Reply

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RE: Traber et al.: Enhanced depth imaging optical coherence tomography of optic nerve head drusen: a comparison of cases with and without visual field loss

(*Ophthalmology*. 2017;124:66-73)

TO THE EDITOR: We read with interest the study by Traber et al, where the presence or absence of visual field defects was correlated with optic nerve head drusen (ONHD) morphology.[1] The ONHD were classified using enhanced depth imaging optical coherence tomography (OCT) morphologic characteristics as either peripapillary, granular, or confluent. The hyperreflective structures classified as peripapillary ONHD in the present study have previously been labeled as ONHD[2]; however, we do not find substantial evidence for this suggestion.

First, we regularly see similar hyperreflective mass-like peripapillary changes in OCT volume scans of patients with papilledema from idiopathic intracranial hypertension, none of whom show other ONHD characteristics (Fig 1). In these patients, the peripapillary changes are thought to be secondary to axoplasmic stasis.

Second, the "peripapillary drusen" also differ from recognized ONHD OCT morphology,[3,4] having a hyperreflective core and no surrounding high-signal border. Furthermore, unlike classic ONHD, they extend across areas of the optic disc circumference corresponding to a blurring of the optic disc margin. If this blurring was caused by superficial ONHD, they should be visible on ophthalmoscopy and exhibit the typical hyporeflective core surrounded by hyperreflective bands on OCT. In the study by Traber et al, the authors found that none of the peripapillary structures exhibited autofluorescence and none were evident as drusen on ultrasound imaging.

No histologic findings have shown a resemblance between these peripapillary structures and regular ONHD. The peripapillary structures have been diagnosed histologically as retinal scarring and, in contrast with ONHD, calcium is not found within them. The finding of endothelial lined channels in one of the retinal scars could indicate blood vessels, which are not found in ONHD.[5] Although the lack of calcium in these peripapillary structures could be a result of immature ONHD, these structures are found in all age groups, including elderly patients in whom noncalcified drusen are not found elsewhere. It is thought traditionally that the more superficial ONHD are the more calcified, making it less likely that these structures are immature noncalcified ONHD.

Although the authors acknowledge some doubt about classifying these changes as ONHD, they argue that the peripapillary changes should be considered ONHD, given that confluent ONHD were found within peripapillary subretinal structures. However, it is just as possible that ONHD developed in this area coincidentally. The authors suggest that the peripapillary structures may be an early form of ONHD, but this is inconsistent with the absence of similar structures where the vast majority of definite ONHD are found (within the substance of the optic nerve itself) and with the observation that the majority of these peripapillary structures do not contain any definite ONHD. In preliminary data from our own ONHD prospective cohort, some degree of peripapillary mass-like structure was found in 28 of 35 patients. In all 28 patients, the blurring of the optic disc corresponded with the peripapillary mass-like structures, which were seen in conjunction with regular ONHD.

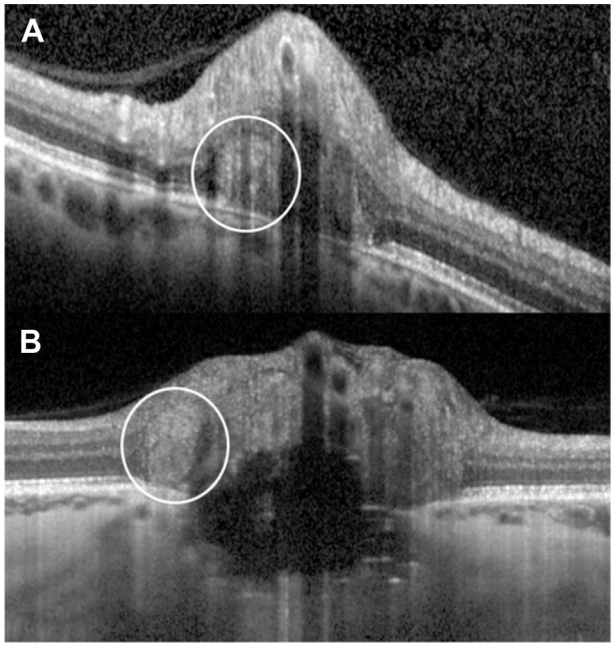

Figure 1. Enhanced depth imaging optical coherence tomography scans showing a peripapillary subretinal hyperreflective structure (*white circle*) (**A**) in a patient with idiopathic intracranial hypertension and (**B**) in a patient with optic nerve head drusen.

The authors suggest that the peripapillary changes could indicate axonal stasis as an early form of ONHD but we find no substantial evidence to diagnose these as ONHD, early ONHD, or even as a parallel form of ONHD, as proposed by Traber et al.[1] Instead, they may be the result of axoplasmic stasis with disruption of retinal layers caused by nonspecific axonal compression. Until there is clarity about the etiology of these structures, we recommend classification systems avoid labeling them as ONHD unless further evidence becomes available.

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REPLY: We thank Malmqvist et al for raising this interesting discussion about the nature of what we described as "peripapillary subretinal hyperreflective optic nerve head drusen" (referred to as peripapillary ONHD). Similar findings have been described by Lee et al[1] and Kulkarni et al.[2] While Malmqvist et al agree that these structures may be the result of axoplasmic stasis, which is what we hypothesized, they object to labelling them as early or parallel forms of ONHD. Although they found these structures in a majority of their own ONHD case series, they prefer to call them peripapillary mass-like structures. The question that arises is principally one of terminology and the definition of ONHD, and we would like to comment on a few points made by Malmqvist et al.

First of all, we observed confluent ONHD within peripapillary ONHD, or within mass-like structures if you will, in a few of our patients, which is against their presence being merely coincidental. Malmqvist et al argue that, unlike classic ONHD, peripapillary ONHD extend across areas of the optic disc circumference and should be visible on ophthalmoscopy. We presume that this refers to calcified ONHD only. We have no reason to believe that peripapillary ONHD do not extend into the optic nerve itself. However, this is difficult to image for the following 2 reasons. The reflectance of the suspected ONHD is similar to the reflectance of the optic nerve itself, and the shadowing artifact from major retinal vessels further interferes with their detection. The fact that peripapillary ONHD seem undetectable by autofluorescence or ultrasound imaging is not necessarily against their being a variety of ONHD, since autofluorescence and ultrasound imaging never had perfect sensitivity of detecting presumed ONHD.[3] This point is particularly true for uncalcified drusen.

The fact that similar structures have been observed in patients with papilledema[2] does not seem to contradict our hypothesis, since axonal stasis occurs in both conditions. There remains uncertainty as to whether these hyperreflective subretinal masses observed in papilledema are related to papilledema itself or reflect coexistent ONHD.[1,2] There may well be overlap in pathology in the 2 conditions. However, it is rare for papilledema to persist for many years, as is the case with the anomalous discs that give rise to drusen formation. Ophthalmologists have been speculating about uncalcified drusen for decades. However, drusen are geodes in geology and, therefore, we might consider not calling them drusen unless they have or will develop some kind of crystalline structure. In that sense, we agree with the arguments against peripapillary ONHD being protodrusen, but consider it unproven that they are not related to the pathogenesis of drusen because we (and the authors of the letter) find them very commonly in discs considered clinically to have drusen. Their presence correlates with aspects of disc morphology (no cup, centrally emerging vessels, elevation) but not with visual field loss which is a major original finding in our article.

Enhanced depth imaging with optical coherence tomography opens new perspectives in ONHD-related research and it seems wise to keep an open mind about interesting new findings despite traditional views about this condition.

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