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Review Paper

Non-glaucomatous Optic Disc Cupping: A Brief Review

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ABSTRACT

Although optic disc cupping is mostly seen in glaucoma patients, it can occur in non-glaucomatous optic neuropathies (NGON). The characteristics of NGON are cupping toxic optic neuropathies, optic neuritis, compressive ischemia, and hereditary nature. The basic components of optic disc cupping are prelaminar and laminar. Prelaminar thinning, which seemed to be non-specific, occurs in all types of retinal ganglion cell axon loss; such as compressive, ischemic, and inflammatory events; glaucoma; and aging. This form of cupping is usually shallow, with less excavation of the optic disc. Laminar type of cupping which is a clinically profound type of cupping, may damage peripapillary scleral and lamina cribrosa. Sometimes experienced clinicians cannot clearly distinguish glaucomatous from non-glaucomatous cupping. The non-glaucomatous optic neuropathy has more neuroretinal rim pallor with less excavation of the disc than in glaucoma. It also involves central visual acuity and color vision in primary levels with visual field defects aligned vertically and respecting the midline. Evaluation of the patient's medical records, disease presentation, ocular function, and examination are also crucial. Secondary examinations, including visual field examination and optical coherence tomography (OCT) or neuroimaging, facilitate the disease's differentiation. This review presents the methods of examining a patient with an increased cup-to-disc ratio.

Keywords: Low tension glaucoma, Pallor, Optic nerve diseases, Glaucoma, Neuritis

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Highlights

• Glaucoma is the most pathologic cause of optic disc cupping and usually occurs with elevated intraocular pressure.

• The non-glaucomatous optic neuropathies have more neuroretinal rim pallor with less excavation of the disc than in glaucoma.

• Visual field examination, optical coherence tomography, or neuroimaging test help differentiate glaucomatous optic neuropathy from non-glaucomatous one.

Introduction

Glaucomatous optic neuropathy is the main cause of pathologic cupping of the optic disc and the second leading cause of irreversible blindness. Nerve fiber layer defects cause the optic nerve cupping in glaucoma in conjunction with altered structural integrity and the posterior transposition of the lamina cribrosa [1]. However, other types of optic neuropathies, like arteritic anterior ischemic optic neuropathy (AAION), methanol toxicity, intracranial tumors, optic neuritis, and Leber hereditary disease, can cause optic nerve cupping [2].

It is difficult to distinguish glaucoma cupping from non-glaucomatous form via clinical presentations. Glaucoma cupping usually accompanies elevated intraocular pressure (IOP) and a typical scheme of visual field defects attributable to retinal ganglion cell loss. Elevated intraocular pressure is considered the most significant factor for optic nerve damage in glaucoma patients. However, in some patients with normal tension glaucoma (NTG), cupping arises at normal levels of IOP. Clinical and paraclinical parameters can help differentiate glaucomatous and non-glaucomatous cupping. Optic disc pallor is greater in non-glaucomatous conditions with less excavation and cupping than in glaucomatous conditions. It also involves central visual acuity and color vision in the early steps of the disease with visual field defects that are aligned vertically and respect the midline [3, 4].

Glaucoma is a well-known cause of optic disc cupping and usually occurs in conjunction with increased intraocular pressure. It often involves peripheral vision, spares central and color vision until the last phases, and has typical glaucomatous field defects as a partial and complete arcuate or nasal scotoma. In cases with elevated IOP, diagnosis, and treatment are not challenging but may be difficult if optic disc cupping is present in the eye with normal IOP [3, 4].

This study reviews the differences in clinical features that help diagnose glaucomatous and non-glaucomatous optic disc cupping.

Materials and Methods

Searching strategy

We looked for articles from the beginning of 2000 to April 2023 in scientific databases: Web of Science, PubMed, Scopus, and Google Scholar. We used relevant MesH terms "retinal ganglion cells," "low tension glaucoma," "scotoma," "pallor," "optic nerve diseases," "glaucoma," and "neuritis." Articles that met the inclusion criteria were entered into the Endnote software, version 8.

Inclusion and exclusion criteria

All articles and reviews with available full texts published in English from 2000 to April 2023 were included. Study protocols, letters to editors, and corresponding and conference papers were excluded. Studies with incomplete resources, inadequate data, or insufficient author information were excluded.

Data extraction

Each author completed a data extraction form including the general author, publication date, journal, general characteristics of the cases, intervention measures, results scales, and statistical methods used in the research.

Quality assessment

Newcastle-Ottawa quality assessment scale (NOS) was utilized for bias measurement by each author. For cross-sectional studies, Herzog et al. checklist [5] was used as below:

Very good articles: 9-10 points, good articles: 7-8 points, satisfactory articles: 5-6 points, and unsatisfactory articles: 0-4 points [5].

Results

A total of 365 studies were collected. After duplication removal, 162 articles remained. Of them, 108 articles were incompatible and excluded after controlling the title and abstract. According to our review's inclusion and exclusion criteria, 54 qualified articles were recognized.

Based on the results of our assessment scale, articles that were systematically reviewed had desirable qualities: 14 studies (26%) as very good, 29 studies (54%) as good, and 11 studies (20%) as satisfactory. Therefore, the systematically reviewed studies had a very good to a satisfactory quality. The results are shown in Figure 1.

Discussion

Cupping in non-glaucomatous optic neuropathies

Although optic disc cupping expansion is common in glaucoma patients, it may occur in non-glaucomatous lesions, including leukomalacia and arteritic anterior ischemic optic neuropathy. Clinical differentiation between glaucomatous and non-glaucomatous cupping (NGC) is difficult. Cupping is deeper in eyes with glaucoma, while eyes with NGC have more scales of neuroretinal rim pallor. Besides, disc pallor is more significant than cupping, and visual field weakness aligning vertically can be considered exclusive traits of non-glaucomatous cupping. The cup deepness is a critical prediction of the optic nerve head (ONH) that assist in the discrimination of glaucoma from non-glaucomatous optic neuropathy caused by the compressive lesion [6].

A survey, which used ONH-enhanced depth imaging optical coherence tomography (EDI OCT), revealed that evaluation of the cup depths and the lamina cribrosa (LC) depth from Bruch's membrane opening (BMO) is useful to distinguish compressive optic neuropathy from a glaucoma-like disc and glaucoma [7].

The optic nerve consists of 1.6 million retinal ganglion cell axons and exits the eye through Bruch's membrane fenestration and the scleral part of the optic canal. Quigley and green demonstrated that ganglion cell axon loss and lamina cribrosa soft tissue remodeling cause enhancement in the cup-to-disc ratio [8].

Kim et al. evaluated 542 eyes to determine the most important factors of glaucoma in patients with large optic disc cupping without retinal nerve fiber layer defect (RNFLD). They revealed that several patients with large optic disc cupping without RNFLD defects developed glaucoma. Fundus photography examination, including

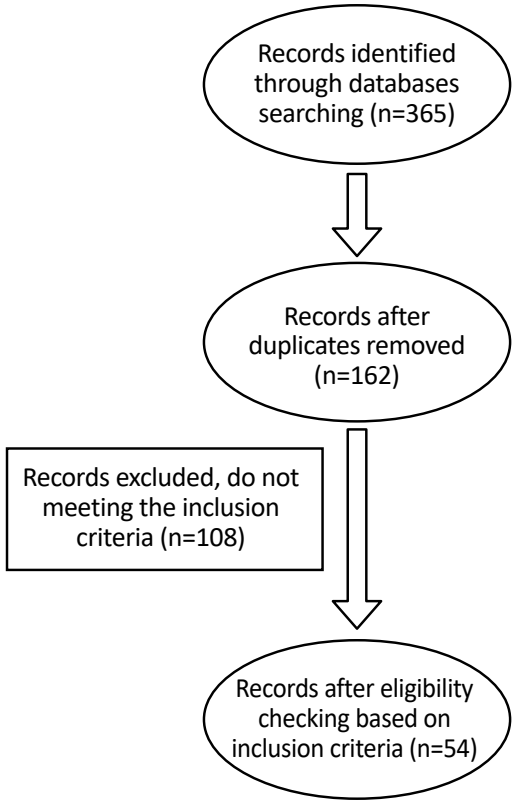

Figure 1. The steps for selecting studies

ONH configuration and retinal vascular changes, is useful for predicting the risk of glaucoma development and the advance of RNFLD defects in these patients [9].

Burgoyne et al. have explained two prelaminar and laminar mechanisms for optic disc cupping. The prelaminar mechanism seems non-specific and is seen in all forms of retinal nerve fiber layer loss, including glaucoma, compressive, ischemic, inflammatory events, and aging. This form of cupping is usually shallow, with less excavation of the optic disc [10]. In the laminar type of optic disc cupping, concomitant retinal nerve fiber loss with peripapillary scleral and lamina cribrosa destruction and remodeling cause posterior bowing of lamina cribrosa and eventually significant cupping [11].

Compressive lesions

Compressive lesions, including pituitary adenoma, craniopharyngioma, aneurysms, and meningioma, can cause optic disc cupping [12]. In a retrospective study, Qu et al. found that patients with parasellar and sellar lesions and larger lesions closer to the entrance of the optic canal were more likely to have glaucoma-like disc cupping [13].

Clinical features of compressive optic neuropathies, unlike glaucomatous optic neuropathy, are painful (such as headache) or subacute progressive visual loss, with loss of central acuity and central visual field, and unilateral or bilateral asymmetric visual field loss, which might respect the vertical meridian. Distinguishing glaucomatous from non-glaucomatous optic disc cupping, particularly when IOP is within a normal range (normal tension glaucoma or low-tension glaucoma), can be difficult on clinical examination [14].

Danesh-Meyer et al. revealed that optical coherence tomography is an important imaging device to appraise the circumpapillary retinal nerve fiber layer (cpRNFL). Optical coherence tomography (OCT) determines types of retinal ganglion cell (RGC) damage, so compressive or glaucomatous optic neuropathy could be distinguished. They showed the differences in cpRNFL profile in these optic diseases [15].

In prospective research, Lee et al. compared compressive optic neuropathy, glaucomatous optic neuropathy, and healthy eyes using spectral-domain optical coherence tomography (SD-OCT) to show its usefulness in determining and comparing retinal ganglion cell damage scheme in the macular and peripapillary areas between CON and GON. They revealed explicit diversities in these diseases' retinal ganglion cell (RGC) damage scheme. SD-OCT is useful for distinguishing these diseases when the visual field test or fundus photography is inconclusive [16].

A study reported patients with primary normal tension glaucoma and the final compressive lesion of the anterior visual pathways [17].

Coincidentally, simultaneous glaucoma and the anterior visual pathway close lesion are possible. For example, Blumenthal et al. showed that optic disc cupping might accompany the gradual development of suprasellar mass lesions, and it is not easy to differentiate it from GON clinically. They identified some patients with normal IOP with glaucomatous optic nerve lesions and cupping. They concluded that typical glaucomatous optic neuropathy may sometimes occur accompanied by gradual-growing suprasellar tumors. For example, a patient (male, 87-year-old) with a cup-to-disc ratio of 0.8 and accurate scotoma in the right eye and IOP<16 or less in all follow up, along with a mass in the suprasellar space without compressive effect on the chiasma [18].

Micieli and Margolin retrospectively evaluated three patients referred to the clinic for a possible non-glaucomatous optic neuropathy. Patients had optic disc cupping without neuroretinal rim pallor and unequivocal radiological finding of the ipsilateral optic nerve compression by an intracranial blood vessel. All patients had IOP within normal limits, preserved visual acuity, and typical glaucomatous field defects. This result suggests that diagnosing glaucoma from non-glaucomatous on purely clinical manifestations is challenging, and neuroimaging might be necessary [19].

The internal carotid artery pressure on the optic nerve can account for some normal pressure glaucoma patients a theory supported by some authors [20].

Inflammation

Optic neuritis is one of the main reasons for optic neuropathy in patients under 50, which is present in subacute vision loss and eye pain [21]. It can occur after a viral infection or vaccination but, in most cases, is associated with demyelinating disorders like multiple sclerosis.

A study evaluated the morphologic characteristics of optic disc atrophy 6 months or more after non-arteritic AION and optic neuritis. A number of 35 optic discs after non-arteritic AION and 24 since optic neuritis, and 17 age-matched normal discs have been evaluated. The

optic discs discovered after AION was more wasted than after ocular neuritis. Rim segmental involvement after AION was usually either superior 'altitudinal' (53%) or inferior 'altitudinal' (29%), whereas, after optic neuritis, it was usually either temporal-central (papillomacular) (42%) or diffuse temporal (42%) [22].

A study investigated some patients with increased optic disc excavation with pallor caused by optic neuritis [23]. In another study, Rebolleda et al. evaluated 50 cases of unilateral optic neuritis and compared them to age- and sex-matched controls. After evaluating the optic disc by OCT device, they found that affected eyes had greater cup-to-disc ratios than healthy controls by an average of 0.12 [24].

Ischemic

Ischemic optic neuropathies consist of any vascular disease of the optic nerve. Typical ischemic optic nerve disease is non-arteritic acute anterior ischemic optic neuropathy. Its main reason remains unrecognized, but a disc at risk (little and crowded optic nerve) may result in non-arteritic ischemic optic neuropathy. There is no curative or preventive treatment. Posterior ischemic optic neuropathy is less common than anterior ischemic optic neuropathy. There is no cure. In all cases of ischemic optic neuropathy, an arteritic cause, must be omitted via clinical and para-clinical examinations. The main reason is giant-cell arteritis, so intravenous methylprednisolone will be prescribed to restrict vision loss in the damaged eye and to intercept vision loss in the other [25]. As previously mentioned, cupping in the arteritic type of anterior ischemic optic neuropathy (AAION) is more common and deeper than the non-arteritic type [26]. In an observational case series, Danesh-Meyer et al. appraise the prevalence of AAION and non-arteritic anterior ischemic optic neuropathy (NAION) cupping. They found a greater ratio of optic disc cupping in patients with AAION secondary to giant cell arteritis of AAION than in patients with NAION (92% and 2%, respectively). In this study, NAION patients had segmental or diffused optic disc pallor (72% and 28%, respectively) rather than cupping [27]. Contreras et al. reported a different cup-to-disc ratio in the affected eyes of NAION patients compared to noninvolved eyes. They showed that 48% of the involved eyes had a cup-disc ratio of more than 0.1 compared to noninvolved eyes [28]. Giant cells arteritis causes complete obstruction of the posterior ciliary arteries with significant ischemia, and NAION causes transient hypoperfusion of the ONH with the preservation of some blood flow. It is also in NAION's eyes presence of in crowded or missing physiologic cup (disc at risk); makes it more difficult to show cupping. Recent studies indicate that for distinguishing glaucomatous and non-glaucomatous optic neuropathies, the minimum thickness of Bruch's membrane inauguration (MRW-BMO) border, measured by Spectralis OCT device, is a valuable parameter. In a study, 54 cases with NGON, (22 eyes with ischemic optic neuropathy and 27 patients with NTG) were included. They reported that for differentiating glaucoma from non-glaucomatous optic neuropathies, the MRW-BMO parameter is crucial [29]. In a cross-sectional study, Fard et al. used enhanced depth imaging OCT (EDI-OCT) to analyze the morphology of the optic nerve head (ONH) in patients with primary open-angle glaucoma (POAG) and eyes with a history of non-arteritic anterior ischemic optic atrophy (NAION). This study included 32 eyes with mild to severe POAG, 30 with visual field mean deviation–matched NAION and their other eyes, and 29 with control eyes. The density and placement of LC in NAION eyes are similar to healthy ones and their fellow eyes. But severe thinning and posterior displacement were different in POAG [30]. Posterior ischemic optic neuropathy (PION) is due to occlusion or hypoperfusion of the surrounding nutrient pial capillary of the optic nerve. In the acute stage, it has optic disc swelling; in the chronic setting, optic disc pallor is the main presentation of the disease. PION can be related to GCA (arteritic) or occur in post-operative conditions (non-arteritic), Hayreh evaluated 42 eyes with non-arteritic PION and found that only two patients had an increased cup-disc ratio [31].

Hereditary optic neuropathies

Hereditary conditions like dominant optic atrophy or Leber optic neuropathy are among the causes of optic disc cupping [32]. They are typically bilateral and primarily affect central and color vision in the primary phase of the disease (glaucoma spares color until the end). The optic disc excavation will increase in the late phases of the disease; consequently, distinguishing it from glaucoma gets tough [33].

Early central visual loss with the temporal pallor of the optic disc and central or cecocentral scotoma are caused by Selective papillomacular involvement in hereditary optic neuropathies. A study revealed that DOA (dominant optic atrophy) and Leber hereditary optic neuropathy) LHON (lead to more shallow cups in contrast with glaucoma (34%, 49%, and 9%, respectively) [34].

DOA is the major ordinary sort of hereditary optic neuropathy. A survey showed that patients with DOA have temporal wedge-shaped excavation (78%) and a cup-to-

disc ratio is more than 0.5 in at least one of their eyes (89%). These characteristics are useful to differentiate DOA and NTG, beginning at a young age, central vision deficiency, preservation of the peripheral fields, neuro-retinal pallor, and explicate visual loss in the family or optic atrophy [35]. A study demonstrated that the distribution of retinal nerve fiber layer damage measured by OCT could be used to distinguish DOA from glaucoma. The temporal clock hour measurement was outside the 95% common range in 29 of the 32 DOA eyes (90.6%). The pattern of RNFL damage was bilaterally symmetrical in location and severity in all patients [36].

Toxic and nutritional optic neuropathies

Some medications or poisonous materials, like ethambutol, linezolid, or methanol, can cause acute toxic optic neuropathy with ocular and systemic presentation that usually occurs 12–24 hours after exposure [37]. Multiple methanol toxicity outbreaks with concomitant optic neuropathies occurred in developing countries during the COVID-19 pandemic [38]. Active products of methanol dissolution cause retinal ganglionic cell loss and subsequent necrosis of nerve fiber layers and optic nerve. In the acute phase, fundoscopic examination shows optic disc hyperemic edema with venous dilation and optic disc excavation and pallor in the late stage. In avoiding unnecessary glaucoma evaluation and workup, taking a careful history is valuable in diagnosing the disease. There are many reports recorded in recent years from developing countries with methanol toxicity and optic disc cupping and pallor [39].

Congenital causes

In optic disc coloboma, an enlarged optic disc is occupied by a white, bowl-shaped excavation. In the literature, numerous optic disc colobomas similar to glaucomatous cupping have been reported [40]. In some cases, with nerve fiber layer defects, differentiation between colobomatous cupping from glaucoma can be difficult. Key features to differentiate optic disc coloboma from glaucoma include the presence of colobomatous defects in other areas of the eye (retina, iris), a larger size of optic disc defect and depression and cupping in colobomatous patients, and an unusual vascular displacement by the coloboma and history of amblyopia in early age.

Periventricular leukomalacia (PVL) is the main cause of visual dysfunction in preterm neonates. This disease results from hypoxic-ischemic injury to periventricular white matter and subsequent periventricular leukomalacia [41]. In many patients, optic disc cupping imitating glaucomatous cupping has been seen in Periventricular leukomalacia [42]. In a study, Jacobson et al. proposed that small-sized optic discs may be associated with primary PVL. However, after 28 weeks of gestation, diminished neuro-retinal rim disc enlargement is seen [41].

Morning glory disc anomaly (MGDA) is hereditary and identified by ONH cupping, abnormal radial retinal vessels appearing from the disc rim, and peripapillary atrophy [43]. Srinivasan et al. evaluated the OCT finding of MGDA patients. They showed an extended optic disc and cup by reduced macular thickness and temporal increase of the retinal nerve fiber layer [44]. A study demonstrated an extended optic cup and disc accompanied by RNFL diminishing and normal macular thickness in a patient with MGDA [45].

High myopia

There is an increased risk of primary open-angle glaucoma in high myopic eyes, and particular attention is needed for eyes with high myopia [46]. Myopic eyes typically have the shallow, oval-shaped, obliquely oriented, larger disc with larger cupping, with significant peripapillary atrophy compared to normal eyes [47].

As high as 16.1% of patients with myopia have visual field defects simulating glaucoma [48]. In myopic, tilted disc patients, the discontinuity between the temporal optic edge border and inferior or superior optic rim margin (crescent moon sign) is extremely important for early diagnosis of glaucoma (90.0%–91.4%) [49].

Approach to the patient with optic disc cupping

As discussed, the entities mimicking glaucoma are non-glaucomatous optic neuropathies. As history taking is very important in this setting. A non-glaucomatous etiology is more probable than glaucoma in a patient with a history of painful eye movements, systemic manifestations (like temporal headache, jaw claudication), or acute and subacute vision loss.

The presence of the normal IOP, significant disc pallor, reduced central acuity in the early stage of the disease, familial history of the optic disc anomaly, and the patient's medical history can help differentiate GON from NOGN. More than in glaucoma, progressive visual field loss in patients with normal or low intraocular pressures is seen in non-glaucomatous optic neuropathies.

While glaucoma spares central and color vision until the end stage of the disease and generates specific visual field defects (nasal step and arcuate scotoma), the visual function must consider. Lack of color vision not coordinated with the visual acuity or a visual field defect regarding the vertical midline are signs of NGOT.

The appearance of the optic disc is also significant. Neuroretinal rim pallor points to the non-glaucomatous etiology. Any mismatch between optic disc notching pattern and visual field defect (an inferior notching accompanied by superior visual field deficiencies) or a visual field d disproportionate to the cupping stage, NGOT should be considered.

In some circumstances, distinguishing between these entities, such as advanced optic atrophy with a full cup or anomalous and hypoplastic optic nerves, is difficult. Orbital imaging to evaluate compressive lesions of the anterior visual paths and blood testing based on history and clinical features helps to differentiate between the two. Finally, in cases where the diagnosis is doubtful, it will regard to consult with a neuro-ophthalmologist or glaucoma specialist.

Conclusion

As mentioned above, non-glaucomatous optic neuropathy includes a variety of disorders. The patient's history, a complete eye examination, and imaging tests such as perimetery or retinal nerve fiber layers or macular ganglion cells OCT are useful in making a definite diagnosis. When the diagnosis is mixed-up, refer to a neuro-ophthalmologist or glaucoma specialist, and additional investigations may be required, including imaging or auxiliary blood testing.

Ethical Considerations

Compliance with ethical guidelines

All study procedures were in compliance with the ethical guidelines of the Declaration of Helsinki (2013).

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Authors contributions

Conceptualization, methodology, software, supervision, project administration, writing the original draft: Ebrahim Azaripour; Validation, formal analysis, investigation, resources, data curation, writing, review, editing and visualization: Ebrahim Azaripour and Hassan Behboudi.

Conflict of interest

The authors declared no conflict of interest.

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References

[1] Quigley HA, Green WR. The histology of human glaucoma cupping and optic nerve damage: Clinicopathologic correlation in 21 eyes. Ophthalmology. 1979; 86(10):1803-30. [DOI:10.1016/S0161-6420(79)35338-6] [PMID]

[2] Ambati BK, Rizzo JF. Nonglaucomatous cupping of the optic disc. Int Ophthalmol Clin. 2001; 41(1):139-49. [DOI:10.1097/00004397-200101000-00013] [PMID]

[3] Soltani-Moghadam R, Azaripour E, Alizadeh Y, Behboudi H, Moravvej Z, Medghalchi A, et al. Clinical outcomes of viscocanalostomy and phacoviscocanalostomy in primary open angle glaucoma: Two years follow-up. Eur J Ophthamol. 2022; 32(5):2880-5. [DOI:10.1177/11206721211064003] [PMID]

[4] Azaripour E, Khakpour Y, Soltani-Moghadam R, Moravvej Z, Medghalchi A, Behboudi H, et al. Outcomes of phaco-viscocanalostomy in primary open angle glaucoma versus pseudoexfoliation glaucoma. J Ophthalmic Vis Res. 2021; 16(4):566-73. [DOI:10.18502/jovr.v16i4.9746] [PMID] [PMCID]

[5] Herzog R, Álvarez-Pasquin MJ, Díaz C, Del Barrio JL, Estrada JM, Gil Á. Are healthcare workers' intentions to vaccinate related to their knowledge, beliefs and attitudes? A systematic review. BMC Public Health. 2013; 13:154. [DOI:10.1186/1471-2458-13-154] [PMID] [PMCID]

[6] Fard MA, Moghimi S, Sahraian A, Ritch R. Optic nerve head cupping in glaucomatous and non-glaucomatous optic neuropathy. Br J Ophthalmol. 2019; 103(3):374-8. [DOI:10.1136/bjophthalmol-2018-312161] [PMID]

[7] Hata M, Miyamoto K, Oishi A, Makiyama Y, Gotoh N, Kimura Y, et al. Comparison of optic disc morphology of optic nerve atrophy between compressive optic neuropathy and glaucomatous optic neuropathy. Plos One. 2014; 9(11):e112403. [DOI:10.1371/journal.pone.0112403] [PMID] [PMCID]

[8] Quigley HA, Green WR. The histology of human glaucoma cupping and optic nerve damage: Clinicopathologic correlation in 21 eyes. Ophthalmology. 2020; 127(4S):S45-9. [DOI:10.1016/j.ophtha.2020.01.035] [PMID]

[9] Kim YW, Yun YI, Choi HJ. Screening fundus photography predicts and reveals risk factors for glaucoma conversion in eyes with large optic disc cupping. Sci Rep. 2023; 13(1):81. [DOI:10.1038/s41598-022-26798-4] [PMID] [PMCID]

[10] Burgoyne C. The morphological difference between glaucoma and other optic neuropathies. J Neuroophthalmol. 2015; 35(Suppl 1):S8-21. [DOI:10.1097/WNO.0000000000000289] [PMID] [PMCID]

[11] Crawford Downs J, Roberts MD, Sigal IA. Glaucomatous cupping of the lamina cribrosa: A review of the evidence for active progressive remodeling as a mechanism. Exp Eye Res. 2011; 93(2):133-40. [DOI:10.1016/j.exer.2010.08.004] [PMID] [PMCID]

[12] Pincelli Netto M, Ferrari PV, Herrerias BT, Hirai FE, Gracitelli CPB. Internal carotid artery aneurysm mimicking normal-tension glaucoma. Arq Bras Oftalmol. 2018; 81(2):148-52. [DOI:10.5935/0004-2749.20180032] [PMID]

[13] Qu Y, Wang YX, Xu L, Zhang L, Zhang J, Zhang J, et al. Glaucoma-like optic neuropathy in patients with intracranial tumours. Acta Ophthalmol. 2011; 89(5):e428-33.[DOI:10.1111/j.1755-3768.2011.02118.x] [PMID]

[14] Pellegrini F, Marullo M, Zappacosta A, Liberali T, Cuna A, Lee AG. Suprasellar meningioma presenting with glaucomatous type cupping. Eur J Ophthalmol. 2021; 31(6):NP36-40. [DOI:10.1177/1120672120937674] [PMID]

[15] Danesh-Meyer HV, Yap J, Frampton C, Savino PJ. Differentiation of compressive from glaucomatous optic neuropathy with spectral-domain optical coherence tomography. Ophthalmology. 2014; 121(8):1516-23. [DOI:10.1016/j.ophtha.2014.02.020] [PMID]

[16] Lee EJ, Yang HK, Kim TW, Hwang JM, Kim YH, Kim CY. Comparison of the pattern of retinal ganglion cell damage between patients with compressive and glaucomatous optic neuropathies. Invest Ophthalmol Vis Sci. 2015; 56(12):7012-20. [DOI:10.1167/iovs.15-17909] [PMID]

[17] Ahmed II, Feldman F, Kucharczyk W, Trope GE. Neuroradiologic screening in normal-pressure glaucoma: Study results and literature review. J Glaucoma. 2002; 11(4):279-86. [DOI:10.1097/00061198-200208000-00002] [PMID]

[18] Blumenthal EZ, Girkin CA, Dotan S. Glaucomatous-like cupping associated with slow-growing supra-sellar intracranial lesions. Neuro-Ophthalmology. 2006; 30(5):111-5. [DOI:10.1080/01658100600980974]

[19] Micieli JA, Margolin EA. Optic disc cupping due to dolichoectatic internal carotid artery optic nerve compression. J Neuroophthalmol. 2021; 41(4):e560-5. [DOI:10.1097/WNO.0000000000001113] [PMID]

[20] Ogata N, Imaizumi M, Kurokawa H, Arichi M, Matsumura M. Optic nerve compression by normal carotid artery in patients with normal tension glaucoma. Br J Ophthalmol. 2005; 89(2):174-9. [DOI:10.1136/bjo.2004.047035] [PMID] [PMCID]

[21] Wilhelm H, Schabet M. The diagnosis and treatment of optic neuritis. Dtsch Arztebl Int. 2015; 112(37):616-25. [DOI:10.3238/arztebl.2015.0616] [PMID] [PMCID]

[22] Rath EZ, Rehany U, Linn S, Rumelt S. Correlation between optic disc atrophy and aetiology: Anterior ischaemic optic neuropathy vs optic neuritis. Eye. 2003; 17(9):1019-24. [DOI:10.1038/sj.eye.6700691] [PMID]

[23] Zhang YX, Huang HB, Wei SH. Clinical characteristics of nonglaucomatous optic disc cupping. Exp Ther Med. 2014; 7(4):995-9. [DOI:10.3892/etm.2014.1508] [PMID] [PMCID]

[24] Rebolleda G, Noval S, Contreras I, Arnalich-Montiel F, García-Perez JL, Muñoz-Negrete FJ. Optic disc cupping after optic neuritis evaluated with optic coherence tomography. Eye. 2009; 23(4):890-4. [DOI:10.1038/eye.2008.117] [PMID]

[25] Tournaire-Marques E. Neuropathies optiques ischémiques [Ischemic optic neuropathies (French)]. J Fr Ophtalmol. 2020; 43(6):552-8. [DOI:10.1016/j.jfo.2019.10.020] [PMID]

[26] Horowitz J, Melamud A, Sela L, Hod Y, Geyer O. Internal carotid artery hypoplasia presenting as anterior ischemic optic neuropathy. Am J Ophthalmol. 2001; 131(5):673-4. [DOI:10.1016/S0002-9394(00)00886-2] [PMID]

[27] Danesh-Meyer HV, Savino PJ, Sergott RC. The prevalence of cupping in end-stage arteritic and nonarteritic anterior ischemic optic neuropathy. Ophthalmology. 2001; 108(3):593-8. [DOI:10.1016/S0161-6420(00)00602-3] [PMID]

[28] Contreras I, Rebolleda G, Noval S, Muñoz-Negrete FJ. Optic disc evaluation by optical coherence tomography in nonarteritic anterior ischemic optic neuropathy. Invest Ophthalmol Vis Sci. 2007; 48(9):4087-92. [DOI:10.1167/iovs.07-0171] [PMID]

[29] Leaney JC, Nguyen V, Miranda E, Barnett Y, Ahmad K, Wong S, et al. Bruch's membrane opening minimum rim width provides objective differentiation between glaucoma and nonglaucomatous optic neuropathies. Am J Ophthalmol. 2020; 218:164-72. [DOI:10.1016/j.ajo.2020.05.034] [PMID]

[30] Fard MA, Afzali M, Abdi P, Chen R, Yaseri M, Azaripour E, et al. Optic nerve head morphology in nonarteritic anterior ischemic optic neuropathy compared to open-angle glaucoma. Invest Ophthalmol Vis Sci. 2016; 57(11):4632-40. [DOI:10.1167/iovs.16-19442] [PMID]

[31] Hayreh SS. Posterior ischaemic optic neuropathy: Clinical features, pathogenesis, and management. Eye. 2004; 18(11):1188-206. [DOI:10.1038/sj.eye.6701562] [PMID]

[32] Souto FM, de Vasconcellos JP, de Melo MB, Sartorato EL, Moura FC. Differentiating leber hereditary optic neuropathy from normal-tension glaucoma. Neuroophthalmology. 2017; 41(2):99-102. [DOI:10.1080/01658107.2017.1279185] [PMID] [PMCID]

[33] Behbehani R. Clinical approach to optic neuropathies. Clin Ophthalmol. 2007; 1(3):233-46. [PMID] [PMCID]

[34] O'Neill EC, Danesh-Meyer HV, Kong GX, Hewitt AW, Coote MA, Mackey DA, et al. Optic disc evaluation in optic neuropathies: The optic disc assessment project. Ophthalmology. 2011; 118(5):964-70. [DOI:10.1016/j.ophtha.2010.09.002] [PMID]

[35] Fournier AV, Damji KF, Epstein DL, Pollock SC. Disc excavation in dominant optic atrophy: Differentiation from normal tension glaucoma. Ophthalmology. 2001; 108(9):1595-602. [DOI:10.1016/S0161-6420(01)00696-0] [PMID]

[36] Kim TW, Hwang JM. Stratus OCT in dominant optic atrophy: Features differentiating it from glaucoma. J Glaucoma. 2007; 16(8):655-8. [DOI:10.1097/IJG.0b013e31804d23aa] [PMID]

[37] Shin YW, Uhm KB. A case of optic nerve atrophy with severe disc cupping after methanol poisoning. Korean J Ophthalmol. 2011; 25(2):146-50. [DOI:10.3341/kjo.2011.25.2.146] [PMID] [PMCID]

[38] Gouda AS, Khattab AM, Mégarbane B. Lessons from a methanol poisoning outbreak in Egypt: Six case reports. World J Crit Care Med. 2020; 9(3):54-62. [DOI:10.5492/wjccm.v9.i3.54] [PMID] [PMCID]

[39] Hassanpoor N, Niyousha M. Severe optic disc cupping following the methanol toxicity in a 20-year-old man: A case report. Iran J Med Sci. 2021; 46(5):395-8. [DOI:10.30476/ijms.2021.88370.1914] [PMID] [PMCID]

[40] Mansoori T, Vemuganthi S, Agraharam SG. Optic disc coloboma: Glaucoma imitator. Indian J Ophthalmol. 2019; 67(10):1735. [DOI:10.4103/ijo.IJO_494_19] [PMID] [PMCID]

[41] Jacobson LK, Dutton GN. Periventricular leukomalacia: An important cause of visual and ocular motility dysfunction in children. Surv Ophthalmol. 2000; 45(1):1-13. [DOI:10.1016/S0039-6257(00)00134-X] [PMID]

[42] Groth SL, Donahue SP, Reddy A, Sarma A, Wushensky C. Periventricular leukomalacia in patients with pseudoglaucomatous cupping. Am J Ophthalmol. 2020; 211:31-41. [DOI:10.1016/j.ajo.2019.10.016] [PMID]

[43] Brodsky MC. Periventricular leukomalacia: An intracranial cause of pseudoglaucomatous cupping. Arch Ophthalmol. 2001; 119(4):626-7. [DOI:10.1001/archopht.119.4.626] [PMID]

[44] Srinivasan G, Venkatesh P, Garg S. Optical coherence tomographic characteristics in morning glory disc anomaly. Can J Ophthalmol. 2007; 42(2):307-9. [DOI:10.3129/can.j.ophthalmol.i07-031] [PMID]

[45] Saraswat N, Ranjan R, Shukla D, Ojha S. Morning glory disc anomaly: A case report. Niger J Ophthalmol. 2017; 25(1):42-7. [DOI:10.4103/0189-9171.207376]

[46] Chen SJ, Lu P, Zhang WF, Lu JH. High myopia as a risk factor in primary open angle glaucoma. Int J Ophthalmol. 2012; 5(6):750-3. [DOI:10.3980/j.issn.2222-3959.2012.06.18] [PMID] [PMCID]

[47] Sampaolesi R, Sampaolesi JR. Large optic nerve heads: Megalopapilla or megalodiscs. Int Ophthalmol. 2001; 23(4-6):251-7. [DOI:10.1023/A:1014409404579] [PMID]

[48] Ding X, Chang RT, Guo X, Liu X, Johnson CA, Holden BA, et al. Visual field defect classification in the zhongshan ophthalmic center-brien holden vision institute high myopia registry study. Br J Ophthalmol. 2016; 100(12):1697-702. [DOI:10.1136/bjophthalmol-2015-307942] [PMID]

[49] Kim MJ, Kim SH, Hwang YH, Park KH, Kim TW, Kim DM. Novel screening method for glaucomatous eyes with myopic tilted discs: The crescent moon sign. JAMA Ophthalmol. 2014; 132(12):1407-13. [DOI:10.1001/jamaophthalmol.2014.2860] [PMID]