Non-Diabetic Diffuse Macular Edema associated with Extrafoveal Vitreous Traction

Samia Fatum MD[1], Aaron Trevino MD[1] and Avinoam Ophir MD[1,2]

[1]Division of Ophthalmology, Hillel Yaffe Medical Center, Hadera, Israel
[2]Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

ABSTRACT: **Background:** The causative role of diffuse macular edema in various etiologies is often undetermined.
Objectives: To describe an association between extrafoveal vitreous traction and non-diabetic diffuse macular edema secondary to various ocular entities.
Methods: In a retrospective study of eyes with non-diabetic diffuse macular edema, charts and optical coherence tomography scans demonstrating extrafoveal vitreous traction were analyzed. Excluded were diabetic patients and eyes that had vitreofoveal traction. A control group (n=12) allowed for mapping of normal macular thickness.
Results: Five eyes with macular edema were associated with extrafoveal traction, each secondary to and representing a different etiology. The causes were penetrating injury, cataract extraction, branch retinal vein occlusion, central retinal vein occlusion, and idiopathic. Vitreous traction was detected either at the papillomacular bundle (n=3), superonasally to the fovea (n=1), and at the optic nerve head (n=1). The associated retinal edema (all eyes) and serous retinal detachment (four eyes) at the traction sites were in continuum with the foveal edema in each eye, manifesting as diffuse macular edema. Of the two modalities – the OCT-Line group program and the OCT-Automatic central program – only the former enabled detection of extrafoveal traction in each.
Conclusions: Diffuse macular edema secondary to various ocular diseases may be associated with extrafoveal vitreous traction. The OCT-Automatic central program may omit some of these extrafoveal traction sites. Further studies are required to validate these findings and to assess whether early vitrectomy may improve visual prognosis in these eyes.

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KEY WORDS: diffuse macular edema, extrafoveal traction, vitreopapillary traction, pseudophakic macular edema, retinal vein occlusion, optical coherence tomography

Macular edema may occur in a variety of pathological conditions including ocular vascular diseases such as diabetic retinopathy, branch and central retinal vein occlusion, as well as circumstances related to pseudophakia, penetrating ocular injury and detectable or subclinical uveitis [1-4]. Breakdown of the inner blood-retina barrier and/or ischemic insult in these conditions may result in either cystic or diffuse type macular edema, with or without associated serous macular detachment [5-7]. Whereas cystoid macular edema is perceived by optical coherence tomography as intraretinal round hyporeflective lacunae with well-defined boundaries, diffuse macular edema is characterized by ill-defined widespread hyporeflective increased retinal thickness that often attains an appearance of sponge-like cavities [8,9].

Another mechanism that might be associated with macular edema is vitreofoveal traction [9,10]. The latter can usually be detected by the Automatic central program of the OCT. Moreover, OCT-related diagnosis of vitreopapillary traction associated with adjacent retinal edema, with or without serous retinal detachment, has been reported as another cause of diffuse macular edema in diabetic eyes [11]. The retinal edema and subretinal fluid adjacent to the optic nerve head were in continuum in each eye with the fovea, presenting clinically as diffuse macular edema. Furthermore, vitreopapillary traction has been associated with serous macular detachment following central retinal vein occlusion [12].

However, since the cause of diffuse macular edema is often obscure, a therapeutic approach is usually insufficient. Grid argon laser photocoagulation was found partially beneficial in eyes with diabetic diffuse macular edema [13] and in one major study following BRVO associated with visual acuity of 6/12 to 6/60 [14]. Due to the fact that intraretinal and intravitreal growth factors have been documented to be associated with long-standing macular edema [15], treatment with anti-inflammatory (e.g., steroids) and/or antivascular endothelial growth factor agents is commonly applied for diffuse macular edema secondary to most of the aforementioned etiologies [16-19]. However, their benefit is by and large temporary and may be associated with ocular and grave systemic complications. Regarding surgery, the beneficial effect of pars plana vitrectomy for macular edema in diabetic eyes as well as those following cataract surgery is still controversial [10,20-22].

OCT = optical coherence tomography

BRVO = branch retinal vein occlusion

This study presents (for the first time, to the best of our knowledge) five non-diabetic patients (five eyes) in whom diffuse macular edema was associated with extrafoveal vitreous traction.

PATIENTS AND METHODS

This retrospective study reviewed the charts and OCT scans (OCT 2000, Humphrey Zeiss Inc., San Leandro, CA, USA) of non-diabetic patients who had macular edema associated with extrafoveal vitreous traction. Evidence of traction was confirmed by the presence of vitreous adherence to the retina or the optic nerve head, associated with tissue elevation and deformity at the traction site. Exclusion criteria were diabetic patients, eyes that had vitreofoveal traction, and eyes with vitreoretinal adherence without signs of retinal traction and for which the quality of scans was not high enough for a proper diagnosis and measurements. As controls, 12 normal eyes (12 age-matched patients) underwent OCT examination of the macula. Based on the latter, the fovea was considered edematous when its center exceeded 200 μm, similar to that previously reported [23]. This research adhered to the tenets of the Declaration of Helsinki, and approval from the Institutional Ethics Committee was obtained.

After ophthalmic examination, each OCT evaluation of the macula was routinely initiated by using the Automatic 6-radial lines program, directed to the fixation point and focused on the fovea. (In this OCT-2000, six radial lines centered on the fovea are obtained individually, oriented 30^0 from one another, whereas the OCT-3 fast macular map protocol provides six scans rapidly obtained in a radial spoke pattern). We then used the Line group program, which can be controlled manually by the examiner. Scans are routinely taken at various sites, angles and lengths (shorter scan increases resolution) to search for a vitreous traction point away from the fovea. When an extrafoveal vitreous traction was detected, that site was examined to verify whether the associated retinal edema or subretinal fluid was in continuum with the fovea. The search for further traction was usually discontinued upon detection of a vitreous traction site.

RESULTS

Patients' characteristics and OCT findings are summarized in Table 1. Each of the five eyes (of five patients aged 45–85 years) with macular edema that was unresponsive to the conservative treatment was confirmed by OCT to have extrafoveal vitreous traction. Vitreoretinal traction was apparent at the papillomacular bundle site in three eyes, in two of which a second traction site was detected, either superotemporally (patient 2) or inferonasally to the fovea (patient 4) [Figure 1]. Vitreous traction was situated in one eye (patient 3) superonasally to the fovea and in the fifth (patient 5) at the optic nerve head, manifesting as vitreopapillary traction. The cause of the vitreous traction was identified as penetrating injury, cataract extraction, branch retinal vein occlusion, central retinal vein occlusion, and idiopathic.

Detection of vitreous traction was not made by the Automatic 6-radial lines program in two eyes (patients 4 and 5), but was possible only by using the Line group program [Figures 1 and 2, Table 1]. In a third eye (patient 3), a vitreous strand was detected close to an extrafoveal retinal site while using the Automatic 6-radial lines program, but proof of adherence was indecisive. The Line group program, however, confirmed vitreoretinal traction at that site.

Localized serous retinal detachment was apparent at or adjacent to the traction sites in four eyes and retinal edema in all eyes [Table 1, Figures 1 and 2]. The localized subretinal fluid (patients 2–5) and the retinal edema underlying the traction site attained direct communication with the foveal edema in each eye, thus presenting as diffuse macular edema with or without serous macular detachment. In comparison with the 6 mm diameter macular map of normal eyes, the macular maps

Table 1. Characteristics of patients with diffuse macular edema and their optical coherence tomography findings

Patient no. Gender/Age	BCVA	Etiology	Foveal thickness (μm)	Site of extrafoveal traction	Serous macular detachment	Detection of traction with the Automatic 6-radial lines
1 M/51	6/18	Penetrating injury	358	Papillomacular bundle	No	Yes
2 M/66	6/24	Pseudophakia	370	Papillomacular bundle & superotemporal to fovea	Yes	Yes
3 F/78	6/24	Idiopathic	505	Superonasal to fovea	Yes	Suspected
4 M/45	6/36	Central retinal vein occlusion	582	Papillomacular bundle & inferonasal to fovea	Yes	No
5 F/85	FC 3 m	Branch retinal vein occlusion	717	Optic nerve head	Yes	No

BCVA = best-corrected visual acuity, FC = finger counts, m = meters.

Figure 1. Diffuse macular edema in the left eye of a 45 year old man with central retinal vein occlusion (Patient 4). **[A]** The Automatic 6-radial lines program demonstrates diffuse macular edema (arrow) and a localized serous retinal detachment (arrow head). Vitreoretinal traction is not detected, though a small epiretinal membrane is identified (thick arrow). **[B]** The Line group program discloses vitreous traction strand located inferonasally to the fovea. A serous retinal detachment (arrow head) and diffuse edema (arrow) are adjacent to the traction site.

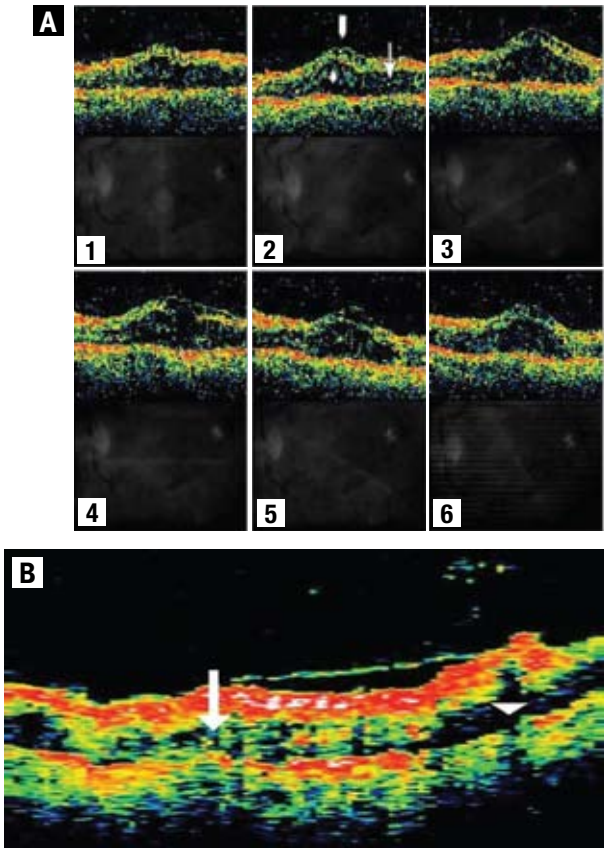
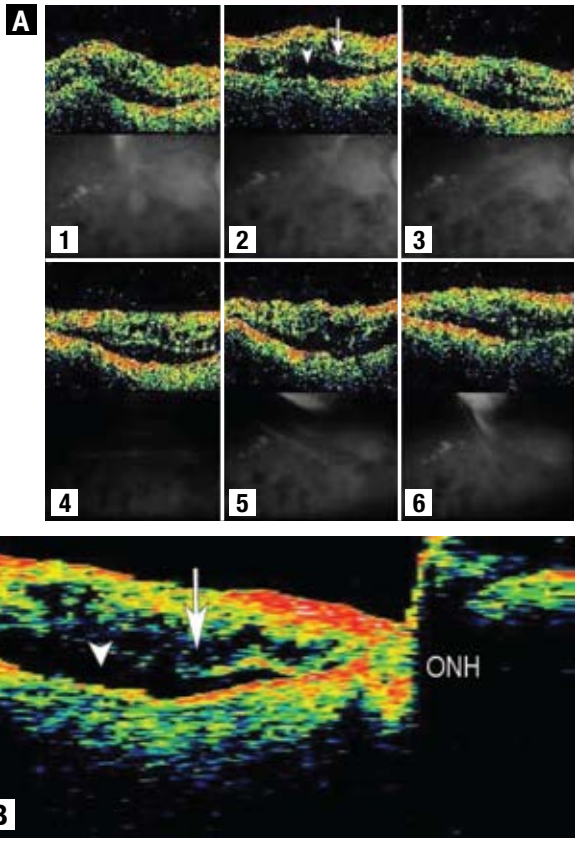


Figure 2. Diffuse macular edema in the right eye of an 85 year old woman with branch retinal vein occlusion (Patient 5). **[A]** The Automatic 6-radial lines program reveals diffuse macular edema (arrow), and a localized serous retinal detachment (arrow head). Vitreoretinal traction is not detected. **[B]** The Line group program shows vitreous traction at the optic nerve head. A diffuse macular edema (arrow) and serous retinal detachment (arrow head) are adjacent to the traction site.



of the five studied eyes presented thickened retina in most of the zones surrounding the fovea [Figure 3].

DISCUSSION

The study presents five eyes (of five patients) with diffuse macular edema secondary to five different etiologies. Extrafoveal vitreoretinal or vitreopapillary traction was associated with an underlying or adjacent retinal edema in all traction sites and serous retinal detachment in four eyes. The edema and subretinal fluid were in continuum with the foveal edema, manifesting in each as diffuse macular edema with or without shallow macular serous detachment.

The origin of diffuse macular edema in eyes without vitreomacular traction is often unidentified. Therefore, for eyes with diffuse macular edema secondary to diabetes or following BRVO without vitreofoveal traction, treatment by argon laser grid photocoagulation or by intravitreal administration of corticosteroid or anti-VEGF agents is only partially beneficial for the former, i.e., laser treatment [13,14], and transient when medications are used [16-18]. Reports on the outcome of PPV in eyes with diffuse macular edema are diverse [10,24], and the causes of success or failure are often obscure. A few authors attribute the surgical benefit, in part, to the removal of growth factors associated with macular edema from the vitreous site. In contrast, La Heij et al. [24] observed that surgical success for diabetic diffuse macular edema was significantly better when not preceded by laser treatment(s). Those authors and others [10] suggested that

VEGF = vascular endothelial growth factor
PPV = pars plana vitrectomy

surgical delay, in addition to the harmful, sometimes repeated laser treatment for diffuse macular edema, may partly explain the functional surgical failure in the relevant studies.

Similarly, several studies on PPV for treating recalcitrant pseudophakic CME have been reported [18-20]. Harbour and colleagues [20] described 24 consecutive patients who underwent PPV for chronic pseudophakic CME that failed to respond medically. The surgery resulted in improved visual acuity in all eyes from a mean visual acuity of 20/190 preoperatively to 20/52 postoperatively, with a mean improvement of 4.7 Snellen lines [18]. Pendergast and co-workers [21] reported the results of PPV for intractable chronic pseudophakic CME in 23 consecutive eyes with no apparent vitreoretinal disturbance. Surgery resulted in resolution of the CME in all cases, though with improved visual acuity in only some of the eyes [21]. This latter, relatively minor functional benefit could be related to the fact that the macular edema was present for a mean of 20 months (range 3–110 months) prior to surgery. Peyman and team [22] reported on the beneficial effect of internal limiting membrane peeling in two eyes with recalcitrant pseudophakic CME. Nevertheless, none of the aforementioned studies used OCT preoperatively, and vitreous traction was not detected. Although speculative, it might be possible that in some of these eyes, as well as in the aforementioned diabetic eyes, PPV released undetected vitreous traction membranes that resulted in the postoperative anatomic improvement.

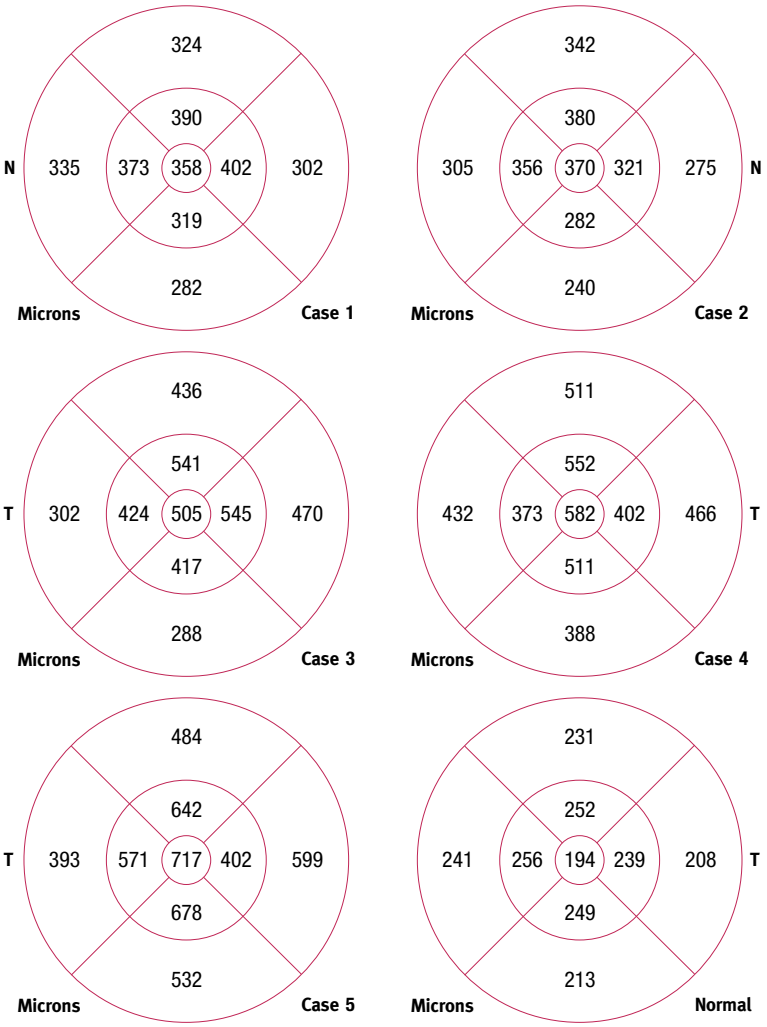
In our study one patient presented with extrafoveal vitreous traction and diffuse macular edema of idiopathic origin. Of the possible causes, the most common is an old, transient subclinical uveitis. In uveitis, clinical observations of macular traction and secondary macular edema, or tractional peripheral retinal tears have been reported [25]. However, none of the uveitic studies related the retinal edema that underlined an extrafoveal traction site to a diffuse macular edema.

The centrally fixated Automatic 6-radial lines program enabled unequivocal diagnosis of extrafoveal vitreous traction in two eyes (patients 1 and 2). However, in two other eyes (patients 4 and 5) the diagnosis of extrafoveal vitreous traction was possible only with the Line group program, with no suspicious signs on the Automatic scans. In the remaining eye (patient 3), a definite diagnosis of extrafoveal vitreous traction could only be made with the Line group program. This may be explained by the fact that the length of each scan in the Automatic 6-radial lines program is ~6 mm and is separated from each other by a 30^0 of arc. This could lead to missing vitreoretinal adherence even in the foveal vicinity, and thus to misdiagnosing the presence of traction membranes. The Line group program can overcome that obstacle. It may be possible that the new generation three-dimensional OCT will detect traction sites faster and with a higher rate of accuracy than the two-dimensional OCT. This is because the 3-D OCT screens the whole area, acquiring an entire A-scan simultaneously, and it promises an image acquisition at 50 to 100 times the current speed with equal or improved spatial resolution.

Limitations of the study are its retrospective design and the small series. Nonetheless, the study raises awareness that a diffuse macular edema in various ocular diseases may appear secondary to extrafoveal vitreous traction. Further studies are required to validate these findings and to assess whether early vitrectomy may improve visual prognosis in these eyes.

CME = cystoid macular edema

Figure 3. Macular maps, 6 mm diameter, of the five eyes studied: patients 1–5 are presented from superior-left to right. The mean of the normal controls (n=12) is presented at the inferior-right. Each of the studied eyes had a thickened retina in most of the zones surrounding the fovea compared to the normal eyes. N = nasal, T = temporal. Diameter of the innermost ring is 1 mm, of the median ring 3 mm, and the outer ring 6 mm.



Correspondence:
Dr. A. Ophir
Division of Ophthalmology, Hillel Yaffe Medical Center, Hadera 38100, Israel
email: ophthalmology@hy.health.gov.il

References

1. Gass JD. A fluorescein angiographic study of macular dysfunction secondary to retinal vascular disease. IV: Diabetic retinal angiopathy. *Arch Ophthalmol* 1968; 80: 583-91.
2. Stark WJ Jr, Maumenee AE, Fagadau W, et al. Cystoid macular edema in pseudophakia. *Surv Ophthalmol* 1984; 28: 442-51.
3. Wolter JR. Foveal pathology following anterior segment injury. *Ophthalmic Surg* 1981; 12: 661-5.
4. Rothova A. Inflammatory cystoid macular edema. *Curr Opin Ophthalmol* 2007; 18: 487-92.
5. Cunha-Vaz JG. The blood-retinal barriers. *Doc Ophthalmol* 1976; 41: 287-327.
6. Vinores SA, Amin A, Derevjanik NL, Green WR, Campochiaro PA. Immunohistochemical localization of blood-retinal barrier breakdown sites associated with post-surgical macular oedema. *Histochem J* 1994; 26: 655-65.
7. Tso MO. Pathology of cystoid macular edema. *Ophthalmology* 1982; 89: 902-15.
8. Yamamoto S, Yamamoto T, Hayashi M, Takeuchi S. Morphological and functional analyses of diabetic macular oedema by optical coherence tomography and multifocal electroretinograms. *Graefes Arch Clin Exp Ophthalmol* 2001; 239: 96-101.
9. Catier A. Tadayoni R, Paques M, et al. Characterization of macular edema from various etiologies by optical coherence tomography. *Am J Ophthalmol* 2005; 140: 200–6.
10. Dillinger P, Mester U. Vitrectomy with removal of the internal limiting membrane in chronic diabetic macular oedema. *Graefe's Arch Clin Exp Ophthalmol* 2004; 242: 630-7.
11. Karatas M, Ramirez JA, Ophir A. Diabetic vitreopapillary traction and macular oedema. *Eye* 2005; 19: 676-82.
12. Rumelt S, Karatas M, Pikkel J, Majlin M, Ophir A. Optic disc traction syndrome associated with central retinal vein occlusion. *Arch Ophthalmol* 2003; 121: 1093-7.
13. Lee CM, Olk RJ. Modified grid laser photocoagulation for diffuse diabetic macular edema: long term visual results. *Ophthalmology* 1991; 98: 1594-602.
14. Branch Vein Occlusion Study Group. Argon laser photocoagulation for macular edema in branch vein occlusion. *Am J Ophthalmol* 1984; 98: 27-82.
15. Vinores SA, Youssri AI, Luna JD, et al. Upregulation of vascular endothelial growth factor in ischemic and non-ischemic human and experimental retinal disease. *Histol Histopathol* 1997; 12: 99-109.
16. Barak A, Regenbogen M, Goldstein M, Loewenstein A. Intravitreal triamcinolone injection for diffuse diabetic macular edema with foveal cystoid changes. *IMAJ* 2006; 8: 83-7.
17. Desatnik H, Habot-Wilner Z, Alhalel A, Moroz I, Glovinsky J, Moisseiev J. The transient efficacy of a single intravitreal triamcinolone acetonide injection for diabetic macular edema. *IMAJ* 2006; 8: 383-7.
18. Jaissle GB, Leitritz M, Gelisken F, Ziemssen F, Bartz-Schmidt KU, Szurman P. One year results after intravitreal bevacizumab therapy for macular edema secondary to branch retinal vein occlusion. *Graefes Arch Clin Exp Ophthalmol* 2009; 247: 27-33.
19. Mason JO 3rd, Albert MA Jr, Vail R. Intravitreal bevacizumab (Avastin) for refractory pseudophakic cystoid macular edema. *Retina* 2006; 26: 356-7.
20. Harbour JW, Smiddy WE, Rubsamen PE, Murray TG, Davis JL, Flynn HW Jr. Pars plana vitrectomy for chronic pseudophakic cystoid macular edema. *Am J Ophthalmol* 1995; 120: 302-7.
21. Pendergast SD, Margherio RR, Williams GA, Cox MS Jr. Vitrectomy for chronic pseudophakic cystoid macular edema. *Am J Ophthalmol* 1999; 128: 317-23.
22. Peyman GA, Canakis C, Livir-Rallatos C, Conway MD. The effect of internal limiting membrane peeling on chronic recalcitrant pseudophakic cystoid macular edema: a report of two cases. *Am J Ophthalmol* 2002; 133: 571-2.
23. Massin P, Vicaut E, Haouchine B, Erginay A, Paques M, Gaudric A. Reproducibility of retinal mapping using optical coherence tomography. *Arch Ophthalmol* 2001; 119: 1135-42.
24. La Heij EC, Hendrikse F, Kessels AG, Derhaag PJ. Vitrectomy results in diabetic macular oedema without evident vitreomacular traction. *Graefes Arch Clin Exp Ophthalmol* 2001; 239: 264-70.
25. Malinowski SM, Pulido JS, Folk JC. Long-term visual outcome and complications associated with pars planitis. *Ophthalmology* 1993; 100: 818-24.