Primary Angiitis of the Central Nervous System

Diagnostic Criteria

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KEYWORDS

• CNS angiitis • CNS vasculitis • Primary angiitis of the central nervous system

KEY POINTS

- Histologically proven primary angiitis of the central nervous system (PACNS) is a rare condition.
- Controversy exists over the means to establish the diagnosis. Some researchers require histologic documentation of angiitis by autopsy or biopsy, whereas others accept cerebral angiographic findings.
- Cerebral arteriography, cerebrospinal fluid (CSF) examination, and MRI singly or in combination have not sufficiently demonstrated positive predictive value to establish the diagnosis. The person with so-called typical changes of angiitis at arteriography is more likely to have a definite diagnosis other than angiitis at biopsy.
- In patients with a nondiagnostic biopsy in the setting of high clinical suspicion, there are no data to demonstrate that PACNS occurs commonly or that immunosuppressive therapy is beneficial and it can be harmful if the patients do not have PACNS.
- Histologic confirmation is required for the diagnosis of PACNS. Patients without histologic confirmation should not be included in case reports, case series, or reviews.

INTRODUCTION

A vasculitis of small arteries and veins of unknown cause restricted to the central nervous system (CNS) was initially described from autopsy material as granulomatous angiitis of the CNS in the 1950s.[1] A variety of other names have been used at different times since the original description of this entity, including isolated CNS angiitis, isolated CNS vasculitis, PACNS, and primary CNS angiitis. Antemortem diagnosis based on biopsy specimens showing the same histologic changes found at autopsy, with no clinical evidence of disease outside the CNS, was put forward in the 1970s.[2,3] In the 1980s, diagnostic criteria not requiring histologic evidence from biopsy or autopsy but rather based on cerebral angiography and laboratory evaluation were proposed.[4,5]

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DISEASE DESCRIPTION

Histologically proven PACNS is a rare condition. In 1991, Hankey[6] found 71 cases published from 1922 to 1989. Alrawi and colleagues[7] reported 17 definite cases at the University of Michigan Medical Center from 1989 to 1996. Schmidley[8] identified 68 cases published from 1922 to 1993 and from his own personal material. From 1986 to 2006, there were no cases at Johns Hopkins Hospital.[9] At Washington University School of Medicine/Barnes Hospital, there were 2 cases from 1992 to 1999.[10] Chu and colleagues[11] report 10 cases at Duke University Medical Center from 1993 to 1996. These reports all document the rarity of the disease. Some of the variation in incidence stems from different diagnostic criteria (see later discussion), but patterns of referral and local practice patterns regarding the frequency of biopsy undoubtedly contribute as well.

Despite its rarity, a diagnosis of PACNS is often entertained for 2 good reasons. Its clinical manifestations are protean, and the course in patients who received no or inadequate immunosuppressive therapy is poor, with 88% mortality reported in one review.[8] The disease may affect the brain, spinal cord, or both. There is no typical or classic presentation. It may present as a focal mass lesion mimicking a brain tumor, seizures (focal or generalized, including status epilepticus), chronic meningitis, myelopathy, intracerebral hemorrhage, focal neurologic deficits (eg, aphasia, hemiparesis), cognitive impairment, and encephalopathy.[8] In 5 series comprising 127 histologically proven cases, headache occurred in two-thirds, cognitive decline in one-half, focal motor deficits (monoparesis, hemiparesis, or quadriparesis) in one-half and seizures in one-third.[8,11–14] (Only data from the lymphocytic and necrotizing groups from Miller and colleagues[14] are included owing to their inclusion of cases of cerebral amyloid angiopathy (CAA) in the granulomatous group.)

As noted earlier, the original description of PACNS was based on autopsy material. In autopsy studies, necrotizing granulomatous lesions were found in the walls of arteries and veins less than 200 μm in diameter. Occasionally larger vessels and capillaries were affected.[15] All fully described autopsy cases had granulomatous inflammation with giant cells of the Langhans or foreign body type.[8] Granulomatous involvement may be segmental within the same vessel.[16] Small lymphocytes and multinucleate giant cells were seen in the vessel walls.[17] Within the same brain, vascular lesions may vary from fibrinoid necrosis with infiltrating polymorphonuclear leukocytes to infiltration by lymphocytes, epithelioid-appearing histiocytes, and giant cells with granuloma formation.[18] Completely sclerosed vessels without perivascular infiltrate may be seen as well.[18] Fibrinoid necrosis may affect only a few vessels or be absent.[1,10,19] These vascular changes were associated with intravascular thrombi, infarcts (ischemic or hemorrhagic), or hemorrhages.[15,18,20] There was uniform involvement of the leptomeninges in 17 autopsy cases in which they were examined.[21] The original description by Kolodny and colleagues[15] noted that some parts of the CNS were more involved than others, but no region was entirely spared. Since then, autopsy findings demonstrating sparing of large brain regions have been reported.[16,22]

THE CONTROVERSY

The 3 essential diagnostic criteria for PACNS are (1) demonstration of CNS angiitis, (2) exclusion of other conditions, and (3) restriction to the CNS. Controversy and disagreement continue over the means to establish each of these, especially the demonstration of CNS angiitis. At present, there are multiple proposed criteria for diagnosis in use.