MR Imaging of Papilledema and Visual Pathways: Effects of Increased Intracranial Pressure and Pathophysiologic Mechanisms

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Papilledema is the term used to describe optic disc swelling associated with ICP. While the pathogenesis of papilledema is not fully understood, recent studies have demonstrated a link between elevated ICP and the development of papilledema. The importance of papilledema as a useful indicator of increased ICP has long been recognized, with this phenomenon posited as early as the 1920s, with 1 pioneering ophthalmologist commenting, “While it is true that papilledema is a variable correlate of increased intracranial pressure, it is, nevertheless, a valuable guide to the necessity for surgical intervention.” Since the first descriptions of papilledema on fundoscopic examination, a variety of diseases have been reported as presenting with papilledema. Modern evidence suggests that papilledema is caused by an increase in ICP that is transmitted to the SAS surrounding the ON, thereby interrupting the metabolic processes of the nerve and consequently leading to edema, ischemia, and eventual visual impairment or loss. The urgency of this condition and the need for its prompt recognition are as important now as they were in 1937 when Dr. Gordon Holmes addressed the Ophthalmological Society, saying: “As the essential etiological factor in papilloedema is increase in ICP, the relief of this pressure will lead to its disappearance and remove the risk of blindness or serious deterioration of vision if it can be effected before secondary changes have developed in the disc. It is therefore natural that those who are primarily concerned in the conservation of the patient’s sight should demand early or immediate operation, for it is only by operation that permanent relief of pressure can be obtained.”

Papilledema has gained increasing interest in recent years among neuro-ophthalmologists as the result of several clinical studies demonstrating that it may have not only diagnostic potential as a measure of increased ICP but also therapeutic potential as a measure of disease severity and response to treatment.

In attempting to detect and diagnose papilledema as early as possible in patients, MR imaging is becoming a useful noninvasive method. Because MR imaging can provide gross visualization of the optic globe, ON, orbits, and optic tract, it is an ideal tool to study the details of papilledema. This review provides a brief outline of the common MR imaging findings of papilledema and its pathologic mechanisms.

ON Anatomy
The ON is a white matter tract of the CNS that passes through the optic canal into the orbit. Anatomically, the nerve can be divided into orbital and intracanalicular components. The orbital portion consists of the bulbar segment and the midorbital segment. The bulbar segment forms the widest part of the orbital portion and is adjacent to the ocular globe. The midorbital segment follows the bulbar segment.

Perioptic Meninges
The perioptic meninges or ONS envelope the length of the ON up to the globe and is continuous with the intracranial meninges. For this reason, pressure changes in the intracranial space can be transmitted to the optic papilla via the SAS accompanying the ONS.

SAS of the ON
The SAS of the ON is a multichambered tubular system with a blind end behind the globe. The SAS of the ON is anatomically classified into a bulbar segment, intraorbital segment, and canalicular portion. These divisions are not uniform in architecture: The bulbar segment consists of trabeculae, the intraorbital segment consists of septa and pillars, and the canalicular portion consists of trabeculae and pillars. This architectural meshwork may play an important role in maintaining the pressure within the nerve.

ABBREVIATIONS: ICP = intracranial pressure; IIH = idiopathic intracranial hypertension; ON = optic nerve; ONS = optic nerve sheath; SAS = subarachnoid space

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A number of studies have used imaging techniques to investigate the anatomic changes of the ON in papilledema.5,6,8,9,12-15 Of the many imaging techniques, MR imaging has been of particular interest because of its ability to provide gross visualization of the optic globe, ON, orbits, and optic tract. Additionally, MR imaging provides higher soft-tissue contrast and free section orientation capabilities compared with CT and appears to be more accurate in assessing the ON than sonography.16

Despite these advantages, the ON has been technically difficult to image because of its small size: It is 0.4 – 0.6 cm in diameter within the orbit.8 T2-weighted FSE sequences with fat-suppression have been found to be optimal for visualizing the ONs and perioptic CSF.6,17-19 Coronal image acquisition is optimal for visualizing the true dimensions of the ON and perioptic CSF relative to the surrounding sheath.12 The most commonly reported macroscopic findings in MR images of patients diagnosed with papilledema are the following: 1) enlargement of the ONS,5,6,8,9,20 2) flattening of the posterior sclera,13-15 3) protrusion of the optic papilla into the globe,6,11 and 4) tortuosity of the ON.6

**Enlargement of the ONS**

The SAS around the ON in the orbit can be observed by using T2-weighted MR imaging with fat-saturation pulse sequences (Fig 1). The ONS diameter can be evaluated by measuring the outer diameter of the SAS.5

The normal ONS diameters just behind and 4 mm posterior to the globe are 5.52 ± 1.11 and 5.2 ± 0.9 mm, respectively.5 The ONS is widest anteriorly behind the globe and narrowed toward the orbital apex; these dimensions are consistent with the results of a histologic study of the ON.12 The sheath of the ON behind the globe is the most distensible part of the ONS, giving it a bulbous appearance.12

ONS enlargement appears as a widened ring of CSF around an ON and as a widened CSF signal intensity on either side of the ON on axial images.6 The finding of ONS enlargement have been reported previously in association with intracranial hypertension on sonography4 and CT.21 Seitz et al9 used MR imaging to examine patients with papilledema and found that the mean width of the ONS directly behind the globe was 7.54 mm (±1.05 mm) in pathologic conditions, compared with 5.52 mm (±1.11 mm) in healthy subjects. In addition, the CSF surrounding the ON from the optic globe toward the optic chiasm was visible over a longer distance (12.4 mm) in patients compared with healthy subjects (6.3 mm).9 Similar findings were noted in patients with IIH, with an enlarged and elongated SAS around the ON.8 The orbital portion of the ON was examined in patients at different stages of papilledema, and the diameter of the ONS was found to be increased compared with that in healthy subjects.20 With severe papilledema, the diameter of the ON just behind the globe was significantly less than that with moderate papilledema; this difference indicates that increased subarachnoid pressure may lead to gradual atrophy of the ON.20 Dilation of the SAS, compression of the ON, and widening of the ONS were also observed with optic disc pallor.12 Broadening of the ON directly behind the optic globe may also occur with papilledema.9

MR imaging has been used to evaluate the effectiveness of treating elevated ICP with ONS fenestration by assessing the
resolution of the optic sheath enlargement. ICP and ONS diameter in patients with chronic subdural hematoma or hygroma who underwent burr-hole craniotomy and continuous drainage have shown significant correlation. ONS diameter before surgery (6.1 mm) was significantly reduced after surgery (4.8 mm). These findings suggest that the ONS diameter is a strong indicator of increased ICP.

Flattening of the Posterior Sclera
Several studies have demonstrated posterior scleral flattening (Fig 2) in patients with elevated ICP. Gibby et al noted this finding on CT scans and considered it to be the mildest in the spectrum of changes leading to the protrusion of the ON head into the globe. Atta and Byrne noted flattening of the posterior sclera on sonography in some patients with choroidal folds and papilledema. Jacobson found bilateral flattening of the posterior sclera and distension of the perioptic SAS on MR imaging in a patient with elevated ICP and unilateral papilledema. These findings suggest that the combination of acquired hyperopia and choroidal folds may indicate pseudotumor cerebri in rare patients whose distal ONs are structurally resistant to developing papilledema.

Protrusion of the Optic Papilla into the Globe
The optic papilla is considered by some to be the site most vulnerable to the effects of elevated CSF pressure in the nerve sheath. Normally, the optic papilla appears as a flat hyperintense (hypointense relative to the vitreous of the globe of the eye) region in the posterior sclera. In pseudotumor cerebri, intraocular protrusion of the optic papilla is occasionally observed on MR imaging. Brodsky and Vaphiades found prelaminar enhancement in 50% of MR images of patients with pseudotumor cerebri. However, they also found an absence of prelaminar enhancement in some patients with florid papilledema. Intraocular protrusion was also demonstrated by Jinkins et al in 10 (67%) of 15 patients with pseudotumor cerebri on MR imaging.

Intraocular protrusion of the optic disc (Fig 3) may not produce a sufficient signal-intensity differential with the vitreous of the globe on routine MR imaging. However, contrast-enhanced MR imaging may demonstrate a focal hyperintensity in the region of papilla protrusion because intraocular protrusion of the optic papilla disrupts blood flow in the optic prelaminar capillaries. The optic papilla usually appears hypointense relative to the vitreous fluid of the globe on T2-weighted images because it is largely composed of myelinated axons. However, extracellular edema generally produces increased signal intensity on T2-weighted images, and this seems to contradict active capillary leakage. Histologic studies in patients with papilledema have demonstrated that despite capillary leakage, prelaminar axons appear distended but show little evidence of extracellular edema. This could explain the hypointensity of the optic papilla relative to the vitreous on T2-weighted images.

Tortuosity of the ON
ON kinking or tortuosity (Fig 4) has also been associated with increased ICP. The ON tortuosity in patients with elevated ICP is attributable to the fixation of the distal and proximal points of the ON. The sensitivity of observing ON tortuosity in either the vertical or horizontal planes also depends on section thickness. The ability of axial MR imaging to display relatively minor degrees of horizontal tortuosity makes it a somewhat nonspecific finding. Tortuosity of the vertical component, which requires a greater deflection of the ON to be visible on axial scans, retains a higher specificity value. Vertical tortuosity of the ON is often accompanied by a “smear sign,” in which the midportion of the ON appears obscured by a “smear” of orbital fat on T1-weighted images.

Brodsky and Vaphiades theorized that periopetic distension would be expected to straighten the ONs if the globes were not tethered in the orbits by their rectus muscles and check ligaments. However, the absence of proptosis in patients with papilledema suggests that the focal pressure exerted by the bulbous portion of the distended periopetic nerve sheaths on the posterior sclera is insufficient to displace the globes anteriorly. Instead, the globe provides resistance to the distal bulbous portion of the ONs, which may kink the inflated ONs.

Pathogenesis of Papilledema
Because all CSF spaces communicate freely, the pressure and composition of the CSF is thought to be the same throughout the CNS. Consequently, researchers have based their theories and experiments on the assumption that the pressure in the SAS surrounding the ON is the same as that in the cerebral and spinal SAS. However, this assumption has not been proved, mainly due to the difficulty in obtaining accurate pressure measurements in the SAS of the ON in vivo. In the SAS of the ON, CSF flows from the chiasmatic cistern through the canaliculic portion and into the intraorbital portion of the ON, a space that becomes a cul de sac at the back of the globe.
A number of theories have been postulated during the past century to explain the pathogenesis of papilledema. In 1911, Leslie Paton, an ophthalmologist and Gordon Holmes, a neurologist, reported the results of the first definitive light microscopic study of papilledema. They concluded that papilledema was due to compression of the subarachnoid portion of the central retinal vein by a high ICP and that this produced dilatation of the optic disc segment of the vein. Leakage from this dilated vein and its feeding capillaries then caused prelaminar optic disc swelling and bending of axons, which occasionally resulted in their fracture.

In the late 20th century, the theory of axoplasmatic stasis replaced the Paton-Holmes venous compression doctrine following electron microscopy evidence of intra-axonal edema of the optic disc in acute glaucoma, ocular hypotony, and increased ICP. Studies of axoplasmic flow within the ON, as measured by the progress of titrated leucine injected into the vitreous cavity and incorporated into retinal ganglion cells, showed that axoplasm was arrested in the region of the lamina cribrosa. It was thought that the high-pressure gradient, present in all 3 conditions, caused or contributed to the axoplasmatic stasis.

Currently, investigators are focusing on uncovering the mechanism by which elevated ICP causes papilledema. Two competing theories are at the forefront of current research—the mechanical theory and the ischemic theory. The mechanical theory postulates that elevated ICP causes direct compression of axons. The high ICP compresses the ON at its junction with the globe and distends its prelaminar axons as their axoplasm piles up at the scleral lamina. Howden et al found that CSF velocity is substantially slower in areas farther away from its inlets and that at certain sites, the flow nearly stagnates. Therefore, any reduction in CSF flow rate should first affect the SAS of the ON, which is farther away from the ventricles and anatomically does not allow continuous flow.

The ischemic theory postulates that elevated ICP causes reduced perfusion of the ON axons. The retrolaminar region of the ON is a watershed area and is prone to ischemic insult. With severe dilation of the distal optic SAS, all the regional neural and vascular structures can become compressed, compromising vascular flow. Trobe proposed that papilledema results primarily from the competitive relationship between the ciliary arterial circle and the choroidal circulation. If the subarachnoid pressure rises, the ciliary circulation becomes the ciliary arterial circle and the choroidal circulation. If the results primarily from the competitive relationship between CSF metabolites may accumulate.

Furthermore, papilledema may be asymmetric or unilateral, and the degree of ON head swelling is poorly correlated with ICP.

In the recent William F. Hoyt Lecture of the American Academy of Ophthalmology, Dr Jonathan Trobe posited that papilledema is only a reliable indicator of chronically high ICP because the development of papilledema tends to lag behind the rise in ICP. Trobe noted that fewer than 20% of patients examined within a few days of head trauma or ruptured aneurysm have papilledema and only 6% of patients with chronically high ICP lack papilledema. On the other hand, intracranial hypertension can occur without the presence of papilledema. Possibly, MR imaging could assess the presence of intracranial hypertension before the development of papilledema. According to Hansen and Helmke, there is a correlation between the width of the ONS and increased ICP. A width of >5 mm in this location is considered abnormal. This may occur because the ONS is not as rigid as other intracranial meningeal structures and can thus react without volume changes of intracranial CSF spaces.

Elevated ICP may lead to several abnormalities on MR imaging, including the following: 1) flattening of the posterior sclera, 2) enhancement of the prelaminar ON, 3) distension of the perioptic SAS, 4) intraocular protrusion of the prelaminar ON, 5) vertical tortuosity of the orbital ON, and 6) empty sella. In patients with pseudotumor cerebri, all neuroimaging signs except for intraocular protrusion of the optic disc have been found to be highly significant for the presence of elevated ICP. Flattening of the posterior sclera was found in 80% of these patients; empty sella, in 70%; distension of the perioptic SAS, in 45%; and enhancement of the prelaminar ON, in 30%. On the basis of these signs, elevated ICP may be predicted in 90% of these cases. Posterior scleral flattening and prelaminar enhancement were thought to be confirmatory for papilledema, whereas distension of the perioptic nerves or empty sella was only considered suggestive for elevated ICP.

Once the diagnosis of elevated ICP is established, the appearance of the discs and the severity of papilledema are commonly used as measures of disease severity and response to therapy. However, the degree of papilledema does not predict the severity of symptoms. Increased CSF pressure might produce different disc abnormalities depending on the normal size of the ONS. Further studies should lead to a better understanding of the mechanisms and augment our ability to detect papilledema on imaging and allow early intervention to maintain or restore vision.

Future Directions of MR Imaging in Papilledema Imaging

MR imaging findings in papilledema only represent 1 aspect of papilledema—the anatomic alterations of the optic disc and nerve. Recent advances in MR imaging make it possible to more closely examine the interface between anatomic disruption and physiologic dysfunction. Theoretically, MR imaging could be used to predict the visual outcome of papilledema as a prognostic test—deficits in functional imaging of the retina or disruption of the optic pathways could suggest a greater risk of vision loss.

A number of advanced MR imaging techniques to enhance image quality have been developed in the past decade and have been found to be valuable in imaging the ON.
High-resolution MR imaging may differentiate papilledema from other optic neuropathies and diagnose it earlier. High-resolution MR imaging has been used to visualize the ON and the smaller structures of the globe, including the lens, ciliary body, choroid, sclera, and retina with a high level of anatomic detail.40–44

fMRI has been used in mapping the function of cortical regions in a variety of healthy and disease states involving vision.45,46 In cases involving papilledema, fMRI of the visual pathway and particularly the retina may offer insight into the effect of papilledema on visual impairment. Retinal fMRI is still in the early stages of development and is currently performed only in animal models, still well below the resolution of optical imaging techniques.47–49 These animal experiments have already shown promise in imaging the activity of the retina in response to visual stimuli50 and can distinguish the 2 retinal layers supplied by the retinal and choroidal arteries with differing responses to hypercapnia and hyperoxia.51

Manganese uptake by active neurons to image neural activity.53–57 The role of manganese in the visualization of the retina has been shown in various studies.58–60 Manganese is a paramagnetic ion, which can be used to image neural activity in the retina.61–63 Manganese uptake by retinal ganglion cells has been demonstrated in vivo using fMRI.64–66 Manganese uptake by retinal ganglion cells can be visualized using fMRI, which can help in the diagnosis of papilledema.

Visualization of the fiber tracts from the retina to the visual cortex is also being investigated with DTI.58,59 DTI can map optic radiations within the brain with a great deal of accuracy compared with postmortem dissections.60 Retinal ischemia in an animal study showed decreased anisotropy within the optic radiations, suggesting that DTI can detect changes in the visual pathways as early as 3 days from injury, well before the potential appearance of papilledema.61 Other experiments in rats have demonstrated decreased anisotropy within the ON following glaucoma induction and ON injury.62,63 DTI has demonstrated decreased anisotropy and increased diffusivity in children with ON hypoplasia in septo-optic dysplasia.64 Disruption of these pathways leading to atrophy of distal axons projecting from the retina65 could predict visual loss from degeneration related to papilledema.

Conclusions

Papilledema represents a serious warning sign for elevated ICP and potential vision loss in a variety of clinical settings. MR imaging may facilitate its detection and demonstrate changes of elevated ICP well before the appearance of papilledema on fundoscopic examination. MR imaging signs such as flattening of the posterior sclera, dilation of the ONS, and protrusion of the optic disc head can be useful in the setting of papilledema. Although the mechanisms causing papilledema and its associated signs are not entirely clear, the role for noninvasive imaging in this clinical condition is evident. Future advances in DTI, fMRI of the retina, and high-resolution MR imaging hold the promise of demonstrating the effects of papilledema on the visual pathway in patients.

References


