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Research Article

Significance of Asymmetric Retinal Vasculature Tortuosity - Report of 10 Consecutive Cases

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Abstract

Retinal vascular appearance is expected to be symmetrical between the two eyes - whether torturous or not. When asymmetric retinal vascular tortuosity (aRVT) is observed, then a question arises: is this finding significant? The ophthalmic literature suggests that asymmetric retinopathy is associated with carotid artery occlusive disease - is the same true for aRVT? This article surveyed the results of carotid ultrasonography for ten consecutive cases of aRVT. In this series, there was no conclusive association between the presence of aRVT and carotid artery occlusive disease. It may be conjectured that aRVT is an anatomical and/or physiological variation manifested in the presence of underlying systemic vasculopathy. In patients not receiving primary medical care, its discovery suggests the need for referral for systemic workup. Otherwise, aRVT appears to be an incidental finding.

Keywords: Asymmetric; Retinal Vasculature; Tortuosity

Introduction

During retinal examinations, ophthalmic providers frequently observe tortuous retinal vasculature. Direct visualization of the retinal circulation *in vivo* is particularly intriguing in medicine because of reported associations between retinal and cerebrovascular disease [1].

Although healthy vessels can also be highly twisted [2], wide variations regarding interpretation of retinal vascular changes [3] have precluded definitive clinical recommendations regarding the significance of changes in the appearance of retinal vascular tortuosity (RVT). RVT with respect to age was variously linked [3], but more recently, again positively associated with aging [4].

RVT has long been associated with hypertensive arteriosclerosis [5]-with the very close association between these two entities recognized [6]-although the diagnostic value in and of itself has been questioned [7]. RVT has also been associated with diabetes mellitus for a long while [8].

In recent years, RVT has been variably linked to other cardiovascular diseases - albeit with sometimes conflicting evidence. RVT has been observed in chronic anemia [9], coronary artery disease [10] and obesity [4] (BMI); whereas ischemic heart disease and stroke (CVA) were not associated with this clinical finding [11]. Conversely, Ong [12] did link CVA with RVT. Hyperlipidemia (HDL) has been both correlated [13] and dissociated [14] with RVT.

A non-cardiovascular confounder in both systemic and ocular health is obstructive sleep apnea (OSA). The high prevalence of OSA in patients with known cardiovascular disease [15] suggests a "synergistic health risk", although the direct relationship is unknown [16]. Indeed, RVT has been reported in a small group of patients with OSA [17], although this clinical consequence remains indeterminate.

The delineation of RVT between arterioles and venules is limited, and much of the research cited above did not make this distinction. Broadly speaking, arteriolar changes have been related to hypertension/arteriosclerosis [3]; whereas tortuosity of the venules has been connected to vascular obstruction [7]. The extent to which both vascular beds are involved seems to be variable.

It is generally expected for RVT-involving arteries, veins or both-to be observable to roughly the same degree in the two eyes; however, occasionally there is a noteworthy difference in the vascular appearance when comparing one eye to the other. Asymmetric RVT (aRVT) is thought to be significant, meriting further investigation into the patient's systemic health.

After the first report of asymmetric retinopathy-albeit not aRVT-and carotid occlusive disease [18] in what is now known as ocular ischemic syndrome (OIS), the role of vascular hypoperfusion was recognised for other ocular conditions. It has been recommended that OIS in the presence of asymmetric diabetic retinopathy be evaluated for possible carotid insufficiency [19].

As the main blood supply to the eye is via ophthalmic artery, a tributary of the internal carotid artery, it is reasonable to expect that the effects of carotid insufficiency might be visible in the retinal vasculature, presumably due to the relative downstream ischemia in the distribution of the ophthalmic artery. Over time, this might result in changes in the vasculature appearance of the eye that become visible to the ophthalmic observer.

Carotid artery occlusive disease was found to be present in unequal diabetic retinopathy [20] and dissimilar hypertensive retinopathy [21]. In both conditions-and perhaps paradoxically-it was discovered that the eye with the normal appearance was ipsilateral to the carotid stenosis. Gay and Rosenbaum [20] proposed that a reduction in intraretinal arterial diastolic pressure retarded the development of retinal hemorrhages associated with diabetic retinopathy. Perhaps in this milieu of non-perfusion, there was some kind of "protective" effect that arose in the presence of carotid artery occlusive disease. However, there was no protective effect of hemodynamically-significant carotid stenosis against the development of proliferative diabetic retinopathy (PDR) in cases of asymmetric PDR [22].

By analogy, other forms of asymmetric retinopathy-perhaps even including aRVT-could also be an indicator of carotid artery occlusive disease. The latter has been suggested by some lecturers, but has not been explored and reported in the ophthalmic literature to date. It might be conjectured that carotid stenosis, leading to reduced blood supply and relative hypoxia might occasionally account for aRVT. Based on the findings in both diabetic and hypertensive retinopathies mentioned above, it might be further proposed that the eye with the normal vascular appearance would be ipsilateral to the carotid stenosis.

This paper discusses the findings of 10 such consecutive cases involving, presumably-acquired aRVT that were not observed within the context of more-marked asymmetry associated with arteriovenous malformations-as in congenital anomalies, retinal racemose hemangioma, ophthalmic manifestations of Wyburn-Mason Syndrome, or Waldenstrom's Macroglobulinemia. The intent of this report is to provide preliminary findings regarding whether there is a direct correlation between aRVT and carotid artery insufficiency.

Methods

Ten consecutive cases of asymmetric retinal vasculature tortuosity were identified between October 2017 and July 2018. The patients were identified by the author through either direct ophthalmic examination or retinal screening photos obtained as part of a standardised retinal screening program. These patients were all Caucasian and between 59 and 79 years of age. Only one was female. The patients' medical records were reviewed to determine pertinent cardiac and vascular surgery histories - including any obvious potential confounders-ophthalmic or vascular-that might affect retinal hypoxia, and, therefore, alter the retinal vascular appearance. These factors specifically included retinal laser or cryopexy and prior history of carotid endarterectomy.

In no case was a patient symptomatic of anything that could be construed as being retinal in origin or in any way related to the vascular appearance. No specific algorithm was followed other than the examiner's subjective interpretation of asymmetric vascular appearance between the two eyes. The eye affected by the tortuosity was recorded, as well as whether the tortuosity included arteries only, veins only, or both vascular beds. A representative case is demonstrated in figure 1.

Carotid ultrasound duplex studies were obtained or reviewed (if results were available for tests performed within the six months prior to the ophthalmic exam/imaging), and the presence of internal carotid stenosis was noted, if present. A chart summarizing all findings is provided in table 1.

Discussion

Autoregulation is defined as the capacity to maintain a generally constant level of blood flow in the presence of changes in ocular perfusion pressure and varied metabolic demand [23] and has been demonstrated in the retinal vasculature [24]. During this process, arteriolar vasodilation results in expansion of cells in three dimensions. The addition of length in the limited anatomical space between the posterior hyaloid membrane of the vitreous and the internal limiting membrane of the retina restricts one of those dimensions. Hypertrophy of the arteriolar walls results in confined extension of the retinal length, which is observed as "tortuosity".

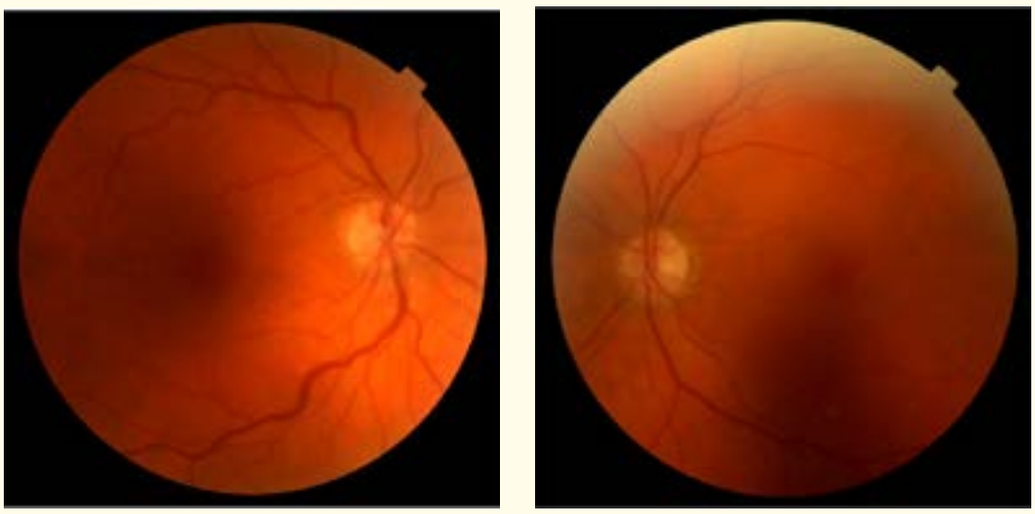

Figure 1: Case 7. Representative photos of asymmetric retinal vascular tortuosity. In this case, arteries and veins of the right eye are involved.

Case Number	1	2	3	4	5	6	7	8	9	10
Age	73	73	79	67	62	72	71	59	72	76
Gender	M	M	M	M	F	M	M	M	M	M
HTN	Y	Y	Y	Y	N	Y	Y	N	Y	Y
DM	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
HLD	Y	Y	Y	N	Y	Y	Y	Y	N	Y
BMI > 30	Y	Y	N	Y	Y	Y	N	Y	N	Y
Other Cardiology*	Y	Y	Y	Y	N	Y	Y	N	N	Y
OSA?	N	N	N	Y	Y	N	Y	N	N	N
Arteries, Veins, Both	Both	Both	Veins	Veins	Both	Veins	Both	Both	Veins	Both
Eye with "NL" Vasculature	R	R	L	L	R	L	L	R	L	L
Carotid Results	R < L	R > L	R = L	R = L	R = L	R = L	R > L	R = L	R = L	R = L
IPSILATERAL Correlation	N	Y	N	N	N	N	N	N	N	N
Potential Confounder**	N	N	Y	N	N	Y	N	N	N	N
***Cardiology Findings**						****Potential Confounders**				
Case 1	Atrial fibrillation									
Case 2	CAD, atrial Fibrillation, aortic valve disorder									
Case 3	CAD + s/p CABG					s/p cryo/retinopexy OS x 2008				
Case 4	PVD									
Case 6	CAD, s/p CABG					s/p L carotid endarterectomy x 2017 at non-VA site				
Case 7	s/p CABG					s/p R carotid endarterectomy x 2010				
Case 10	IHD, s/p 4 stents									

Table 1: Summary of 10 Cases. Outliers are highlighted.

Key: HTN: Hypertension; DM: Type 2 Diabetes Mellitus; HLD: Hyperlipidemia; BMI: Body Mass Index (>30 = "obese"); OSA: Obstructive Sleep Apnea; NL: Normal; CAD: Coronary Artery Disease; PVD: Peripheral Vascular Disease; IHD: Ischemic Heart Disease.

The local process whereby retinal arterioles become tortuous in appearance appears to be mechanical in nature, although related to multiple factors, including: blood pressure, blood flow, axial tension (vector force imposed on a body that tends to cause it to become longer), and anatomical structural changes [25]. Retinal venous tortuosity has been described in terms of increased vascular transmural pressure, i.e. the difference in pressure between the two sides of the vascular wall [26]. Chronic vascular in response to systemic vasculopathies results in permanent changes in the retinal architecture.

Although all eye care providers have an idea of what constitutes retinal vascular tortuosity, there is no standardised definition or consensus regarding normal or abnormal vascular appearance [27]. Many objective RVT measures have been developed [28], but without widespread application to date. Therefore, the cases identified for this report were subjectively determined by a single observer. Intriguingly, aRVT has not been reported to date.

Interestingly, several conclusions can be drawn based on the results of this limited case series.

First, these 10 consecutive cases of unambiguous asymmetric retinal vascular tortuosity were identified over a period of nine months. During the same time frame, the author had a total of 3926 patient encounters. At an incidence < 1%, the preliminary inference that may be drawn is that such a retinal appearance is rare - even in an older patient population.

Second, this particular case series included only Caucasian patients, just one female patient, and only one patient who was slightly under the age of 60. So, these clinical assumptions are necessarily limited by multiple demographic indices. The extent to which the results of this case series can be generalised to other groups is uncertain.

Third, regarding the carotid studies themselves: the results of these 10 cases suggest that the presence of aRVT does not correlate well with ipsilateral carotid insufficiency. Only one patient in this series (Case 2) was found to have ipsilateral carotid insufficiency for eye with normal retinal vascular appearance, whereas two cases (1 and 7) has contralateral carotid insufficiency (i.e. ipsilateral to eye with RVT). It should be further noted that for 7 of the 10 cases carotid insufficiency was symmetric, and was < 50% in each of those cases, with 3 of those 7 cases noted to have negligible carotid findings altogether. It seems that individual structural or biological variations may account for such results.

Fourth, even the confounders are confounding. The retinal vascular appearance in both Cases 3 and 6 could have been affected by retinal cryopexy and endarterectomy (respectively), thereby reducing the oxygen demand of the retina and leading to a "normal" vascular appearance. By the same analogy, though, Case 7-also with a history of R endarterectomy-should have had a normal vascular appearance in the R eye; however, the reverse was observed.

Fifth, at a cost of approximately €250 (£220, $280) per carotid ultrasound test (https://www.mdsave.com/procedures/carotid-ultrasound-doppler/d783feca), it is not financially prudent to order carotid studies based solely on the presence of aRVT).

Sixth, the presence of aRVT itself cannot be wholly explained by extraocular factors. It may be conjectured that the presence of aRVT is the result of an intraocular anatomical or physiological variation, which may possibly be related to an underlying systemic vasculopathy; however, this supposition cannot be confirmed with current clinical technology.

Finally, none of these patients was free of cardiovascular disease. Due to the high number of these patients with hypertension and/or diabetes, plus significant cardiovascular histories for most of this cohort (7/10 patients), the presence of aRVT may be more clinically useful when noted in patients with no known systemic vasculopathy. For those cases, referral to a primary care provider for physical examination and basic laboratory testing, may be indicated.

Conclusion

While aRVT has been suggested to be related to carotid artery occlusive disease, the results of this clinical case series did not support that theoretical supposition. If aRVT is observed, then the most prudent clinical recommendation is referral to primary care medicine for basic labs and physical examination. In patients with known cardiovascular disease, aRVT appears to be an incidental ophthalmic finding.

Disclosures

The views expressed in this article are those of the author and do not necessarily represent the positions of the Department of Veterans Affairs.

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