Atypical Lymphocytic Angiitis of the Optic Nerve and Central Nervous System

Primary angitis of the central nervous system (PACNS), also known as primary vasculitis of the central nervous system, is a rare, poorly understood, and often fatal disorder. Although the association of PACNS with optic neuropathy has been documented, this is the first report to our knowledge of visual loss with histopathologic involvement of the optic nerves.

Report of a Case | Our patient developed decreasing visual acuity and right-sided weakness in his 40s after falling from a height of 3 m. Neuroimaging revealed normal blood vessels on computed tomographic angiography and irregular large areas of hyperintensity in the brain and cervical spine on magnetic resonance imaging, consistent with demyelinating processes of different ages. He was treated for multiple sclerosis with interferon beta-1a (Avonex, Rebif) and natalizumab (Tysabri) for 4 years but then experienced altered mental status and left-sided weakness. He developed bowel and bladder incontinence, monoplegia of the left lower extremity, spasticity, and loss of vision in the left eye. During the last month of life, he was treated for multiple urinary tract infections and died of acute aspiration bronchopneumonia.

The brain was normal sized with multiple circular granular lesions ranging in diameter from 1 to 3 mm. The largest lesion was in the mid–corpus callosum at the level of the caudate nucleus, and multiple small lesions surrounded the calcarine fissure. Both eyes had indistinct borders of the optic nerve, suggestive of optic edema.

Microscopic examination of the brain revealed no multiple sclerosis plaques. Instead, there were prominent eosinophilic (Figure 1A), well-circumscribed nodules of fibrotic tissue (Figure 1B) in the white and gray matter of the right occipital lobe and medulla. The nodules had a central, cellular core containing a mixture of macrophages and CD3+ T lymphocytes (Figure 1C) and CD20+ B lymphocytes (Figure 1D), with T cells predominating. Lymphocytic vasculitis (angiitis) involved arterioles. Reactive astrocytes surrounded arterioles within the nodules. Reactive microgliosis with a few macrophages surrounded the nodules. We interpreted the nodules as representing areas of fibrosis secondary to chronic inflammation, consistent with a partial response to immunosuppressive therapy.

Figure 1. Histopathologic Findings in the Brain

A, Section of the right occipital lobe shows well-circumscribed, eosinophilic nodules with demyelination indicated by loss of blue staining (hematoxylin-eosin and Luxol fast blue, scale bar = 500 μm). B, The nodules were fibrotic as highlighted by the green staining using Masson trichrome stain (scale bar = 500 μm). C, The nodules had a central, cellular core containing a mixture of macrophages and CD3+ T lymphocytes (C) and CD20+ B lymphocytes (D), with T cells predominating. The lymphocytes surroundcd and infiltrated the wall of an arteriole.

Letters
Both eyes had bilateral lymphocytic angiitis with vascular fibrosis of the optic nerve as well as optic nerve demyelination (Figure 2). There was a scant mononuclear infiltrate in the optic nerve meninges bilaterally, similar to that in the leptomeninges of the brain.

Discussion | The diagnosis of PACNS is extremely challenging owing to the limited diagnostic performance of current neuroradiologic studies and the large number of conditions that can mimic PACNS. The diagnostic criteria for PACNS are the presence of an acquired neurological or psychiatric deficit, the classic angiographic or histopathological features of PACNS, and no evidence of systemic vasculitis or any disorder that can cause or mimic this condition. Only histopathology can definitively confirm the diagnosis of PACNS.

Visual loss has rarely been described in PACNS, but without corresponding histopathologic analysis. Four cases of bilateral visual loss have been reported secondary to cortical infarction. Optic disc edema has also been rarely reported in patients with PACNS, most commonly in association with increased intracranial pressure, which was not documented in our patient. In another case of PACNS with bilateral optic disc edema, a relative sparing of the visual acuity suggested an optic perineuritis pattern. The histopathologic picture of non-granulomatous PACNS in our patient resembles that described by Solis et al in the absence of a clinical history of decreased visual acuity.

In conclusion, visual loss may be associated with involvement of the optic nerve in PACNS. Primary angiitis of the central nervous system and optic nerve should be considered in the differential diagnosis of optic disc edema and magnetic resonance imaging findings resembling a primary demyelinating illness.

Eleonora M. Lad, MD, PhD
Christine M. Hulette, MD
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Eleonora M. Lad, MD, PhD
Christine M. Hulette, MD
Alan D. Proia, MD, PhD

Author Affiliations: Department of Ophthalmology, Duke University Medical Center, Durham, North Carolina (Lad); Department of Pathology, Duke University Medical Center, Durham, North Carolina (Hulette, Proia).


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Acquisition, analysis, or interpretation of data: All authors.

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OBSERVATION

Optic Disc Pit Maculopathy Recurring in the Absence of Vitreous Gel
Optic disc pit (ODP) is a rare congenital cavitation in the optic nerve head frequently associated with serous detachments of the macula, ODP maculopathy (ODP-M), and subsequent visual decline.\(^1\) Optic disc pit maculopathy is preceded by development of a schisis cavity due to accumulation of intraretinal fluid from the ODP. The source of the fluid remains controversial and 4 mechanisms have been hypothesized: (1) fluid from the vitreous cavity\(^2\); (2) cerebrospinal fluid originating from the subarachnoid space\(^3\); (3) fluid originating from the orbital space surrounding the dura\(^4\); and (4) fluid from leaky blood vessels at the pit base.\(^1\)

We report the long-term follow-up of a patient diagnosed in his teens as having bilateral ODPs with ODP-M in the left eye. He underwent 3 pars plana vitrectomies (PPVs), with endolaser and gas, within a 2-year period. The last PPV was performed nearly 16 years ago by one of us (B.F.G.), with resolution of the maculopathy and restoration of visual acuity.

Report of a Case | A man in his 30s with bilateral ODPs presented with decreased vision in his left eye. He was diagnosed as having ODP-M in his left eye 18 years earlier and underwent PPV with gas. Six months later, his ODP-M did not resolve. He underwent a second PPV with endolaser and gas. After initial improvement, his maculopathy recurred with subretinal fluid (SRF) extending through the fovea. One year later, he underwent a third PPV by one of us (B.F.G.) with barricade endolaser, gas, and prone positioning. His subsequent examinations revealed resolution of his maculopathy with best-corrected visual acuity of 20/20 OD and 20/30 OS 3 years later.

His dilated fundus examination revealed bilateral inferotemporal ODP with temporal juxtapapillary retinal atrophy and peripapillary SRF in the left eye (Figure 1) extending to the fovea, confirmed by spectral-domain optical coherence tomography (Figure 2A). Surgical repair was performed with 23-gauge PPV, with peripapillary barricade endolaser, internal limiting membrane peel, endolaser of the temporal peripapillary retina, air and fluid exchange with drainage through retinal fenestration, and 18% sulfur hexafluoride gas. No SRF drainage was performed during the intervention. The absence of vitreous in the peripapillary or macular retina was confirmed with intravitreal triamcinolone acetate. At 10 weeks after surgery, his uncorrected visual acuity was 20/70 +1 OS with resolution of metamorphopsia and near resolution of SRF and intraretinal fluid (Figure 2B).