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Magnetic resonance imaging of limbic encephalitis

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Summary. In two patients with limbic encephalitis serial magnetic resonance (MR) imaging showed evolution of abnormal high-signal intensity in both hippocampal formations on T2-weighted images.

Key words: Magnetic resonance imaging – Encephalitis – Limbic system

Limbic encephalitis was initially described in 1960 as a subacute encephalitis predominantly involving the limbic system [1] and frequently associated with malignant tumors [2]. This disorder has previously been diagnosed on clinical and pathological grounds. Its MR findings have been described in a limited number of reports [3–8]. Two cases of limbic encephalitis whose serial MR imagings documented the evolution of the lesions are reported here.

Case reports

Case 1

This 34-year-old woman presented with dysphagia, lethargy and diplopia. She also complained of diminished job performance, citing forgetfulness and disorientation. Neuropsychiatric testing revealed limited recall of recent events. Neurological examination was normal except for left lateral rectus paresis. Head CT was normal. Cerebrospinal fluid (CSF) showed mild lymphocytic pleocytosis. Oligoclonal band tests for infectious diseases were all negative. Initial T2-weighted spin echo (SE) MR showed abnormal high-signal intensity along the orbital surface of the left frontal lobe (Fig. 1 a, b). No abnormalities were detected in either temporal lobe.

Chest radiography and CT revealed a mediastinal mass suggestive of thymoma. Tensilon test revealed moderate subjective improvement of dysphagia and diplopia. A malignant thymoma was partially resected.

Following surgery, the patient became more disoriented and experienced severely impaired short- and long-term memory. A second T2-weighted MR 2 weeks after her first showed abnormal increased signal in the hippocampal formations, predominantly on the right (Fig. 1 c). There was no abnormal enhancement after IV administration of gadopentetate dimeglumine (Gd-DTPA). The abnormal signal intensity previously noted in the left frontal lobe had nearly resolved (Fig. 1 d). Open biopsy of the right hippocampus revealed a mild mononuclear infiltration of the subarachnoid space with reactive astrocytes, rod cells and clustering of microglia in the subjacent cortex (Fig. 1 e). Scattered neurons acute ischemia and edema. No inclusion bodies were observed. No immunoreactivity for the herpes simplex virus (HSV I/II) was detected immunocytochemically. Meningoencephalitis was diagnosed. A third MR 2 weeks after the biopsy showed nearly complete resolution of the high-intensity lesions in the hippocampal formations (Fig. 1 f).

Case 2

This 55-year-old woman had a 2-week history of temporal lobe seizures and progressive alteration in her mental status. Mastectomy had been performed for breast cancer 15 years prior to admission, but without recurrence or metastasis. Neuropsychological examinations revealed moderately impaired recent and mildly impaired remote memory. She had no abnormal neurological signs. CSF revealed mild lymphocytic pleocytosis and slightly elevated protein. All examinations for infectious disease were negative. Initial CT and MR revealed a small enhancing lesion attached to the falx, compatible with a meningioma. No abnormalities were observed in either temporal lobe (Fig. 2 a). Follow-up MR 16 days later showed abnormal high-signal intensity in the right hippocampal formation (Fig. 2 b). A third MR with coronal T2-weighted images performed 5 days after the second showed high-signal intensity in the hippocampal formations bilaterally and symmetrically (Fig. 2 c). Open biopsy of the right hippocampal formation disclosed meningoencephalitis histo-

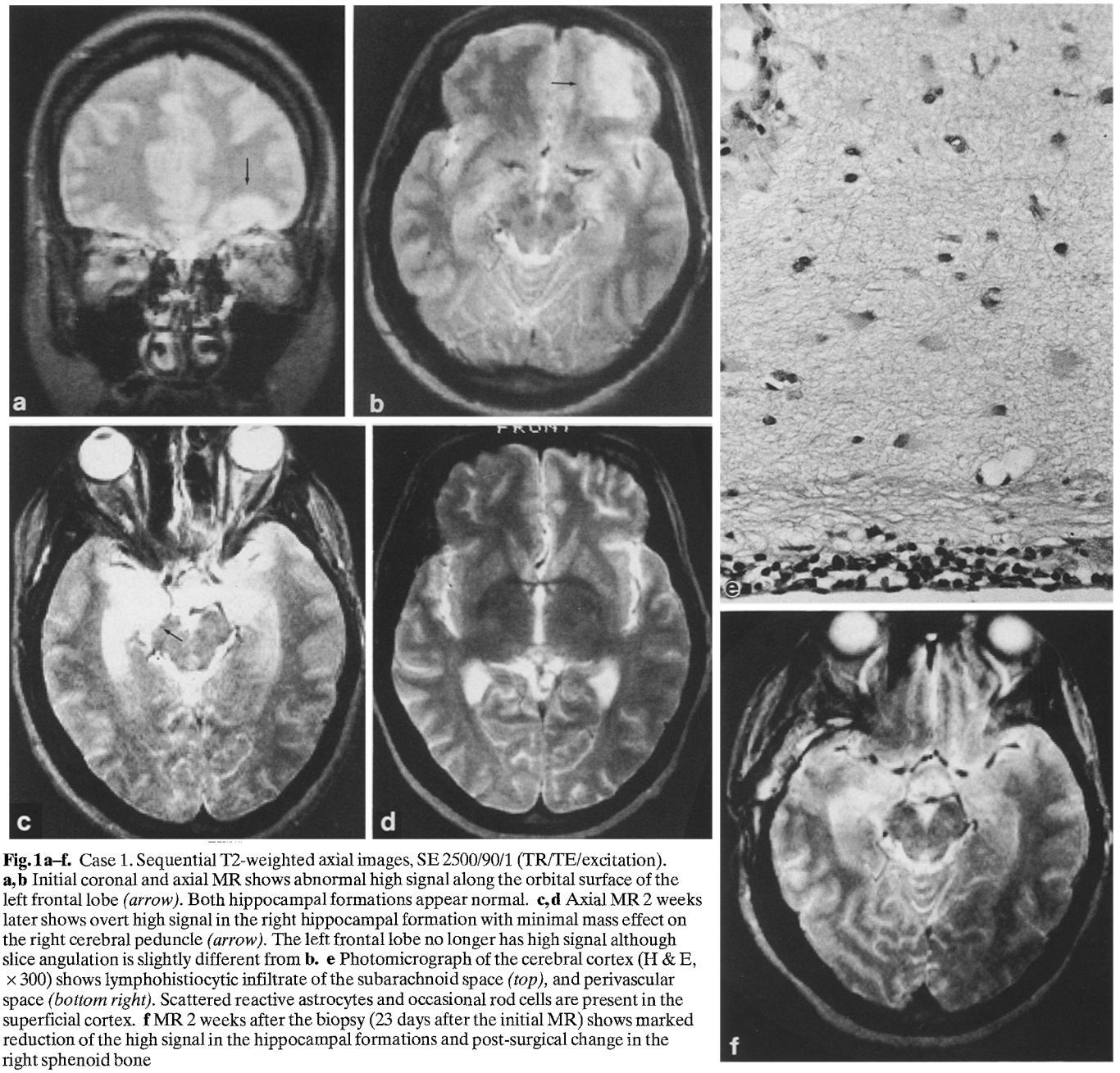

Fig. 1a–f. Case 1. Sequential T2-weighted axial images, SE 2500/90/1 (TR/TE/excitation). **a,b** Initial coronal and axial MR shows abnormal high signal along the orbital surface of the left frontal lobe *(arrow)*. Both hippocampal formations appear normal. **c,d** Axial MR 2 weeks later shows overt high signal in the right hippocampal formation with minimal mass effect on the right cerebral peduncle *(arrow)*. The left frontal lobe no longer has high signal although slice angulation is slightly different from **b.** **e** Photomicrograph of the cerebral cortex (H & E, × 300) shows lymphohistiocytic infiltrate of the subarachnoid space *(top)*, and perivascular space *(bottom right)*. Scattered reactive astrocytes and occasional rod cells are present in the superficial cortex. **f** MR 2 weeks after the biopsy (23 days after the initial MR) shows marked reduction of the high signal in the hippocampal formations and post-surgical change in the right sphenoid bone

pathologically similar to that of case 1. No organisms or inclusion bodies suggestive of viral encephalitis were detected. No immunocytochemical reactivity for HSV (I/II) was noted. The patient's mental status was stable throughout the hospital course. She was discharged because of the lack of seizures. Follow-up MR 3 months after the biopsy showed only subtle high-signal intensity in the right hippocampal formation (Fig. 2 d).

Discussion

Limbic encephalitis is a rare paraneoplastic disorder most commonly associated with lung cancer, especially with small-cell carcinoma [8]. However, an identical clinical and pathological syndrome has also been noted in the absence of cancer [5, 8, 9]. The hallmarks of this disease are changing mental status consisting of affective symptoms and striking memory impairment. Hallucinations and overt psychosis are less common. CSF often reveals lymphocytic pleocytosis and elevated protein [3]. No spontaneous clinical remissions have been reported, but treatment of the primary malignancy may reverse the course of this syndrome [4, 8]. Histopathologically, neuronal loss with reactive gliosis, perivascular monocytic infiltration and microglial nodules are observed predominantly in the hippocampal formations, amygdalae and other medial temporal lobe structures [8]. The clinical features, CSF findings, and histopathology of our patients were compatible with limbic encephalitis, although there was no

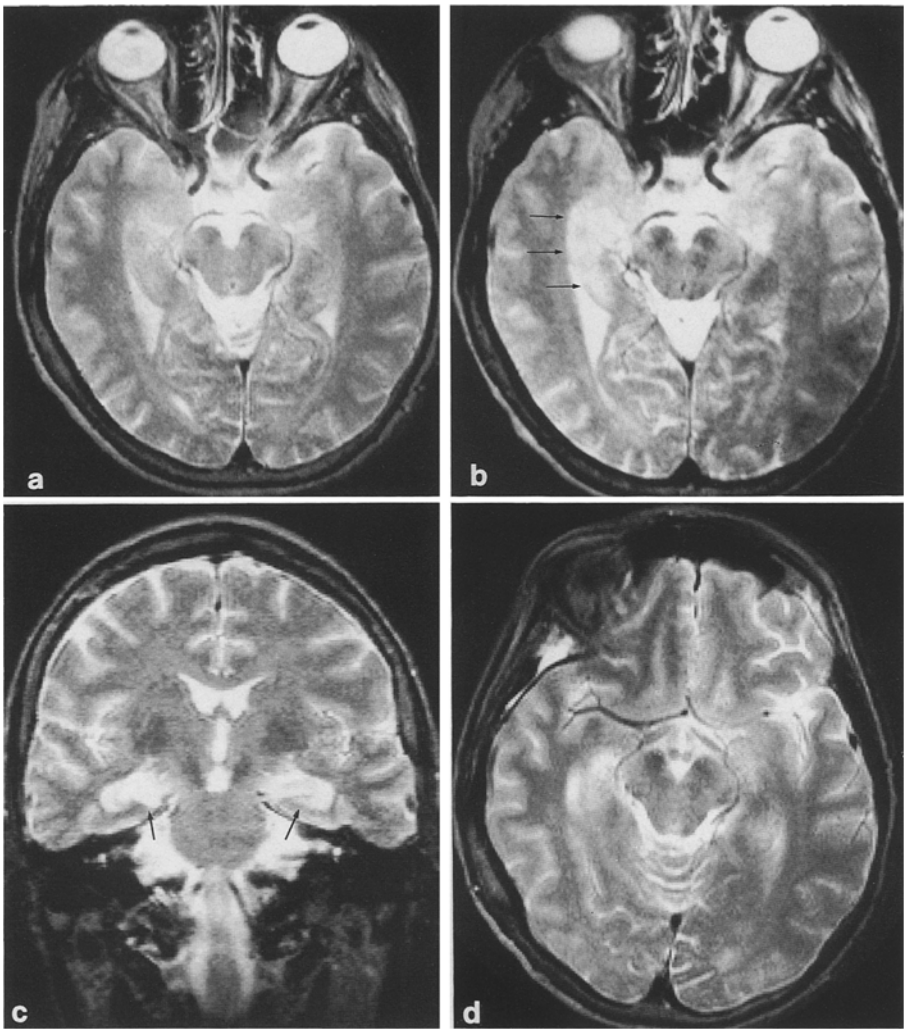

Fig. 2 a–d. Case 2. Sequential T2-weighted images, SE 2500/90/1. **a** Both temporal lobes are normal on the initial scan. **b** Axial MR 16 days later shows abnormal high signal in the right hippocampal formation *(arrows)*. **c** Coronal MR 5 days later demonstrates symmetrical high signal in both hippocampal formations *(arrows)*. **d** MR 3 months later shows only subtle high signal in the right hippocampal formation and post-surgical change in the right sphenoid bone. Coronal T2-weighted images were not obtained during that study

evidence of a malignant neoplasm in case 2, except for a past history of breast cancer.

Neuroimaging played little role in the diagnosis of limbic encephalitis during the CT era. CT studies were normal or showed only mild ventricular dilatation in most reported cases [5–8, 10–12]. The initial CT of one patient showed an enhancing lesion in the right temporal lobe; follow-up CT 10 months later showed low attenuation in both medial temporal lobes [4]. MR imaging has proven helpful for the diagnosis of temporal lobe lesions [13]. Literature review revealed only six cases of limbic encephalitis with MR imaging (Table 1). MR failed to show abnormalities compatible with limbic encephalitis in three patients [3, 7, 8]. MR obtained in the later phase of one patient showed only temporal lobe tissue loss [4]. MR revealed abnormal signal intensity in the medial temporal lobes bilaterally in only two of the six patients [5, 6]. The most striking T2-weighted MR findings in the previously reported cases, as well as our own, are the high-signal intensities in both medial temporal lobes, including the hippocampal formations and amygdalae. The cortex was predominantly involved, and there was little or no mass effect in the surrounding structures. Involvement of the insula, cingulate gyrus, pyriform cortex, orbital surface of the frontal lobe, and the hypothalamus in limbic encephalitis has been reported pathologically [8]. However, successful display of the involvement of these structures, as shown in our first case, has not previously been documented in the radiological literature.

Initial MR imaging failed to demonstrate temporal lobe abnormalities in both of our patients. Abnormal signal intensity first appeared in the hippocampal formations on follow-up MR examinations. From these findings, we conclude that the clinical symptoms of limbic encephalitis can present at a time when inflammatory changes are too mild to produce abnormal signals on MR images. Therefore, repeat MR examination is mandatory even if the initial study fails to reveal any abnormalities. Furthermore, our present cases suggest that the inflammation in limbic encephalitis does not necessarily occur simultaneously throughout the brain, and acute inflammatory changes can resolve without any residual radiologically detectable abnormalities. The latter does not necessarily imply that microscopic abnormalities are absent.

Differential diagnosis of limbic encephalitis from gliomatosis cerebri may be difficult on the basis of MR images alone. Bilateral temporal lobe involvement has been reported in gliomatosis cerebri. The gray matter can be in-

Table 1. MR findings in reported and present cases of limbic encephalitis

Authors	Age/sex	Associated cancers	CT findings	MR findings
Camara et al. [3] (1987)	61F	Lung	Normal	Normal
Burton et al. [4] (1988)	26M	Testis	Enhancing lesions in the temporal lobes	Volume loss in the temporal lobes[a]
Kohler et al. [5] (1988)	52M	None	Normal	High intensity in both medial temporal lobes on T2W
Lacomis et al. [6] (1990)	42F	Breast	Normal	High intensity in both medial temporal lobes on T2W, CE (–)
Ingenito et al. [7] (1990)	59M	Benign thymoma	Normal	Normal
Newman et al. [8] (1990)	76M	Lung, kidney	Normal	Normal
Kodama et al. (1991)	34F	Malignant thymoma	Normal	High intensity in left frontal lobe cortex on initial T2W, and high intensity in both hippocampal formations on T2W of second MR
	55F	None	Normal	High intensity in both hippocampal formations on T2W, CE (–)

[a] MR 1 year after completion of all therapy
T2W: T2 weighted images; CE (–): no abnormal enhancement on Gd-DTPA

volved as well as the white matter [14]. Bilateral temporal lobe involvement can also occur in viral encephalitis such as herpes encephalitis [15]. Indeed, the neuropathological findings of limbic encephalitis can simulate those of viral encephalitis. Based on the latter findings, a viral etiology has been suggested for limbic encephalitis, although direct evidence of viral infection has not been demonstrated [8, 16].

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