Benign focal cerebral vasculitis: Case report

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Article abstract—We report a 47-year-old man who presented with partial seizures complicating focal cerebral vasculitis of the right temporal lobe. Excisional biopsy of the mass lesion revealed fibrinoid necrosis of small vessels. These vessels were infiltrated by neutrophils, eosinophils, lymphocytes, and plasma cells. Despite extensive evaluation, no etiology was apparent for the vasculitis. No immunosuppressive agents were administered, and 4½ years after the diagnosis, he remains healthy except for an incongruous left homonymous hemianopia. Follow-up cranial magnetic resonance images revealed only postoperative changes. This case demonstrates that focal lesions and a benign course may represent one end of the spectrum of primary angiitis of the central nervous system.

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A classification of the CNS vasculitides includes those illnesses in which the CNS is affected in the course of a systemic vasculitis and those in which the vasculitis occurs solely in the CNS. Granulomatous angiitis of the CNS is the prototypical illness of the latter category. It affects men more than women, has an average age of onset of 46 years, and typically results in death in untreated cases within 1 year. A benign course with recovery in the absence of treatment and with prolonged survival is uncharacteristic.2 In rare instances, it may present as a focal lesion. 1-13 In 12% of patients, seizures are the presenting manifestation of the disorder.14 We describe an individual presenting with seizures caused by focal cerebral vasculitis who has remained healthy more for than 4½ years after diagnosis.

Case report. On November 18, 1990, while playing tennis, this 47-year-old man developed recurrent waves of a peculiar odor described as "like tar" and associated with intense nausea and an incapacitating malaise. During the initial episode, he may have had a brief loss of consciousness. The spells recurred at 5- to 10-minute intervals and were accompanied by pallor and diaphoresis. He was quickly taken to a local emergency room where a diagnosis of partial seizures was suspected. Following the intravenous administration of valium 10 mg and phenytoin 1,000 mg, the episodes stopped.

Two days earlier, he had had an uncharacteristically intense headache that prevented him from engaging in his scheduled social activities. Although he had no history of a seizure disorder, he recalled that, 3 weeks earlier, he found himself in the middle of a wide thoroughfare without any recollection of having driven through a stop sign. He had driven this route many times and was

quite perplexed by the experience. Additionally, his wife related that his memory had been a "bit off" in the preceding weeks. He denied any systemic illnesses.

He was afebrile and his general physical examination was unremarkable. Neurologic examination revealed him to be alert and oriented. Funduscopy was normal. There was a suggestion of a left superior-quadrant visual field defect to confrontation. Muscle strength and tone were normal, and his muscle stretch reflexes were brisk and symmetric. Sensory perception to all modalities was normal. Chest x-ray, ECG, and results of routine laboratory studies, including complete blood count with differential, chemistries, rapid plasma reagin, fluorescent treponemal antibody test, and urinalysis, were normal or negative. A head CT without contrast (figure 1) showed a focal hypodense lesion within the medial right temporal lobe associated with minimal mass effect. The lesion had associated areas of calcification. Cranial MRI (figure 2) on admission showed this same mass lesion with associated areas of signal void, consistent with calcification. The lesion enhanced irregularly with gadolinium. A glioma was suspected, and on November 19, 1990, he underwent a right temporal craniotomy with temporal lobectomy and removal of an intratemporal mass, and was started on acyclovir 10 mg intravenously every 8 hours for possible herpes simplex virus (HSV) encephalitis.

Sections from the convexity cortex and underlying white matter showed no significant changes. However, in the hippocampus, several small blood vessels showed marked fibrinoid necrosis of their walls, which were infiltrated by acute and chronic inflammatory cells including neutrophils, eosinophils, lymphocytes, and plasma cells (figure 3). The adjacent neuropil was edematous, and a few necrotic neurons were present. Rare psammomatous bodies were noted. There were no microglial nodules, perivascular lymphocytic infiltrates, or intranuclear inclusions. The meninges were free of pathologic changes. There was no evidence of a neoplastic process. Im-

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munoperoxidase staining and polymerase chain reaction for HSV 1 and 2 were negative.

Following surgery, he had dysprosodic speech, a denial of the left side, difficulty with visual tracking leftward, and a left homonymous hemianopia. Because of

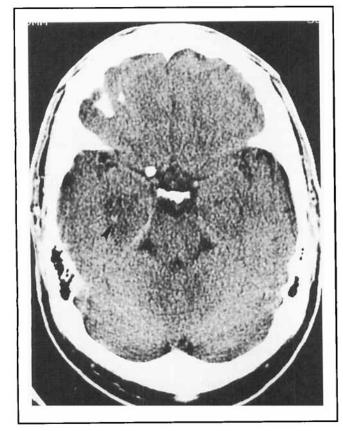


Figure 1. CT (General Electric, Milwaukee, WI) without contrast reveals a focal hypodense lesion in the right medial temporal lobe with a small area of high density within the lesion (arrowhead), consistent with calcification and minimal associated mass effect.

the nature of the pathology observed on brain biopsy, further studies were performed. His ESR was 4 seconds. Other studies included serum immunoelectrophoresis, serum complements (C3, C4, and CH₅₀), ANA, rheumatoid factor, anti-DNA antibodies, anti-neutrophil antibodies, cryoglobulins, Lyme antibody, serum HSV 1 and 2 IgG and IgM antibodies, cryptococcal antigen, angiotensin-converting enzyme, prolactin, and follicle-stimulating and luteinizing hormones. All results were either negative or normal. Examination of the CSF showed 1 white blood cell per mm³, 0 red blood cells per mm³, protein 68 mg/dl (normal, 15 to 45 mg/dl), glucose 66 mg/dl, IgG 4.7 mg/dl (normal, 2.2 to 4 mg/dl), and IgG index 0.49 (normal, 0.3 to 0.7). On CSF electrophoresis, two oligoclonal bands were present. An abdominal CT revealed a liver cyst.

Within 2 months of surgery, his examination was remarkable for an incongruous left homonymous hemianopia compatible with optic tract disease (N. Schatz, Bascom Palmer Eye Institute, Miami, FL, personal communication). A cranial MRI obtained in December 1990 revealed postoperative changes that included an abnormal signal in the distal end of the right optic tract and the right geniculate body. A detailed neuropsychological battery revealed distinct abnormalities in his Performance IQ, but he retained a high Verbal IQ. He was able to return to full-time work as a pediatrician and has had no seizures on carbamazepine 800 mg daily. As of May 1995, he remains healthy. Repeat cranial MRI revealed only postoperative changes.

Discussion. The remarkable features of this case are the exquisite focality and the benign course of pathologically confirmed cerebral vasculitis. The illness presented with focal seizures. The radiographic properties suggested the possibility of a neoplastic process that was not confirmed by biopsy. HSV encephalitis was also seriously considered in light of the partial seizures with a medial temporal lobe lesion. However, the patient remained afebrile; there was no CSF pleocytosis;



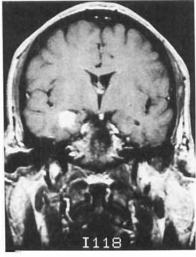


Figure 2. (A) Axial T_2 -weighted (TE 90, TR 2,000) MRI obtained on a 1.5-tesla imager (Signa, Milwaukee, WI) shows a large, oblong, hyperintense signal abnormality in the medial aspect of the right temporal lobe. There is minimal mass effect. A signal void in the lesion is consistent with calcium. (B) Coronal T_1 -weighted (TE 14, TR 516) MRI with gadolinium contrast shows irregularly enhancing lesion abutting the temporal horn.

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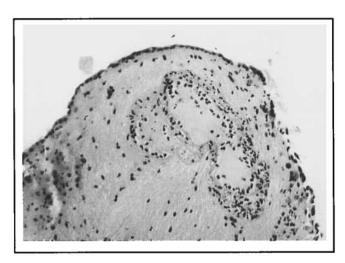


Figure 3. Histopathology. Fibrinoid necrosis of vessel with infiltration of vessel wall with neutrophils, eosinophils, plasma cells, and lymphocytes. (Hematoxylin and eosin; ×240 before 48% reduction)

serum HSV antibody titers were negative; and the pathology, including immunoperoxidase staining and polymerase chain reaction for HSV 1 and 2, was negative. There were no clinical or laboratory features to suggest the diagnosis of a systemic vasculitis. Certain infections, such as syphilis, tuberculosis, and herpes zoster, may also result in a CNS vasculitis, but none was demonstrated. Additionally, there was no history of toxin exposure or drug use. The significance of calcification in the lesion detected both radiographically and histopathologically remains obscure. The sizable lesion evident on radiographic imaging was likely the consequence of multiple confluent infarcts due to the angiitic process⁵ and associated edema.

"Vasculitis" refers to a broad group of conditions characterized by inflammation of the vessel wall. Vasculitis may result from different pathophysiologic mechanisms.3 In immune complex-mediated vasculitis, soluble immune complexes are formed in the presence of slight antigen excess, which results in increased vascular permeability with infiltration of the arterial elastic walls and basement membranes of venules. 15 Activation of complement attracts polymorphonuclear cells that release proteolytic enzymes, with further injury to vascular structures. This mechanism is the presumed mechanism for polyarteritis nodosa and hypersensitivity vasculitis. In cell-mediated injury, macrophages may be activated by phagocytosing immune complexes, by Fc receptor interaction, or by lymphokines released by antigen-sensitized T cells.16 Activated macrophages releasing lysosomal enzymes cause, by granulomatous reaction, vascular damage. Vasculitis may also result from neoplastic cell invasion, as in lymphomatoid granulomatosis. 17 Other, as yet unproven, possibilities of vessel wall injury include damage arising from cellular T-cell activity, natural killer cell activity, and antibodies directed against components of the vessel wall.3

Among the primary vasculitides, polyarteritis nodosa, hypersensitivity vasculitis, Wegener's granulomatosis, and lymphomatoid granulomatosis frequently affect the CNS. To the best of our knowledge, none of these primary vasculitides affects the CNS in an isolated and focal manner. Furthermore, a benign course in the absence of immunosuppressive therapy is unexpected.

The primary CNS vasculitis, primary angiitis of the CNS (PACNS) or granulomatous angiitis of the nervous system, affects small vessels, chiefly small arteries and arterioles (200 to 500 microns in diameter) of the leptomeninges and brain parenchyma, in a segmental fashion. 1,2,4 The infiltrate is composed of mononuclear cells, giant multinucleated cells, and plasma cells with a granulomatous reaction.^{2,4} There are no polymorphonuclear cells or eosinophils. Most patients present with a diffuse encephalopathy. 1,2,18 Focal lesions tend to develop gradually when they occur. 18 The pathophysiologic mechanism is believed to be chiefly cerebral ischemia, but hemorrhage may be observed. 19 Seizures have been reported in 23% of patients, but headache, confusion, and cognitive changes are more common.² Neuroimaging often reveals hypodensities with enhancement and occasional mass effect.^{5,13} Angiography lacks diagnostic specificity.²⁰ In their original description, Cravioto and Feigin⁴ initially suspected brain tumor in two of their patients. Even with the application of more sophisticated brain imaging techniques, misdiagnosis as brain tumor occurs. 5,8,13,21 Cerebral biopsy remains the standard for diagnosis.⁵ Death generally occurs within 1 year in untreated cases, 2,4 but corticosteroids and cyclophosphamide treatment have had favorable results.22

In summary, we describe a unique illness characterized by a focal vasculitis that was heralded by partial seizures. Other than a brief course of corticosteroids, no immunosuppressive treatment was administered, and the patient remains well 41/2 years after presentation except for a visual field deficit. Benign isolated arteritis of the CNS has been previously observed. 1-13 Calabrese et al23 argue that there is a spectrum of PACNS. In a subset of patients in whom the diagnosis was established angiographically without histopathologic confirmation, the disease was often heralded by focal neurologic deficit and typically occurred in young women who had relatively unremarkable CSF findings. A benign course was often observed. However, in the absence of pathologic confirmation, the true nature of this disorder remains suspect. Another explanation for the angiographically observed changes is vasospasm caused by migraine, drugs, head trauma, or other etiologies. 20,24 Few cases of focal cerebral vasculitis 5,7,8,12 have been confirmed histologically. Among the pathologically proven cases of benign focal cerebral vasculitis, the patient described by Beresford et al7 was very similar to our patient. Features that either preclude comparison or distinguish other cases from our own include insufficient follow-up to determine the benign or non-recurrent nature of the disorder⁵; the presence of a positive ANA and mild leukopenia, suggesting a systemic vasculitis⁸; and the admixture of amyloid in the cerebral biopsy.¹²

In our patient, a middle-aged man with no history of migraine, head trauma, drug use, or preceding or concomitant infectious illness, the diagnosis was confirmed by biopsy. As in other cases of focal cerebral vasculitis, a brain tumor was initially suspected. Whether this entity is truly one end of the spectrum of PACNS remains uncertain, as vascular inflammation may be a physiologic or pathologic process. Despite that, this case confirms the existence of an entity of focal cerebral vasculitis with a benign course that does not require corticosteroid or other immunosuppressive therapy.

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