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Letter to the Editor

Optical Coherence Tomography Angiography in patients with Neurofibromatosis type 1: a quantitative vascular prospective study

Gilda Cennamo,[1] Daniela Montorio,[2] Maria Paola Laezza,[2] Piera Giunta,[2] Pasquale Fabio Barra[3] and Iris Scala[3]

[1]Eye Clinic, Public Health Department, University of Naples "Federico II", Naples, Italy; [2]Department of Neurosciences, Reproductive Sciences and Dentistry, University of Naples "Federico II", Naples, Italy; [3]Department of Maternal and Child Health, Federico II University Hospital, Naples, Italy

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Editor,

Neurofibromatosis type 1 (NF1) is an autosomal neurogenetic disorder, and its main clinical phenotype is the development of optic pathway gliomas (OPGs). The most common ophthalmological signs at diagnosis are proptosis, strabismus, nystagmus and excavation of the optic disc with glial tissue (Kaufman et al. 2006). The main symptom of clinical progression is considered to be visual acuity loss which depends on the lack child's collaboration (Pasmant et al. 2012). It is crucial to develop an objective diagnostic method not influenced by attention-deficit disorders occurring in this disease (Listernick et al. 1997).

Spectral-domain optical coherence tomography (SD-OCT), a rapid diagnostic tool, detects changes in the retinal ganglion cell complex (GCC), the retinal nerve fibre layer (RNFL) and their relationship to vision loss in patients with OPGs (Topcu-Yilmaz et al. 2014). The introduction of OCT angiography (OCTA) allowed for non-invasive quantification of the retinal perfusion in macular and papillary regions (Wang et al. 2018). We prospectively evaluated the changes in retinal vessel density (VD) detected by OCTA and structural SD-OCT parameters in 34 NF1 patients with OPG (mean age 10.23 ± 3.86 years) involving the intraorbital optic nerve in one eye and 46 eyes of 46 NF1 patients without OPG (mean age 11.32 ± 4.25 years) and compared results to those from 40 eyes of 40 healthy subjects. The Institutional Review Board of the University of Naples Federico II (protocol number: 315/18) approved this study.

Each subject in the study underwent a complete ophthalmological examination, including OCT and OCTA. Fundus examination of all patients with OPG revealed the optic disc had oedema and a blurred margin, while no papillary alteration was detected in subjects without OPG. All patients showed normal visual acuity (0.05 ± 0.11 logMAR).

Ganglion cell complex (GCC) and Retinal nerve fibre layer (RNFL) parameters were significantly reduced in the OPG group compared to controls. No statistically significant difference was found in structural SD-OCT parameters between the group without OPG and controls ($p > 0.05$). The comparison between groups revealed a statistically significant reduction in GCC and RNFL parameters in NF1 patients with OPG compared to those without OPG ($p < 0.001$). OCT angiography (OCTA) examination revealed a reduction in the

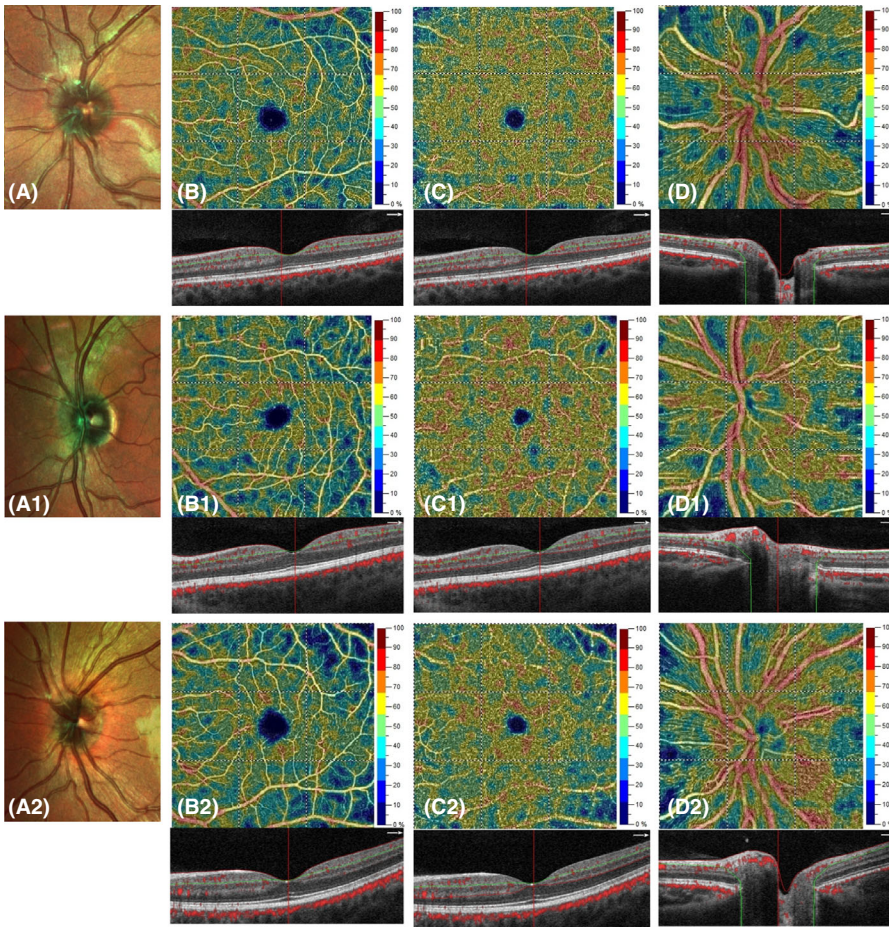

Fig. 1. Optical coherence tomography angiography images of a healthy eye, an eye from a NF1 patient without glioma of the optic nerve, and an eye from a NF1 patient with glioma. The left eye of a 9-year-old healthy female subject in the top row shows normal features of the optic disc at multicolour imaging (A), normal vessel density in the superficial capillary plexus (SCP) (B), deep capillary plexus (DCP) (C) and radial capillary plexus (RPC) (D). The second row in the left eye of a NF1 patient (10-year-old female) without glioma of the optic nerve reveals normal optic disc features (A1) and a focal reduction of the vessel density in SCP (B1) without changes in DCP and RPC (C1, D1). The bottom row shows in the left eye of a NF1 patient (10-year-old male) with glioma of the optic nerve, blurred margins in the nasal sector of the optic disc (A2), a decreased vessel density in SCP (A2) and RPC (D2) while no change was found in vessel density of the DCP (C2)

VD of the superficial capillary plexus (SCP) and radial peripapillary capillary plexus (RPC) that was statistically significant in the OPG group compared to controls ($p < 0.001$). In contrast, no significant difference was found in the deep capillary plexus (DCP). The patients without OPG revealed a lower VD only in SCP respect to controls ($p < 0.05$). Comparing the study groups, the OPG group showed a statistically significant reduction in VD of SCP and RPC compared to the group without OPG ($p < 0.001$) (Fig.1).

The retinal structural and vascular impairment associated with glioma could be due to a compressive effect of this lesion on the optic nerve that may have determined progressive damage of the neuronal component and vascular perfusion. Moreover, the reduced macular and papillary VD in NF1 patients without glioma despite no retinal structural abnormalities suggests that even in the absence of optic nerve compression, the retinal vascular damage may precede the appearance of GCC and RNFL loss. This result assumes that the structural degeneration may be due to the interference in axoplasmic flow induced by local ischaemia at the level of the optic nerve.

In conclusion, OCTA could have a valid role in the management of NF1 patients because it provides an objective, automatic and quantitative evaluation of retinal microvasculature and requires only a few seconds of collaboration. OCT angiography (OCTA) was revealed to be a useful biomarker to distinguish the early changes in retinal perfusion before the appearance of structural damages and in absence of visual acuity abnormalities in NF1 patients.

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Correspondence:
Gilda Cennamo MD
Department of Public Health
University of Naples Federico II
Via S. Pansini 5
80133 Naples
Italy
Tel: +00 390 817 143 731
Fax: +00 390 817 462 383
Email: xgilda@hotmail.com