A characteristic type of retinal microvascular abnormalities in a patient with Neurofibromatosis type 1

A. Moramarco¹, A. Lambiase¹, F. Mallone¹, E. Miraglia², S. Giustini²

¹Department of Organ of Sense, Sapienza University of Rome, Rome; ²Department of Dermatology, Sapienza University of Rome, Rome, Italy

Abstract

This study aims to describe a typical retinal microvascular abnormality in patients with neurofibromatosis type 1 (NF-1). A 64-year-old man with diagnosis of NF-1 was evaluated by complete ophthalmological examination, including fluorescein angiography and spectral Domain OCT in Near-Infrared (NIR-OCT) modality. Slit lamp exam showed the presence of more than 10 Lisch nodules for each eye. Ophthalmic examinations and NIR-OCT scans showed the presence of retinal tortuous vessels ending in a ‘puff of smoke’ arrangement. The clinical significance as diagnostic and prognostic factor of this novel type of retinal microvascular abnormality in NF-1 should be further investigated. Cl. Ter. 2019; 170(1):e4-9. doi: 10.7417/CT.2019.2101

Key words: retina, microvascular abnormalities, neurofibromatosis, NIR-OCT, Moya-Moya disease

Case History

We report the case of a specific type of retinal microvascular involvement in NF1. A 64-year-old man with diagnosis of NF1, showed the presence of axillary freckling, café-au-lait macules, one plexiform neurofibroma on the left arm, and hundreds of cutaneous and subcutaneous neurofibromas spread over the entire body. His family history was positive for Neurofibromatosis type 1. Cervical and spinal MRI, laboratory analysis and abdominal ultrasound were normal. Slit lamp exam showed the presence of more than 10 Lisch nodules for each eye. Choroidal abnormalities were observed in both eyes under Spectral Domain OCT in Near-Infrared (NIR-OCT) modality. NIR-OCT scans revealed retinal abnormal microvessels in the right eye (Fig. 1). The lesions consisted of tortuous vessels ending in a ‘puff of smoke’ arrangement (Fig. 1). They were located within the posterior pole, and consisted in small (second or third order venules) tributaries of the superior and inferior temporal veins. In addition, simple vascular tortuosity in the superonasal region of the same eye, was observed. The patient was completely asymptomatic. Cross sectional SD-OCT images through the ‘puff of smoke’ area were also performed (Figures 2-5). We observed a normal retinal vascular appearance, with vessels at the level of the retinal nerve fiber layer and inner nuclear layer, and the typical shadowing effect to interrupt the underlying structures. In our opinion, it can be related to the completely unaffected visual acuity of the patient. Fluorescein angiography did not show any leakage (Fig. 6). More in detail, we enclosed blu-light autofluorescence (BAF) (Fig. 7) image and artero-venous early and late-phases acquired images (Fig. 6,8-10). We observed a rapid intake of the contrast agent in early arterial-venous phase (19 sec) and a persistent hyperreflexivity in the late stages. We didn’t describe any leakage in early phases. There was a substantial reduction in reflectivity at the late time of 4 min and 30 sec of FAG-examination, and a slight physiological papillary impregnation.

Correspondence: Alessandro Lambiase MD, Department of Sense Organs, “Sapienza” University of Rome, Viale del Policlinico 155 00161 Rome, Italy. Fax +390649970752. E-mail: alessandro.lambiase@uniroma1.it.
Fig. 1. Near infrared reflectance (NIR) imaging showing the 'puff of smoke' arrangement of retinal microvascular abnormalities in a 64 years-old patient with NF1.

Fig. 2.

Fig. 3.
Fig. 4.

Fig. 5.

Fig. 2, 3, 4, 5. Cross sectional SD-OCT images through the ‘puff of smoke’ area: normal vascular representation
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Fig. 6

Fig. 7

Fig. 8

Fig. 9
Fig. 10

Fig. 6, 7, 8, 9, 10. Fluorescein angiographic (FA) images of retinal microvascular abnormalities: blue-light autofluorescence (BAF) (Figure 7) image and artero-venous early and late-phases acquired images (Figures 6, 8, 9, 10). No leakage was detected.

Discussion

Moya-Moya disease is a rare, progressive, occlusive cerebrovascular disorder with particular involvement of the Circle of Willis. The main manifestations are represented by stroke and recurrent transient ischemic attacks. The name “Moya-Moya” means "puff of smoke" in Japanese, and describes the look of the tangle of tiny vessels in an apparent attempt to distally supply blood. The Moya-Moya like pattern of NF1-related retinal microvascular abnormalities is characterized by tortuous vessels that end in a 'puff of smoke' arrangement to remember the collateral circulation of the Moya-Moya Syndrome. We consider the Moya-Moya like vessels as a vascular extension from the spiral-shaped pattern that should be differentiated from the spiral arrangement. We hypothesize that the proliferative attitude that involves different vascular wall cells, can lead to anatomic modifications and consequent different vascular arrangements (4, 5). We speculate that a large spectrum of retinal microvascular lesions, all resulted from the same pathogenesis, may reflect a progressive trend of complexity from the spiral attitude to the more grotesque Moya-Moya like type.

Moreover, Parrozzani et al. recruited one patient presenting with Moya-Moya syndrome and retinal microvascular abnormalities, underlying the relationship between the vascular configuration in collateral cerebral circulation of Moya-Moya syndrome and our identified Moya-Moya like pattern (6).

NF-1 retinal vascular alterations have rarely been reported in literature. “Corkscrew” retinal vessels of diverse complexity were described in 12 of 32 patients with NF-1 (37.5%) (7). Similarly, Abdolrahimzadeh et al. observed retinal microvascular abnormalities in 35% of 17 patients (8). Moreover, Makino et al. reported the association between NF1 and congenital retinal macrovessel (9) In addition, distinctive corkscrew retinal vessels superior and inferior to the fovea in a single patients with NF1 were previously described (10, 11).

NF1 vasculopathy is a significant but underrecognized complication of the disease, affecting both arterial and venous blood vessels of all sizes (12). Oderich et al. identified 76 vascular abnormalities among their cohort of 31 NF-1 patients, including: 38 aneurysms, 20 arterial stenoses, 5 arteriovenous malformations, 5 arteries compressed or invaded by neural tumors, and 6 abnormalities of the heart valves (13). Kaas et al. reported a prevalence rate of 8% for both peripheral and cerebral vasculopathy associated with pediatric neurofibromatosis type 1, based on confirmed findings in 14 of 181 children seen in a large neurofibromatosis clinic (14). Previous studies in mice have suggested an important role of smooth muscle cells and bone marrow cells in neointimal hyperplasia, inflammation and exaggerated response to injury including enhanced angiogenesis (4, 15, 16). Shields et al. described the presence of retinal vasoproliferative tumors (RVPT) among 6 NF1 young patients, revealing early hyperfluorescence, late staining and leakage of each case (17). Moreover, Ocular Vascular alterations are widely described as part of the phakomatoses: Sturge–Weber syndrome (SWS), Neurofibromatosis, Klippel–Trenaunay syndrome, tuberous sclerosis, and von Hippel–Lindau syndrome (VHL) (18, 19). Approximately 50% of SWS patients showed pathologic ocular changes, involving the eyelid, anterior chamber, cornea, choroid, and retina (18, 19). Toy et al. described that 154 out of 249 patients with von Hippel–Lindau syndrome had clinical evidence of ocular disease in at least one eye, with involvement being bilateral in 33% and unilateral in 29% of participants (20). Moreover, different phakomatosis are reported to be coexisting in the same individual on the basis of their identical mesodermal origin (21, 22, 23).

In conclusion, we described a characteristic retinal microvessels’ change in a patient with NF1. This retinal abnormality has a 'puff of smoke' appearance, resembling the collateral circulation of Moya-Moya disease. We speculate a possible inclusion of this peculiar retinal sign among NF1 diagnostic criteria, although further studies are required to assess the clinical significance of this finding (24).

References

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