parietal lobe.
g: enhanced T1 weighted MR image also showing gyral enhancement (arrows).

Discussion

Diagnosis of herpes simplex encephalitis is crucial because the success of antiviral treatment depends on the early diagnosis of the disease[6]. The workup for suspected herpes encephalitis may include cerebrospinal fluid (CSF) studies, especially polymerase chain reaction (PCR) in CSF; electroencephalography (EEG); computed tomography (CT); magnetic resonance imaging (MRI); single photon emission computed tomography (SPECT); and brain biopsy[7-10]. Initial CSF profile can show increased or normal white blood cells, usually with mononuclear predominance, and elevated protein. Glucose is usually normal[1]. Blood and CSF antibody titers against HSE do not increase until the second or third week of illness. A rapid diagnostic test would offer immense advantages in care of these patients. The use of PCR to detect HSV in CSF within 25-45 hours has therefore been an exciting breakthrough in recent years. Polymerase chain reaction uses oligonucleotide primers to probe and amplify a portion of the HSV DNA polymerase gene which then can be detected by gel

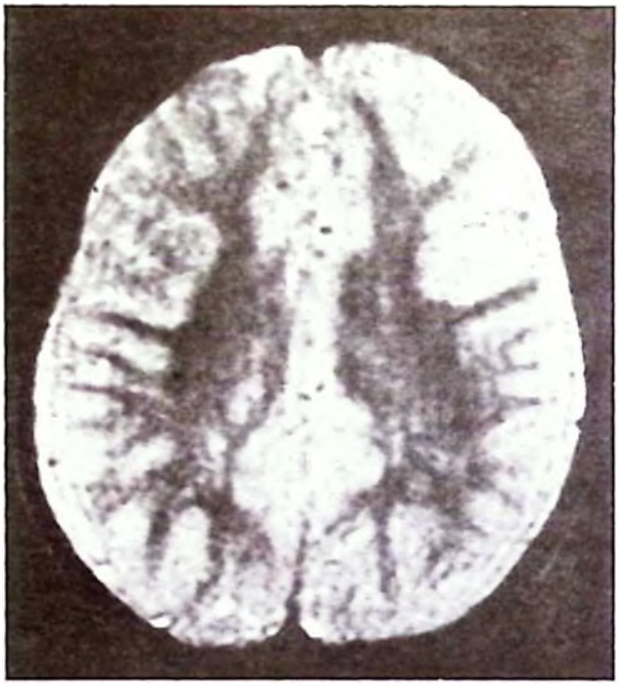

Fig. 2a

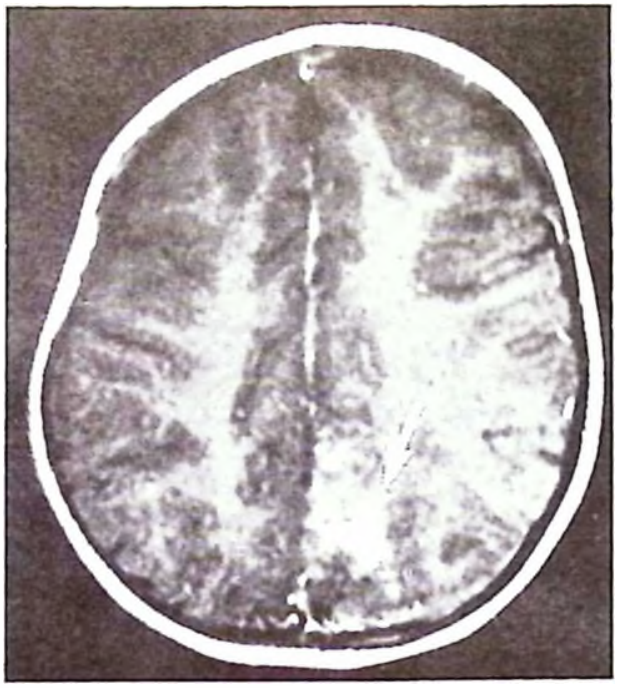

Fig. 2b

Figure 2: Case 11. Herpes virus encephalitis involving left parietooccipital lobe.
a: T2 weighted axial image showing no signal change in the affected area.
b: enhanced T1 weighted axial MR image showing disrupted blood-brain barrier due to infection in the corresponding region (arrow).

electrophoresis. The primer used in most reports will detect DNA of both HSV-1 and-2, but it does not cross-react with other herpes viruses, including Epstein-Barr virus, cytomegalovirus, Varicella, and HSV-6[7].

A characteristic temporal EEG focus and appropriate clinical signs and symptoms of acute encephalitis are indicative for HSE. However, EEG abnormalities are not consistently characteristic[1,6].

The most common CT findings in HSV infections are a poorly marginated hypodense area, mass effect and nonhomogeneous contrast enhancement. Low density usually centered in the temporal (limbic system) and frontal lobes may extend to involve cingulate gyrus, thalamus, and deep frontal and occipital lobes. Early CT scans may be inconclusive due to partial volume or beam hardening artifacts in the temporal fossa[2,5]. In this study, early CT examination demonstrated the pathology in only 57 percent of the cases.

The multiplanar capability of MRI allows a fast and accurate assessment of the temporal lobe. Subtle gyral effacements in the temporal lobe can easily be detected in the coronal plane. Because encephalitis leads to a rapid increase in water content, the involved brain parenchyma appears mildly hypointense on

T1 weighted images and markedly hyperintense on T2 weighted images. An abrupt transition to normal density at the lateral margin of the lenticular nucleus sparing the putamen has been a characteristic feature of herpes encephalitis on MRI[2-4]. Disruption of blood-brain barrier results in parenchymal and meningeal contrast enhancement on T1 weighted images[11]. In this study, with the exception of one patient, parenchymal involvement manifested as hypointensity on T1 weighted images and hyperintensity on T2 weighted images. The non-contrast T1 weighted images and the T2 weighted images were negative in a patient (Case 11) with a highly suspected clinical history of herpes encephalitis. However, the post-contrast images revealed the disruption of the blood-brain barrier in the left parietal lobe, which is a hallmark of the disease (Fig. 2). It should be noted that new sequences such as FLAIR (fluid attenuated inversion recovery) demonstrate the pathological changes much better than spin echo sequences[8,9].

Typical necrotizing HSE affects the limbic temporal lobe. Involvement of neurons through axonal transport of the virus may explain the systemic and even transhemispheric extension of the inflammation via the limbic pathways. The temporal lobe preference which was a dominant feature in this study (78%) appears to remain one of the most useful distinguishing features in addition to its bilaterality. Isolated basal ganglia and parietooccipital lobe involvement were also seen.

In the subacute phase, parenchymal petechial hemorrhage, which is consistently seen on pathological specimens, was rarely seen on CT images but may be more readily detected on MRI[2-5]. In this study, follow-up MRI demonstrated encephalomalacia and gyral and basal ganglia hemorrhages in four patients.

Recent SPECT studies suggest that an increased radionuclide uptake in the limbic temporal lobe and anterior basal ganglia in patients with acute encephalitis reflects distinct pathomorphological features in HSE rather than coincidental features[10].

The diagnosis of HSE may be delayed due to the non-specific nature of the earliest symptoms. Initially, CT findings may be equivocal, and the wait for serological results protracted. Magnetic resonance imaging is the most sensitive imaging modality in the early diagnosis of herpes encephalitis.

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