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Case Report

Disabling amnestic syndrome following stereotactic laser ablation of a hypothalamic hamartoma in a patient with a prior temporal lobectomy☆

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ABSTRACT

A 19-year-old man with cortical dysplasia and intractable focal seizures underwent a right temporal lobectomy. A hypothalamic hamartoma was subsequently recognized, and he then underwent MRI-guided stereotactic laser ablation. Unfortunately, he sustained damage to the bilateral medial mammillary bodies and suffered significant memory loss. We review laser ablation therapy for hypothalamic hamartomas and the anatomy of the memory network. We postulate that his persistent memory disorder resulted from a combination of the right temporal lobectomy and injury to the bilateral medial mammillary bodies.

1. Introduction

One-third of patients with epilepsy have seizures that are resistant to pharmacological therapy [1]. Resective surgery is effective for patients with pharmacoresistant epilepsy who have a localized area of epileptogenic tissue in noneloquent cortex. Hypothalamic hamartomas are a rare cause of intractable epilepsy [2]. These masses of disorganized neuronal tissue are usually associated with gelastic seizures, intellectual disabilities, and behavioral changes. Tissue destruction can achieve seizure freedom rates ranging from 30 to 50% in mixed adult–pediatric populations [3]. A recent series of 14 patients treated with MRI-guided stereotactic laser ablation of hypothalamic hamartomas achieved seizure freedom in 86% with a mean follow-up of nine months [4]. None of these patients suffered focal neurological deficits, neuroendocrine disturbances, or memory losses.

We present a young man who underwent MRI-guided stereotactic laser ablation of a hypothalamic hamartoma following a right temporal lobectomy for resection of a focal cortical dysplasia. His case illustrates the need to assess for dual pathology in treatment of pharmacoresistant epilepsy and the potential complications of MRI-guided stereotactic laser ablation.

2. Case presentation

A 19-year-old right-handed man had attention deficit disorder and treatment-resistant focal epilepsy with weekly seizures (behavioral arrest, incomprehensible speech, and postictal confusion) since the age of nine. Seizures persisted despite trials with 12 antiepileptic drugs used in up to three-drug combinations, steroids, intravenous gamma globulin, modified Atkin's diet, and a vagus nerve stimulator.

On video-EEG, seizures involved bilateral changes evolving more over the right hemisphere. Magnetoencephalography showed multifocal bilateral polyspike-and-wave discharges as well as right frontal–temporal–occipital discharges. Magnetic resonance imaging demonstrated a subtle cortical abnormality in the right insula and frontal operculum, with subtle atrophy of the right fornix and mammillary body. Positron emission tomography showed mild hypometabolism in the right anteromedial temporal lobe.

Neuropsychological testing targeting delayed memory recall showed Story Memory Delayed Recall (DR) 50th percentile, List Learning DR 75th percentile, and Figure Copy DR 14th percentile (Table 1). Intracarotid amobarbital testing revealed left language dominance and right hemispheric memory impairment (right hemisphere memory [left injection] score: 7/12; left hemisphere memory [right injection] score: 12/12).

When the patient was 17 years old, intracranial EEG monitoring with right hemispheric grids, strips, and depths captured 49 seizures: 32 had broad onset over the right lateral–temporal, mesial temporal, frontal, and occipital lobes and insula, while 17 arose from depth electrodes in the right posterior mesial temporal lobe. He underwent resection of the right lateral temporal and mesial cortex, along with

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Table 1
Memory recall across neuropsychological assessments.

	Story Memory IR	Story Memory DR	List Learning IR	List Learning DR	Figure IR	Figure DR
Before surgery	37th percentile	50th percentile	75th percentile	75th percentile	7th percentile	14th percentile
After temporal lobectomy	–	–	35th percentile	50th percentile	18th percentile	18th percentile
After ablation surgery	1st percentile	<1st percentile	2nd percentile	1st percentile	–	1st percentile
After ablation, 8-month follow-up	14th percentile	2nd percentile	18th percentile	<1st percentile	–	<1st percentile

Note: IR = immediate recall, DR = delayed recall. All scores represent percentile ranks.

the inferior insula and frontal operculum. Neuropathology showed Type I microdysplasia.

After surgery, he experienced less intense, briefer simple partial seizures twice daily. He remained active in varsity lacrosse, maintained a 3.5 GPA in a competitive high school, had a close circle of friends, and was accepted to his first-choice college. A brief neuropsychological screen revealed List Learning DR 50th percentile, Figure Copy immediate recall (IR), and DR 18th percentile (Table 1).

When he was 18, repeat MRI demonstrated the right temporal lobectomy and now an 8-mm hypothalamic hamartoma on the right, not recognized on multiple previous MRI studies (Fig. 1A). In retrospect, the patient now admitted that his seizures both before and after the lobectomy included mirthless laughter. He was referred to a center with expertise at MRI-guided stereotactic laser ablation and underwent this procedure.

A severe impairment of memory and attention was observed immediately after laser ablation. He reported feeling as though he was in a dream with events happening in a disjointed fashion. Three weeks postoperative, he required hospitalization for agitation and suicidal ideation and was diagnosed with a severe amnestic syndrome with confabulation. Video-EEG monitoring captured several complex partial seizures with impaired responsiveness and bilateral ictal discharges.

Repeat MRI showed not only successful ablation of the hamartoma but also unexpected contrast enhancement that crossed the midline involving the bilateral medial mammillary bodies and adjacent anteromedial left thalamus (Fig. 1B). There was persistent right fornix and mammillary body atrophy. Neuropsychological testing (Table 1) revealed a dense anterograde amnesia (Story Memory IR 1st percentile, DR 0.1 percentile; List Learning IR 2nd percentile, DR 1st percentile; and Figure Copy DR 1st percentile), with impaired attention and processing speed. These findings were attributed to bilateral mammillary body involvement.

He underwent intense cognitive and psychological rehabilitation. Neuropsychological testing (Table 1) eight months after hamartoma ablation demonstrated improved attention, concentration, and immediate recall but severe deficits in delayed recall (Story Memory IR 13th percentile, DR 2nd percentile; List Learning IR 18th percentile, DR <0.1 percentile; and Figure Copy Memory DR <0.1 percentile). Clinically, he has a disabling amnestic syndrome. He deferred his college education plans and is unable to drive because of ongoing seizures.

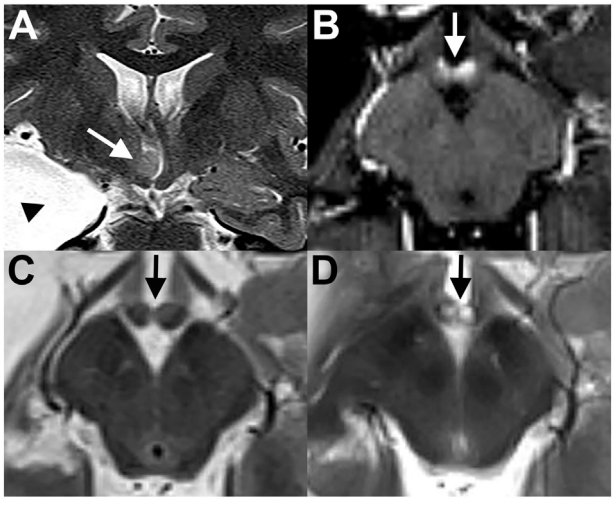

Fig. 1. Coronal T2-weighted MRI demonstrating prior right temporal lobectomy (black arrowhead) and ectopic gray matter along the right lateral wall of the hypothalamus (white arrow) (A). There is also subtle right mammillary body atrophy at this time. Panels B and C show cropped axial postcontrast T1 and axial T2 of the midbrain and mammillary bodies 3 weeks after successful MRI-guided laser ablation of the hypothalamic hamartoma. There is new enhancement (white arrow, panel B) and subtle T2 hyperintensity in the medial aspects of both mammillary bodies (black arrow, panel C) concerning perioperative tissue injury. Follow-up axial T2 MRI 6 months later shows abnormal T2 hyperintensity and atrophy of both mammillary bodies (black arrow, panel D), confirming that significant tissue injury occurred.

3. Discussion

Hypothalamic hamartomas are nonneoplastic developmental lesions with disorganized normal-appearing neurons. They cause medically refractory epilepsy associated with some combination of gelastic and other seizure types, cognitive impairment (epileptic encephalopathy), and behavioral changes including aggression. Removal or destruction of the hamartoma can control seizures and improve cognition [2], especially in children. Only a third of adults achieve seizure freedom with surgery [5].

Magnetic resonance imaging-guided laser ablation is a minimally invasive technique that uses MRI-guided placement and application of thermal heat to destroy a tissue focus [6]. Among 14 patients with medically refractory epilepsy due to hypothalamic hamartoma who underwent stereotactic laser ablation, 11 (79%) became seizure-free after a single treatment; another patient became seizure-free after a second ablation (12/19; 86%) [4]. There were no surgical complications previously associated with traditional operative techniques, such as neuroendocrine disturbances, visual changes, or hemiparesis. No patient suffered memory impairment.

Our patient's case is the first reported serious complication of MRI-guided stereotactic laser ablation of hypothalamic hamartoma. The presence of bilateral postoperative changes in the mammillary bodies suggests that the laser ablation may have been sufficient to account for his deficits. However, his prior right temporal lobectomy may have influenced the postoperative cognitive changes. One group [7] reported on a patient who also presented with such dual pathology: a 35-year-old man who underwent removal of a left temporal subarachnoid cyst and resection of temporal neocortex for treatment of intractable complex partial seizures. These did not recur, but he subsequently presented with status gelasticus. Similar to our patient, targeted questioning revealed that he had always experienced short outbursts of "genuine" laughter, which he had not felt was abnormal. Postoperative MRI, ictal PET, and SPECT revealed an 8-mm hypothalamic hamartoma retrospectively present on preoperative scanning. Gelastic seizures were controlled with medication.

Three other patients underwent partial or total resection of a hypothalamic hamartoma and later had temporal lobectomies [3,8]. In two of these cases, there were no pathological abnormalities found in the resected temporal lobe tissue [3]; pathology in the third case is not

described [8]. Secondary epileptogenesis was postulated as the cause of the temporal lobe focus after removal of the hypothalamic hamartoma [3]. Transient memory loss (two months) following lesionectomy of the hamartoma was seen in one of the cases but did not worsen further after the temporal lobectomy. By contrast, a fourth patient had mesial temporal sclerosis and a 5-mm hypothalamic hamartoma and presented with epigastric rising sensation, dizziness, and fear [9]. Video-EEG recording localized seizure onset to the right temporal lobe, and she became seizure-free after a right temporal lobectomy.

Gelastic seizures not only are associated with hypothalamic hamartomas but also occur with seizure foci due to diverse pathologies, including focal cortical dysplasias in the temporal [10,11], frontal [12,13], and parietal lobes [10,14,15]. Our case was unique in having both a hypothalamic hamartoma and pathologically confirmed focal cortical dysplasia. The hypothalamic hamartoma was missed at several academic medical centers but was present before the right temporal lobectomy, although subtle. Mild brain shift from the original resection widened the appearance of the third ventricle and made the hamartoma obvious. Our patient's original seizures may have been attributable to the right temporal focal cortical dysplasia, the hypothalamic hamartoma, or a network involving the two abnormalities.

Our case illustrates the effects of graded interventions involving the temporolimbic system on memory. Anterograde amnesia can result from disruption of mesial temporal lobe structures or the mesial diencephalon [16,17]. Diencephalic (mammillary bodies and medial thalamus) pathology can result from alcoholism, malnutrition, infection, trauma, or infarct [17–19]. Selective involvement of the mammillary bodies can cause Korsakoff's syndrome [20]. However, many cases show damage involving other portions of the memory network, including the hippocampus. Our case is unique since anterograde amnesia resulted from a right temporal lobectomy followed by an ablative lesion that unfortunately extended into both medial mammillary nuclei with greater involvement contralateral to the lobectomy. It is likely that the bilateral nature of the temporal–diencephalic lesion led to amnesia. The role of the prior temporal lobectomy in the amnesia is uncertain.

This case illustrates the potential for severe memory deficits following laser ablation of hypothalamic hamartomas. The dangers may be greatest in patients with normal or high intellectual function. Since many children who undergo this procedure are very young or have moderate-to-severe intellectual disability, it may be difficult to assess memory function in these individuals. It is worthwhile to consider dual pathology in epilepsy and the potential morbidity of MRI-guided laser ablation of hypothalamic hamartomas, especially in a patient with a prior temporal lobectomy.

Disclosure

None of the authors has any conflict of interest to disclose.

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