Cupped disc with normal intraocular pressure: The long road to avoid misdiagnosis

Nikhil S Choudhari[1,2], Aditya Neog[1,2], Vimal Fudnawala[2], Ronnie George[1]

We present a series of six patients who had been receiving treatment for normal tension glaucoma (NTG; five patients) or primary open angle glaucoma (one patient). All of them were found to have optic neuropathy secondary to compression of the anterior visual pathway. Even though uncommon, compression of the anterior visual pathway is an important differential diagnosis of NTG. Diagnosis of NTG should be by exclusion. Here the possible causes of misdiagnosis are discussed. We present an approach to distinguish glaucomatous from nonglaucomatous optic neuropathy. The article also emphasizes how important it is for the clinicians to consider the total clinical picture, and not merely the optic disc morphology, to avoid the mismanagement of glaucoma, especially the NTG.

Key words: Optic disc cupping, optic disc pallor, suprasellar tumor, glaucoma, neuroimaging

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Glaucomatous optic neuropathy is characterized by progressive loss of the nerve fiber layer resulting in diffuse loss or notching of the neuroretinal rim especially to the optic disc margin.[1] Other characteristic features of glaucomatous optic neuropathy include optic disc hemorrhage crossing the neuroretinal rim, intereye asymmetry of cupping in the absence of asymmetry of disc size, and parapapillary atrophy.[1]

The current definition of glaucoma precludes intraocular pressure (IOP) as a defining feature.[2] One can diagnose glaucoma even when the IOP is "normal." Unfortunately, in day-to-day practice, excessive cupping of the optic disc is considered to be pathognomonic of chronic glaucoma. One tends to diagnose "normal tension glaucoma" (NTG) if the IOP falls within the acceptable range often without investigating nonglaucomatous causes. In fact, in many cases, long-standing optic neuropathy can result in optic disc cupping. Causes of nonglaucomatous optic disc cupping include methanol poisoning,[3] arteritic anterior ischemic optic neuropathy,[4] and rarely chronic compressive lesions of the optic nerve.[5-8]

In the present series, we report six patients, who were misdiagnosed and treated as having glaucoma, in whom bilateral optic disc cupping simulating glaucomatous optic neuropathy was a feature of compression of the anterior visual pathway. We discuss an approach to the not so rare clinical presentation of cupping of the optic nerve head associated with normal IOP to prevent similar occurrences in future.

Case Report

The cases are summarized in Table 1.

Discussion

The patients in this series ranged in age from 40 to 69 years. All of them had presented to their treating ophthalmologist with painless, gradually progressive vision loss. Except for a diffuse, dull headache at presentation to us in only one patient, none of them had any neurological symptoms. All were diagnosed to have glaucoma and were treated with IOP lowering measures. Three of them had undergone trabeculectomy. All, except the last, presented to us with progressive vision loss despite adequate treatment for glaucoma.

Pruett *et al*.[8] cited "a low index of suspicion" as a main culprit in the delayed diagnosis of chiasmal compression in 1973. This series illustrates why one should be extra-vigilant when diagnosing NTG even today.

All these patients had signs that should have raised suspicion about the presumptive diagnosis of NTG [Table 2]. Notably, the morphology of the pupils and that of the optic nerve head excepting the vertical cup-to-disc ratio were not recorded in any of these patients. Prominent pallor that was more than loss of the neuroretinal rim, at least when we examined, was seen in all, except the fifth patient. Misinterpretation of the visual fields is another significant factor for the misdiagnosis in these cases. For example, patchy visual field loss in the right eye of the second patient's earliest visual field [Fig. 6B] could be mistaken for glaucomatous biarcuate visual field loss. On careful evaluation, the visual field defects in the earliest visual field respected the vertical meridian. Thinning of retinal nerve fiber layer (RNFL) on optical coherence tomogram might have been considered to represent glaucomatous optic neuropathy in the fourth patient [Fig. 10A]. Thinning of RNFL is the end result of any pathological process causing optic neuropathy and does not necessarily mean glaucoma. A comprehensive ophthalmic evaluation and appropriate interpretation of the clinical and/or investigational findings could have saved the second, third, and fifth patients from an erroneous diagnosis of glaucoma and glaucoma filtering surgeries. Moreover, neuroimaging at least when the visual loss was progressive despite achieving low IOP could have prevented further visual loss in them as well as in the first patient.

Distinguishing glaucomatous from nonglaucomatous optic disc cupping on clinical examination is difficult. Generally, the optic disc in patients with intracranial compressive lesions

[1]Jadhavbhai Nathamal Singhvi Glaucoma Department, [2]Neuro-Ophthalmology Department, Medical Research Foundation, Sankara Nethralaya, 18, College Road, Chennai, India

Correspondence to: Dr. Nikhil S Choudhari, Medical Research Foundation, Sankara Nethralaya, 18, College Road, Chennai – 600 006, India. E-mail: nkl164@gmail.com

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Table 1: Details of cases

Case no.	Age/ Sex	Presentation to treating ophthalmologist	Earlier records	Presentation to us	Examination findings	Investigations
1	56/M	LE Decreased vision (2003)	Vision RE: 20/30, LE: 20/200; IOP BE: 17.3 mmHg (Schiotz); Visual fields: Fig. 1; Dx: NTG; Mx: Topical AGM	Occasional frontal headache, further decrease in LE vision and side vision RE (2008)	Vision RE: 20/30, LE: PL; CV RE: 16/16; LE: grade 2 RAPD; IOP BE: 12 mmHg; Open angles, Lens BE: NS 1; Optic disc RE: CDR 0.6:1, Temporal pallor, LE: CDR 0.9:1, gross pallor [Fig. 2]	Pachymetry BE: 516 µ, Progression in RE visual field [Fig. 3]; MRI: Pituitary macroadenoma compressing optic chiasm [Fig. 4]
2	43/M	LE Decreasing vision (2002)	Dx: POAG; MX: BE Trab	BE progressive decrease in vision despite surgery (2007)	Vision RE: 20/30, LE: no PL; LE grade 3 RAPD; BE thin conjunctival bleb; IOP BE: 12 mmHg; Open angles, Lens BE: clear; Optic disc BE: large, residual thin, pale NRR [Fig. 5]	Pachymetry RE: 525,LE: 516 µ; Visual field RE: temporal hemi field loss [Fig. 6A]; CT: supra sellar pituitary adenoma [Fig. 7]
3	40/F	BE: Decreased vision (2004)	IOP: Multiple readings in low teens, latest single reading BE 28 mm Hg; Mx: LE trab, BE AGM	BE Progressive decrease in vision despite LE surgery (2008); BE on 4 topical AGM	Vision RE: PL, LE: counting fingers @ 1m; sluggish pupils; LE shallow conjunctival bleb; IOP BE: 10 mmHg; Lens RE: grade 2 PSC[9], LE: clear; Optic disc BE: moderate sized, CDR 0.8:1, pallor > cupping [Fig. 8]	MRI: supra-sellar meningioma [Fig. 9]
4	69/M	BE: Decreased vision (April 2008)	IOP BE: 15 mm Hg; OCT RE: gross RNFL thinning, LE: borderline superior thinning [Fig. 10A]; Dx: NTG; Mx: BE Timolol, Brimonidine combination eye drop	Diffuse, dull headache; BE further decrease in vision (July 2008)	Vision RE: HM, LE: 20/80; CV LE: 0/16; RE grade 1 RAPD; IOP RE: 16, LE 14 mmHg; Open angles, Lens BE: grade 2 NS[9]; Optic disc RE: CDR 0.7:1, inferior polar excavation, pale nasal and inferior NRR and temporal beta parapapillary atrophy, LE: healthy	Pachymetry BE: 508 µ; visual field LE: advanced defect respecting vertical meridian [Fig. 10B] MRI: cystic supra-sellar craniopharyngioma [Fig. 11]
5	65/M	RE: Gradually progressive vision loss (2007)	`Normal' IOP; BE: optic disc cupping, Dx: POAG, Mx RE: Trab	RE further decrease in vision despite surgery (2008)	Vision RE: counting fingers @ 1 m, LE: 20/30; CV LE: 8/16; RE grade 2 RAPD; RE non-functional conjunctival bleb; IOP RE: 20, LE 16 mmHg; Open angles, BE Pseudophakia, no PCO; Optic disc BE: large disc, CDR 08:1, pink NRR, RE: inferior notch, LE: inferior incomplete notch [Fig. 12]	Pachymetry RE: 550, LE: 533 µ; visual fields not corresponding with fundus, RE: advanced loss, LE: temporal hemi-field loss [Fig. 13]; CT: cystic, supra-sellar calcified craniopharyngioma [Fig. 14]
6	59/M	LE: Gradually progressive vision loss (July 2009)	Vision BE: 20/20, IOP RE: 12.2, LE: 14.6 mm Hg (Schiotz); visual field RE: normal, LE: early, superior arcuate scotoma; Dx: POAG; Mx: Timolol, Dorzolamide eye drop	Came for another opinion (Oct 2009)	Vision RE: 20/16, LE: 20/25; CV RE: 16/16, LE: 2/16; LE grade 1 RAPD; IOP RE: 12, LE: 14 mmHg; Open angles, Lens BE: clear; Optic disc BE: large disc, CDR 0.65:1, sloping inferior NRR, LE: prominent temporal pallor [Fig. 15]	Pachymetry BE: 532 µ, visual field defect respecting vertical meridian [Fig. 16]; MRI: Pituitary macroadenoma [Fig. 17]

M: Male, F: Female, RE: Right eye, LE: Left eye, BE: Both eyes, CV: Color vision, IOP: Intraocular pressure, NS: Nuclear sclerosis, PSC: Posterior subcapsular cataract, PCO: Posterior capsular opacity; CDR: Cup-to-disc ratio, NRR: Neuroretinal rim, CT: Computed tomography, MRI: Magnetic resonance imaging, OCT: Optical coherence tomography, Dx: Diagnosis, Mx: Management, POAG: Primary open angle glaucoma, NTG: Normal tension glaucoma, AGM: Antiglaucoma medication(s), Trab: Trabeculectomy. Note that at our hospital, all IOP measurements were done with the Goldmann applanation tonometer and all color vision recordings were done with Ishihara pseudoisochromatic plates.

Table 2: Probable factors that lead to misdiagnosis in the presented cases

Factors	Case number						Total cases
	1	2	3	4	5	6	
Failure to attend grossly asymmetric vision loss	Y	Y	–	Y	Y	–	4
Failure to document morphology of pupils	Y	Y	Y	Y	Y	Y	6
Failure to document optic disc morphology besides vertical cup-to-disc ratio	Y	Y	Y	Y	Y	Y	6
Considering unacceptable cupping of the optic disc to be synonymous with glaucoma	Y	Y	Y	Y	Y	Y	6
Failure to correlate visual acuity with cupping of the optic disc	Y	Y	Y	Y	Y	Y	6
Failure to obtain visual field examination	–	–	Y	Y	Y	–	3
Misinterpretation of visual field defect	Y	Y	–	–	–	Y	3
Misinterpretation of RNFL thinning	–	–	–	Y	–	–	1
Failure to obtain neuroimaging despite a progressive visual loss	Y	Y	Y	–	Y	–	4
Follow-up visual field examinations inadequate	Y	Y	–	–	–	–	2

RNFL: retinal nerve fiber layer, Y: yes (present).

is pale and lacks cupping as seen in glaucoma.[10] However, this is not the rule. Kupersmith[7] demonstrated cupping of the optic nerve resembling glaucoma in 16 patients with lesions compressing the anterior visual pathway. Bianchi-Marzoli[11] demonstrated an increased median cup-to-disc area in patients with compressive lesions compared to age-matched controls. Similarly, pallor of the optic disc might also be lacking in intracranial compressive lesions (e.g., in the

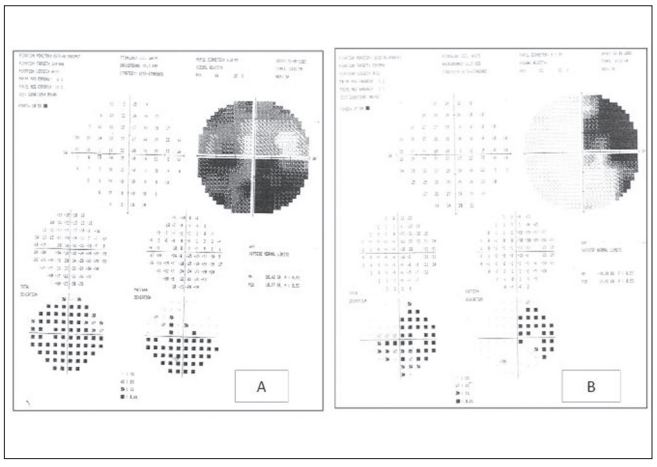

Figure 1: Case 1 – The earliest available visual field in 2003; left eye (A) and right eye (B). Advanced field loss in the left eye and superotemporal quadrantanopia in the right eye

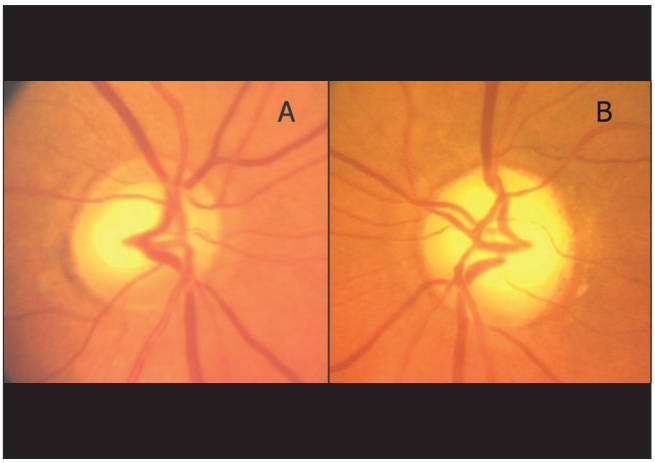

Figure 2: Case 1 – Minimal pallor of the temporal rim in the right eye (A) and gross pallor of the rim in the left eye (B)

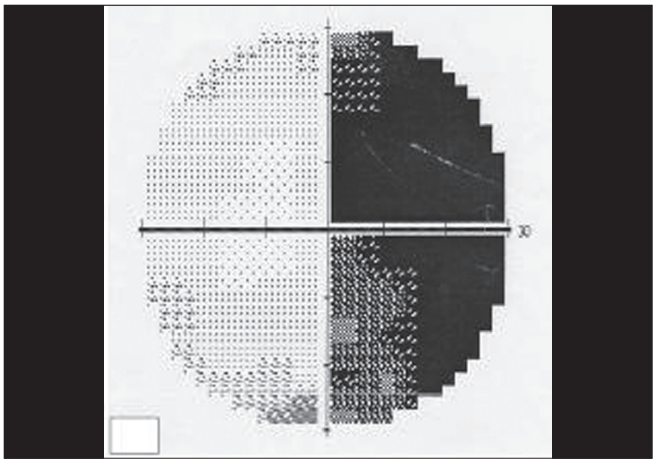

Figure 3: Case 1 – The visual field of the right eye at presentation to us in February 2008. Note the progression in the field defect

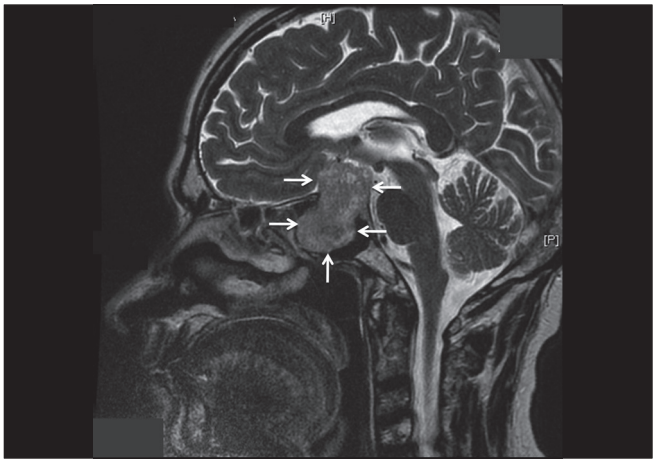

Figure 4: Case 1 – Magnetic resonance imaging of brain (sagittal section) shows a well-circumscribed, lobulated sellar mass lesion suggestive of pituitary macroadenoma (outlined by arrows). Superiorly, it is displacing and compressing the optic chiasm

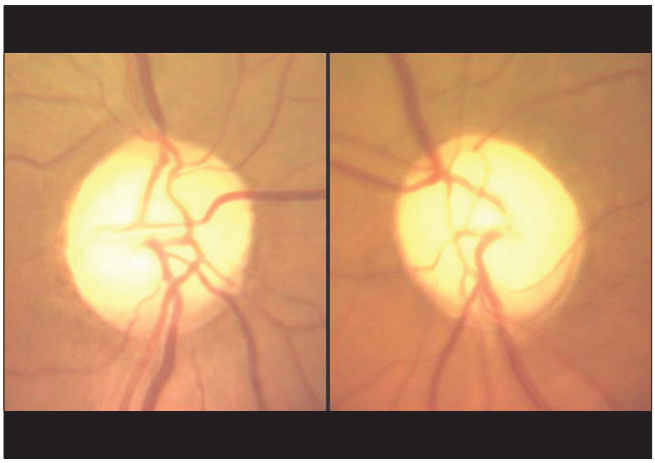

Figure 5: Case 2 – Thin and pale neuroretinal rim of both optic discs

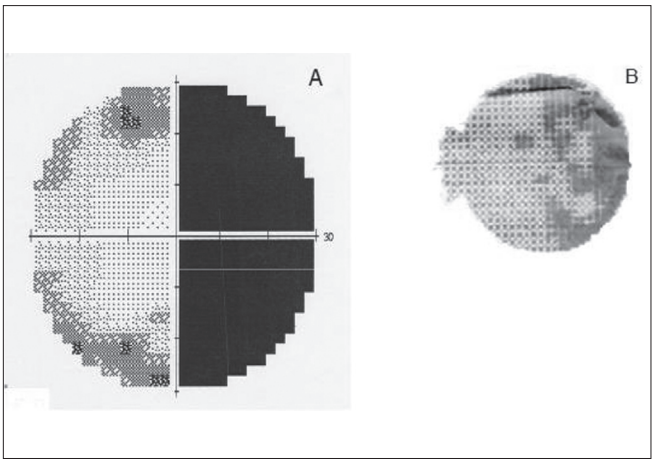

Figure 6: Case 2 – (A) The visual field of the right eye in 2007. (B) The visual field of the right eye in 2002. Note the defects respect the vertical meridian

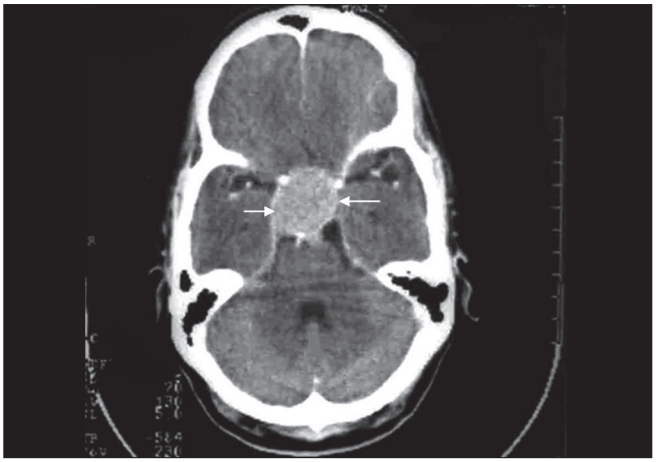

Figure 7: Case 2 – Axial computed tomography scan shows a suprasellar mass (outlined by arrows) suggestive of pituitary adenoma

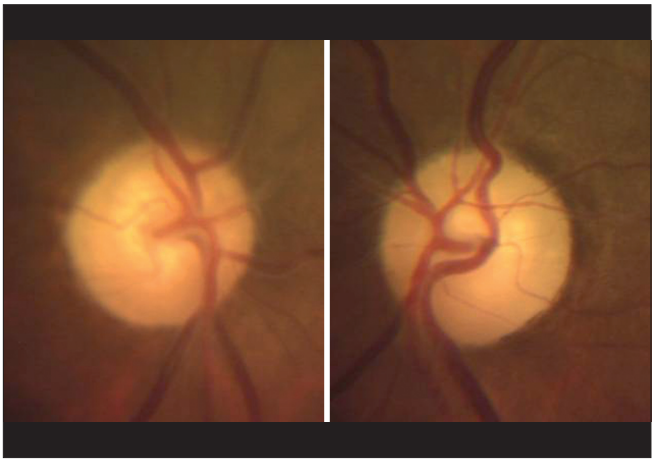

Figure 8: Case 3 – Area of pallor more than that of cupping in both optic discs

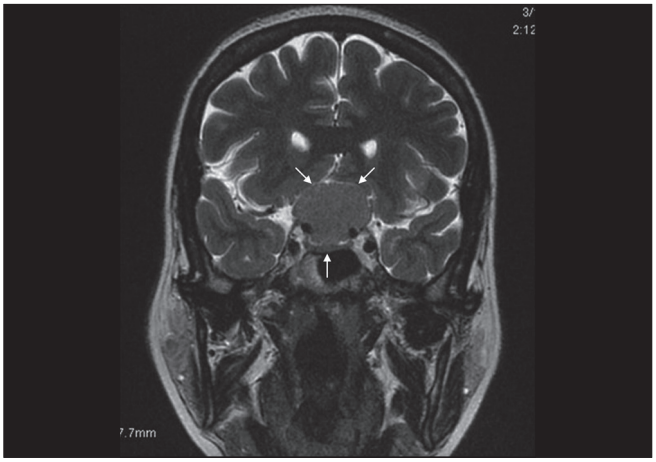

Figure 9: Case 3 – Coronal section on magnetic resonance imaging of brain shows a well-circumscribed, lobulated, homogeneous, solid suprasellar mass lesion consistent with meningioma (outlined by arrows). Intracranial optic nerves and optic chiasm could not be identified separately from the lesion

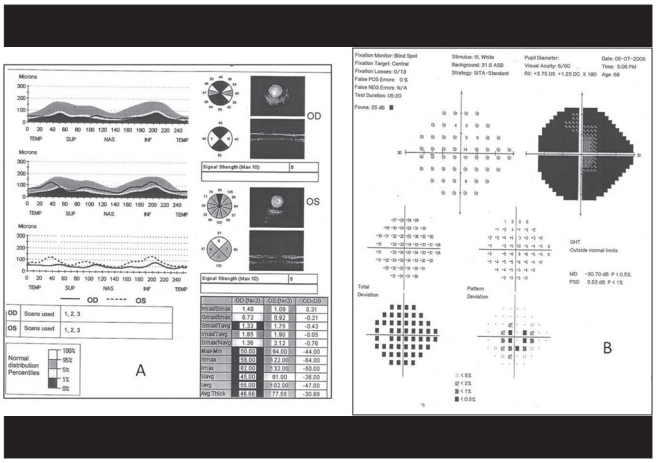

Figure 10: Case 4 – Optical coherence tomogram (A) and automated perimetry (B) in the left eye. Note the gray scale; the visual field defect respects the vertical meridian. The pattern deviation is misleading in advanced visual field loss

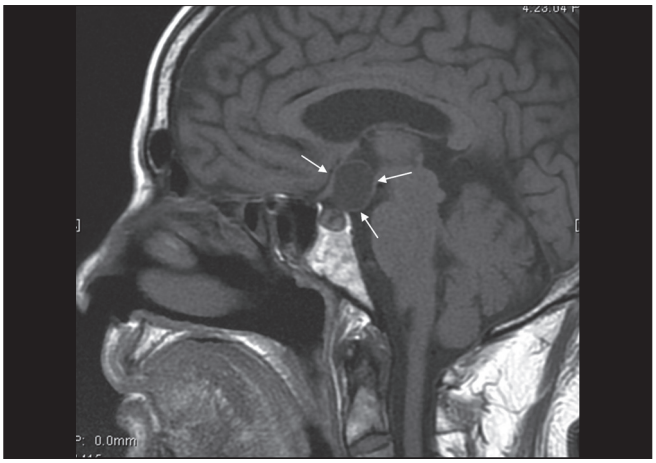

Figure 11: Case 4 – Magnetic resonance imaging of brain (sagittal section) shows a cystic lesion in the suprasellar cistern (outlined by arrows) suggestive of craniopharyngioma

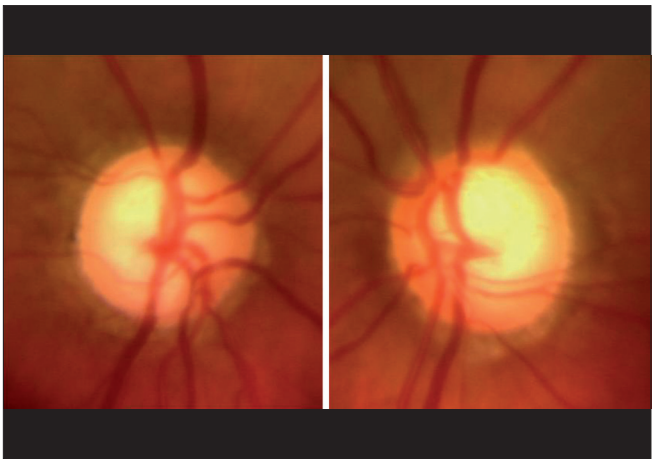

Figure 12: Case 5 – Optic disc photographs. Note the absence of pallor of the neuroretinal rim

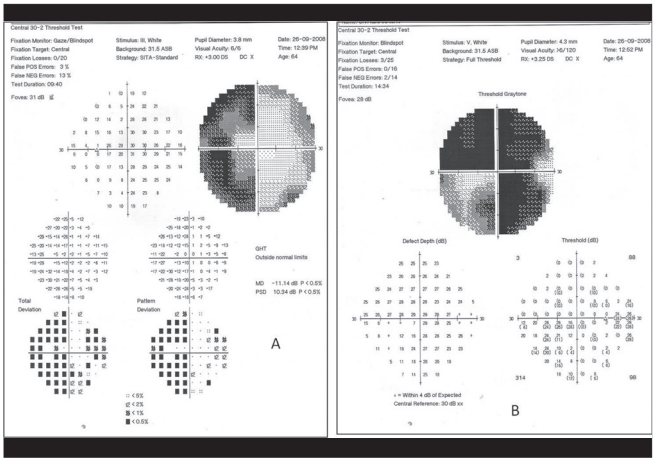

Figure 13: Case 5 – Visual field in the left (A) and right (B) eye. Note gross intereye asymmetry in the visual field despite symmetrical optic disc cupping [Fig. 12]. The field defect in the left eye respects the vertical meridian

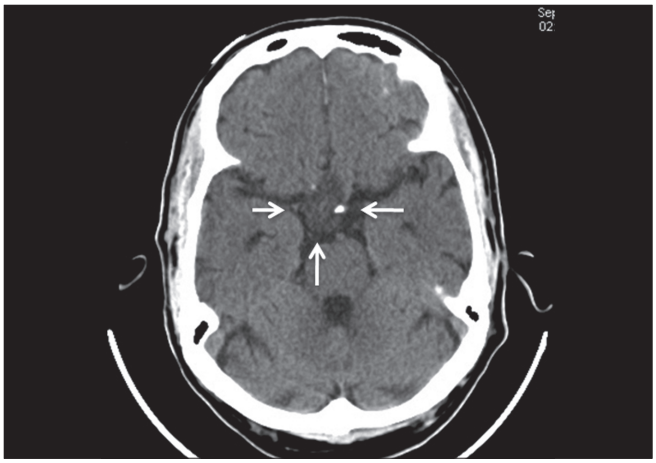

Figure 14: Case 5 – Computed tomography scan of brain (axial section) shows a well-defined, cystic suprasellar lesion with calcification (outlined by arrows) suggestive of craniopharyngioma

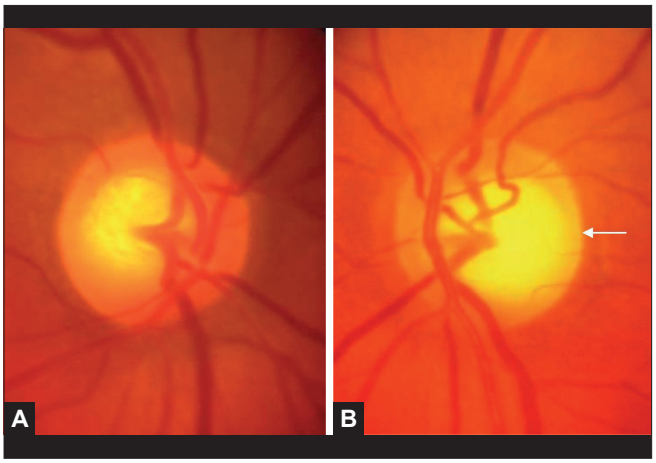

Figure 15: Case 6 – Right (A) and left (B) optic disc photographs. Note appreciable pallor only of the temporal rim in the left eye (arrow)

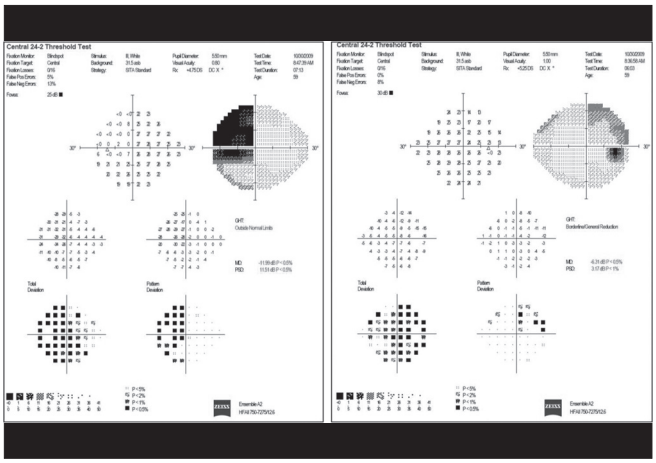

Figure 16: Case 6 – Asymmetric bi-superotemporal quadrantanopia. Note that the visual field respects the vertical meridian in both eyes

fifth case), especially in early compression. At presentation, unequivocal pallor of one or both optic discs was noted in only 28 of 50 (56%) patients with chromophobe pituitary adenoma causing visual field defects.[12] Pallor of the optic disc can also be masked by lenticular changes. Trobe[13] tested whether glaucomatous and nonglaucomatous optic disc cupping can be distinguished ophthalmoscopically. Two glaucoma specialists and one neuro-ophthalmologist independently analyzed optic disc stereo photographs. A total of 13 out of 29 (44%) eyes with nonglaucomatous optic neuropathy were classified as glaucomatous by at least one observer, demonstrating that even experts can misdiagnose glaucomatous cupping on isolated stereo photographs.

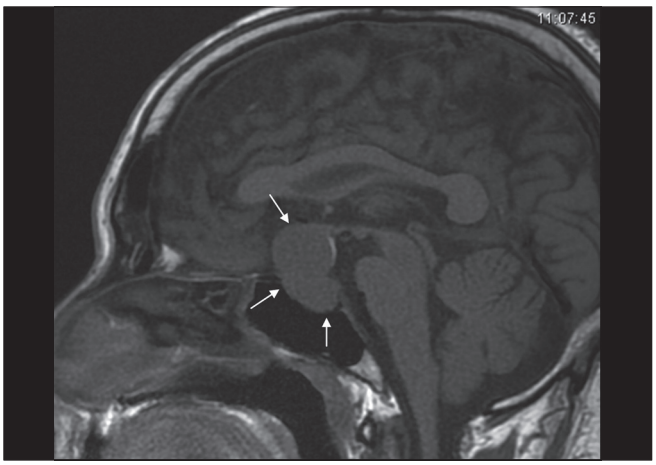

Figure 17: Case 6 – Magnetic resonance imaging of brain (sagittal section) revealing a pituitary adenoma

Visual field examination is another important factor to distinguish glaucomatous from nonglaucomatous optic neuropathy. However, since the arcuate distribution of the optic nerve fiber bundles remains intact as distal as the anterior chiasm, compression of the intracranial optic nerve or the anterior chiasm can produce arcuate visual field defects resembling glaucoma with sparing of central vision. Ahmed[14] prospectively performed neuroimaging in NTG patients who presented with classic glaucoma features without overt neurologic signs. Compression of the anterior visual pathway was found in 4 of 62 (6.5%) patients, all of whom had visual field defects typical of glaucoma.[14]

Routine neuroimaging for patients with presumed NTG is considered unnecessary due to a low yield for detecting intracranial pathology.[10] The South East Asia Glaucoma Interest Group (SEAGIG) recommends appropriate neuroradiological investigation only in a small proportion of patients with NTG, especially those who are younger and/or have unilateral disease, optic disc pallor out of proportion with cupping, atypical visual field defects, and color deficiency.[15] These factors, even though highly specific, have low sensitivity.[10] Greenfield compared eyes of 23 NTG patients with eyes with optic disc cupping associated with intracranial masses.[10] Age younger than 50 years, optic nerve pallor in excess of cupping, and vertically aligned visual field defects individually were only 46.4%, 45.5%, and 47.7%, respectively, sensitive for nonglaucomatous cupping.[10] One needs a highly sensitive examination or test to rule out nonglaucomatous

Table 3: Distinguishing glaucomatous from nonglaucomatous optic neuropathy

Factors	Glaucomatous optic neuropathy	Nonglaucomatous optic neuropathy
Age of patient	NTG more common in elderly; glaucoma in young patients is usually developmental or secondary	Optic disc cupping with normal IOP at young/ middle age (as in the second case)
Presenting history	Most patients are asymptomatic except in end-stage disease	Sudden, rapidly progressive vision loss, diplopia, headache
Family history	May be present	Absent
Visual acuity	Central vision preserved until end-stage disease	Vision loss relatively early in disease
Correlation between visual acuity and color vision	Generally both maintained until the end stage wherein color deficit is possible with preserved central vision	Impairment in color vision parallels reduction in visual acuity
Correlation between visual acuity and pupil	Often symmetric disease, especially POAG. Worst eye in asymmetric disease can have RAPD with good central vision	Reduced vision in one eye and ipsilateral RAPD is not uncommon
Correlation between visual acuity and optic disc cupping	Central vision often better despite advanced optic disc cupping	Visual acuity generally poor compared to the amount of optic disc cupping
Nature of neuroretinal rim	Initially vertical extension of the cup, splinter shaped disc hemorrhage(s), residual rim pink unless in the advanced stage of glaucoma	Area of pallor of the rim usually larger than that of the cup (stereoscopic optic disc evaluation is recommended)
Nature of visual field defects	Typically, nasal step or arcuate visual field defect	Typically central, cecocentral, altitudinal, and bitemporal or hemianopic defects that respect the vertical meridian
Correlation between optic disc cupping and visual field loss	Generally good correlation	Often poor correlation
Laterality of disease	All primary glaucomas are typically bilateral and generally symmetrical	Often unilateral or highly asymmetric optic neuropathy

NTG: normal tension glaucoma, IOP: intraocular pressure, POAG: primary open angle glaucoma, RAPD: relative afferent pupillary defect.

cupping in patients with presumed NTG if a routine neuroradiological investigation is to be avoided.[16] In day-to-day clinical practice, we suggest combining the results of one or more factors listed in Table 3 to distinguish glaucomatous from nonglaucomatous cupping. If a patient lacks one characteristic of nonglaucomatous visual loss, there is a significant likelihood that another characteristic is present. For example, even though there was no neuroretinal rim pallor in either optic disc in the fifth patient, the nature of the visual field defect was a tipoff for the nonglaucomatous etiology. Performing a careful evaluation of the total clinical picture initially and maintaining a high index of suspicion during follow-up, while investigating appropriately if visual acuity, optic disc, or visual fields do not follow the expected pattern, we can minimize the chance of a potential diagnostic error.

In conclusion, it is important to remember that space occupying lesion in the parasellar and suprasellar region may be associated with contour abnormalities of the optic disc ophthalmoscopically indistinguishable from glaucomatous optic neuropathy. An accurate and early diagnosis can make a real difference to the lives of such patients by preventing visual impairment and significant morbidity. Similar to the article by Thomas,[17] this report points toward nonadherence to the routine comprehensive eye examination. This practice should change.

References

1. South East Asia Glaucoma Interest Group. Asia Pacific Glaucoma Guidelines. 2008:12. Available at:http://www.seagig.org/toc/APGG2_fullversionNMview.pdf.2009.
2. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol 2002;86:238–42.
3. Sharma M, Volpe NJ, Dreyer EB. Methanol-induced optic nerve cupping. Arch Ophthalmol 1999;117:286.
4. Hayreh SS, Jonas JB. Optic disc morphology after arteritic anterior ischemic optic neuropathy. Ophthalmology 2001;108:1586-94.
5. Drummond SR, Weir C. Chiasmal compression misdiagnosed as normal-tension glaucoma: Can we avoid the pitfalls? Int Ophthalmol; 2009.
6. Blumenthal EZ, Girkin CA, Dotan S. Glaucomatous-Like Cupping associated with Slow-Growing Supra-Sellar Intracranial Lesions. Neuro-Ophthalmology 2006;30:111-5.
7. Kupersmith MJ, Krohn D. Cupping of the optic disc with compressive lesions of the anterior visual pathway. Ann Ophthalmol 1984;16:948-53.
8. Pruett RC, Wepsic JG. Delayed diagnosis of chiasmal compression. Am J Ophthalmol 1973;76:229-36.
9. American Optometric Association. Optometric Clinical Practice Guideline, Care of the adult patient with cataract 2004:6. Available at: http://www.aoa.org/ documents/CPG-8.pdf.2010.
10. Greenfield DS, Siatkowski RM, Glaser JS, Schatz NJ, Parrish RK II. Cupped disc. Who needs neuroimaging? Ophthalmology 1998;105:1866-74.
11. Bianchi-Marzoli S, Rizzo JF, Brancato R, Lessell S. Quantitative analysis of optic disc cupping in compressive optic neuropathy. Ophthalmology 1995;102:436-40.
12. Wilson P, Falconer MA. Patterns of visual failure with pituitary tumors. Clinical and radiological correlations. Br J Ophthalmol 1968;52:94–110.
13. Trobe JD, Glaser JS, Cassady J, Herschler J, Anderson DR. Non glaucomatous excavation of the optic disc. Arch Ophthalmol 1980;98:1046-50.
14. Ahmed II, Feldman F, Kucharczyk W, Trope GE. Neuroradiologic screening in normal-pressure glaucoma: Study results and literature review. J Glaucoma 2002;11:279-86.
15. South East Asia Glaucoma Interest Group. Asia Pacific Glaucoma Guidelines. 2008:64. Available at:http://www.seagig.org/toc/APGG2_fullversionNMview.pdf.2009.
16. Parikh R, Mathai A, Parikh S, Chandra Sekhar G, Thomas R. Understanding and using sensitivity, specificity and predictive values. Indian J Ophthalmol 2008;56:45-50.
17. Thomas R, Dogra M. An evaluation of medical college departments of ophthalmology in India and change following provision of modern instrumentation and training. Indian J Ophthalmol 2008;56:9-16.