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# Unusual Findings in Brain Biopsies of Two Patients with Acute Magnetic Resonance Imaging Lesions Associated with Focal Seizures

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**Summary**: *Purpose:* Patients with focal seizures often have magnetic resonance imaging (MRI) abnormalities in the brain region of their presumed seizure focus. Neoplasms, ischemic infarctions, inflammatory processes, and other specific pathologic entities have been diagnosed by biopsies of such MRI abnormalities. Two patients with this presentation had brain lesion biopsies with a leading presumptive diagnosis of glial neoplasm but were found to have indistinct histopathology.

*Methods:* Each patient was initially seen with focal seizures (right parietal region, right hippocampus) corresponding with focally increased $T_2$ signal on MRI. In both patients, the preoperative clinical suspicion was for neoplastic or inflammatory processes.

*Results:* Several weeks after seizure onset, craniotomy in patient 1 and stereotactic needle biopsy in patient 2 revealed mild gliosis with reactive vascular changes and perivascular hemosiderin deposition, not diagnostic of but compatible with venous congestion (or possibly venous thrombosis). Postoperatively, patient 1 had brief sensory seizures that stopped 5 months after surgery, whereas subsequent seizures did not develop in patient 2. Both patients had normalization of their MRI (except for postoperative changes) and have remained seizure free.

*Conclusions:* We describe two patients who had brain biopsies of striking focal increased $T_2$ signal MRI abnormalities associated with seizures. Pathologic findings contradicted our preoperative suspicions (neoplasm or inflammatory process), compatible with (but not conclusive for) subacute venous congestion/thrombosis. These findings indicate that patients with seizures may have an associated discrete intraaxial MRI lesion that is not neoplastic. To our knowledge, this is the first report of focal seizure–associated MRI lesions with biopsy findings compatible with venous congestion/thrombosis.
**Key Words:** Focal epilepsy—Magnetic resonance imaging—Biopsy—Venous thrombosis.

Patients with focal seizures often have magnetic resonance imaging (MRI) abnormalities in the brain region of their presumed seizure focus (1–5). Multiple pathologic entities have been diagnosed by biopsies of such MRI abnormalities, including neoplasms, vascular malformations, ischemic infarctions, hemorrhages, cortical dysplasia, inflammatory processes, and demyelinating diseases (6–10). Recently at our medical center, two patients with this presentation had brain lesion biopsies with presumptive diagnosis of glial neoplasm versus inflammatory process and were subsequently found to have indistinct histopathology.

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## Presentation and intervention

*Case 1*

Our first patient was a 38-year-old woman with a history of focal-onset seizures and normal MRI in 1995. Seizures were controlled on antiepileptic medication (AED) through 2000, and then medication was discontinued. Seizures recurred in January 2004, manifesting as nocturnal convulsions 8 days and 5 days before her MRI. Over the 24-h period before her MRI, she experienced a flurry of sensorimotor seizures involving her left hand and face. The sensorimotor seizures each lasted ~30 s but recurred every 30 min for a number of hours. MRI showed a sharply defined increased $T_2$-signal right parietal lesion (extending into the primary sensory cortex) with no definite gadolinium enhancement (Fig. 1). Clinical suspicion was highest for intraaxial neoplasm (inflammatory process was thought to be a less likely possibility), and the patient was recommended for surgery. The goal of

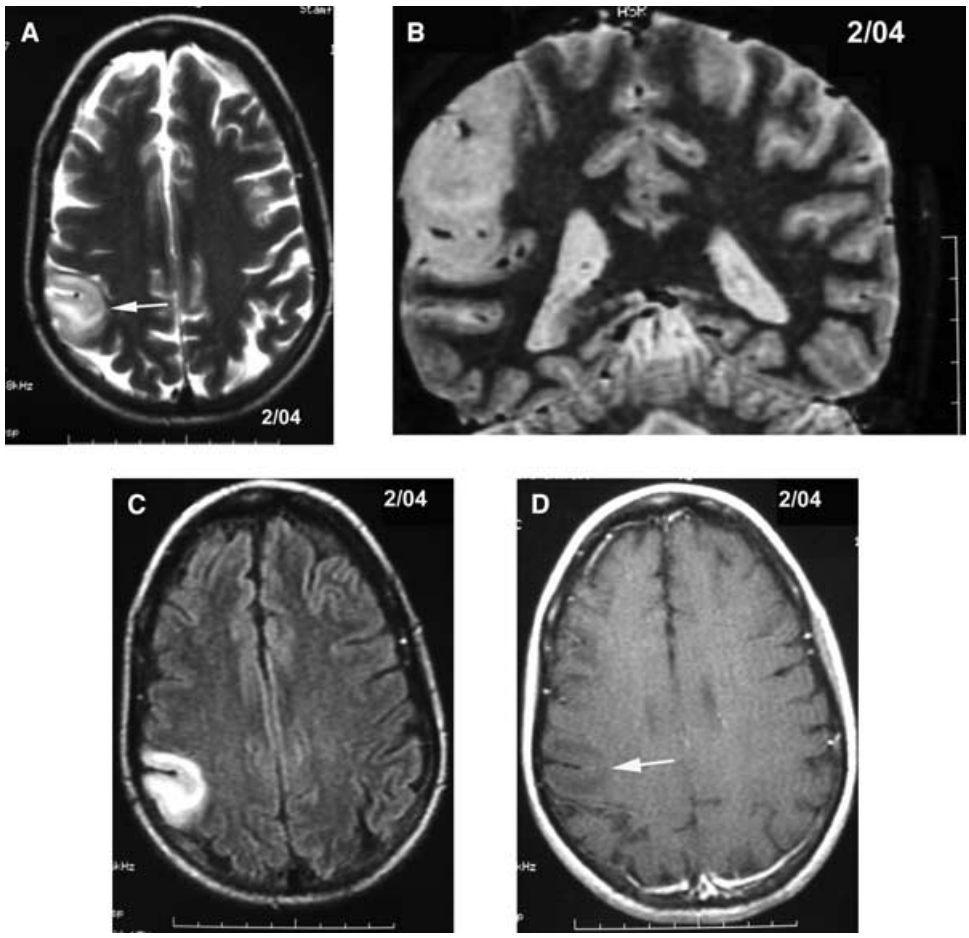



**FIG. 1.** Preoperative brain MRI of Patient 1. A) $T_2$-weighted axial image with discrete right parietal area of intraparenchymal increased signal (arrow). The same abnormality is seen in: B) $T_2$-weighted coronal, C) Axial FLAIR, and D) Axial $T_1$ with gadolinium (arrow).

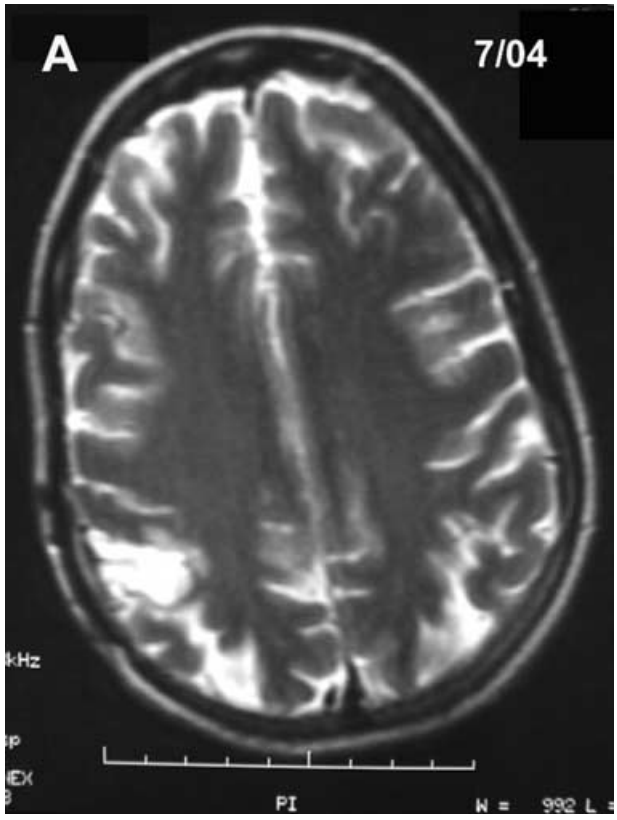
the surgery was largely to obtain a definitive diagnosis, a subtotal resection (limited by functional cortex), and had the additional goal of possibly facilitating seizure control.

Surgery was performed (10 days after her flurry of focal seizures) with awake intraoperative sensorimotor cortex mapping. The majority of the MRI abnormal tissue was posterior to the sensory cortex, and it was excised. She has been neurologically intact since the surgery. She reported several episodes of brief sensory seizures of the left lower lip and thumb, but these stopped 5 months after surgery, with the addition of a second AED. Postoperative MRI showed the resection cavity, some adjacent increased signal suggestive of postoperative gliosis, and normalization of signal in the residual primary sensory cortex (Fig. 2). Pathology revealed mild gliosis, widened perivascular spaces, mild perivascular inflammation, and hemosiderin deposition, with no evidence of cortical malformation, neoplasm, or infection (Fig. 3).

*Case 2*

Our second patient was a purely left-handed 52-year-old man with an unprovoked nocturnal convulsion that was estimated to last for 3 min. He was started on phenytoin (PHT; Dilantin) and had no further seizure activity. MRI (within 24 h of his seizure) demonstrated increased $T_2$ signal throughout the right hippocampus, with some preservation of the internal architecture (Fig. 4). $T_1$ pregadolinium MRI demonstrated low signal in the right hippocampus with apparent enlargement of the hippocampus and some preservation of the internal architecture. Postgadolinium $T_1$ images had punctate areas of increased signal within the hippocampus that may have represented prominent vessels. No definite abnormal enhancement of the tissue was identified. Clinical suspicion was for an intraaxial neoplasm versus inflammatory process, and he was recommended for surgery.

The patient had a stereotactic MRI-guided needle biopsy (3 weeks after the diagnostic MRI) of the hippocampal abnormality in October 2003. Pathology was nondiagnostic, and the biopsy was repeated 1 week later, to ensure that a diagnostic area had not been missed (although postoperative MRI indicated that the biopsy needle track was in the abnormal hippocampus). The patient has remained neurologically intact and seizure



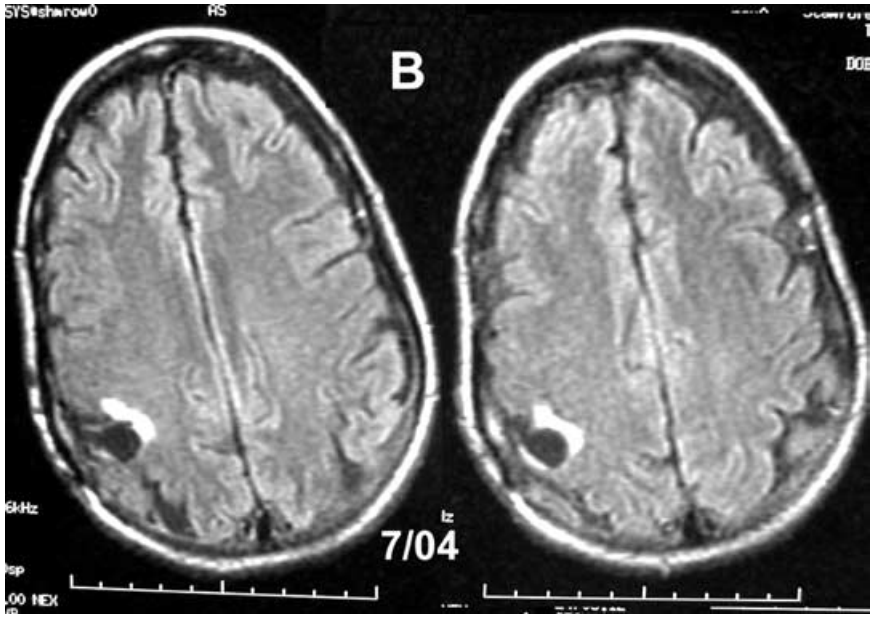




**FIG. 2.** Postoperative brain MRI of Patient 1. A) Axial $T_2$-imaging reveals the resection cavity with adjacent increased signal suggestive of postoperative gliosis and normalization of signal in the residual primary sensory cortex anterior to the cavity. B) Axial FLAIR images showing the same normalization.

free since the biopsies. Postoperative MRI in September 2004 showed complete normalization of the hippocampus (Fig. 5). Pathology revealed mild gliosis, reactive vascular changes, focal perivascular hemosiderin deposition, and a few neuritic plaques with no evidence of neoplasm, infection, inflammation, or malformative changes (Fig. 6). Despite the presence of neuritic plaques, no evidence was indicative of amyloid angiopathy.

## DISCUSSION

Many pathologic entities have been reported as causes of focal increased MRI signal abnormalities associated

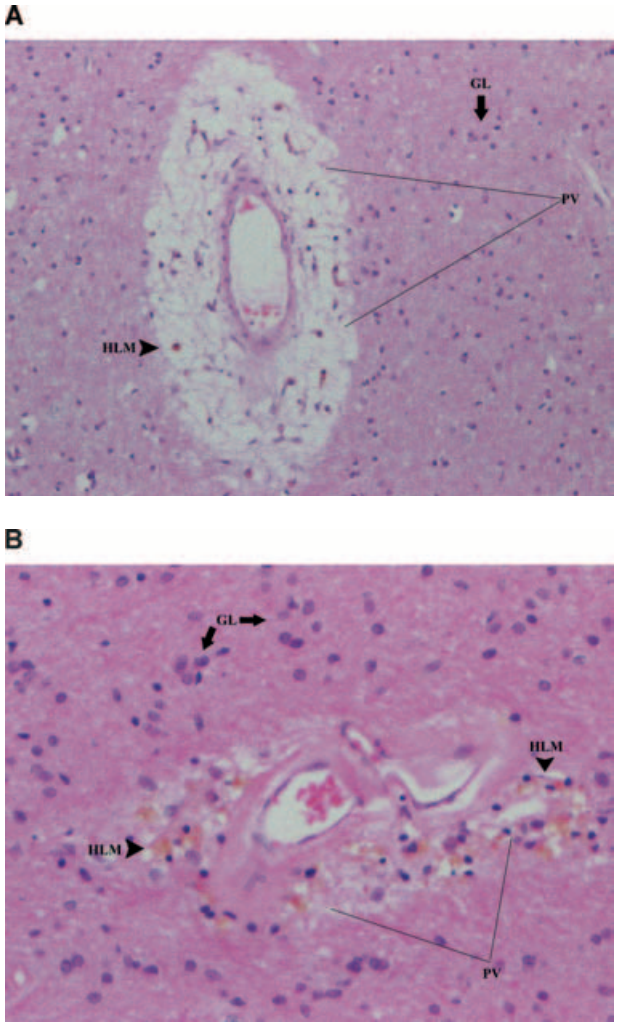



**FIG. 3.** Biopsy of patient 1. Right posterior sensory cortex showing hemosiderin deposition in widened perivascular spaces and mild gliosis. (Hematoxylin and eosin, original magnification × 100, and × 200; GL = gliosis, HLM = hemosiderin-laden macrophage, PV = perivascular space).

with seizures, including neoplasms, vascular malformations, inflammatory processes, cytotoxic edema, and demyelinating diseases (6–12). Of these entities, the most common causes are cerebrovascular disease and tumor (11). Multiple tumor subtypes have been reported to manifest as a nonenhancing increased $T_2$ signal change associated with focal seizures, including low-grade gliomas, de novo glioblastoma multiforme, gliomatosis cerebri, papillary glioneuronal tumor, ganglioglioma, and hamartoma (13–18). In our patient with the hippocampal abnormality (case 2), it is worthwhile to mention that subtle hippocampal abnormalities have been associated with seizures, such as hippocampal sclerosis or malformation, and may be associated with increased signal on $T_2$ MRI. The normalization of his MRI eliminates these possibilities in this patient. Given the commonality of tumor as a cause of this manifestation, and that neither patient demonstrated any history of cerebrovascular disease, tumor became first on our differential diagnosis, with inflammatory process becoming second. Inflammatory processes reported to manifest with increased $T_2$ signal and seizures include focal meningoencephalitis, cysticercosis, central nervous system angiitis, multiple sclerosis, and severe cerebral cortical gliosis (19–23). Pathologic examination of biopsy material, however, revealed nondiagnostic perivascular hemosiderin deposition and reactive vascular changes in both patients, eliminating the majority of these disorders. Such hemosiderin deposition has been reported in multiple sclerosis and angiitis (21,22,24). The lack of white matter involvement on MRI in both cases essentially rules out multiple sclerosis, whereas the lack of slow-evolving waxing and waning neurologic symptoms likewise makes central nervous system angiitis highly improbable (21,22). Although the radiologic, operative, and pathologic findings could be explained by reversible seizure-related changes, such changes are usually due to prolonged seizures, which neither of our patients experienced (23).

The presentation of our second patient (case 2) could be attributed to one of the following: (a) an unexplained seizure that caused venous congestion (or possibly a venous thrombosis) in the right medial temporal region, or (b) a spontaneous venous thrombosis that caused the changes in the temporal lobe and a single convulsion. The fact that he had no further seizures suggests that the MRI abnormality was not strongly epileptogenic (such as a cavernous malformation or a neoplasm), and given this, it seems more likely that a spontaneous seizure produced the structural change in the brain that ultimately was proven to be transient. The pathologic findings are not definitive for any specific entity but certainly are compatible with a venous congestion scenario. Given all that we know now, our leading hypothesis is that this patient had a venous thrombosis in the context of a spontaneous seizure.

The presentation of our first patient (case 1) was more complicated because of her preexisting seizure disorder and the nocturnal convulsions that occurred several days before her flurry of focal seizures. One possible explanation for this patient's findings is that one of her nocturnal convulsions induced a venous thrombosis in the region of her right central cortex and precipitated a flurry of focal seizures, the MRI changes, and the pathologic findings. This would be very similar to our stated theory for case 2. Because of the abrupt change in her seizure frequency/presentation after her nocturnal convulsions, it seems less plausible to postulate that the structural change was present at the time of this patient's nocturnal convulsions 8 and 5 days before her flurry of focal seizures and abnormal MRI. Given the pathologic findings and the normalization of their MRIs, in retrospect, both patients would have been better managed by observation without a biopsy.

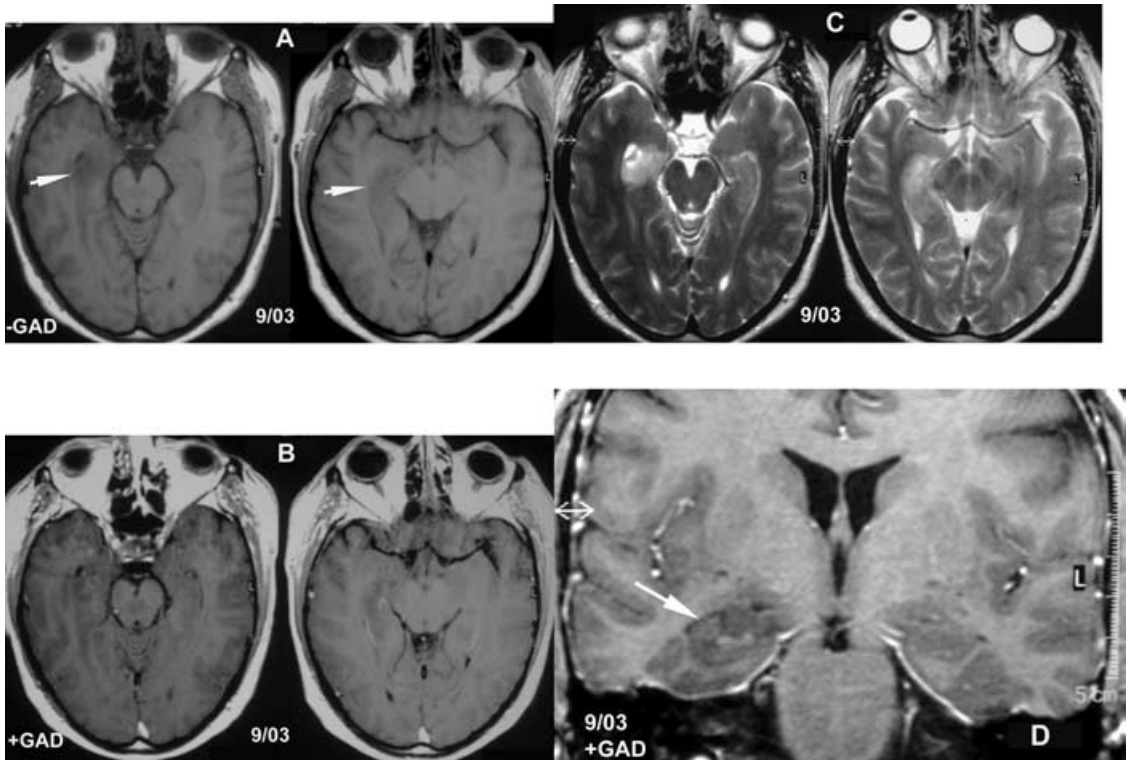



**FIG. 4.** Preoperative brain MRI of Patient 2. A) Axial $T_1$-weighted images (pregadolinium) demonstrating abnormal low signal in the right hippocampus (arrows). B and D) Axial and coronal $T_1$-weighted images (postgadolinium) demonstrating punctate areas of increased signal within the hippocampus which may represent prominent vessels (arrow). No definite abnormal enhancement of the tissue was identified. C) Coronal $T_2$-imaging demonstrates increased signal throughout the right hippocampus with some retention of internal architecture.

Our usage of the term venous congestion is not meant necessarily to imply venous thrombosis. This may represent venous congestion in the context of increased regional blood flow in the context of a seizure and that the venous congestion resolved after cessation of the seizures.

The MRI findings in both patients ($T_2$ hyperintensity of lesions at presentation, subsequent normalization of signal intensity, hemorrhagic nature of lesions) are all consistent with previously reported findings of cytotoxic edema (25,26). This finding actually lends support to our hypothesis, because cytotoxic edema has been reported to play a role in the pathogenesis of cerebral venous infarction, because increased venous pressure may cause reduced cerebral blood flow, resulting in cytotoxic edema that decreases over time (27). Although the actual explanation for these patients' pathologies may be something other than venous congestion/thrombosis, we do not have any specific alternate hypotheses.

The dramatic transient MRI changes associated with seizures that we report here may not be a rare occurrence. Because our two patients did not have serial imaging, it is not known how long the MRI abnormality existed. It is possible that the abnormality may be fairly brief, and discovering it might depend on imaging at the ideal time point relative to the seizures. Alternatively, this abnormality may be a rare event that occurred because of some unusual feature of the anatomy of these patients or some unusual aspect of their seizures. The authors were recently informed about two patients at an epilepsy center in Brazil who had similar MRI changes in the context of a flurry of seizures (Palmini A, Paglioti-Neto N, personal communication, 2004).

Given the combination of clinical, radiologic, operative, and pathologic findings, we propose the possibility of associated subacute venous congestion, which has yet to be reported as being associated with seizures and focal increased $T_2$-signal MRI. The preoperative imaging and events are consistent with two possibilities: (a) a seizure precipitating a venous congestion, or (b) a spontaneous venous thrombosis precipitating the brain tissue changes and seizures. Our experience does not allow us to determine definitively if the MRI and tissue abnormalities preceded, or were caused by, the seizures.

## Conclusions

We describe two patients who had brain biopsies of striking focal increased $T_2$-signal MRI abnormalities associated with seizures. Pathologic findings contradicted our preoperative suspicions and were compatible with (but not conclusive for) subacute venous thrombosis. Our findings indicate that patients with new-onset seizures may have an associated discrete intraaxial MRI lesion that is

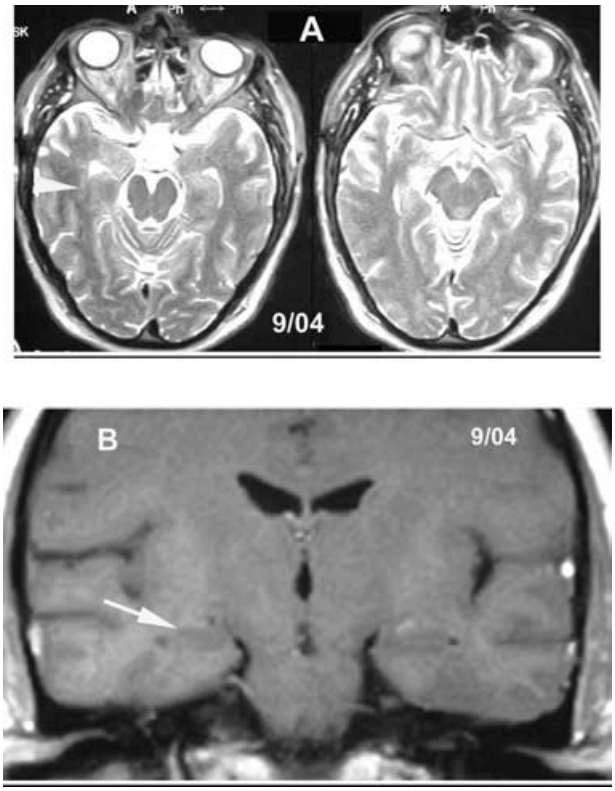



**FIG. 5.** Postoperative brain MRI of Patient 2. A) Axial $T_2$-weighted images revealing complete normalization of the right hippocampus, also seen on B) Coronal $T_1$-weighted post-gadolinium image.

not a neoplasm, infection, or inflammatory process. To our knowledge, this is the first report of focal seizure–associated MRI lesions with biopsy findings compatible with venous thrombosis.

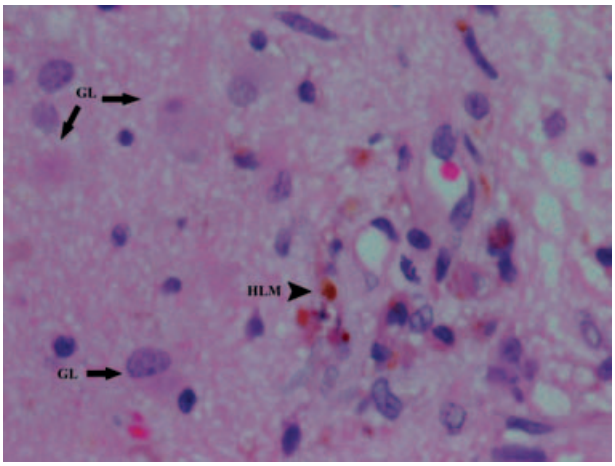



**FIG. 6.** From second biopsy of patient 2. Photomicrograph of the right hippocampus demonstrating mild gliosis and a reactive blood vessel with perivascular hemosiderin deposition. (Hematoxylin and eosin, original magnification × 200; GL = gliosis, HLM = hemosiderin-laden macrophage).

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