

Optic disc swelling in the paediatric population



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HIGHLIGHTS

The discovery of optic disc swelling during fundus examination should trigger a comprehensive investigation to rule out sight- or life-threatening disease.

ABSTRACT

Swelling of the optic disc may result from inflammation, infiltration, optic nerve compression or ischaemia, as well as increased intracranial pressure. It can be imitated by local structural features of the optic disc leading to pseudopapilloedema. Disease entities leading to optic disc swelling can take different courses in the paediatric population compared to the adult population. Investigations used to confirm diagnosis include optical coherence tomography (OCT), ocular ultrasound, fluorescein angiography, visual evoked potentials (VEP), and imaging studies of head and orbits.

Key words: optic disc swelling, papilloedema, optic neuritis, pseudopapilloedema

INTRODUCTION

Optic disc swelling in children might be a manifestation of ophthalmological, neurological or systemic disease. Because of its potentially sight- or life-threatening implications it should always concern the observing clinician. The paediatric population differs from the adult population in the prevalence of diseases causing optic disc swelling, as well as their course and prognosis. This article presents the most common causes of optic disc swelling in children along with the differential diagnostic methods.

PAPILLOEDEMA

The term papilloedema is used to describe optic disc swelling caused by elevated intracranial pressure.

Fundus appearance and development of papilloedema

Usually, the development of papilloedema requires several days, but it can also develop more rapidly, within hours, if there is a sudden rise in the intracranial pressure, caused by e.g. subarachnoid haemorrhage. Early signs of papilloedema include slight optic disc elevation with blurring of the disc margin, first nasally, then involving superior, inferior and temporal sides of the optic disc. Established papilloedema occurs when the usual features of the optic disc are completely obscured by oedema and there is an absence of the physiological cup. Flame haemorrhages and also frequently 'cotton-wool-spots'-type soft exudates caused by ischaemia of the nerve fiber layer may develop. Circumferential retinal folds known as Paton's lines might appear around the temporal region of the optic disc. Chronic papilloedema, when swelling persists for weeks or months, shows 'Champagne-cork' appearance of the optic disc, the signs of hyperaemia are less pronounced and peripapillary haemorrhages are absent. Optociliary shunt vessels, as well as drusen-like crystalline deposits might appear overlying the disc. Subsequently, disc becomes atrophic, greyish in colour, elevated, and develops blurred margins [1–4].

Clinical features

Symptoms reported by patients with increased intracranial pressure include headache, typically present on waking up and worsening in the supine position, transient visual obscurations, pulsatile tinnitus, and horizontal diplopia due to unilateral or bilateral sixth nerve palsy. Nausea and vomiting might also occur. In infants, increased intracranial pressure may cause open fontanelles to tense and bulge [5]. Patients with papilloedema usually have normal visual acuity, unless there is chronic disc atrophy or oedema present [1, 6, 7].

Diagnosis of papilloedema

First noticeable visual field defect is enlargement of the blind spot. Inferonasal field loss and peripheral constriction of

isopters might also manifest [1, 6]. OCT demonstrates increased peripapillary retinal nerve fiber layer (RNFL) thickness; that can decrease in time, due to resolution of disc swelling or disc atrophy. OCT can also show the peripapillary retinal pigment epithelium (RPE) and Bruch's membrane to be angulated inward, towards vitreous, at the disc margin. This sign is not present in optic disc swelling due to other aetiologies, e.g. papillitis [1, 8]. During ocular ultrasound one can perform a '30° test'. It consists of measuring the optic nerve sheath width using probe A (B-scan mode is less reliable) when the patient looks straight ahead, and then again after re-fixating 30° laterally. In papilloedema, this results in the reduction of optic nerve sheath width by at least 10%, compared to its width in the primary gaze [7, 9, 10]. In children with suspicion of increased intracranial pressure, it is necessary to perform head and orbits imaging: magnetic resonance imaging (MRI), MR angiography when suspecting angiopathy, and in time-sensitive cases also computer tomography (CT). MRI allows to image increased intracranial pressure caused by a brain tumour or hydrocephalus, as well as non-specific indicators of increased intracranial pressure. When aetiology is not possible to establish using imaging, lumbar puncture and cerebrospinal fluid analysis can provide additional information [6, 11]. Papilloedema can be caused by central nervous system tumours, hydrocephalus, developmental disorders, demyelinating and infectious diseases, as well as pseudotumour cerebri syndrome.

Pseudotumour cerebri syndrome

Idiopathic intracranial pressure (IIP), also known as pseudotumour cerebri syndrome, is a disease defined by the elevated intracranial pressure in the setting of normal brain parenchyma and cerebrospinal fluid [12]. In the paediatric population the most common symptom is headache. Older children may complain of neck and shoulder pain, pulsatile tinnitus, diplopia, or transient visual obscurations. Younger children may present with apathy or irritability. It differs from other causes of increased intracranial pressure in that the level of consciousness is not altered. In the adult population IIP is a disease of young, obese women. In the paediatric population the male to female ratio for IIP in prepubescent children is approximately equal and there is no connection to obesity. With increasing age, however, there is more resemblance to the adult population in gender distribution and inclination to obesity [1, 11, 12]. Diagnosis of secondary intracranial hypertension is established in the presence of neurologic disorder or systemic disease. These include vascular causes, for example dural venous sinus thrombosis, superior vena cava syndrome, jugular vein thrombosis, or altered cerebrospinal fluid flow and absorption due to intracranial infection or bleeding. Furthermore, dural venous sinus thrombosis can be associated with mastoiditis, otitis media or head trauma. Secondary intracranial hypertension can

be precipitated by medications, e.g. tetracycline, minocycline, nalidixic acid, sulphonamides, nitrofurantoin, growth factor, vitamin A, all-trans retinoic acid, isotretinoin, as well as, discontinuing corticosteroids. It can also be related to systemic disease, e.g. kidney disease, severe anaemia, sleep apnoea; genetic disorders, e.g. Down syndrome, Turner syndrome; and endocrine disorders, such as Addison disease, or hypoparathyroidism [1, 6, 11–13].

OPTIC NEURITIS

Optic neuritis can be an isolated finding, a post-infectious or post-immunisation condition, or occur in conjunction with autoimmune disorders. Symptoms include reduced visual acuity, dyschromatopsia, afferent pupillary defect or central and paracentral scotoma in visual field testing.

Optic neuritis in demyelinating disorders

Optic neuritis can occur in autoimmune disorders, such as multiple sclerosis, neuromyelitis optica spectrum disorder (NMOSD), acute disseminated encephalomyelitis (ADEM) [1]. Optic disc oedema in demyelinating disorders is usually less pronounced compared to papilloedema [3]. Optic neuritis in the paediatric population is often bilateral and is generally considered to be a postinfectious condition, in contrast to the adult population where optic neuritis is usually unilateral and retrobulbar [1, 6]. After puberty the differences in the disease course are diminishing between the paediatric and adult populations. A meta-analysis from 2011 showed that 72% of children under 10 years presented with bilateral optic neuritis, whereas 70% of children over 10 years had unilateral optic neuritis [14]. In children, optic neuritis has a characteristic course, manifesting as bilateral papillitis, that can mimic pseudotumour cerebri syndrome. However, these two disease entities differ in presenting symptoms. In optic neuritis there is a sudden, and in children often profound, decrease in visual acuity, dyschromatopsia and relative afferent pupillary defect. Despite initial severe reduction, visual acuity recovers in most cases [6, 15]. Pain with eye movement does not consistently occur in paediatric patients, therefore lack of pain is not a negative symptom [16]. In many children visual field testing cannot be achieved due to lack of cooperation. If it is carried out, it might show central or paracentral scotoma, which differentiates it from optic disc swelling secondary to intracranial hypertension, in which case there would be blind spot enlargement present in visual field testing [1, 6]. Prolonged P100 latencies on VEP testing occur in the acute phase. On the other hand, OCT can reveal neuronal injury in RNFL and ganglion cell complex (GCC) after episode of optic neuritis [6, 16]. MRI with contrast shows signal enhancement along optic nerve lesion [14]. After optic neuritis as a clinically isolated syndrome in children the risk

of conversion to multiple sclerosis is smaller than in adults and increases with age. Meta-analysis of available optic neuritis studies in children showed that for every 1-year increase in age the odds of developing multiple sclerosis after an isolated optic neuritis increased by 32%. White matter changes in brain MRI scans also increased the risk of developing multiple sclerosis [14]. In contrast, optic neuritis is more likely to be an initial manifestation of ADEM in the paediatric population [15].

Para-infectious and post-immunization optic neuritis

Apart from isolated optic neuritis or optic neuritis caused by demyelinating diseases, optic neuritis might occur following an infection or inoculation. The former generally presents 1–2 weeks after the febrile illness, with either unilateral or bilateral optic disc swelling. Post-immunization optic neuritis, in turn, can develop a few days post vaccination [6].

Neuroretinitis

Neuroretinitis can cause uni- or bilateral optic disc swelling [6]. Within weeks, the swelling begins to subside, and a characteristic star-shaped pattern of macular exudate within the fiber layer of Henle appears and can persist longer than optic disc swelling itself. Decreased visual acuity, dyschromatopsia and an afferent pupillary defect are present, and visual field testing shows a central and centrocecal scotoma [1]. Fluorescein angiography shows abnormal capillary permeability, whereas OCT can show serous retinal detachment, early in the disease course, before the appearance of the star-shaped pattern [17]. Cat scratch disease caused by Gram-negative bacillus, *Bartonella henselae*, is the most common infectious cause of neuroretinitis. The disease is transmitted by a bite or a scratch of an infected animal – often a cat, but also e.g. a dog. General symptoms of the disease can include regional lymphadenopathy, fever and fatigue. Lyme disease is another cause of neuroretinitis. It is caused by the spirochete *Borrelia burgdorferi*, which is transmitted by *Ixodidae* ticks that are most active from May to September. Physical findings may include fatigue, erythema migrans, carditis, arthritis, or facial and oculomotor nerve palsies. In both aetiologies serology testing including specific IgG and IgM antibodies should be carried out to confirm diagnosis [1, 17, 18].

OPTIC DISC SWELLING IN SYSTEMIC DISEASE

Optic neuropathy in leukaemia

Optic nerve leukaemic infiltration occurs mainly in children with acute leukaemia. Optic nerve invasion may appear as a swelling of the optic disc with disc haemorrhages causing decreased visual acuity. It can be accompanied by leukaemic retinopathy manifesting with tortuous vessels, vein dilata-

tion, retinal haemorrhages and cotton wool spots. It is important to remember that leukaemic infiltration of the optic nerve is a visual emergency requiring immediate treatment to prevent visual loss [1, 6].

Optic neuropathy in sarcoidosis

Sarcoidosis is a multiorgan inflammatory disease associated with formation of granulomas. Neurosarcoidosis develops when CNS is affected, that can lead to optic disc swelling due to optic nerve infiltration (granulomatous optic neuritis, with lumpy, 'cauliflower' appearance of the optic disc, causing decreased visual acuity), or increased intracranial pressure (following e.g. hydrocephalus or mass effect) [1, 6, 19].

Anterior ischaemic optic neuropathy

Anterior ischaemic optic neuropathy (AION) is a very rare cause of optic disc swelling in children. If present, it is usually associated with hypotension and hypoperfusion, leading to sudden visual loss. Fundoscopy reveals swelling of the optic disc with associated flame haemorrhages. It is a recognised complication in children who underwent major surgery or are subjects to continuous peritoneal dialysis [20, 21].

Malignant hypertension

Malignant hypertension can lead to optic disc swelling in association with a headache. In addition to optic disc swelling, signs of hypertensive retinopathy and choroidopathy manifest. Malignant hypertension in children is seen in the course of several diseases including severe glomerulonephritis, vasculitis e.g. in lupus, renal artery stenosis, as well as in transplant patients with rejection, and in children with pheochromocytoma [1, 22, 23].

OPTIC DISC SWELLING DUE TO OCULAR DISEASE

Ocular hypotony

Ocular hypotony can manifest in children e.g. following uveitis, or as a postoperative complication e.g. following glaucoma surgery [1].

Uveitis

Optic disc swelling can be caused by posterior as well as anterior uveitis with accompanying symptoms including hypotony, macular oedema and decreased visual acuity. There was a 21% chance of optic disc swelling in chronic anterior uveitis in children recorded. Uveitis and associated optic disc swelling can be caused by both autoimmune e.g. juvenile rheumatoid arthritis, as well as infectious diseases [1, 24].

Posterior scleritis

Posterior scleritis is an autoimmune disorder. Patients can present with ocular pain, conjunctival injection, and ocular

motility disturbances. Slit lamp examination may reveal anterior uveitis, whereas fundoscopy can show cystoid macular oedema, retinal and choroidal striae, choroidal detachment, as well as exudative retinal detachment, in addition to the optic disc swelling [1, 25]. The diagnosis can be confirmed by ocular ultrasonography, which demonstrates a 'T-sign' – a fluid-filled space in subarachnoid space of the optic nerve, and in the space behind Tenon's capsule [9].

Optic nerve tumours

Optic nerve tumours interrupt axonal transport by compressing or infiltrating the optic nerve, initially causing swelling and then atrophy of the optic disc. Fundoscopy can show opticociliary shunt vessels. Other symptoms include gradual decrease in visual acuity and proptosis [1, 2, 6, 26]. The most common primary tumours of the optic nerve in children are optic nerve gliomas; in the paediatric population, in contrast to the adult population, they are relatively benign. Optic nerve glioma can involve the optic nerve, as well as optic chiasm and the hypothalamus area. This neoplasm arises in association with neurofibromatosis type 1 in 30% of cases [1, 2, 6, 26]. Less common optic nerve tumour in children is optic nerve sheath meningioma, which can be more aggressive in the paediatric population. It can be associated with neurofibromatosis type 2 [1, 6, 26].

PSEUDOPAPILLOEDEMA

Pseudopapilloedema is described as an apparent elevation of the optic disc secondary to local structural features of the optic disc [7].

Drusen

The most common cause of pseudopapilloedema in children are optic disc drusen – calcified to varying degrees hyaline deposits within the optic nerve head. It is estimated that drusen are present in 0.4% of the paediatric population [7, 27]. They rarely cause visual disturbances during childhood [1]. On ophthalmoscopic examination the optic disc is elevated, can be cupless, with uneven, lumpy-bumpy margin, and characterised by anomalous vascular branching and tortuosity on its surface. Surface drusen may partially appear on the optic disc as yellowish, globular conglomerations [1, 7]. In the paediatric population buried drusen prevail, they become more superficial, and thus more visible with time at the average age of 12 years [28]. Ancillary studies that can show calcifications within the optic disc include CT scanning and ocular ultrasonography [7]. On ocular ultrasonography optic disc drusen have hyper-echogenic appearance. It is recommended to decrease gain to around 50–65 dB during the examination, in order to achieve a better image [9]. It is important to remember that in children optic disc drusen are less likely to be calcified and there-

fore more difficult to detect using ocular ultrasonography [29]. Other studies include fluorescein angiography and OCT. Fluorescein angiography shows increased fluorescein staining of the optic disc without swelling of the surrounding retina, or leakage from the optic disc [30]. Fundus autofluorescence pictures of superficial drusen taken by fundus camera exhibit autofluorescence of the optic disc [7]. OCT studies show a thickening of the peripapillary nerve fiber layer in both papilloedema and pseudopapilloedema caused by drusen. In case of the papilloedema, however, the peripapillary nerve fiber layer is thickened in all sections, whereas in pseudopapilloedema with drusen RNFL tends to be thinner nasally and thicker temporally [1]. Spectral domain OCT (SD-OCT) studies may reveal hyper-reflective mass underlying optic disc in some drusen cases [31]. Enhanced depth imaging OCT (EDI-OCT) studies and swept source OCT (SS-OCT) studies may expose drusen as a region of low reflectivity with hyper-reflective borders [32]. Systemic disorders associated with more frequent occurrence of optic disc drusen include: retinitis pigmentosa, Alagille syndrome, pseudoxanthoma elasticum and angioid streaks [28, 33].

Differential diagnosis for pseudopapilloedema

Apart from optic disc drusen there are other causes for elevated appearance of the optic disc or blurring of its margin, thus imitating optic disc swelling. These include: persistent hyperplastic primary vitreous causing vitreopapillary traction, glial tissue on the optic disc (Bergmeister papilla), juxtapapillary myelinated nerve fibers, or 'crowded nerve' in hyperopic eyes or nanophthalmos [1, 33]. Peripapillary tumours e.g. astrocytic hamartoma can be another example. This tumour, due to its 'mulberry-like' appearance, can

be easily confused with optic disc drusen, however, fluorescein angiography characteristically shows a superficial network of blood vessels within the mass during the arterial phase [1, 2, 34].

Leber hereditary optic neuropathy

It is a rare disease caused by a point mutation in the maternally inherited mitochondrial DNA. It is characterised by heavy, painless, bilateral vision loss. Typically one eye is affected first, weeks to months before the other. During the acute phase, funduscopy may reveal hyperaemia of the optic disc (pseudopapilloedema), with accompanying dilatation and tortuosity of vessels, and peripapillary telangiectatic microangiopathy. Fluorescein angiography can show no fluorescein leakage, helping to distinguish the Leber hereditary neuropathy optic disc from true optic disc swelling. Genetic testing confirms the diagnosis [2, 6].

CONCLUSION

Optic disc swelling may be caused by inflammation, infiltration, optic nerve compression or ischaemia, as well as increased intracranial pressure. Pseudopapilloedema arising from local structural features of the optic disc can imitate optic disc swelling. Ancillary ophthalmological studies that can help establish aetiology of optic disc swelling include: OCT, ocular ultrasound, fluorescein angiography, VEP, and imaging studies of head and orbits. Fundus examination showing optic disc elevation and blurring of disc margins should always lead to comprehensive diagnostics towards ophthalmological, neurological or systemic disease, as this can be a first symptom of sight- or life-threatening disease in children.

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The content presented in the article complies with the principles of the Helsinki Declaration, EU directives and harmonized requirements for biomedical journals.