The Diagnostic Dilemma of Pseudopapilledema

Tiffenie Harris, OD, FAAO
Associate Professor
Western University College of Optometry

Author’s Bio

Dr. Harris is a graduate of Indiana University School of Optometry. She practiced primary care optometry in the Detroit Metropolitan Area for 10 years prior to starting her academic career in 2004 at her Alma matter. She joined Western University College of Optometry in 2008. Dr. Harris is the Course Director for Principles and Practice of Anterior Segment and Posterior Segment courses.

Diagnostic Dilemma

Optic nerve head (ONH) elevation tends to be the most intimidating ocular finding especially when it presents bilaterally. The purpose of this article is to provide the clinician with clinical strategies that will enhance their assessment and management of bilateral disc elevations. In addition, this topic is important to review because effective management will reduce over-referrals for neurological evaluations, thus decreasing health care costs while avoiding needless and expensive neurological testing.

The optometrist’s role includes detection of disease with a timely and appropriate referral to specialists as well as co-management and/or monitoring once under the care of a physician. A clinical case in which the optic nerves are severely swollen is easy to diagnose. Yet, a case in which the nerves appear to be mildly or moderately elevated or swollen makes the diagnosis more challenging, especially when the patient presents with symptoms of headaches. This type of quandary frequently can cause alarm for the clinician, which often eclipses the fact that the patient has no other signs or symptoms of increased intracranial pressure (ICP).1,2 Thus, the diagnostic dilemma begins with making the clinical decision and answering the question, “Is it or is it not swollen?”

The foremost clinical goal is to differentiate congenital causes of disc elevation from acquired disc edema. Papilledema (PE) is acquired bilateral optic disc swelling attributed to increased intracranial pressure as listed in Table 1. Pseudopapilledema (PPE) is the appearance and false impression of bilateral disc swelling that is associated with an underlying anomalous condition as listed in Table 2. A thorough history and a dilated fundus examination will often facilitate the diagnosis. However, the use of current diagnostic technologies can increase clinician confidence and augment our ability to diagnose and manage these challenging cases.
Table 1
Differential Diagnosis of PE

<table>
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<tr>
<th>Diagnosis</th>
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<tr>
<td>Mass or Space Occupying Lesion</td>
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<tr>
<td>Malignant HTN (Hypertensive Crisis)</td>
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<tr>
<td>Idiopathic Intracranial Hypertension</td>
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<td>Intracranial Hypertension Secondary to:</td>
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<tr>
<td>Subdural Venous Thrombosis</td>
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<tr>
<td>Saggital Sinus Thrombosis</td>
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<td>Chiari I Malformation</td>
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<tr>
<td>Arteriovenous Malformation</td>
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<td>Menigitis/Encephalitis</td>
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Table 2
Differential Diagnosis of PPE

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<tr>
<th>Diagnosis</th>
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<tr>
<td>Optic Nerve Head Drusen (ONHD)</td>
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<tr>
<td>Congenitally Full Disc (CFD)</td>
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<tr>
<td>Malinserted (Oblique insertion)</td>
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<tr>
<td>Tilted Disc Syndrome</td>
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<tr>
<td>Optic Nerve Hypoplasia</td>
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<td><strong>DDx for bilateral presentations</strong></td>
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Background on Papilledema

In papilledema the acquired bilateral, occasionally asymmetrical, ONH swelling is due to increased intracranial pressure. The term papilledema should be strictly reserved for optic disc edema as a result of increased cerebral spinal fluid (CSF), which bears specific etiologic implications. The most important entity to consider in cases of increased intracranial pressure is a space occupying lesion of the brain. This is often done with diagnostic tools such as Magnetic Resonance Imaging (MRI) and/or Computerized Tomography (CT) scans in conjunction with a lumbar puncture (LP). Computerized Tomography has traditionally been the imaging study of choice because of its availability and lower cost per patient than MRI. However, MRI has emerged as the technically optimal imaging modality.

Papilledema due to increased CSF in the absence of mass lesion on brain imaging has been historically associated with the term Pseudotumor Cerebri (PTC). The nomenclature of the syndrome of elevated CSF with no mass effect, no ventriculomegaly, and with normal CSF composition remains controversial, yet, Benign Intracranial Hypertension is no longer accepted. Current literature based on clinical experiences and advances in neuroimaging technology supports the terminology of Idiopathic Intracranial Hypertension (IIH). The pathogenesis underlying the increased cerebral spinal fluid in IIH is not fully understood. Apparently, there is a disruption of the CNS homeostasis resulting in increased CSF production and decreased CSF absorption. Several mechanisms have been proposed. Sugerman et al suggested that intra-abdominal obesity causes increased intrathoracic pressure resulting in a decrease in cranial venous flow. Conversely, most of the clinical evidence points to an overall decrease of CSF absorption by the arachnoidal villi concurrent with intracranial venous hypertension.
The treatment and management of the underlying condition is crucial in the resolution of papilledema. In the presence of chronic PE the swelling eventually subsides leaving the nerve atrophic. The loss of axons is considered to begin with the peripheral axons with sparing of central axons explaining why in cases of PE the acuities and pupils are rarely affected. The rate at which a patient develops optic atrophy from PE is not specific. It depends upon many factors such as severity and prolonged duration of the increased ICP.\textsuperscript{1,4} It can take anywhere from days, months, to even years. On rare occasions a patient can present with no evidence of PE, yet still have increased ICP.\textsuperscript{1,4} Again, there is the diagnostic dilemma of optic nerve elevation as compared to swelling. Knowing that some cases of increased CSF may not present with overt PE, making the diagnosis of PPE is even more crucial. The conundrum can also lie in the fact that congenitally anomalous nerves can become swollen.

Help in piecing the puzzle together comes in the differential diagnosis of the underlying conditions. The basic pathophysiology of conditions that cause bilateral optic nerve swelling and that of congenital elevation can help in differentiating PE from PPE. The pathophysiology of papilledema is a reaction to the increased CSF as it passes from the subarachnoid space to the prelaminar optic nerve via the optic nerve sheath.\textsuperscript{1} The end result causes axoplasmic flow stasis and swelling of the axons in the prelaminar optic nerve. The pathophysiology of PPE is determined by the congenital anomaly associated with the disc elevation. In fact, congenitally anomalous disc elevation must be included in the differential etiologies of presumed PE before referring a patient for neuroimaging and a lumbar puncture.\textsuperscript{1,2}

**Background on Congenital Disc Anomalies**

PPE, encompasses anomalies of the optic nerve head such as congenitally full discs (CFD), malinserted discs (MID) and optic nerve head drusen (ONHD). Crowded Disc also known as CFD is the result of a normal number of retinal axons passing through a small posterior scleral foramen. The resulting appearance is that of a densely packed or crowded optic nerve head as the axons exit the globe.\textsuperscript{2,8} This is a nerve that is smaller than the average sized optic disc and is often associated with hyperopic eyes. Typically, it is slightly hyperemic in color with little to no physiological cupping along with superonasal and inferonasal blurred margins.\textsuperscript{2,9} Knowledge and appreciation of the appearance of the normal disc and its anomalies are required to distinguish between the healthy and the abnormal. This is true in the assessment of the optic disc appearance associated with malinserted discs.

The typical disc elevation seen in MID is due to the oblique insertion of the nerve to the globe. Primarily the nasal portion is elevated with the temporal portion depressed and often associated with a sclera crescent.\textsuperscript{2,9} It gives a swollen-like appearance because the nasal margins are often blurred. They typically have mirror images in the right and left eyes and a high association with moderately myopic corrections. Malinserted disc are tilted along its vertical axis such that the disc appears to have the nasal rim and margin raised or “heaped-up”.\textsuperscript{2} This type of tilt should not be confused with that of tilted disc syndrome. Tilted disc syndrome refers to
a triad of tilted discs, decreased visual acuities, and bi-temporal visual field defects that do not respect the midline. In tilted disc syndrome the disc’s vertical axis itself is tilted downward nasally giving the superior temporal aspect of the nerve an elevated appearance with the inferior portion depressed. Therefore, “tilted” discs are better described as “malinserted” discs in order to avoid confusing the term’s etiology with that of the syndrome.

Although it is not uncommon to encounter PPE as a result of crowded disc and/or malinserted disc, they are not the most frequent. By far the next entity frequently encountered that gives the false impression of disc elevation is ONHD. It is the most common cause of PPE, accounting for 75% of diagnostically challenging disc anomalies.  

**Background on ONHD**

ONHD are congenitally inherited as an autosomal dominant trait occurring approximately 1% of the population with an increasing prevalence of 10-fold in family members. The scleral canal and optic disc of eyes with drusen are much smaller than average. This is seen clinically where ONHD predominately occurs in Caucasians and rarely in African Americans, whose scleral canal size is often larger. There are two types of ONHD, visible and buried.

Buried ONHD are located beneath the disc surface and are not directly visible. They can cause elevation of the optic disc with or without blurred margins. They can often have a very dramatic appearance giving the impression of PE. In young children, the elevated optic nerve can present an ominous finding, as seen in Figure 1. Current research and studies suggests that an abnormally narrow opening of the scleral canal can cause a stasis of axoplasmic flow. This leads to abnormal axonal metabolism and mitochondrial calcifications creating calcium-like globular deposits within the papilla.

![Figure 1](image)

Congenial disc anomalies often have in common a particular “look” such as anomalous disc vasculature including early branching of the retinal vessels at the disc and secondary tortuosity. In addition, atypical vascular loops or corkscrew vessels at the papillary border are associated with congenitally anomalous discs.
In cases of ONHD, 10% will have some type of vasculature anomaly.\textsuperscript{9,10} ONHD is associated with peripapillary retinal pigment epithelial changes (33%) and an absent to very small cup-to-disc ratio.\textsuperscript{2,9} Drusen of the optic nerve head have no histopathologic relationship to retinal drusen and are not considered age-related. However, they have a tendency to become more visible as the patient ages as seen in Figure 2.

Figure 2

In early life, ONHD remain deep in the nerve and always anterior to the lamina cribosa. They become more visible at the disc surface in the second to third decades.\textsuperscript{10} In adulthood, ONHD appear as spherical nodules on the disc surface that are highly reflective by the ophthalmoscope light and give the disc a scalloped margin. When illuminated with a red-free light these retractile bodies will auto fluoresce.

Most patients with ONHD are asymptomatic. However, many can present with visual field defects and rarely with decreased visual acuities. ONHD can shear and damage the nerve fibers and vascular supply as they move to the disc surface. The reduction of RNFL thickness results in visual field defects including enlarged blind spots, localized depressions, arcuate nerve fiber bundle defects, or constrictions. Visual field defects are present in 73% of visible drusen and 36% of buried disc drusen with no significant difference in the severity.\textsuperscript{11,12} Spontaneous disc hemorrhages can occur in, around, and over the optic nerve head if progression of the drusen interferes with the nerve’s blood supply. The incidence of retinal hemorrhage is between 2% and 10%.\textsuperscript{10} Visible disc drusen may cause peripapillary atrophy and a break in Bruch’s membrane. As a result, the patient is at risk of the development of peripapillary choroidal neovascular membranes, which may extend to the macular or subfoveal area and compromise the patient’s vision.\textsuperscript{10,13,14}

Conditions known to be associated with ONHD include Retinitis Pigmentosa (RP) and Angioid Streaks with or without Pseudoaxanthoma Elasticum (PXE). The ONHD in PXE are similar but in RP they do not have the same appearance.\textsuperscript{2,10} They tend to be more visible adjacent to a normal-sized nerve. In addition, there have been reports of non-arteritic anterior ischemic optic neuropathy (NAION) associated with ONHD.\textsuperscript{2,10,15}

Building upon the pathophysiolgy of various disorders which can result in a bilateral elevated disc appearance, the clinician can now approach the case with a systematic framework using information established in a checklist approach. In every case of ONH elevation there should be an “instant checklist” in order to help the practitioner to effectively determine if the nerve is in fact “swollen” or “elevated”. A review of this checklist provides clinical strategies to effectively manage this diagnostic dilemma. The checklist consists of the following elements:
A comprehensive history to illicit symptoms associated with increased intracranial pressure (ICP) (Table 3)
- Assessment of cranial nerve function
- Assessment of optic nerve function
- Stereoscopic examination of the optic nerve appearance and peripapillary area
- Diagnostic and ancillary testing

Table 3.
Symptoms of PE

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<th>Symptom</th>
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<tr>
<td>Headaches (HA)</td>
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<tr>
<td>Transient Visual Obscurations (TVO)</td>
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<tr>
<td>Tinnitus – “Whooshing” sound</td>
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<tr>
<td>Diplopia</td>
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** HA and/or TVO are most common**

Diagnostic Testing

Differential diagnoses include any entity that can cause bilateral optic disc elevation. This includes increased intracranial pressure and congenital disc anomalies. Special investigations for the definitive diagnosis of bilateral disc elevation include the following: Magnetic Resonance Imaging (MRI) and/or Computerized Tomography (CT) scans of the orbit and brain, Fluorescein Angiography (FA), B-scan ultrasonography, and Optical Coherence Tomography (OCT). The CT scan can detect intracranial tumors as well as ONHD. However, it is not sensitive enough to pick up subtle calcific drusen in the disc and is not reliable for ONHD diagnosis.¹² The MRI is superior to CT scan for soft tissue structures and is the preferred imaging test to rule out the etiology of increased intracranial pressure. FA can be helpful in papilledema where the optic nerve head will show hyperfluorescence and peripapillary leakage of the dye. In congenital disc elevation, there is no peripapillary leakage of the dye especially in the late phase. In addition, the red-free barrier used in the pre-injection phase illuminates the autofluorescent properties of disc drusen. Buried ONHD with both of these techniques can be missed. Less invasive diagnostic investigations are available to differentiate disc edema and buried disc drusen.

B-Scan ultrasonography has been shown to be the most sensitive and diagnostically relevant test to aid in the differential diagnosis of ONHD.²¹⁰,¹²,¹⁶ B-scan ultrasonography uses high-frequency sound waves. The sound waves are reflected back to the probe, converted into an image, which is used to make a dynamic evaluation of the optic disc. When calcification of tissue is present, there is a very strong reflection of the echo back to the probe. Therefore, B-scan ultrasonography is the single most important ancillary test to perform in the diagnosis of ONHD. The results for ONHD will show a highly reflective nodule within the optic nerve even at a low gain level as seen in Figure 3. In the presence of acquired disc edema, the B-scan will demonstrate a circle within the optic nerve sheath, separating the sheath from the optic nerve at a standard gain level. This is called a “crescent sign” produced by the increased cerebral spinal fluid transmitted along the subdural space within the optic nerve.¹⁶
Optical Coherence Tomography (OCT) is analogous to the B-Scan except light, rather than sound is used to provide images of the ocular structures. OCT is an objective, noninvasive alternative to analyze the optic nerve head. More importantly, it is useful in quantifying the status of the retinal nerve fiber layer (RNFL). In papilledema, the OCT shows an elevated nerve head along with excessive thickening of the RNFL as seen in Figures 4 and 5. In Figure 6, the OCT shows the elevation of the disc and the underlying nodular shadows caused by the ONHD. The key differential between ONHD and acquired disc edema is significant thinning of the retinal nerve fiber layer with ONHD (Figure 7) and thickening in disc edema. In cases of papilledema the RNFL curve falls above the normative, age-adjusted scale exceeding 200 microns. Many cases of early papilledema as seen in Figure 8 can clinically mimic buried ONHD. The nasal margins are blurred and the disc has anomalous vasculature branching. The OCT results for this example are shown in Figure 5 and clearly show that the RNFL layer is thickened as seen in early papilledema. In cases of CFD and MID, the OCT will show a normal to slightly thickened retinal nerve fiber layer curve that stays within the age-adjusted scale. Figures 5 and 7 demonstrate the application of testing RNFL to aid in differentiating early PE from PPE.
Making the Diagnosis

Making the clinical diagnosis begins with a working checklist starting with a comprehensive history. During the history, the practitioner is listening for symptoms associated with increased intracranial pressure and any associated neurological defects. Table 3 highlights the symptoms of PE that can often serve as the “red flag” of increased intracranial pressure. Medical, family, and social history are also helpful in suspected cases of increased intracranial pressure. Always include in the checklist the patient’s age, demographics, general appearance, and ocular/medical history, medication review, and in-office blood pressure readings.

Visual acuities, pupils, color vision, extraocular muscles, and visual field screening are important to determine if there is any optic nerve or cranial nerve dysfunction associated with elevated optic discs. Acuities are normal in most cases of PE until optic atrophy or macular edema develops. Most patients with ONHD, CFD, and MID are asymptomatic with normal acuities, color, and visual fields. Conversely, many cases of ONHD can present with visual field defects and rarely with decreased visual acuities. In rare cases, ONHD can cause an afferent pupillary defect. The pathophysiology of the pupil defect can be a direct result of the drusen’s effect on the RNFL as well as a result of asymmetric RNFL loss.

Cranial nerves of the extraocular muscles (EOMs) must also be assessed. Patients with CFD, ONHD, and MID will not exhibit any deficits of the EOMs. But, patients with PE need to be screened for a sixth nerve palsy (SNP). Approximately 38% of patients with IIH will present with a sixth nerve palsy. The patient will report horizontal diplopia during motility examination. In fact, the SNP is a non-localizing sign of increased ICP from any etiology. The sixth cranial nerve is vulnerable to the effects of elevated ICP. As the nerve courses the base of the posterior fossa, it runs along the petrous portion of the temporal bone. The increased ICP cause the nerve to compress against this boney structure. A posterior fossa brain lesion can produce a bilateral SNP. There has been a less frequent association of cranial nerves III, IV, and VII palsies with increase intracranial pressure.
A dilated fundus examination including stereoscopic views of the disc provides the most effective optic nerve evaluation. There are key characteristics to look for in determining disc edema from elevation. Start with the overall disc appearance looking at the size, cup, margins, neuroretinal rim tissue color, and taking note of any spontaneous venous pulsation (SVP). SVP is present in about 20% of the normal population. Next, study the vasculature of the disc and surrounding tissue. In the presence of papilledema, the optic nerve will appear elevated and hyperemic with blurred margins that will obscure peripapillary vessels as they leave the disc. The swelling includes no SVP along with venous congestion with flame-shaped hemorrhages and cotton wool spots. Buckling or retinal folds of the temporal aspect of the disc (Paton’s lines) may be present. In contrast, congenitally anomalous discs will not have peripapillary vessel obscuration nor will there be any cotton wool spots. In addition, Paton’s lines are not associated with pseudopapilledema. Look for anomalous vascular patterns including tortuosity. Clinical diagnosis and decisions are made based on the appearance of the optic nerves and information provided by the ancillary tests.

Now what to do about it?

Once the clinician determines that the discs are in fact swollen, the patient must be sent for neuroimaging within 24 hours to identify the source of increased ICP. Take stereo disc photos, get a baseline threshold visual field, and order the MRI. The visual field defects associated with papilledema start as an enlarged blind spot. Depending on location and severity of a brain lesion, neurological visual field defects such as quadranopsia or hemianopsia can occur.

In addition to visual field testing, the OCT provides an available option for long-term follow-up of the changes in RNFL thickness. This is helpful in monitoring the resolution of papilledema as well as monitoring RNFL loss in ONHD. Patients with ONHD can develop visual field defects and RNFL loss that resembles glaucoma. Glaucoma and ONHD can coexist. The OCT cannot distinguish nerve fiber layer loss that occurs from ONHD from that which occurs as a result of glaucoma. Documentation of visual field loss and RNFL provides a baseline measure to track progression. The lack of significant disc cupping of nerves with drusen contributes to the difficulty in managing these patients who also develop glaucoma.

There is no existing treatment for ONHD. An annual comprehensive eye examination along with proper diagnosis and patient education is the best available modality of care. Generally, ONHD is without visual significance. However, patients need to be aware of potential complications that could affect vision. Patients with ONHD should undergo regular dilated fundus examinations along with visual field testing (HVF 24-2), stereoscopic disc photos, IOP measurement, and nerve fiber layer examinations for future monitoring.

The optometrist’s role in bilateral disc elevation includes recognition, timely and appropriate referral to specialists, and co-management when required. In addition, the clinician must rule out pathological presentations that can be misinterpreted as anomalous while being mindful that anomalous optic nerves can become swollen. With the aid of diagnostic tests such as Bscan and OCT, clinicians can avoid unnecessary doubts and concerns along with expensive neurological investigations while targeting the correct diagnosis in bilateral optic nerve elevation.
The Diagnostic Dilemma of Pseudopapilledema

CE Questions December 2012

Name____________________________   License #_______________________________

1. Every elevated optic nerve is the same as a swollen optic nerve.
   a. True
   b. False

2. Which of the following are optic nerve characteristics should be evaluated in cases of bilateral optic nerve elevation:
   a. Overall disc diameter or size
   b. Examination of the peripapillary vessels
   c. Neoretinal rim tissue color
   d. All of the above

3. Optic nerve head drusen (ONHD) is associated with all of the following, EXCEPT:
   a. Thinning of the RNFL
   b. Large optic disc diameters
   c. Glaucoma-like visual field defects
   d. Small optic disc diameters

4. The most common cause of pseudopapilledema, accounting for 75% of diagnostically challenging disc anomalies is which of the following?
   a. Crowded discs
   b. Malinserted discs
   c. Tilted disc syndrome
   d. Optic nerve head drusen

5. The differential etiologies of bilateral disc swelling and/or elevation include which of the following?
   a. Malignant hypertension
   b. Optic nerve head drusen
   c. Increased intracranial pressure
   d. All of the above

6. Patients with increased intracranial pressure will MOST often complain of the following symptom:
   a. Headache
   b. Earache
   c. Vertigo
   d. Diplopia

7. All of the following diagnostic tests can be utilized in determining the cause of bilateral optic nerve elevation, EXCEPT:
   a. X-ray of head
   b. CT scan of brain
   c. OCT of optic nerve
   d. Humphrey visual fields

8. Tilted disc syndrome is associated with all of the following clinical findings, EXCEPT:
   a. Arcuate visual field defects
   b. Decreased visual acuities
   c. Bitemporal visual field defect
   d. Tilted disc along the vertical axis

9. B-Scan ultrasonography has been shown to be the most sensitive and diagnostically relevant test to aid in the differential diagnosis in which of the following?
   a. Diabetic retinopathy
   b. Optic atrophy
   c. Optic nerve head drusen
   d. Retinitis Pigmentosa

10. Congenitally Full Disc (CFD) is most commonly associated with which of the following?
    a. Myopic patients
    b. Hyperopic patients
    c. Visual field defects
    d. Large optic nerve diameters