LETTER TO THE EDITOR

Microcystic macular degeneration from optic neuropathy: not inflammatory, not trans-synaptic degeneration

Piero Barboni,1,2 Valerio Carelli,3,4 Giacomo Savini,5 Michele Carbonelli,5 Chiara La Morgia3,4 and Alfredo A. Sadun6

1 Istituto Scientifico San Raffaele, Milano, Italy
2 Studio Oculistico d’Azeglio, Bologna, Italy
3 IRCCS, Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy
4 Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, Bologna, Italy
5 IRCCS Fondazione Bietti, Roma, Italy
6 Doheny Eye Institute and Department of Ophthalmology, Keck School of Medicine at the University of Southern California, Los Angeles, CA, USA

Correspondence to: Piero Barboni MD, Studio Oculistico d’Azeglio, Via d’Azeglio, 9 40123 Bologna, Italy
E-mail: p.barboni@studiodazeglio.it

Sir, we read with great interest the article by Gelfand et al. (2012) in the June issue of Brain in which they describe ‘microcystic macular oedema in multiple sclerosis’. They concluded that these changes in the inner nuclear layer of the retina were best seen by spectral domain optical coherence tomography and were due to inflammatory conditions that produced a breakdown in the blood–retinal barrier. In response, Abegg et al. (2012) noted similar changes in a case of compressive optic neuropathy due to glioma and suggested retrograde trans-synaptic degeneration as an alternative explanation. Furthermore, Balk et al. (2012) also noted similar features in a case of recurrent optic neuritis not due to multiple sclerosis, adding evidence of inflammation as the key aetiology.

However, we have seen several hundred patients with severe optic atrophy secondary to two non-inflammatory hereditary conditions, i.e. Leber’s hereditary optic neuropathy (LHON) and dominant optic atrophy. These conditions have been shown to cause severe losses of retinal ganglion cells and their axons in the range of 75–99% (Carelli et al., 2004). These patients with hereditary optic neuropathy have been systematically studied by optical coherence tomography and other methodologies in a large Brazilian LHON pedigree and many other smaller LHON and dominant optic atrophy, genetically confirmed, families in Italy and the USA (Barboni et al., 2005; Ramos et al., 2009; Barboni et al., 2011). We have found these microcystic-like changes in the macular inner nuclear layer, but it is important to note, only in 10 such patients (Fig. 1). Furthermore, fluorescein angiography did not disclose any leakage (Fig. 1), as expected for the non-inflammatory conditions of LHON and dominant optic atrophy. Hence, this could not be a process associated with the breakdown of the blood–retinal barrier. It is also important to note that in the vast majority of cases, despite devastating and longstanding optic atrophy, no such microcystic-like changes were found on optical coherence tomography. Hence, this also could not be due to retrograde trans-synaptic degeneration alone.

Therefore, we can say that optic atrophy is necessary, but not sufficient to produce these microcystic-like changes in the inner nuclear layer of the macula. We agree with Abegg et al. (2012) that this degeneration is non-specific and non-inflammatory. With regards to what might be a critical second factor, we propose vitreous traction. As noted by Gelfand et al. (2012), the microcystic-like changes were more likely in cases of severe macular ganglion cell complex volume loss and we noted that the vitreous remained attached in this area of the macula (Fig. 1). We propose that the vitreous traction bears directly on the next retinal layer, the inner nuclear layer, and produces a schesis. The spaces between the remaining bipolar cell axons look like microcystic changes but they do not reflect true oedema (Fig. 1).

Insofar as this schesis is associated with optic atrophy and vitreous traction, but not due to inflammation or retrograde trans-synaptic degeneration, it is unlikely to be useful as a marker of multiple sclerosis.
References


Figure 1 Images from (A–C) a patient with LHON, and (D–F) a patient with dominant optic atrophy. (A) Fundus photograph depicting the horizontal plane of the optical coherence tomography scan shown in C. (B) Fluorescein angiography showing lack of leakage in late phase. (C) Optical coherence tomography scan through the macula showing the occurrence of cystic-like structures between bridging tissue in the inner nuclear layer. (D) Fundus photograph depicting the horizontal plane of the optical coherence tomography scan shown in F. (E) Severe loss of retinal ganglion cells and plexiform layer in the macular region as demonstrated in a pseudo-colour map of pattern deviation. (F) Optical coherence tomography scan through the macula showing the occurrence of cystic-like structure between bridging tissue in the inner nuclear layer. Note that in both LHON (C) and dominant optic atrophy (F), the vitreous remains attached.