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Primary Angiitis of the Central Nervous System: Unusual MR Appearance

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Summary: The MR findings of a biopsy-proved case of primary angiitis of the central nervous system are described and compared with previously reported cases. Multiple punctate and linear areas of gadopentetate dimeglumine enhancement were present in the brain stem and white matter and appear to correspond to the inflammatory reaction of the small perforating vessels and perivascular tissues seen in the pathologic specimen.

Index terms: Angiitis; Nervous system, diseases; Brain, magnetic resonance

Primary angiitis of the central nervous system (PACNS) is a rare disease of unknown cause. Although any vessel of the brain or spinal cord can be affected, the disease most commonly occurs in the small leptomeningeal vessels (1). Because of the segmental involvement, a biopsy may show a false-negative result, and both computed tomography and angiography studies may appear normal. Therefore, the diagnosis is frequently one of exclusion (1). We found 11 cases in the literature with reported magnetic resonance (MR) findings in PACNS (2–6). This case demonstrates an unusual MR appearance.

Case Report

A 45-year-old man without any significant medical history developed tingling dysesthesias involving his anterior left thigh with aching of the posterior neck. Symptoms resolved after 5 days. Three months later, unsteadiness of gait developed with partial loss of sensation over the lower abdomen, constipation, and loss of sexual function. These symptoms persisted, and 1 month later the prior neck and thigh symptoms returned with new paresthesia of his hand and left upper lip. Within 2 months he developed fatigue, vertigo, and a tendency to drag his left leg.

After his symptoms had persisted for 6 months, the patient presented for examination. There was mild incoordination, increased tone in the legs, and two to three beats of clonus at the ankles. He had no pin and temperature sensation in his entire left leg and left groin. An L-1 sensory level was present. An MR examination of the lumbar spine was normal. His condition continued to deteriorate. MR examination of the brain (Figs 1A and 1B) was obtained, and he was admitted to the hospital. Intravenous methylprednisolone, 1 g daily for 5 days, resulted in dramatic improvement. A cerebral angiogram was also performed (Fig 1C), as were MR studies of the cervical and thoracic spine. These studies were all normal.

Four months later, his symptoms recurred, and there was marked improvement after treatment with oral prednisone. A follow-up MR examination of the brain was performed (Figs 1D-1F), 5 months after the first study. The patient remained stable until 2 months later, when he developed a Lhermitte phenomenon, a 2-month progression of unsteady gait, clonus, and blurred vision. Again, symptoms resolved with oral steroid treatment.

After he received monthly intravenous methylprednisolone treatments for 3 months, the patient was admitted to the hospital again. A third MR of the brain was obtained (Figs 1G and 1H) a total of 11 months after the first study. Also, cerebellar and leptomeningeal biopsies were performed without complication. During the patient's extensive workup, no cause could be found for his neurologic problems. Some of his normal studies included antiphospholipid antibodies, lupus anticoagulant, antinuclear antibody, lyme titer, human immunodeficiency virus, and human T cell lymphotropic virus type 1. On three occasions the cerebrospinal fluid showed elevated protein and lymphocytes, with all other values normal. There were no oligoclonal bands.

Right cerebellar biopsies extended to a depth of 3 cm and included white matter (Fig 1I). There were small arteries with the muscular walls infiltrated by lymphocytes, macrophages, and occasional polymorphonuclear leukocytes (Fig 1J). The infiltrate extended into the immediate surrounding gray and white matter. One vessel showed almost complete destruction of the wall, with obliteration of the lumen by inflammatory cells. The surrounding cerebellar tissue showed a reactive gliosis.

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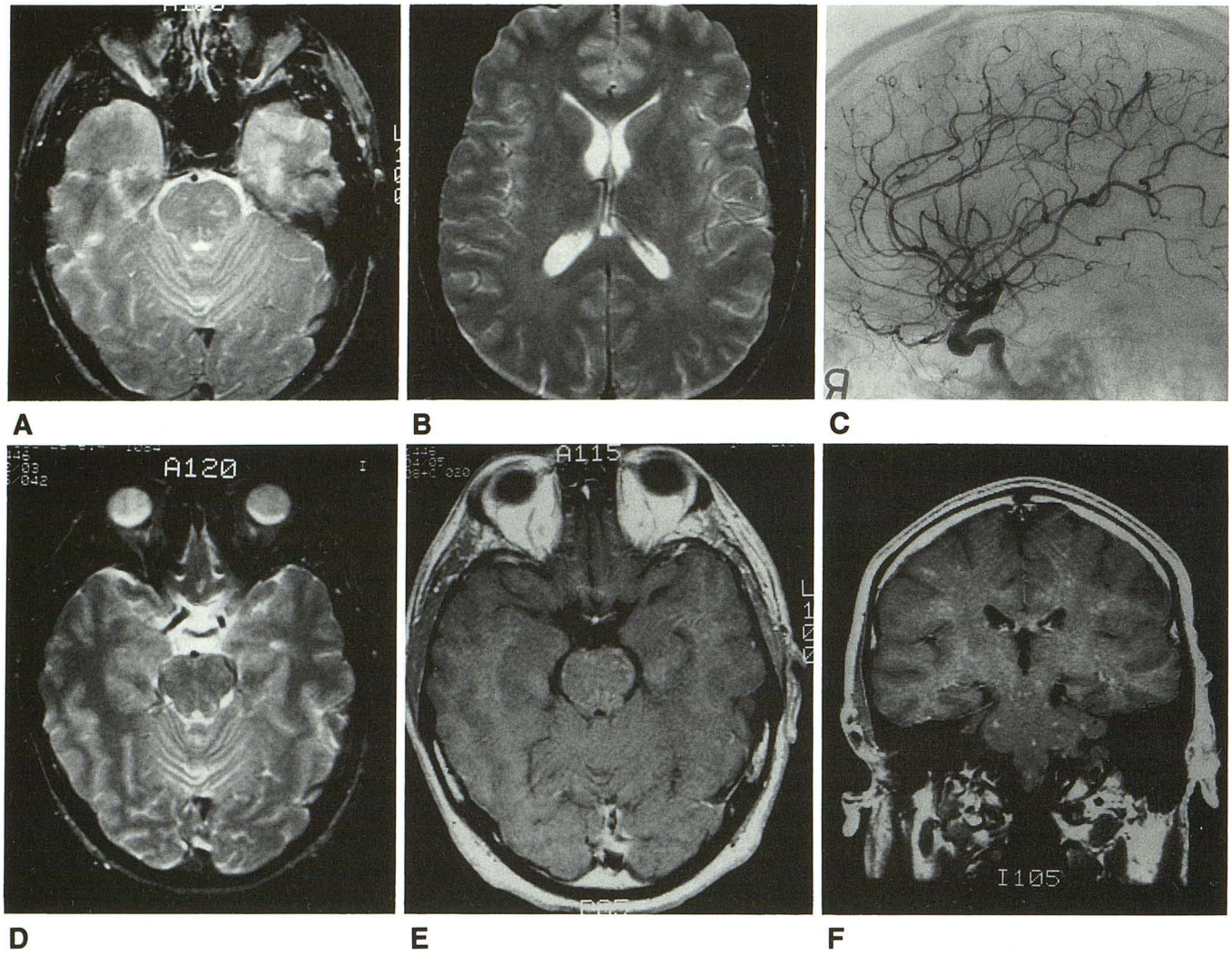


Fig. 1. *A*, Axial T2-weighted (2800/90/1 [repetition time/echo time/excitations]) image from first study shows focal areas of hyperintensity in the brain stem.

B, Axial T2-weighted (2800/90/1) image from same study shows focal high signal in left frontal white matter, with a faint second lesion in the right frontal lobe.

C, Lateral view; right carotid artery angiogram is normal.

D, Axial T2-weighted (2857/80/1) image from second study 5 months later again shows focal areas of high signal in the brain stem.

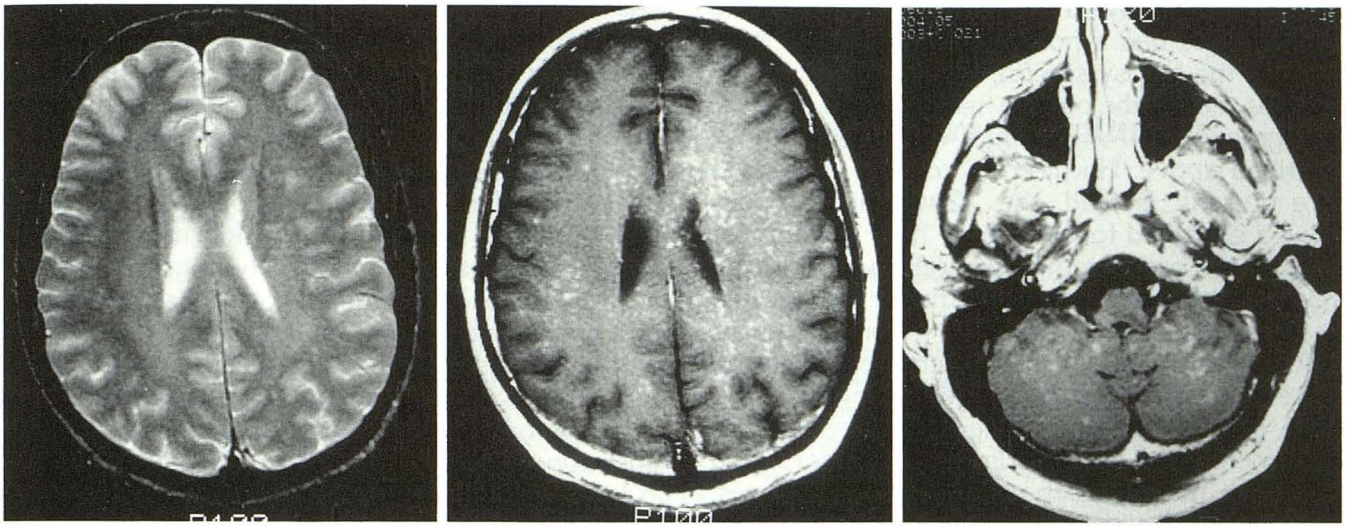
E, Axial T1-weighted (750/20/2) gadolinium-enhanced image at same level as D shows multiple focal areas of enhancement in the brain stem.

F, Coronal T1-weighted (750/20/2) gadolinium-enhanced image from second study shows multiple areas of enhancement in the brain stem and cerebral white matter.

Discussion

PACNS has been defined as a clinical disease characterized by central nervous system (CNS) dysfunction that remains unexplained after thorough clinical, laboratory, and neurologic investigations; it seems to be unassociated with a systemic illness. There is evidence of a vasculitis confined to the CNS, as demonstrated by cerebral angiography or brain biopsy (1). Other names that have been used include *cerebral granulomatous angiitis, granulomatous angiitis of the CNS, isolated angiitis of the CNS, granulomatous giant-cell angiitis of the CNS, and noninfectious granulomatous angiitis with a predilection for the CNS* (1).

Symptomatology can vary, and though early treatment is recommended to prevent recurrent episodes, the diagnosis may not be certain after the first presentation (7). Early symptoms include headache, confusion, intellectual deterioration, memory loss, and malaise (7). The process is complicated by the fact that these signs and



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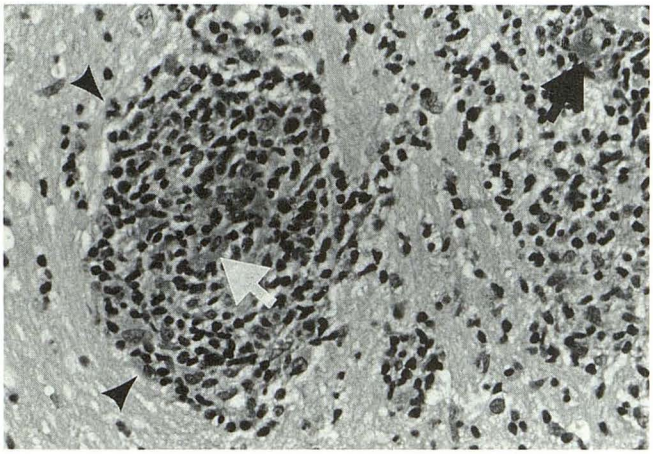

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Fig. 1—(continued)

G, Axial T2-weighted (2800/90/1) image from third study, 11 months after first study, shows faint areas of high signal in periventricular white matter, most prominent on the *left.* The two lesions present in B were still present on images through that region (not shown).

H, Axial T1-weighted (650/12/2) contrast-enhanced image at the same level as G shows multiple areas of focal enhancement in white matter, including corpus collosum.

I, Axial T1-weighted (650/12/2) contrast-enhanced image from third study shows the level of biopsy site of right cerebellum.

J, Specimen of right cerebellar biopsy at gray matter–white matter junction shows lymphocytic vasculitis (*black arrowheads*) surrounding hypertrophied endothelial cells (*white arrow*) of a small vessel in the superficial white matter. On the *right* side of this photograph is the cortical gray matter. Cytoplasm of a possible Purkinje cell (*black arrow)* is present within the granular cell layer of the gray matter with minimal inflammation (magnification 850×; hematoxylin and eosin stain).

symptoms can be caused by a variety of other conditions, and the diagnosis is usually one of exclusion. Treatment regimens include prednisone and cyclophosphamide (1).

Cerebral angiography plays an important role in the diagnosis of PACNS. One review found that 65% of patients with PACNS had angiographic findings of classic arteritis (1). This number should be interpreted cautiously, because in some cases of PACNS a positive angiogram and negative workup for an underlying cause has been used to establish a diagnosis; this may bias the sensitivity. Also, the many other causes of arteritis must be excluded, including infection and drugs. Atherosclerosis, a common cause of arterial alterations on angiography, may mimic arteritis (8). A negative angiogram does not exclude the diagnosis (7). The computed tomographic findings in PACNS tend to be variable, with local areas of decreased attenuation, a mass lesion, and normal scans having been reported (1).

We found 11 cases in the literature that described the MR findings in PACNS. A recent series of seven cases, one of these biopsy proved, had a total of 36 lesions seen with MR, all supratentorial, mainly consisting of cortical or deep white matter lesions. In those patients receiving gadopentetate dimeglumine, five of eight lesions showed enhancement (2). Four other cases in the literature are all biopsy proved. One had deep gray and white matter areas of signal abnormality (3), with another demonstrating multiple areas of high signal consistent with recent infarction (5). The third case described bilateral parieto-occipital white matter high signal, with extension across the splenium of the corpus collosum (4). The suspected diagnosis was a primary cerebral neoplasm. Biopsies in this patient included the corpus

collosum and showed no evidence of neoplasm. The last case had a normal MR, except for high signal at the biopsy site (6).

In this report, the patient had a normal cerebral angiogram. The MR findings were unlike those described above. No discrete cortical infarctions were present. Instead, the T2-weighted images showed scattered focal areas of high signal most noted in the brain stem and cerebellum, but also present in the cerebral white matter. These had a nonspecific appearance. New lesions appeared on follow-up studies; others decreased in prominence or disappeared. After injection of gadopentetate dimeglumine, multiple focal areas of enhancement were present in the posterior fossa and white matter of the cerebral hemispheres, many of these without corresponding signal abnormality on the T2-weighted images. Some were linear. Between the second and third studies, their number increased. These areas of signal abnormality seem to correspond to the location of perforating arteries of the brain stem and the cerebral and cerebellar hemispheres. The enhancement with gadopentetate dimeglumine can be attributable to a combination of vascular and perivascular inflammatory changes, which include both the meninges and surrounding gray and white matter. The T2-weighted images were less sensitive in the detection of these areas.

The cause of PACNS remains unknown. Many cases have granulomata without antibodies or immune complexes in the vessel walls; this has raised the question of cell-mediated immunity. There are no clinical, serologic, or hereditary features suggesting an autoimmune process (7). Even though a similar vasculitis has been seen in patients with Hodgkin disease and herpes zoster, patients with PACNS have no clinical evidence of a viral infection, nor has neoplasia developed in most patients (7).

Pathologically, the lesions are segmental and associated with a high degree of variation among cases. Usually there are multiple foci of infarction or hemorrhage, but occasionally large areas are seen. Any vessel, including the large intracranial vessels, can be involved, although there is a predilection for the small unnamed leptomeningeal vessels, usually affecting the media and adventitia. The inflammatory process can also involve veins. Because of the skip nature of the lesions, a biopsy may be falsely negative. There are reports of vasculitis discovered at postmortem examinations of patients whose previous biopsy results were negative (1). It is important to include samplings of both the leptomeninges and the cortical tissue, with the latter best demonstrating the abnormalities in our patient.

In conclusion, PACNS is a rare disorder with nonspecific symptomatology, and MR is useful in ruling out other disease processes. Diagnosis solely with MR does not appear possible given the varied and nonspecific appearance in the cases reported.

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