Title

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Journal

Journal of Neuro-Ophthalmology, 43(4)

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Publication Date

2023-12-01

DOI

10.1097/WNO.0000000000001874

Peer reviewed

Original Contribution

OPEN

Section Editors: Clare Fraser, MD
Susan Mollan, MD

Peripapillary Vitreous Traction Syndrome: Expanding the Spectrum of Anterior Optic Neuropathies

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Background: Peripapillary vitreous traction (PVT) occurring without any underlying eye disease has been contemplated as a distinct entity from nonarteritic ischemic optic neuropathy (NAION) for many years and is sometimes difficult to differentiate from classical NAION. We report 6 new cases to analyze the clinical features of PVT syndrome that would expand the clinical spectrum of anterior optic neuropathies.
Methods: Prospective case series.
Results: PVT syndrome seems to affect optic discs with a small area with a small cup-to-disc (C/D) ratio. The C/D ratio does not significantly increase in the chronic stage, as in NAION. Vitreous traction without detachment can either lead to mild retinal nerve fiber layer (RNFL) injury with attendant ganglion cell layer/inner plexiform layer (GCL/IPL) thinning in 29% or no injury at all in 71%. Eighty-six percent had good visual acuity (VA) and had no relative afferent pupillary defect (RAPD), whereas 14% had a transient RAPD; 71% had no color defect. Vitreous detachment after a period of severe and persistent traction can lead to more damage to the optic nerve head and RNFL that may look like NAION. Our hypothesized mechanically induced injury to the superficial optic nerve head may not lead to much visual impairment. In our study, no further therapeutic interventions were required.
Conclusions: Based on our analysis of previously published cases and our own prospective case series of 6 patients, the PVT syndrome falls within the spectrum of anterior optic neuropathies, often affecting small optic discs with a small C/D ratio. Vitreous traction can lead to a partial or complete anterior optic neuropathy. The PVT syndrome may be a "more" anterior optic neuropathy distinct from classical NAION.

Journal of Neuro-Ophthalmology 2023;43:514–519
doi: 10.1097/WNO.0000000000001874

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Supported by the Kuen Lau Research Foundation.

The authors report no conflicts of interest.

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The concept of disc edema in acute nonarteritic ischemic optic neuropathy (NAION) as a misclassification of peripapillary vitreous traction optic neuropathy was put forth by William F. Hoyt who first noted the relationship between acute NAION and the vitreous at the Aspen Retina meeting in 1978.[1] Cameron Parsa and Bill Hoyt[2] proposed that the vitreal stretching forces onto the optic disc, the retinal nerve fiber layer (RNFL), and onto the adjacent retinal vessels may occasionally lead to optic nerve damage. Peripapillary vitreous traction detachment optic neuropathy (PVT-DON) causes a mechanically induced injury to the peripapillary RNFL and superficial peripapillary vessels that may readily be misclassified as acute classical NAION.[2] It can present primarily as optic disc elevation, affecting the disc segmentally, mimicking acute NAION or involving the entire disc, mimicking papilledema. Furthermore, it can result from any disorder causing structural changes to the optic disc that would predispose to the weakening of the vitreoretinal interface around the optic disc. Underlying ocular diseases may also increase the risk of disruption of the vitreoretinal interface around the disc. Previous case reports in the literature failed to document initial eye examination details with longer periods of follow-up, which limited the accurate understanding of the natural history of PVT syndrome. In this study, we would like to provide more detailed clinical evidence regarding the onset and temporal progression of PVT syndrome.

METHODS

Seven of a total of 12 eyes were diagnosed with PVT syndrome. Subjects enrolled in this study were referred to the University of California, Los Angeles (UCLA) neuro-ophthalmology clinics for optic disc elevation, and PVT was identified on Heidelberg SD-OCT by the presence of vitreous band attachments to the peripapillary region at the initial visit. To be included, subjects had to have follow-up visits at 3- to 4-month intervals for ≥6 months. Elevation of the RNFL from sustained traction or thinning of the

RNFL presumably from traction- or detachment-related injury was noted. Neuro-ophthalmological symptoms, examination findings, retinal imaging studies, and visual outcomes were reported and analyzed. All cases were reviewed by an imaging reading center expert (SRS).

This study adhered to the Declaration of Helsinki and was approved by the institutional review board at the UCLA Geffen School of Medicine. Informed consent was obtained from all patients when applicable.

RESULTS

In our single-center prospective study, 7 of a total of 12 eyes from 6 patients were affected, in which 1 had bilateral presentation, and the remaining 5 had a unilateral onset. Visual symptoms included blurred vision, photopsias, floaters, "spider webs" in the periphery, a central field defect, or no symptoms at all. None of our patients had myopia >4.00 diopters. Vitreous traction without detachment can either lead to mild RNFL injury with attendant GCL/IPL thinning in 29% (2/7 affected eyes) or no injury at all in 71% (5/7 affected eyes) (Table 1). Eighty-six percent (6/7 affected eyes) had good VA and had no RAPD, whereas 14% (1/7 affected eyes) had a transient RAPD; 71% (5/7 affected eyes) had no color defect.

Humphrey visual field testing 30-2 revealed the following: 1) normal field, 2) superior or superior-nasal arcuate defect, 3) paracentral central defect, and 4) mild superior or mild generalized peripheral depression. The average disc area of all affected eyes at onset was 1.75 mm^2 ± 0.42. The median vertical C/D ratio of all affected eyes at onset was 0.07 ± 0.081. The median vertical C/D ratio at final follow-up was 0.21 ± 0.23, and the median change was +16.4% (Table 2).

At presentation, optic disc elevation from PVT affected the superior-temporal and temporal RNFL sectors (2/7 eyes), inferior-nasal sectors (1/7 eyes), and the inferior-temporal sectors (1/7 eyes). By contrast, RNFL thinning at presentation was present in the inferior and inferonasal RNFL sectors (2/7 eyes).

Initial elevation and subsequent thinning of all RNFL sectors from vitreous detachment injury occurred in Patient #5 who underwent pars plana vitrectomy (PPV). Despite the complete vitreous detachment, the RNFL thickness returned to normal baseline without evidence of permanent RNFL injury. In Patients #1, 2, and 3, chronic vitreous traction on the disc margin persisted from 6 to 12 months; yet, none had an RAPD. A transient RAPD was notable in Patient #6, which was indicative of reversible RNFL injury (Table 1). None had PVT-associated disc hemorrhages.

Regarding demographic and other information, the median age was 54.5 ± 19 years with a range of 23–71 years. The male-to-female ratio was 1:6. The initial diagnoses from referring physicians included acute NAION (3/7), papilledema (1/7), and optic disc edema (2/7). Comorbidities included hypertension (4/7), hyperlipidemia (1/7), and none (2/7). Follow-up until 24 months showed that they ultimately had good visual prognosis that did not require further treatment, except for Patient #5, who was given intravitreal corticosteroids and oral acetazolamide for her diffuse disc elevation and cystoid macular edema before PPV (Table 1).

A similar detailed quantitative analysis of the examination findings, OCT findings, and demographic information for the PVT syndrome in previous publications was not feasible because these data were not available in most of them.

DISCUSSION

In our single-center prospective study, we present new evidence for clinical features that further characterize and differentiate it from classical acute NAION. Isolated PVT syndrome represents part of the spectrum of "more anterior" optic neuropathies and should be recognized as a distinct type of optic neuropathy related to mechanical-induced inflammation and possibly decreased axoplasmic flow in the nerve fibers occurring at the vitreous peripapillary interface.

Without healthy age- and sex-matched controls for comparison, we used the vertical C/D ratio normative value from Caucasian eyes of 0.41 (SD ± 0.01) and the disc area of 1.74 mm^2–2.47 mm^2 from a study by Hoffman et al.[3] Our findings showed that 100% (7/7 affected eyes) at onset had a relatively small vertical C/D ratio that was typical of the "disc-at-risk." The initial average disc area was also relatively small at 1.75 ± 0.42 mm^2, compared with the normative range for Caucasian eyes of 1.74 mm^2–2.47 mm^2.[3] Although our Caucasian patients had a small disc area and a small C/D ratio, none of them presented with peripapillary disc hemorrhages, as observed by Katz and Hoyt in their Asian case series.[1] The relatively constant C/D ratio over the course of disc swelling in all our PVT syndrome patients is suggestive of some preservation of the optic nerve tissue architecture, which was observed in most of our patients (Table 2). A striking example of sparing of the C/D ratio after 6 months occurred in Patient #5 (Table 2) who underwent PPV complicated by the onset of vitreopapillary and vitreomacular swelling. After complete resolution of her right disc edema, her C/D ratio increased by 11%. Only Patient #3 had a C/D ratio that significantly increased over a 21-month period of follow-up. We hypothesize that the tractional force onto a smaller disc area of vitreous adhesion (force/mm^2) would be greater compared with that onto a disc of larger area. Unlike the atrophic enlargement of the C/D ratio by about 50% after 6 months in chronic NAION,[4] the C/D ratio in most of our PVT syndrome patients remained relatively stable from the acute to the chronic stage (This particular morphological feature was often observed by Bill Hoyt). Remarkably, the "disc-at-risk" phenomenon not only contributes to the compartment syndrome theory in NAION, but may also pose as a risk factor for the PVT syndrome, which would explain the frequent coexistence of vitreous traction with NAION observed by Thompson et al[5] and Molaie et al.[6] A larger sample size of patients with the PVT syndrome would be needed to confirm whether a smaller C/D

TABLE 1. Clinical features of our 6 cases of PVT syndrome

Patient Number	1	2	3	4	5	6
Age/sex	41/M	69/F	59/F	23/F	71/F	64/F
Laterality	Unilateral	Unilateral	Bilateral sequential	Bilateral at onset	Unilateral	Unilateral
Referring diagnosis	Optic disc edema OS	Optic disc edema OD	Acute NAION OD	Papilledema OU	Acute NAION OD	Acute NAION OS
Visual symptoms	Photopsias; floaters OS	Photopsias; floaters, mild blurred vision OD	Floaters; dim vision OD	Floaters OU	Floaters OD	Floaters OS
Comorbidities	Hypertension	Hypertension	Hypertension	None	Hypertension, hyperlipidemia; pars plana vitrectomy performed after "dropped nucleus" during cataract surgery OD	None
Best-corrected visual acuity	20/20 OU	20/25 OD	20/20 OD followed by 20/25-3 OU	20/20 OU	20/80 OD	20/30 OS
Relative afferent pupillary defect	None	None	RAPD OD	None	None	Transient RAPD OS
Humphrey visual field 30-2	Within normal limits OU	Mild generalized peripheral depression OD	OD: superior arcuate defect 6 mo later, OS: I/N arcuate defect	Within normal limits OU	Mild superior peripheral depression OD	Superior-nasal arcuate defect OS
Ishihara color plates	14/14 OU	14/14 OU	10/14 OD and 11/14 OS	14/14 OU	14/14 OU	14/14 OU
Disc anatomy	Small disc area with small cup/disc ratio OU	Tilted; small disc area with small cup/disc ratio OU	Small disc area with small cup/disc ratio OU	Small disc area with small cup/disc ratio OU	Small disc area with small cup/disc ratio OU	Small disc area with small cup/disc ratio OU
Neuroretinal rim elevation	Superior, inferior and temporal neuroretinal rim elevation OU	None	OD: 2 separate foci of neuroretinal rim elevations in the superior-temporal (S/T) and temporal-inferior (T/I) sectors OS: S/T neuroretinal rim elevation	None	360° neuroretinal rim elevation OD	None
Vitreous traction or detachment on optic disc seen on SD-OCT	Traction at nasal disc OS	Traction at nasal disc OD	OD: traction on S/T and T/I disc then complete detachment 1 mo later	Traction on temporal and I/N disc OU	Complete detachment OD	Traction at nasal disc OS

(Continued)

Patient Number	1	2	3	4	5	6
RNFL thickness on SD-OCT	Normal RNFL thickness OU	Inferior RNFL thinning	OD: S/T and T/I RNFL thickening followed by S/I thinning 6 mo later, OS: superior thinning followed by I/N thickening, and then S/I thinning consistent with classical NAION	Temporal RNFL thickening; I/N RNFL thinning	Diffuse circumpapillary RNFL thickening returning to within normal limits and resolved cystoid macular edema OD 6 mo later	I/N RNFL thickening OS followed by returning to within normal limits 1 mo later
Visual follow-up duration	Stable over 12 mo	Stable over 8 mo	Stable over 20 mo	Stable over 6 mo	Stable over 6 mo	Stable over 12 mo

F, female; I/N, inferior-nasal; M, male; OD, right eye; OS, left eye; OU, both eyes; RNFL, retinal nerve fiber layer; S/T, superior-temporal; SD-OCT, spectral-domain optical coherence tomography; T/I, temporal-inferior.

ratio at onset is a risk factor of PVT syndrome and whether this C/D ratio remains relatively unchanged in the chronic stage.

Although the PVT syndrome can cause the elevation of a small disc with a small C/D ratio and appear like classical acute NAION, none of our patients had the typical altitudinal defect of classical acute NAION. The visual field defects, if any, corresponded to RNFL damage. We showed that axonal damage after disc swelling in PVT-DON occurred most often as RNFL thinning in the superior sector (23.08%) and in the inferior sector (15.38%). Disc swelling from vitreous traction occurred most often as RNFL elevation in the temporal sector (30.77%) and in the inferior sector (23.08%) at the 7 o'clock region. Compared with acute classical NAION, the most severe RNFL thinning occurs at the 1 and 2 o'clock regions in PVT syndrome.[7] Unlike the more severe macular involvement in NAION, the GCL/IPL thinning in our PVT syndrome patients was less than 30%. Unlike the GCL/IPL thinning that occurs within 1–2 months before the resolution of RNFL disc swelling in acute NAION,[8] the GCL/IPL thinning in our PVT syndrome patients occurred only if the peripapillary traction-related RNFL disc elevation was causing sufficient neuroaxonal injury. It has been hypothesized that the interaction of the gravitational forces and the vitreomacular-peripapillary traction drive the vitreous detachment from the relatively less adherent superior/temporal region to the more adherent inferior/nasal peripapillary region. This vitreous traction/detachment was demonstrated in Patient #6. We inferred that the superior vitreous detachment occurred before we were able to capture the superior elevation, and that gravitational forces were greatest at the superior and inferior peripapillary regions to cause the most RNFL damage. This pattern of vitreous membrane separation because of normal aging often progresses from the superior-temporal to the inferior aspect of the disc, with the nasal-inferior disc edge the last to separate. In Patient #3, vitreopapillary traction occurred in 2 separate and discrete zones around the optic disc in the right eye and was documented as a superior-temporal elevation and an inferior-temporal elevation at the peripapillary region in the right eye (Fig. 1). The progression in vitreous traction detachment usually ends at the nasal peripapillary region where the vitreous strands are most adherent before

TABLE 2. Vertical cup-to-disc (C/D) ratios in 7/12 eyes affected with PVT syndrome measured at initial visit and at final follow-up visit

Patient #	Initial Vertical C/D	Final Vertical C/D	% Change
1 OS	0.13	0.17	31
2 OD	0.44	0.45	2.7
3 OD	0.06	0.35	483.33
4 OD	0.07	0.07	0.00
4 OS	0.07	0.07	0.00
5 OD	0.19	0.21	11
6 OS	0.27	0.33	22

OD, right eye; OS, left eye; OU, both eyes; PVT, peripapillary vitreous traction.

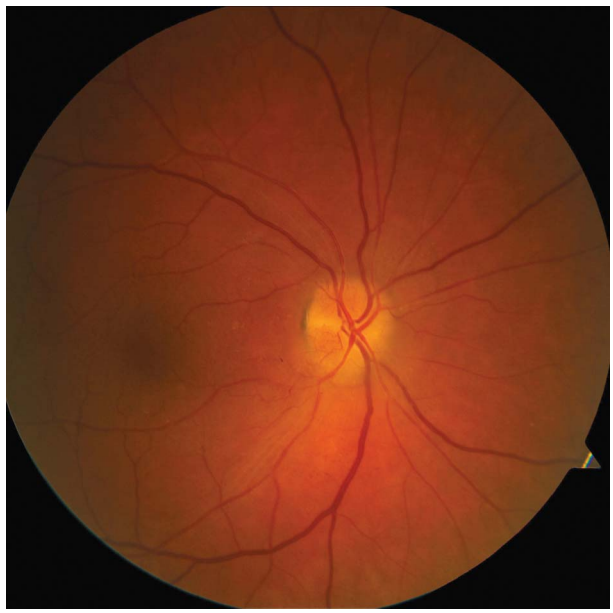

FIG. 1. Two distinct foci of vitreous traction are manifest as elevations in the superior-temporal and the inferior-temporal peripapillary regions in the right eye.

they detach to form a Weiss ring. A vitreous band pulling up axonal bundles at the nasal peripapillary region in the left eye in Patient #1 (Fig. 2) persisted for 12 months. Although it was not technically feasible to document the entire temporal sequence of vitreous traction/detachment stages from the superior temporal disc ending at the nasal disc, we showed a representative stage in each of our cases.

The spectrum of mechanically induced RNFL injury ranges from no neuroaxonal damage to mild isolated RNFL sectoral thinning to RNFL ± GCL/IPL thinning, to a more severe PVT resulting in a complete optic neuropathy, functionally defined as having decreased VA, an RAPD, and nerve fiber layer field defect. The PVT variant with milder neuroaxonal damage than classical NAION could be labeled as "very anterior optic neuropathy" (VAON) (Table 3). The PVT syndrome and acute classical NAION seem to be both due to mechanical injury in which the former is from tractional forces and the latter is a consequence of severe compression from the compartment syndrome affecting the prelaminar optic nerve head. The sharply demarcated altitudinal field defect may be a critical finding in NAION that differentiates it from other types of anterior optic neuropathies and might represent injury more proximally in the short posterior ciliary artery distribution. Ganglion cell loss might be a better metric for optic nerve injury in NAION because it can occur from 2 to 4 weeks after onset,[9] whereas in PVT-DON, there may not be a corresponding GCL/IPL defect. Larger studies are needed to confirm whether the "disc-at-risk" is, indeed, a major risk factor for the PVT syndrome.

The prospective recruitment of study participants is a major strength of this study. To observe the natural history of the PVT syndrome, follow-up duration ranged from 6 to 20 months. Our study was limited by the technical feasibility to document the entire temporal sequence of vitreous traction/detachment stages in each eye. We were only able to show representative stages of this process in each of our cases. Although we were able to visualize vitreous traction bands on the Heidelberg SD-OCT, more advanced swept-source OCT equipment have better capability to visualize the vitreous in greater detail and clarity. Another limitation was our small sample size. We think the lower incidence of the PVT syndrome in our study was due to our rigorous and stricter criteria for establishing the diagnosis based on eye findings and OCT-documented evidence of

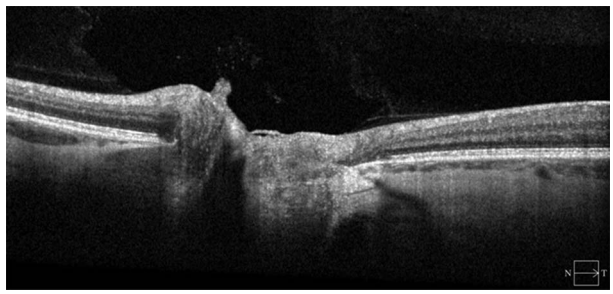

FIG. 2. A peripapillary vitreous band can be seen pulling some axon bundles anteriorly in the nasal optic nerve head.

TABLE 3. The PVT syndrome expands the spectrum of anterior optic neuropathies

	Vitreous Traction and/or Detachment Without Neuroaxonal Damage	Vitreous Traction and/or Detachment With Neuroaxonal Damage or "VAON"	NAION
Visual acuity	20/20	20/20 to 20/40	<20/50
RAPD	—	+/−	+
Visual field defects	—	Arcuate or paracentral defect	Altitudinal defect
Color defect	—	—	+
Optic disc appearance	Elevated	Elevated	Elevated
Initial C/D ratio	Small	Small	Small
SD-OCT RNFL and GCL/IPL thinning	—	RNFL thinning +/− GCL/IPL thinning	RNFL thinning + GCL/IPL thinning
SD-OCT peripapillary vitreous visualization	Traction +/− detachment to optic disc	Traction +/− detachment to optic disc	+/− adherence to optic disc

C/D, cup-to-disc; GCL/IPL, ganglion cell layer/inner plexiform layer; NAION, nonarteritic ischemic optic neuropathy; PVT, peripapillary vitreous traction; RAPD, relative afferent pupillary defect; RNFL, retinal nerve fiber layer; SD-OCT, spectral-domain optical coherence tomography; VAON, very anterior optic neuropathy.

traction and not just adherence or presumed detachment without previous visualization of traction. Our cases were also reviewed by an image reading center expert (SRS) to enhance consistency of our interpretations.

In conclusion, PVT syndrome is a "more" anterior optic neuropathy that is distinct from acute classical NAION and should be considered as part of the spectrum of anterior optic neuropathies. Because the PVT syndrome can occur secondary to disorders, such as posterior uveitis, affecting the vitreoretinal interface, definitive treatment would depend on the underlying disease. In our case series, the PVT syndrome was a complication of anomalous PVD related to normal aging and usually did not require further treatment. Pharmacologic vitreolysis with agents, such as ocriplasmin, is no longer performed by most clinicians because of concerns for potential photoreceptor toxicity. In cases of symptomatic vitreomacular traction with visual loss, vitrectomy to relieve the traction is commonly considered. Finally, the PVT syndrome should be excluded in the recruitment criteria for acute NAION treatment trials.

STATEMENT OF AUTHORSHIP

Conception and design: J. W. Chan, H. Liu; Acquisition of data: J. W. Chan, H. Liu, E. L. Ma, A. A. Sadun, S. R. Sadda; Analysis and interpretation of data: J. W. Chan, H. Liu, A. A. Sadun, S. R. Sadda. Drafting the manuscript: J. W. Chan, H. Liu; Revising the manuscript for intellectual content: J. W. Chan, A. A. Sadun, S. R. Sadda. Final approval of the completed manuscript: J. W. Chan, A. A. Sadun, S. R. Sadda.

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