Videocapillaroscopy and Marfan syndrome: a 2-case report

Sirs,

Marfan syndrome (MFS) is an autosomal dominant connective tissue disorder that affects the cardiovascular, ocular and skeletal systems and is mainly caused by mutations in the fibrillin-1 gene (FBN1) on chromosome 15. Fibrillin-1 is an extracellular glycoprotein that is the major component of the microfibrils, which forms a sheath surrounding the elastin. The estimated incidence of MFS is approximately 1 in 5,000 of the general population, affecting both sexes equally (1).

Although a great range of research has reported on the structural alterations that occur on the large vessels in MFS, the field of microcirculation remains still poorly investigated. There are only a few studies that mention the abnormalities of the capillary morphology. Martinez R. *et al*. have investigated the capillary morphology by nailfold capillaroscopy on patients with MSF and mytral valve prolaps (MVP), and have described the altered architecture of microvessels with reduced compactness of the whole microvasculature when compared to healthy controls (MVP in non-MFS subjects) (2). The study on flow-mediated vasodilatation in MFS has shown impaired flow-mediated but preserved agonist-mediated endothelium-dependent vasodilatation, and suggests also a role for fibrillin in endothelial cell mechanotransduction (3).

The idea of endothelium involvement in MFS has come about thanks to the newest insights in the pathogenesis of aneurysm formation. However, recent findings using genetically engineered mouse models of MFS have mentioned that fibrillin also takes part in the regulation of various cytokines and the growth factor (TGF-β). In particular, fibrillin-1 interacts with latent TGF-β–binding proteins and controls TGF-β bioavailability, which in turn controls a variety of cellular processes including proliferation, differentiation, and apoptosis (1, 4, 5).

Furthermore, MMP-2 and -9 have been identified as latent TGF-β activators, which highlight the link between all of these components (6).

Fibrillin-containing microfibrils have also been described in abundance in the connective tissue matrix close to the arterial endothelial cells (7) that may indicate also its functional as well as structural roles (3).

All items mentioned above provide indirect evidence of endothelial dysfunction with possible further capillary structure alterations in MFS patients.

To visualise the microvascular alteration in patients with MFS, a nailfold videocapillaroscopy (NVC) was performed. NVC represents today the most efficient method for assessing the presence of microvascular alterations and is used in patients with connective tissues diseases, especially systemic sclerosis and Raynaud phenomenon. NVC describes the following parameters: number of capillary, morphology of capillary loops, its dimension and length, the distribution of capillary loops, capillary density and microbleeding. NVC can also detect dynamic parameters such as flux features (8, 9).

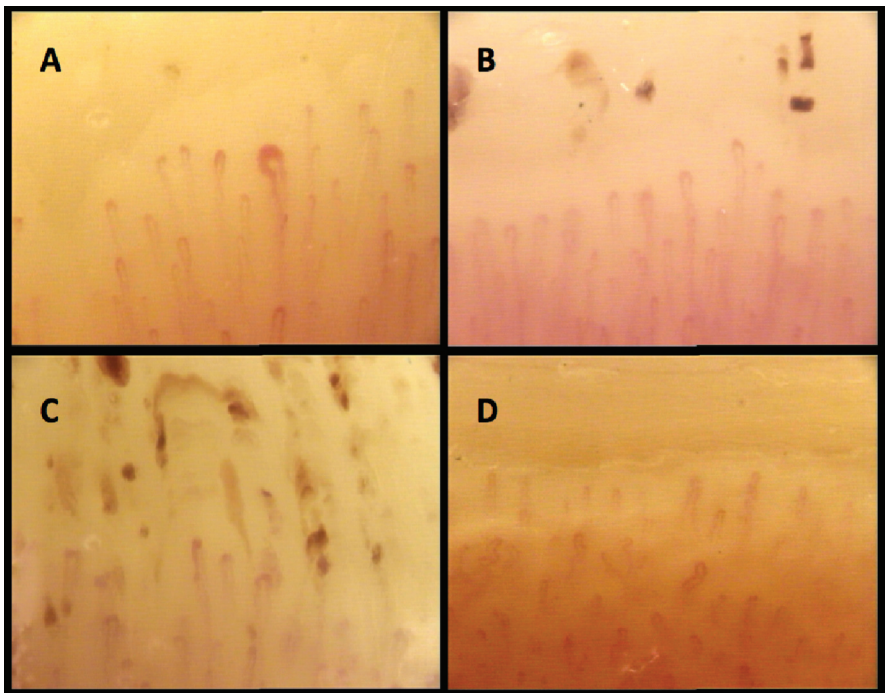

Fig. 1. Videocapillaroscopic findings in the patient with Marfan syndrome.
(A, B, C – Marfan patient's NVC images, D – patient's daughter's NVC image)

Our patient is a 47-year-old, female, with clinical diagnosis of MFS and recent mitral anuloplastica (performed in 2004) for MVP and atrial fibrillation. The diagnosis of MFS was established in 2000, based on skin biopsy. From the anamnestic data, we found out that her daughter, sister and nephew are also suffering from MFS. The recent examinations of her aortic root have not found any alteration of its diameter.

The NVC was carried out at the Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, using an optical probe videocapillaroscopy, equipped with 100× and 200× contact lenses and connected to image analyse software (Videocap; DS MediGroup, Milan, Italy). The nailfolds of all 10 fingers were examined and the following parameters were observed (Fig. 1): normal dermal transparency without pericapillar oedema. The number and direction of capillaries were preserved.

The lengths of the capillaries appeared to be increased. The morphology of capillary loops was normal with a mild tortuosity and a frequent number of irregular ectasias, whereas no giant capillaries or abnormal ramifications were observed (Fig. 1A, B, C). The interesting point was the finding of an increased number of deposits of haemosiderin in almost all the nailfold beds (Fig. 1B, C). The blood flux parameters did not show any abnormalities. We also performed a NVC on the patient's daughter without describing any specific features, with preserved number of capillary, regular morphology of capillary loops with mild turtuosity and with the tendency to an increased length of capillaries. In this case, no deposits of haemosiderin were detected on NVC (Fig.1 D).

The very few existing studies on capillary morphology in MFS patients have not described any specific alteration so far. In particular, the present NVC examination did not find specific patterns of microvascular alteration in our patients. The increased length of capillaries observed in both cases may be the only aspect that might be reported as an anatomical peculiarity in MFS patients. On the other hand, the increased numbers of haemosiderine deposits in the main case may well be due to anticoagulant treatment administered to the patient for her cardiovascular risk condition.

In order to realise more consistent results, a larger number of MFS patients should be observed by NVC and, from our point of view, especially in patients who also present functional/morphological alterations of large vessels.

L. VREMIS[1], *MD*
C. PIZZORNI[1], *MD*
F. RAVERA[1], *MD*
M. CUTOLO[1], *MD*

Letters to the Editor

[1]*Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Italy.*

Address correspondence to: Laura Vremis, MD, Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Viale Benedetto XV, 6, 16132, Genova, Italy.
E-mail: lauravremis@yahoo.com

Competing interests: none declared.

References

1. BACKER J, LOEYS B, PAEPE A: Marfan and Marfan-like syndromes. *Artery Res* 2009; 3: 9-16.
2. MARTINEZ R, DRAGAGNA G, SAPONARO A *et al*.: Microcirculatory changes in mitral prolapse as an expression of a systemic change in the connective tissue. *Cardiologia* 1992; 37: 285-9.
3. WILSON DG, BELLAMY MF, RAMSEY MW *et al*.: Endothelial Function in Marfan Syndrome: Selective Impairment of Flow-Mediated vasodilatation. *Circulation* 1999; 99: 909-15.
4. BRAVERMAN AC: Transforming Growth Factor-2: A Biomarker in Marfan Syndrome? *Circulation* 2009; 120: 464-6.
5. WIPFF J, ALLANORE Y, BOILEAU C: Interactions between fibrillin-1 and TGF-beta: consequences and human pathology. *Med Sci* (Paris) 2009; 25: 161-7.
6. CHUNG AWY, YEUNG K, SANDOR G, JUDGE DP, DIETZ HC, BREEMEN C: Loss of elastic fiber integrity and reduction of vascular smooth muscle contraction resulting from the upregulated activities of matrix metalloproteinase-2 and -9 in the thoracic aorta aneurysm in marfan syndrome. *Circ Res* 2007; 101: 512-22.
7. KIELTY CM, WILSON DG, STUART G *et al*.: Fibrillin expression and deposition by vascular endothelial cells: implications for Marfan syndrome. *Circulation* 1996; 94: I-350 (Abstract).
8. DE ANGELIS R, CUTOLO M, SALAFFI F, RESTREPO JP, GRASSI W: Quantitative and qualitative assessment of one rheumatology trainee's experience with a self-teaching programme in videocapillaroscopy. *Clin Exp Rheumatol* 2009; 27: 651-3.
9. CUTOLO M, MATUCCI-CERINIC M: Nailfold capillaroscopy and classification criteria for systemic sclerosis. *Clin Exp Rheumatol* 2007; 25: 663-5.