

**Letter to the Editor:** Comment on 'Retinal vascular abnormalities in children with Neurofibromatosis type 1'

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To the Editor:

We read with interest the article by Touzé et al.<sup>1</sup> entitled ‘Retinal vascular abnormalities in children with Neurofibromatosis type 1’.

The Authors assessed clinical retinal microvascular abnormalities (RVAs) characteristics in a large series of children affected by NF1 on near-infrared imaging. The overall prevalence of RVAs was 37.1% in accordance with the results of Moramarco et al.<sup>2</sup>. This is notable as vascular tortuosity is a phenotype reported with variable appearance and frequency in clinical studies as opposed to corkscrew pattern, for whom an excellent interobserver agreement was observed<sup>1</sup>.

The Authors classified RVAs based on degree of vascular tortuosity as per Moramarco et al.<sup>2</sup>, reporting 96% of simple vascular tortuosity and 17% of corkscrew arrangement. No moyamoya-like pattern was observed. Evolution of RVAs from simple vascular tortuosity to corkscrew pattern was observed in 5 cases (9%)<sup>1</sup>. While investigating the nature of vessel involvement, tortuous vessels were reported to affect both arteries and veins, whereas only small second-order or tertiary-order venules progressed to highly tortuous corkscrew pattern, possibly because of their more deformable properties<sup>1</sup>. These results support the hypothesis by Moramarco et al.<sup>2</sup> of dynamic nature of RVAs, evolving from simple tortuosity to more complex patterns over time. Thus, the natural history of RVAs might explain why the most complex forms were only found in series of patients older than those included in Touzé et al.<sup>1,2</sup>. This questions the reliability of previous descriptions of congenital and stable nature of RVAs<sup>3</sup>. Interestingly, the prevalence of RVAs evolving over time presented by Touzé et al.<sup>1</sup> differs from that of Parrozzani et al.<sup>4</sup> reporting only one patient out of 473 to develop de novo RVAs and two patients showing progressive changes during the follow-up. This may be related to the higher mean age of the study participants in Parrozzani et al.<sup>4</sup> compared to Touzé et al.<sup>1</sup> (mean age: 17.8 years Vs 8.8 years), suggesting that variations in the RVAs may have developmental features in children with a tendency to stabilize in the more advanced age.

The Authors questioned the use of the term moyamoya-like first introduced by Moramarco et al.<sup>2</sup> to describe a complex RVA phenotype, since Moyamoya syndrome is a vasculopathy that affects cerebral arteries while RVAs mainly affect retinal veins<sup>1,5</sup>. The term moyamoya, from the Japanese ‘cloud of smoke’, refers to the angiographic aspect of the collateral vessels that develop downstream of the stenotic arterial cerebral vessels<sup>5</sup>. Therefore, although the syndrome affects the cerebral arteries, the term itself does not refer to arterial involvement. The term moyamoya-like, chosen by the Authors<sup>2</sup>, is intended to highlight the morphological aspect of the RVAs, regardless of the nature of involved vessels. Moreover, the same Authors (Touzè et al.<sup>1</sup>) observed that although RVAs affect second and third order veins in corkscrew vessels, the arterial system can also be affected in vascular tortuosity. Similarly, Parrozzani et al.<sup>6</sup>, found that the network of congested capillaries in the deep capillary complex on OCT-A has anastomotic connections both with the arterioles and venules in the superficial capillary complex. Therefore, we agree with Touzé et al.<sup>1</sup> that venous involvement is definitely more frequent in RVAs due to the increased flexibility of the venous wall compared to arteries; however, arterial vessels also appear to be involved. In our opinion, the nature of vessel involvement in RVAs related to NF1 should be further investigated. Moreover, since the association between NF1 and Moyamoya syndrome is widely reported<sup>5,7</sup>, it would be interesting to evaluate the presence of RVAs, and especially the moyamoya-like pattern, in patients affected by both of these conditions.

### **Authors’ Contributions**

Fabiana Mallone and Luca Lucchino conceived and wrote the Letter. Antonietta Moramarco conceived of the study and critically evaluated the accuracy and integrity of the work. All authors contributed to refinement of the study and approved the final manuscript. Each author believes that the manuscript represents honest work. All authors meet the requirements for authorship and all express full consent for publication on our esteemed Journal.

### **Competing Interests**

All authors certify that they have no financial or proprietary interest in the subject matter or materials discussed in this manuscript. The authors declare that they do not have any conflicts or potential conflicts of interest

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