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Bilateral disc edema in hypertensive emergency

Bilateral optic disc edema can be a result of several etiologies and deserves a thorough work-up. Neuroimaging and laboratory studies should be performed to rule out neoplastic, vascular, infectious, ischemic, or inflammatory etiologies, and a lumbar puncture (LP) should be performed to measure intracranial pressure (ICP) if necessary after performing the appropriate imaging studies. Patients with papilledema should be evaluated for alternative causes of increased ICP. We present the case of a patient who presented with bilateral optic disc edema and was found to have increased ICP. Although it is true that the systemic blood pressure (BP) should be checked in every case of bilateral optic disc edema to exclude hypertensive emergency, the presence of severe hypertension does not obviate the need for either neuroimaging or evaluation for increased ICP-related papilledema (i.e., LP).

Case

A 35-year-old obese African American male (body mass index of 35.9 kg/m^2) presented with bilateral optic disc edema and vision loss. He had a history of multiple hypertensive emergency episodes and uncontrolled essential hypertension complicated by congestive heart failure (with an ejection fraction of 20%). He had chronic kidney disease and focal segmental glomerular sclerosis. The patient did not have a history of sickle cell disease or obstructive sleep apnea. Medications included hydrochlorothiazide and lisinopril. Family history included hypertension in his father. All other histories were noncontributory. He was not taking any medications that could produce increased ICP.

He presented to the emergency department with acute loss of vision OD. He was found to have a systolic BP of 230/146 mm Hg. Visual acuity was hand-motion OD and 20/40 OS. Funduscopic examination showed Friesen grade IV optic edema OD with hemorrhages and cotton wool spots contiguous to the nerve and grade III–IV optic edema OS (Fig. 1). He was subsequently diagnosed with hypertensive emergency and admitted for BP control. The BP improved but did not normalize on medical therapy. Three weeks later he presented to the neuro-ophthalmology clinic with bilateral vision loss. He also reported headaches and tinnitus, but denied nausea, vomiting, or weakness. BP measurements at home had remained over 200 mm Hg systolic since discharge despite multiagent antihypertensive therapy with carvedilol, hydralazine, and isosorbide dinitrate.

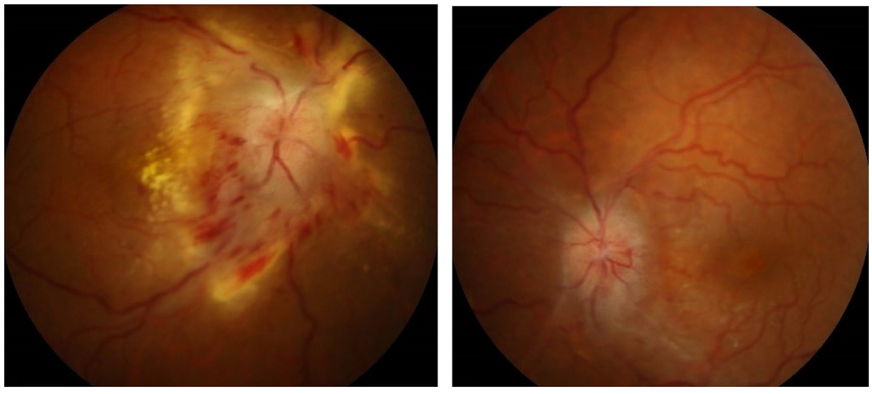

Fig. 1—Fundus photos OU showing marked disc edema, peripapillary flame shaped hemorrhages, and cotton wool spots.

Examination demonstrated that visual acuity was hand-motion OD and counting fingers OS. Pupils were equal and reactive with a relative afferent pupillary defect OD. Ishihara colour plates were 0/14 OD and 14/14 OS. Findings of motility, slit-lamp, intraocular pressure, and external examinations were all normal. Humphrey visual field testing with the stimulus size 5 test object showed diffuse depression consistent with hand-motion vision OD and diffuse depression with a superior and inferior arcuate defect consistent with counting fingers vision OS. Funduscopic examination showed Frisen grade IV optic edema OU with no other signs of hypertensive retinopathy.

Magnetic resonance (MR) imaging of the brain and MR venogram were normal. The orbital MR scan demonstrated increased cerebrospinal fluid signal around the optic nerve sheaths and flattening of the globes OU, consistent with increased ICP. LP showed an opening pressure of 55 cm of water, and cerebrospinal fluid analysis was within normal limits. A diagnosis of pseudotumour cerebri secondary to hypertensive emergency was made. Oral acetazolamide was initiated, and a lumbar drain was placed in an attempt to lower the ICP. A ventriculoperitoneal shunt was performed urgently but was complicated by a subarachnoid hemorrhage. An optic nerve sheath fenestration (ONSF) was scheduled, but the patient was medically unstable and could not undergo additional anaesthesia or procedures. In the intensive care unit, the patient suffered a cardiac arrest and was unable to be resuscitated. Postmortem examination showed that the cause of death was bilateral pulmonary emboli.

Discussion

Although it is well known that bilateral disc edema and retinal hemorrhages can occur in hypertensive retinopathy and optic neuropathy, these ophthalmoscopic features are markers of end-organ damage and hence define it as a hypertensive emergency.[1] However, in the setting of elevated systemic BP concurrent with bilateral optic disc edema, the diagnosis of malignant hypertension should not be used to explain the disc edema without a complete work-up to rule out other causes, including elevated ICP. In the most recent Joint National Committee (JNC) 8 report, 9 recommendations were presented to guide physicians on the treatment of hypertension. This report provided new recommendations on treatment of hypertension in the outpatient setting but did not comment on the treatment for hypertensive urgency or emergency. In the JNC 7 report, hypertensive emergency was defined as BP greater than 180/120 mm Hg with end organ dysfunction. In contrast, hypertensive urgency was defined as the same degree of BP elevation without end organ damage. Neither JNC 7 nor 8 comment on the intracranial evaluation of patients with optic disc edema.

The differential diagnosis for bilateral disc edema in the setting of elevated BPs includes hypertensive optic neuropathy, nonarteritic anterior ischemic optic neuropathy, and hypertensive papilledema from increased ICP. The mechanisms are not mutually exclusive and difficult to differentiate on clinical grounds alone. We therefore recommend neuroimaging and LP in all patients with bilateral optic disc edema even in the setting of elevated BP. The radiological signs of elevated ICP (e.g., increased cerebrospinal fluid in the optic sheath, flattening of the globe, or an empty sella) should be considered additional evidence to support proceeding with an LP to measure ICP.

While the work-up is being performed and the hypertension is being treated, clinicians should consider placing a lumbar drain as a temporizing measure and empiric treatment for increased ICP if needed. Hypertensive emergency should not be used as the sole explanation for bilateral disc edema in the setting of elevated BPs without thorough work-up, excluding increased ICP as another or concurrent etiology. In the literature, cases of concurrent hypertensive emergency and intracranial hypertension have been reported. Abbasi et al. reported a young female who was found to have malignant hypertension and later to have intracranial hypertension.[2] The authors in this case also argue for LP in patients presenting with bilateral disc edema in the setting of severe hypertension.

The relationship of optic disc edema, hypertension, and ICP is multifaceted. The well-known Cushing reflex describes how an increase in ICP will be compensated for by an increase in BP. Malignant hypertension is thought to cause end organ damage via 2 processes: either (*i*) excessive cerebral blood flow leading to breakdown of the blood–brain barrier and secondary vasogenic edema, or (*ii*) an ischemic process leading to fibrinoid necrosis and cytotoxic edema (hypertensive disc edema).[3] Although hypertensive retinopathy and hypertensive choroidopathy may be present in patients with hypertensive optic disc edema, the ophthalmoscopic findings (hypertensive retinopathy, choroidopathy, and optic neuropathy) may occur in isolation or in combination.

In 1932, Shelburne et al. reported a cohort of 50 patients with hypertension, of whom 22 had increased ICP or disc edema, and headache was seen in 80% of these patients (compared with headache in only 40% of the patients with normal ICP).[4] In 1934, Pickering described a cohort of 37 patients with hypertension and increased ICP.[5] Recently, Hayreh et al. suggested the mechanism of disc edema in hypertensive emergency to be (*i*) increased ICP and hypertensive encephalopathy, (*ii*) failure of autoregulation of the optic nerve head, (*iii*) hypertensive retinopathy with optic neuropathy, or (*iv*) ischemia of the optic nerve.[6] In an update, Hayreh explained how disc edema in the setting of increased ICP most likely represents a mechanical phenomenon with the increase in the optic nerve sheath producing axoplasmic flow stasis in the optic nerve fibers, resulting in disc swelling.[7]

Conclusions

Patients presenting with bilateral optic disc edema, even in the setting of hypertensive emergency, should still receive a full work-up to rule out increased ICP or other etiologies of bilateral disc edema, including neuroimaging

and LP. Patients with normal ICP and bilateral optic disc edema likely have hypertensive optic neuropathy alone, but patients with elevated ICP should undergo medical and, if necessary, surgical treatment (e.g., ONSF, CSF diversion procedures) of papilledema to avoid inappropriate delay in therapy and permeant visual loss. Temporizing measures (e.g., lumbar drain) should be considered during the interval when more urgent treatment of systemic BP is necessary before treatment of the ICP.

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Late-onset Leber hereditary optic neuropathy presenting after intraocular surgery

Leber hereditary optic neuropathy (LHON) is a retinal ganglion cell degeneration characterized by bilateral, typically sequential, acute/subacute central visual loss. This maternally inherited condition arises from point mitochondrial DNA (mtDNA) mutations, and more than 90% of affected individuals harbour 1 of 3 primary mtDNA variants, m.11778G>A, m.14484T>C, or m.3460G>A.[1] Intriguingly, (*i*) the majority of subjects harbouring mtDNA mutations do not develop visual symptoms, (*ii*) a striking number of LHON patients have no family history, and (*iii*) there is significant male predominance (male:female, ~3:1).[1–3] These observations suggest significant variability in disease penetrance and point to a complex disease model with interacting environmental and genetic factors.

Environmental factors increasing penetrance in mutation carriers include smoking and heavy alcohol consumption.[3] Other possible environmental triggers described in case reports include head trauma, raised intraocular pressure (IOP), industrial toxins, and drugs with mitochondrial toxicity.[3,4] We report 2 individuals in the seventh decade of life who presented with visual loss within days after penetrating ocular surgery.

The first study subject is a 69-year-old female diagnosed with ocular hypertension at age 55 years. She subsequently developed narrow angles treated with bilateral iridotomies and cataract surgery. At age 68 years, she underwent a left trabeculectomy procedure; this failed to control the IOP and left glaucoma drainage implant surgery was undertaken 1 year later. There were no visual complaints in the first postoperative week, but soon after, she reported blurring in her left temporal subfield; at 1 month postoperatively, left IOP was 43 mm Hg and left visual acuity (VA) was 0.4 logMAR. Subsequently, the IOP reduced, but vision continued to deteriorate (Fig. 1). A left relative afferent pupillary defect was noted 3 months after the procedure. Five months postoperatively, deterioration of the right eye vision was reported, with the right VA dropping to 0.3 logMAR. Extensive investigations for optic neuropathy (including head magnetic resonance imaging before and after involvement of the right eye, lumbar puncture, temporal artery biopsy, and autoimmune/paraneoplastic antibody screen) were unremarkable. MtDNA analysis revealed a homoplasmic m.11778G>A mutation; this change is the most common LHON-associated mtDNA defect,[1] and a diagnosis of LHON was made. At 6 months postoperatively, VA was counting fingers OD and hand movements OS. Optic disc appearance over time is shown in Figure 2, and visual field tests before and after visual deterioration can be found in Supplementary Data (available online).

The second study subject is a male who underwent uneventful right cataract surgery at age 68 years.