Brain Tumor or Infectious Disease?

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Encephalitis is usually an acute or subacute infectious disease presenting variable symptoms including headache, confusion, seizures and obnubilation, with Herpes simplex virus (HSV) as one of its most frequent etiological agents²,³.

Occasionally, clinical presentation may be subtle, chronic and more like a brain tumor, making correct diagnosis difficult and misleading.

A few cases have been reported in which brain tumors mimic herpetic encephalitis at onset, however very little information has been published on the opposite situation, namely herpetic encephalitis masquerading as a CNS neoplasm.

Although it is important to bear this possibility in mind in patients suffering from an expansive temporal mass and presenting an atypical clinical course, infectious encephalitis is not often considered as a potential diagnosis in patients with typical signs and symptoms of a brain tumor.

This case is therefore interesting as it represents an unusual form of herpetic encephalitis (HE).

CASE

We report a 49 year-old diabetic and hypothyroid female referred to our neurological department because of a single and brief episode of behavioral arrest, followed by urinary incontinence two months prior to consultation. She had been receiving antibiotic therapy for a tooth abscess one week before a partial complex crisis. Although the patient’s personal history was uneventful, she did have three family members with a positive history for cancer. No abnormalities were noted on physical examination. A brain MRI carried out at this time to evaluate seizure etiology revealed an extensive right temporal and insular lesion, hypointense on T1, and hyperintense on T2 and flair weighted images, with mass effect and enhancing after gadolinium administration. Four months later, MRI images remained the same and myoinositol and choline peaks were reported elevated on spectroscopy sequence analysis (Fig 1).

Based on clinical course and MRI imaging results, an oligodendroglioma/ oligoastroctoma tumor was initially suspected. A right-side pterional craniotomy, sylvian fissure dissection and medial temporal lobe exposure was indicated with corticectomy of the anterior portion of the uncus. An intrasurgical biopsy showed edematous changes in the uncus and anterior portion of the hippocampus together with lymphocytic infiltration and gemistocytic astrocytes, some with bizarre nuclei. Postoperative course was uneventful. Pathological examination of the whole biopsy sample showed diffuse meningeal and cortical brain tissue and vascular lymphocyte infiltration with reactive gemisto-

cytic astrocytes, some with “bizarre” nuclei. Shrunken neurons with eosi

philic intranuclear inclusions were also observed (Fig 2). HVS I PCR in brain tissue was positive. Definitive diagnosis was established as active encephalitis with extended cortical involvement. Analysis of cerebrospinal fluid showed mild lymphocytic pleocytosis and moderate hyperproteinorrraquia. An HIV test was negative and no other serum abnormalities were found.

Patient completed acyclovir treatment following a standard regimen, no complications ensued. Her neurological examination continued normal. One year after surgery, MRI shows a T2 and flair weighted hyper intense temporal and occipital lobe retraction lesion, with no edema or gadolinium enhancement, which was interpreted as gliosis.

Specific cognitive testing performed after surgery showed slight impairment in recent memory with no consequences on daily life activities. The patient was prescribed carbapazemine and has referred no further ictal manifestations.

**DISCUSSION**

Herpetic encephalitis is a rare complication of HSV in CNS with a yearly incidence of 0.2–0.4 cases per 100,000 inhabitants. For every 1,000,000 individuals suffering HSV infection, only 1 to 2.3 have CNS involvement, and of these 70% have antibodies against the virus at illness onset, indicating prior exposure. Herpetic encephalitis is the most common cause of fatal sporadic encephalitis in untreated patients. Morbidity from the condition is also high, with serious neurological sequelae present in about 50–70% of untreated survivors.

Classical clinical presentation includes an acute onset syndrome characterized by fever, headache, focal motor seizures and changes in personality. Severe progressive neurological deterioration, including impaired consciousness usually follows over the next few days.

Primary CNS neoplasm has an overall incidence of 15 cases per 100,000 inhabitants. Multiform glioblastoma, anaplastic astrocytoma, oligodendroglioma and lymphoma can undergo diffuse brain infiltration suggesting a differential diagnosis more like herpetic encephalitis. However, glioblastoma and lymphoma usually show callosal involvement and a more protracted clinical course than herpetic encephalitis, including headache, seizures or focal signs depending on the lobe affected.

This patient suffered a single partial seizure two months prior to hospital admission. Initial MRI imaging showed an extensive temporal lesion, enhancing gadolinium and with mass effect, interpreted as a possible primary neoplasm. New studies repeated 6 months later showed an identical lesion, and the patient was referred to neurosurgery for excision.

Her final pathology report refuted the original diagnosis suspected, and confirmed typical findings of active encephalitis with extended cortical involvement.

Case reports on atypical presentation of CNS herpes infection have included those with brainstem involvement, others presenting as a psychiatric syndrome, or benign recurrent meningitis or myelitis. Few communications have been published in which herpetic encephalitis did not present typical MRI abnormalities or had been confused with other diseases, including a postpartum brain venous thrombosis, neurosyphilis mimicking HE, as well as HE mimicking anaplastic oligoastrocytoma, lymphoma or astrocytoma. We found only one report of chronic encephalitis diagnosis and subtle neurological manifestations in childhood. Fodor et al. reported 24 herpetic encephalitis cases, 4 of which had had atypical presentation, and of these, three had occurred in immunosuppressed hosts.

The fact that active herpetic infection is fatal if untreated, and that chronic active encephalitis in an immunocompetent host is transient and therefore clinical signs and symptoms of disease presence are extremely rare, would both help explain our initial diagnosis bias in favor of a brain tumor. The pathology results obtained, the patient’s clinical course and ultimate resolution of her radiological lesion were consistent with herpetic encephalitis.

In conclusion, although typically acute in presentation and with ominous clinical prognosis if untreated, rare cases of VSH infection can follow an atypical course and/or present with only subtle neurological signs, making it necessary to consider this infection as differential diagnosis for other diseases including CNS neoplasm.
REFERENCES