Retrobulbar optic neuropathy: “neither the patient nor the doctor can see”

Abstract
Retrobulbar optic neuropathy (RBON) is a characterized by normal optic disc appearance and specific visual symptoms. As the injury site of the pathologic process in this optic neuropathy (ON) is behind the optic nerve head, in the other words, behind the lamina cribrosa, or in the intra-orbital or intra-canicular or intracranial parts of the optic nerve, the optic disc seems normally. RBON may occur as retrobulbar optic neuritis, traumatic ON, toxic ON, posterior ischemic ON, infiltrative ON, compressive ON, radiation-induced ON or hereditary ON with the classic phrase “neither the patient nor the doctor does not see”.

Keywords: retrobulbar optic neuropathy, normal appearing optic disc, normal optic disc appearance, optic neuropathy with the normal disc

Abbreviations: RBON, retrobulbar optic neuropathy; VF, visual field; RAPD, relative afferent pupillary defect; OD, optic disc; CVD, color vision deficiency; RON, retrobulbar optic neuritis; TrON, traumatic optic neuropathy; TxON, toxic optic neuropathy; PION, posterior ischemic optic neuropathy; CON, compressive optic neuropathy; RION, radiation-induced optic neuropathy; LHON, leber’s hereditary optic neuropathy

Introduction
Optic neuropathies can present with clinical findings including visual loss (involving visual acuity, contrast sensitivity, color vision, or visual field (VF)), relative afferent pupillary defect (RAPD) and ophthalmoscopic signs including a hyperaemic, swollen, pale, or anomalous optic disc (OD) and/or peripapillary splinter hemorrhages. However, it may occur especially in early stages or the beginning of the disease in the manner of the retrobulbar optic neuropathy (RBON) characterized with normal OD appearance with above mentioned visual symptoms. Retrobulbar optic neuropathy presents with the loss of visual acuity or/and contrast sensitivity, acquired color vision deficiency (CVD), sometimes ocular pain induced by the eye movements without OD edema. The injury site of the pathologic process in RBON is behind the OD, in the other words, behind the lamina cribrosa, in the intra-orbital, intra-canicular or intracranial parts of the optic nerve. RBON may develop following demyelinating, compressive, infiltrative, inflammatory, traumatic, and ischemic events involving the optic nerve. The optic neuropathies such as retrobulbar optic neuritis (RON), traumatic optic neuropathy (TrON), toxic optic neuropathy (TxON), posterior ischemic optic neuropathy (PION), compressive optic neuropathy (CON), radiation-induced optic neuropathy (RION) which may cause normal OD appearance may be included in RBON. Additionally, ODs may be observed as normal in Stage 0 papilledema. Actually, RBONs are the causes of the classic phrase “neither the patient nor the doctor does not see”. Eventually, OD atrophy may develop following almost all types of optic neuropathy. Unilateral RBON include RON, CON and infiltrative optic neuropathy related with neoplastic diseases such as leukaemia, multiple myeloma or lymphoma while TxONs including tobacco-alcohol induced optic neuropathy, nutritional optic neuropathy (vitamin B12 and folate deficiency), drug-induced optic neuropathy, and Leber’s hereditary optic neuropathy (LHON) can cause the appearance of bilateral normal ODs.

Retrobulbar optic neuropathies
A list of the RBONs and their typical OD appearances were given in Table 1.

| Retrobulbar optic neuropathy | Optic disc appearance | Common laterality |
|-----------------------------|-----------------------|------------------|
| Demyelinating optic neuritis (Retrobulbar optic neuritis) | Usually Normal (65-75% of the cases)/sometimes swollen | Unilateral |
| Infiltrative optic neuropathy | Usually Normal/sometimes swollen | Unilateral |
| Compressive optic neuropathy | Normal (a half of the patients)/pale | Unilateral |
| Toxic/nutritional optic neuropathy | Usually normal/sometimes mildly swollen | Bilateral |
| Traumatic optic neuropathy (indirect posterior) | Usually Normal | Unilateral/Bilateral |
| Radiation-induced optic neuropathy | Usually Normal | Bilateral |
| Hereditary optic neuropathy (Leber’s) | Sometimes normal (20-33% of the cases) in acute stage/usually mildly swollen with peripapillary telangiectasia | Bilateral |
| Papilledema (Stage 0) | Normal or blurring of nasal, superior and inferior poles | Bilateral |

*Correspondence: Burak Turgut, Professor of Ophthalmology, Yuksek Ihtisas University, Faculty of Medicine, Department of Ophthalmology, 06520, Ankara, Turkey, Tel: +90 312 2803601, Email: burakturgut@yu.edu.tr

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Retrobulbar optic neuritis

Retrobulbar optic neuritis (RON) is mainly caused by multiple sclerosis, a common demyelinating disease. The cardinal signs of RON are the loss including visual acuity or/and contrast sensitivity, periculocar pain induced with ocular movements, RAPD and CVD. OD has a normal appearance in 65-75% of cases with RON in initial stages and it is edematous in the rest.

Traumatic optic neuropathy

Traumatic optic neuropathy (TON) is an important cause of severe visual loss occurring following blunt or penetrating head or ocular trauma. TON is usually diagnosed based on the clinical, ophthalmoscopic, radiologic examination findings and trauma story. Ocular examination shows a RAPD except in bilateral symmetric cases, variable loss of visual acuity, CVD, and variable VF defects. TON is classified as direct or indirect. Direct TON is caused by a direct penetrating damage to the optic nerve resulting a severe visual loss. Indirect TON is usually caused by acceleration/deceleration forces due to the blunt head or closed globe trauma. Although TON can occur in any region such as intraocular, intra-orbital, intracranial and chiasmal parts of the optic nerve, it usually occurs at the intra-canicular part of the optic nerve (inside sphenoidal optic canal). Ophthalmoscopic examination reveals the OD with a normal appearance at the presentation and initial stages especially in the cases with indirect posterior (injuries to the optic nerve parts behind lamina cribrosa) TON. However, the OD pallor will develop in about 3-6 weeks following orbital or cranial trauma.

Toxic optic neuropathy

Toxic optic neuropathy (TxON) is resulted from toxicity of nutrients, toxins, drugs or chemotherapeutic agents such as ethambutol, cloquinol, isoniazid, amiodarone, linezolid, methotrexate, sildenafil, oxymetazoline, infliximab, vincristine, carboplatin, paclitaxel, cyclosporine, cisplatin and chloramphenicol, carbon monoxide, ethylene glycol, perchorloethylen, methanol, phosphodiesterase 5 inhibitors, tumor necrosis factor alpha inhibitors and tobacco, and metabolic or nutritional problems (vitamin B12 and folate deficiency). TxON occurs usually as a chronic, slowly progressive optic nerve dysfunction with bilateral and simultaneous involvement resulting early CVD (red-green), the loss of visual acuity and centrocaecal scotoma. Although TxON may cause mild and bilateral OD edema and sometimes OD hemorrhages, ODs usually appear normal in the early stages of TxONs. In the later stages, optic atrophy, most commonly in the temporal OD region develops.

Posterior ischemic optic neuropathy

Posterior ischemic optic neuropathy (PION) is a rare form of ischemic optic neuropathies. PION is usually caused by an acute reduction of the blood flow to the retrobulbar optic nerve and acute ischemic damage. It should be considered in the diagnosis in each patient with acute painless vision loss, a RAPD or sluggish pupillary response, and a normal-appearing OD in one eye. PION is classified as surgical (postoperative or perioperative), arteritic (due to temporal arteritis) or non-arteritic. If rarely, bilateral PION occurs, it should be considered that the underlying cardiac or spinal surgery may be in the etiology. In the etiopathogenesis, it has been considered that some risk factors including anemia, hypertension, hemodialysis, severe blood loss during the surgery, surgeries longer than 6.5 hours such as the spine, cardiac, head-neck surgeries from prone positions, ocular surgery, carotid atherosclerosis, and diabetes. The OD has initially normal appearance without edema as the injury is in the retrobulbar optic nerve. However, an OD pallor will develop within 4-6 weeks of the initial injury.

Infiltrative optic neuropathy

Infiltrative optic neuropathy is an optic neuropathy caused by the infiltration of neoplastic or inflammatory cells of the optic nerve in diseases such as leukemia, lymphoma, or any neoplastic disease (multiple myeloma, malignant glioma, breast carcinoma, lung carcinoma), granulomatous inflammation from sarcoidosis, syphilis, TB, and fungal infections. The patients experience gradual and progressive loss of visual acuity in days or weeks. OD may be observed as normal or swollen in appearance at initial presentation. If a retrobulbar involvement is present, OD will have normal appearance. CVD, VF defect and RAPD may be detect or the patient may be asymptomatic.

Radiation-induced optic neuropathy

Radiation-induced optic neuropathy (RON) is a late complication due to the necrosis of the anterior visual pathway, the brain or orbit following radiotherapy. RION presents with acute, painless, visual loss (involving visual acuity and VF) usually three years (mean 1-1.5 years) after completion of radiation exposure. It may cause a severe and irreversible visual loss and the second eye may be involved within weeks or months. The diagnosis is performed with the evidence of impaired visual function, a story of the radiation exposure and, the absence of another optic neuropathy causes. As RION is a result of the retrobulbar ischémie process and the endothelial cell injury from radiation, OD usually seems as normal with ophthalmoscopy in the acute phase, however, it can be observed as swollen.

Leber’s hereditary optic neuropathy

Leber’s hereditary optic neuropathy (LHON) is an inherited optic neuropathy from the mutation in maternal mitochondrial DNA. LHON affects predominantly affects men and presents with acute, severe, painless and usually irreversible visual loss (including central scotoma and color vision deficiency). The other eye is usually involved within weeks or months after the first eye. Funduscopy examination usually reveals a circumpapillary telangiectasia with OD hypopigmentum. Approximately 20-33% of the patients with LHON show a normal-appearing disc in initial stage. The classic triad of LHON is circumpapillary telangiectasia, swelling of peripapillary nerve fiber layer and the absence of leakage from the disc on fluorescein angiography. After the telangiectasia and nerve fiber layer swelling disappear, eventually, OD pallor appears in especially in the temporal area with coexistent damage of the papillo-macular nerve fiber layer.

Compressive optic neuropathy

Compressive optic neuropathy (CON) is commonly caused by directly compression to the intraorbital, intracranial, or pre-chiasmal optic nerves by a mass such as tumor, aneurysm enlarged extracranial muscles. The common causes of CON are orbital and intracranial meningioma, pituitary adenomas, intracranial aneurysm (involving internal carotid artery or anterior cerebral artery), cranialpharyngioma, glomma in the anterior visual pathway, metastatic carcinomas such as glioma, meningioma, astrocytoma, hemangiomas, lymphangiomata, teratoma, lymphoma, sarcoma, multiple myeloma, nasopharyngeal carcinoma. However, it may also be caused by sinus mucoceles, sphenoid crest and olfactory groove meningioma, tuberculoma, cryptococcal disease, sarcoidosis, thyroid eye disease and mass.
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Stage 0 papilledema

Papilledema is optic disc swelling due to elevated intracranial pressure. Optic nerve damage develops due to intraneuronal ischemia secondary to the stasis in the axoplasmic flow. Main causes of papilledema include intracerebral tumors, cerebral haemorrhage, meningitis, cranial trauma, hydrocephalus, impairment of the circle of cerebrospinal fluid and idiopathic intracranial hypertension. In the acute stage of this optic neuropathy, in contrast to others which vascular alterations in OD, in Stage 0 papilledema OD seems normal or blurring of nasal, superior and inferior poles.

Conflicts of interest

The author declares that there is no conflict of interest regarding the publication of this paper.

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