OPTIC NERVE SWELLING IN CHILDHOOD

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One of the main findings on a pediatric neurologic examination that can instill fear and lead to an urgent referral to neuro-ophthalmology is the finding of optic nerve elevation. This sense of urgency is often warranted as the optic disc swelling may be an ominous clinical sign for intracranial mass or elevated intracranial pressure. In this section, we are going to tackle how to approach, diagnose and treat/manage optic nerve swelling in children.

Let us begin by clarifying the terminology as there are many words used to describe this type of optic nerve appearance. When should we use the term "papilledema," "optic nerve swelling," "optic disc edema" or "elevation of the optic nerves?" For the purposes of this topic, I will use the term "optic disc swelling" as a general term for when one looks into the eye and sees that the optic disc is swollen due to a pathologic process. Of course, optic disc swelling can be due to raised intracranial pressure, inflammation, ischemia or infection. The topic of optic neuritis will be covered elsewhere, so I will restrict my comments to other causes of optic nerve swelling. When I refer to optic disc elevation, it will be in reference to a more benign process such as pseudopapilledema.

Papilledema is defined as optic disc swelling caused by **elevated intracranial pressure**. Clinical symptoms that a child may present with include: headache, nausea, vomiting, blurred vision, double vision, intracranial noises, and transient visual obscurations. As for the optic nerve appearance, in addition to the optic disc elevation, other early signs can include hyperemia of the optic disc, venous distention, absent spontaneous venous pulsations and vessel obscuration. Later on, flame hemorrhages, peripapillary hemorrhages and cotton wool spots can present.

The first thing to determine is whether or not the papilledema is secondary to an intracranial mass via emergent neuro-imaging. Space occupying lesions can cause blockage of CSF flow, produce cerebral edema or compromise venous sinuses. In children, if there is a CNS tumor, it is more likely to be infratentorial because such tumors can compress the cerebral aqueduct or venous sinuses. Tumors that are associated with papilledema in children include midbrain and cerebellar gliomas, medulloblastomas and ependymomas. If there is no space occupying mass, what next?

Pseudotumor cerebri syndrome (PTCS)

If a child is alert and oriented with signs and symptoms of elevated intracranial pressure without mass or CSF ventricular flow obstruction on neuroimaging, the next consideration on your differential diagnosis could include primary or secondary pseudotumor cerebri syndrome. Careful history-taking will help to identify any secondary PTCS causes such as systemic or neurologic conditions or medication/drug exposures (see tables below). I always obtain a careful weight, diet, exercise and sleep history as well. The lumbar puncture is the next management step to assess for opening pressure (OP) and CSF evaluation. In 2013, Friedman, Liu and Digre revised the diagnostic criteria for PTCS in adults and children to include updated lumbar puncture opening pressure norms for children. (Table 1) For children with papilledema and a normal neurologic exam and neuroimaging, if the OP is either ≥ 280 mm H_2O or ≥ 250 mm H_2O (if child is not sedated or obese) with normal CSF composition, this would meet diagnostic criteria for PTCS.

A few clinical pearls: The visual acuity is usually normal in patients with papilledema. Exceptions to this rule would be the presence of macular edema, chronic optic nerve swelling or atrophy. What you do find, however, even in early papilledema, are visual field defects. These defects would be noted on formal computerized visual field testing, and most commonly manifest as blind spot enlargement from mechanical displacement of the peripapillary retina. The tough part is getting accurate visual field testing in younger children. In my experience, I typically have children attempt a computerized visual field test around age 12. Any younger, and the results are far less reliable. When you do notice that the visual acuity is abnormal, even mildly, the visual field loss may already be severe and the child could be at serious risk for vision loss. Remember to test color vision. It can help you to distinguish between an optic nerve versus a macular pathology (macular disease tends to affect visual acuity but spares color vision). However, if you are seeing a child with an optic nerve issue that is still progressing, color vision may be involved. Once the diagnosis of PTCS is established, if there is visual loss, I initiate acetazolamide (250-500 mg BID). If acetazolamide is not tolerated, furosemide (20—40 mg, monitor

potassium) or topirimate (1.5-3.0 mg/kg/day divided into 2 doses) can also be utilized. If the patient is overweight/obese, I recommend weight loss and carefully review with the patient and parent strategies for improvement in diet, exercise and sleep. Generally, I establish weight loss goals of a 10% weight loss over the next 6 months and closely follow the patient during that first year of diagnosis in conjunction with their ophthalmologist. If there is fulminant or severe vision loss, I will obtain an emergent oculoplastic surgical consultation for optic nerve sheath fenestration of the eye with the most severe vision loss.

Revised Diagnostic Criteria for the Pseudotumor Cerebri Syndrome

Diagnosis of PTCS	a	Papilledema		
	b	Benign neurologic exam	May have cranial nerve abnormalities	
	c	Normal cerebrospinal fluid (CSF) composition		
	d	Normal neuro-imaging without signs of hydrocephalus, mass or structural defect, and without meningeal enhancement on MRI	MRI +/- contrast MRI +/- contrast with MRV *May use contrast CT if MRI is unavailable*	Obese females All others
	e	Elevated lumbar puncture opening pressure	≥ 250 mm H_2O ≥ 280 mm H_2O ≥ 250 mm H_2O	Adults Children Children: not sedated or obese
Diagnosis of PTCS without Papilledema	1	b-e from above are satisfied		
	2	Unilateral or bilateral abducens nerve palsy		
Probable PTCS	1	a-d from above are satisfied		
	2	Normal lumbar puncture opening pressure		
Suggested PTCS	1	b-e from above are satisfied		
	2	Neuro-imaging shows at least 3 of:	Empty sella Flattening of posterior globe Distension of perioptic subarachnoid space tortuous optic nerve Transverse venous sinus stenosis	 +/-

Table 1 Diagnostic criteria for pseudoutumor cerebri syndrome (adapted from Friedman DI, Liu GT, Digre KG, Neurology 2013;81:1159-1165.

Secondary PTCS syndrome

There can also be secondary causes for PTCS. In tables below, I have included systemic and vascular conditions along with medications that have been associated with PTCS.

Systemic diseases:

Severe anemia
Down syndrome
Turner syndrome
Sleep apnea
Malnutrition
Addison disease
Renal failure

Table 2 Systemic diseases associated with PTCS

Vascular anomalies:

Cerebral venous sinus thrombosis
Superior vena cava syndrome
Arteriovenous fistulas
Bilateral jugular vein thrombosis/ligation
Increased right heart pressure

Table 3 Vascular anomalies associated with PTCS

Drug induced or exogenous substances:

Endocrine (thyroid replacement, synthetic growth hormone, leuprorelin acetate, levonorgestrel, anabolic steroids)
Antibiotics (nalidixic acid, tetracycline derivatives)
Withdrawal of long-term use corticosteroids
Vitamin A intoxication and its derivatives (all-trans retinoic acid, isotretinoin)
Lithium
Chlordecone (banned insecticide)
Chemotherapeutic agents (cytarabine, cyclosporine)

Table 4 Medications and drugs associated with PTCS

Optic nerve swelling

Optic nerve swelling can be secondary due to neurologic conditions, systemic diseases and infections. These are listed below in Table 5.

Optic nerve swelling due to neurologic conditions or systemic disease:

Hydrocephalus
Neurofibromatosis
Spinal cord tumors
Diabetes
Malignant Hypertension
Sarcoidosis
Leukemia
Leber's Hereditary Optic Neuropathy
Neuroretinitis (Cat Scratch, Lyme, Toxoplasma, Tb, Syphilis, Chicken Pox)
Craniosynostosis
Mucopolysaccharidosis
Multiple sclerosis/ADEM/NMO
Ischemic optic neuropathy
Uveitis
Tumors (hemangioma, tuberous sclerosis, optic gliomas)

Table 5 Optic nerve swelling due to neurologic or systemic conditions

Pseudopapilledema

Pseudopapilledema is also part of the differential diagnosis for childhood optic disc swelling. Pseudopapilledema describes optic nerves that mimic the appearance of swollen optic nerves. This can include normal variants or congenital anomalies of optic nerves including optic nerve tilting, myelinated nerve fibers, crowded hyperopic disc s or optic nerve hypoplasia.

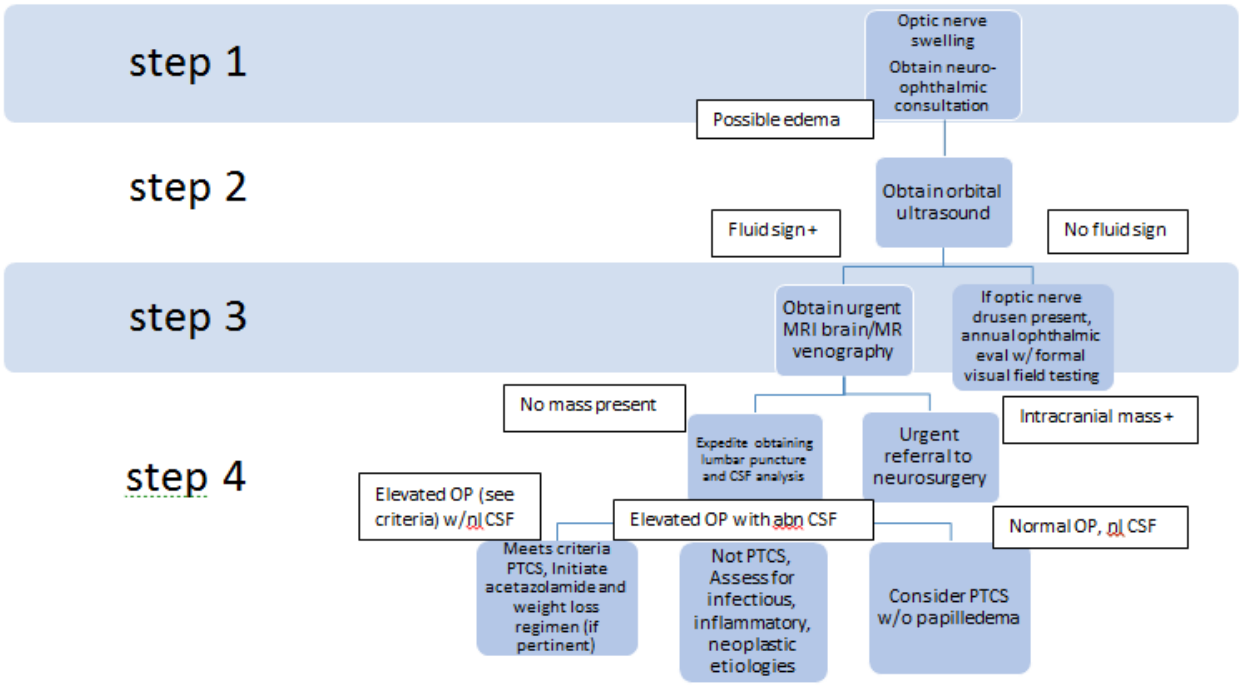
Optic nerve drusen is the most common type of pseudopapilledema in children. The drusen are typically buried and concentrated at the nasal portion of the disc. With age, the drusen can become more apparent. The tricky part is distinguishing buried drusen from papilledema. A few pointers: children with buried drusen are typically asymptomatic compared to children with papilledema (although subtle visual field defects can sometimes be identified at formal perimetry). Those with drusen are generally referred after the incidental finding of optic disc elevation on routine ophthalmic examination. On exam, those with drusen have optic disc elevation that is contained to the optic disc with the vasculature still visible and no venous congestion, exudates, hyperemia or cotton wool spots present. Additionally, there is absence of a central cup and anomalous retinal vessels. At the histopathological level, optic nerve drusen are globular concretions and are thought to occur from impairment of axoplasmic transport anterior to the lamina cribosa.

In practice, if there are prior funduscopic photographs available, I recommend trying to retrieve them from other providers, as the appearance of pseudopapilledema is generally stable compared to the dynamic appearance of acute papilledema. Additionally, I utilize A and B-scan echography to diagnose the drusen and to avoid any unnecessary exposure of a child to radiation from CT head or sedation for a brain MRI or lumbar puncture. Clinically, children with optic disc drusen have good visual acuity and function, but patients can over time experience insidious and progressive visual field loss. Rarer complications may occur in the setting of optic nerve drusen, including ischemic optic neuropathy, loss of central vision, or peripapillary subretinal neovascularization. I advise these children to have at minimum annual routine eye care and visual field evaluation via their pediatric ophthalmologist or neuro-ophthalmologist (if available) to ensure that their vision and visual fields remain stable. Listed below in Table 6 are systemic conditions associated with pseudopapilledema.

Down syndrome
Alagille Syndome (autosomal dominant genetic disorder affecting liver, heart, kidney)
Kenny-Caffey Syndrome (dwarfism, hypocalcemia, tetany)
Leber Hereditary Neuroretinopathy
Mucopolysacchariodosis (lysosomal storage diseases)

Table 6 Systemic conditions associated with pseudopapilledema

Below is a simplified algorithm for how I evaluate and manage optic nerve swelling in children



References and Recommended Resources:

1. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology 2013;81:1159-1165.
2. Avery RA, Shah SS, Licht DJ, et al. Reference range for cerebrospinal fluid opening pressure in children. N Engl J Med 2010;363:891-893.
3. Andrews LE, Liu GT, Ko MW. Idiopathic intracranial hypertension and obesity. Horm Res Paediatr. 2014;81(4)217-25.
4. Liu GT, Volpe NJ, Galetta SL. "Optic disc swelling: papilledema and other causes." Neuro-ophthalmology Diagnosis and Management.2nd Ed. Liu GT, Volpe NJ, Galetta SL. Philadelphia: Saunders, 2010. 199-231.
5. Brodsky MC. "The Swollen Disc of Childhood." Pediatric Neuro-ophthalmology. 2nd Ed. Brodksy MC. New York: Springer 2010. 97-154.