**Polidistrectual videocapillaroscopic evaluation in a patient with prolidase deficiency**

Sirs,

Prolidase deficiency (PD) is a rare autosomal recessive disorder caused by mutations in the **PEPD** gene and defined by a protein clinical spectrum including recalcitrant lower limb ulcers, facial dysmorphisms, deafness, splenomegaly, cognitive impairment and recurrent infections (1). Given the rarity of PD and the limited number of cases investigated, genotype-phenotype correlations have not been yet identified. Also, anatomopathological reports describing the vascular changes and ultimately its histopathological hallmark are currently limited. To date the pattern of vasculopathy has been only marginally studied. We here report our experience of a PD patient focusing on its microcirculation net analysed by videocapillaroscopy in several districts. The patient’s clinical picture was dominated by multiple necrotic skin lesions of the lower limbs and buttocks, hypertelorism, splenomegaly, mild difficulties of speech. Skin lesions were frequently complicated by infections including one episode of septicemia that required hospitalisation in an intensive care unit. A detailed description of the biopic findings, molecular characterisation, enzymatic activity and urine dipeptide analysis has been previously described (2).

Videocapillaroscopy (Videocap 3.0™,DS Medica) was performed in the following districts: conjunctiva, gingival edge, labial mucosa, anterior tibial region, hand nailfold (II, III, IV, V finger) before and after thermal stress (10 minutes in melting ice at 4°C). Quantitative morphological analysis of microvascular changes was done by Marricq, Merlen and Lee score (3-5). A full and detailed description of videocapillaroscopic and biopic findings is given in Figure 1.

Interesting and worth-discussing findings comprise neoangiogenesis (detected in the nailfold and anterior tibial region) and ectasia in the intermediate capillary loops found on labial mucosa and nailfold. Additionally, nailfold tissue and perivascular oedema identified in basal conditions experienced an increase after thermal stress along with a slow, granulated flow with frequent stop flows, thus displaying an acrocyanotic type. These videocapillaroscopic results are compatible with some histological findings such as microcirculatory stasis, moderate vasculitis and abnormal dermal structure that ultimately lead to the clinical manifestations including persistent/refractory cutaneous ulcers. Early ulceration has been biopically characterised by vessel wall thickening which may be partially explained by the slowed down capillary flow on videocapillaroscopy, whereas massive deposits of fibrin in vessel walls and a thick fibrotic floor found on chronic ulcers may be responsible for a later development of neoangiogenesis (6). Interestingly, ultrastructural studies have reported a lamellated and interrupted basal membrane of dermal blood vessels (7). Indeed, most of the cutaneous lesions may be attributed to an altered connective tissue metabolism of capillary blood or lymphatic vessels (8). In this regard, an impaired collagen synthesis as a consequence of decreased prolidase activity (9) could explain the ectasic capillaries found in our patient.

A skin biopsy in our patient showed leukocytoclastic vasculitis involving the vessels of dermis and subcutaneous tissues, with extensive periartrial fibrinoid necrosis, occlusion of vascular lumen, spongiosis, and ischaemic necrosis of the superficial portion of Malpighian layer. Some of the capillaroscopic microvascular changes in our patient are of inflammatory nature, while others highlight tissue repairing processes of more long-term lesions. Prolidase deficiency is a rare disorder with an under-studied aetiopathogenesis and a not fully understood histopathological picture. Properly designed studies investigating its microcirculation may clarify these aspects and stimulate an oriented therapeutic approach.

Fig. 1. A. Conjunctiva. Hyperemic conjunctiva. Reduced diffusion distance. Finely granular and fragmented flow (score 1) with sporadic stop flows in every district. Two venular thrombosis (arrows) in the right eye without re-population, haemorrhage or consensual dilatation. Curvilinear venule with some dilatations, kinking and coiling, fork angle <90°, no parietal alteration. Straight arteriole, some sporadic kinking, fork angles <90°, no parietal alteration. Reduced A/V ratio. B. Labial mucosa and gingival edge. Sporadic ectasies of the intermediate loop. Rare tire-bouchon aspects, granular TM and winding with a normal diameter of the afferent and efferent loop and ectasia of the intermediate loop. Presence of some abnormal morphologies. Presence of neoangiogenesis, ectasia of intermediate and efferent loop, sporadic parietal alterations. Fused dermal papillas (Merlen 1, Marricq 3, Lee 0/1). After thermal stress: Increase of tissue and perivascular oedema. Dark red colouring. Unaltered diameter and number of patent capillaries. Slow, granular flow, frequent stop flows. C. Anterior tibial region. Type 2 network. Sporadic neoangiogenesis with aspects of pedicel, four-leaf clover and blackberry (Lee 0, Merlen 2).

A skin biopsy of leg ulcers, high magnification: haematoxylin-eosin staining revealing an inflammatory infiltration of the vessel wall. Picro-Mallory staining showing an occluded vessel with fibrinoid material.
Research Center of Systemic Autoinflammatory Diseases and Behçet’s Disease Clinic, Department of Medical Sciences, Surgery and Neurosciences, University of Siena; 2Department of Medical Sciences, Surgery and Neurosciences, University of Siena; 3Department of Clinical Sciences and Community Health, University of Milano; 4Rheumatology Unit, Istituto Gaetano Pini, Milano, Italy.

Please address correspondence to:
Luca Cantarini,
Centro di Ricerca delle Malattie Autoinfiammatorie Sistemiche e Malattia di Behçet,
U.O.C. Reumatologia, Policlinico Le Scotte,
viale Bracci 16, 53100 Siena, Italy.
E-mail: cantariniluca@hotmail.com

Competing interests: none declared.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2020.

References