

## Report

# Leucocytoclastic vasculitis associated with acquired reactive perforating collagenosis

## A diagnostic mimicry

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Reactive perforating collagenosis (RPC) is a rare dermatosis, firstly described in 1967 by Mehregan et al.<sup>1</sup> and known to manifest as two distinct clinical variants: (1) a rare inherited autosomal recessive form occurring in childhood and (2) a sporadic, acquired form. Accepting the proposal of Faver<sup>2</sup> in 1994, at least three clinicopathologic criteria are required to diagnose the acquired form of RPC: (1) histopathologic findings of transepidermal elimination of necrotic basophilic collagen bundles into a cup-shaped epidermal depression; (2) umbilicated papules or nodules with a central adherent keratotic plug; and (3) onset of the lesion after 18 years of age. Until now, the detailed pathomechanism leading to the genesis of RPC has been largely unknown, whereas leucocytoclastic vasculitis (LV) is the hallmark of type-III-immune reactions. Frequently, the direct cause of LV remains unclear in most of the clinical cases. To the best of our knowledge, there is no report of an association between perforating collagenosis and cutaneous vasculitis until now. Thus, we report of a 54-year-old female patient that presented with two distinct clinical features. Initially, 1 year before her first dermatologic consultation, dome-shaped papules with central hyperkeratotic plugs appeared on her trunk, progressing slowly to involve the upper extremities and associated with slight burning and intense pruritus. The eruptions were usually scraped off by the patient. Some of these lesions healed spontaneously with atrophic scars and pigmented macules. However, in the following weeks, the patient developed a distinct, palpable purpura with progression to ulcerated and necrotic petechial skin lesions involving the lower extremities (Fig. 1). Social and family history gave no further information. Neither diabetes mellitus nor renal diseases were reported. Cutaneous examination revealed a palpable purpura with central necrotic and ulcerated lesions predominantly



Figure 1. Palpable purpura, ulcerations and umbilicated papules with hyperkeratotic plugs on the lower extremities. Clinically, no discrimination between vasculitic lesions and RPC lesions was made.

involving the lower extremities and petechial skin lesions on the trunk and forearms. There were no mucosal findings. Additionally, the patient had multiple, solitary, tender, skin-coloured papules with a central umbilication containing an adherent plug on her upper extremities, trunk and legs. The laboratory findings were unrevealing. Light microscopy, as well as cultures of scales, were negative for fungi. Treatment in our hospital was initiated based on the clinical diagnosis of allergic vasculitis.

Histopathological confirmation from representative sites of the lower leg primarily revealed features of all the above mentioned criteria of Faver with strong transepidermal elimination of necrotic basophilic collagen bundles into a cup-shaped epidermal depression with a slight perivascular lymphohistiocytic dermal infiltration (Fig. 2). No findings of a vasculitis were observed initially; in particular, no endothelial swelling or transmural neutrophils were accompanied by leucocytoclasia. No immunoglobulin deposits were detected by direct immunofluorescence.

Because the clinical and histopathologic findings differed with respect to the purpuric aspect of the disease, a further specimen was obtained from a macroscopically non-ulcerated lesion of the

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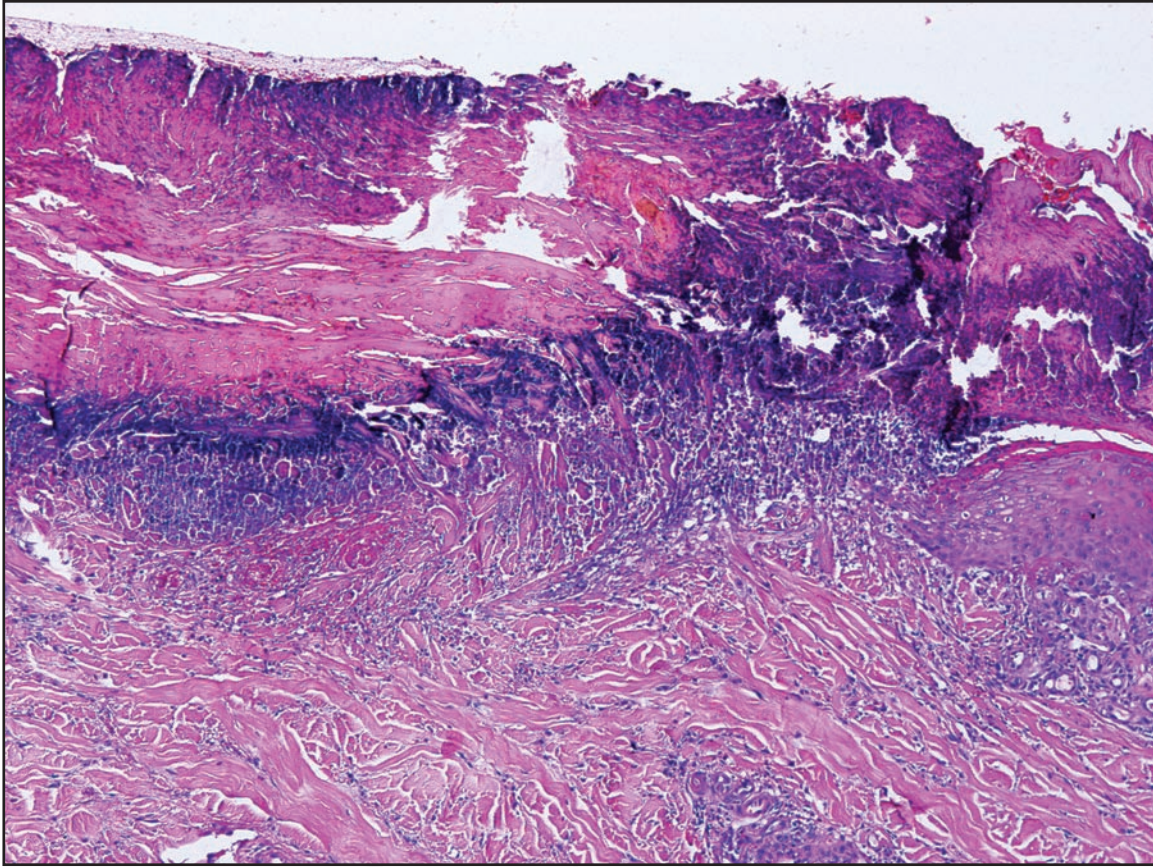


Figure 2. Transepidermal elimination of necrotic basophilic collagen bundles into a cup-shaped epidermal depression. HE stain, magnification 100x.

lower leg. This specimen demonstrated all of the typical signs of a leucocytoclastic vasculitis (Fig. 3). This clinical and histopathologic constellation prompted us to diagnose a leucocytoclastic vasculitis in association with acquired reactive perforating collagenosis. In the case presented herein, no underlying factors of either entity (RPC and LV) were identified; the lesions completely disappeared by systemic glucocorticosteroid therapy.

Recapitulating, the sporadic, acquired form of RPC can be observed in adults and is frequently associated with diabetes mellitus or renal failure. Numerous other systemic disorders have been described to co-exist with RPC.<sup>3</sup> Besides RPC, the following three entities are also considered to be acquired perforating dermatoses: Kyrle's disease, perforating folliculitis and elastosis perforans serpiginosa.<sup>4</sup> Hyperkeratosis follicularis et parafollicularis in cutem penetrans, known as Kyrle's disease, is a recessive inherited genodermatosis. Kyrle's disease is often associated with hepatic, renal or diabetic disorders, and can emerge as a paraneoplastic disease. Clinically, yellow-to-brownish horny papules in the proximity of follicles occur on otherwise healthy skin. Typically, no pruritus is reported.<sup>7</sup> Perforating folliculitis is characterized by asymptomatic-to-severely pruritic folliculocentric, keratotic papules on hair-bearing extremities. Histopathologically, disruption of the infundibular portion of the follicular wall, with transepidermal (transfollicular) elimination of connective tissue elements and cellular debris, can be observed.<sup>8</sup> Elastosis perforans

serpiginosa is an uncommon skin disease characterized by transepidermal elimination of abnormal elastic fibers, frequently associated with congenital connective tissue disorders or Down's syndrome. Clinically, solitary serpiginous lesions with hyperkeratotic papules, central healing and peripheral progression are seen.<sup>9</sup>

The clinical hallmark of the perforating dermatoses is multiple, dome-shaped papules with a central hyperkeratotic plug occurring on otherwise healthy skin. The perforating dermatoses differ mainly in histopathologic findings; differential diagnosis based only on clinical morphology seems to be nearly impossible.

The skin presents a wide spectrum of vasculitides, reflecting injury by circulating immune complexes, antibodies against endothelial cells, or cell-mediated immunity. LV is a common dermatologic disease and results from type III immune mechanisms, when antigen complexed to IgM or IgG activates the complement cascade sequence. Within the term "leucocytoclastic vasculitis," numerous clinical entities are assumed to share the affinity for small vessels in the skin and/or other organs. The characteristic clinical pattern of LV is the palpable purpura affecting dependent areas of the skin, mostly the lower extremities. LV might encompass a large variety of systemic diseases, but there is usually a reaction pattern to exogenous factors (e.g., drug-induced LV) or infectious disorders leading to LV, such as infection with *Mycobacterium* spp.<sup>6</sup>

The pathogenesis of all the perforating diseases is still unclear. Associations with chronic renal failure, diabetes mellitus,

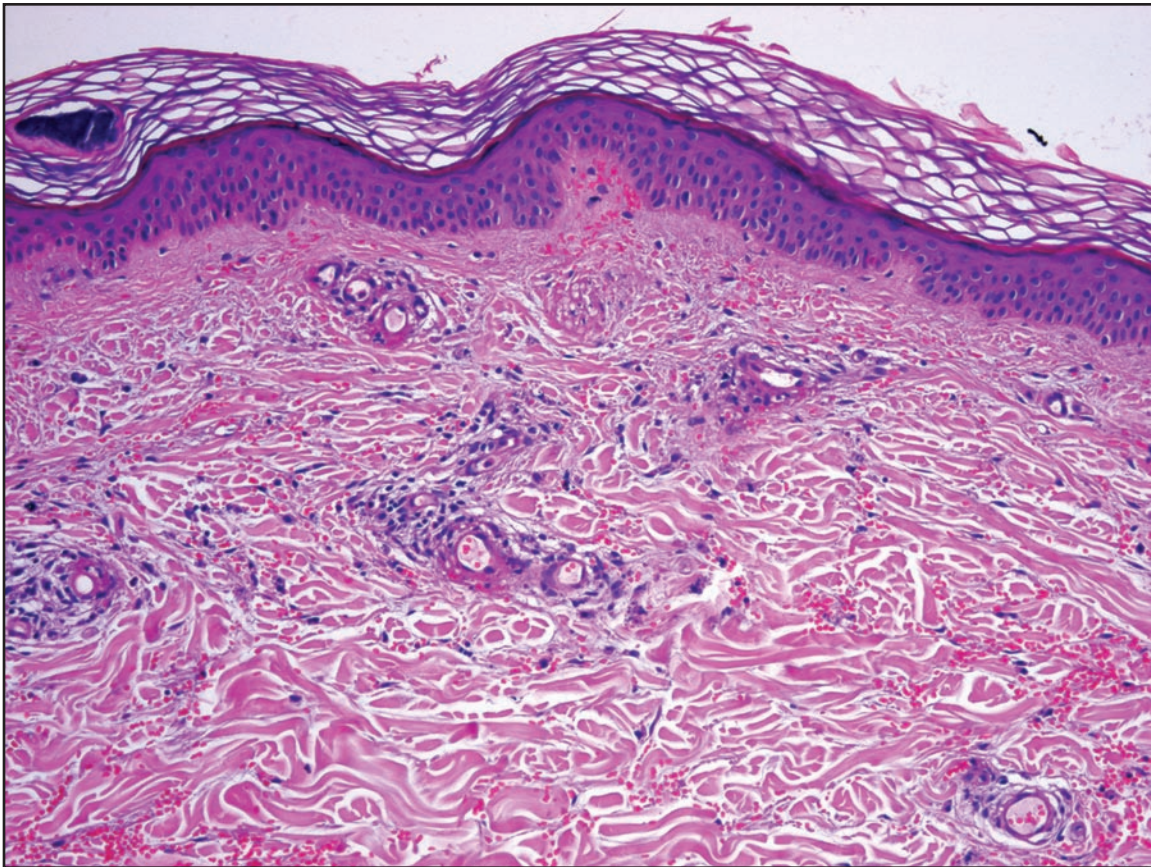


Figure 3. Perivascular infiltration with lymphocytes and neutrophils, transmural neutrophils; endothelial swelling with fibrin deposition. HE stain, magnification 100x.

psoriasis, juvenile acanthosis nigricans, hypertension, atherosclerotic cardiovascular disorders, primary sclerosing cholangitis, HIV infection and trauma have been described in the literature.<sup>8</sup> Up to now, numerous mechanisms of the genesis of RPC have been discussed; specifically, superficial trauma leading to necrobiosis of the dermal collagen and oxidative stress, as well as microvasculopathy, in diabetic individuals resulting in damage to collagen bundles.<sup>1,5</sup> Here, it can be discussed if the vasculopathy due to the leukocytoclastic vasculitis combined with mechanical manipulations invoked by the patient herself led to the distinct feature of perforating collagenosis. We must consider in this case that RPC was manifested primarily by vasculitic lesions, so additional factors in the pathogenesis of RPC apart from vasculopathy do exist. However, a combination of superficial epidermal trauma and microvasculopathy may cause or aggravate predisposed individuals to develop the typical clinical and histopathologic reaction pattern of RPC. Diagnostic procedures in this case were complicated by RPC lesions mimicking vasculitic sites, so that histopathologic investigations solely provide feasibility to make the correct diagnose. Thus, the presented case is unique concerning two characteristics: (1) the occurrence of an acquired reactive perforating collagenosis lacking classical associations, such as diabetes mellitus or renal disorders and (2) the coincidence of a perforating disease with LV.

#### References

1. Mehregan AH, Schartz OD, Livingood CS. Reactive perforating collagenosis. *Arch Dermatol* 1967; 96:277-82.
2. Faver IR, Daoud MS, Daniel Su WP. Acquired reactive perforating collagenosis: report of six cases and review of the literature. *J Am Acad Dermatol* 1994; 30:575-80.
3. Kawakami T, Saito R. Acquired reactive perforating collagenosis associated with diabetes mellitus: eight cases that meet Faver's criteria. *Br J Dermatol* 1999; 140:521-4.
4. Hoque SR, Ameen M, Holden CA. Acquired reactive perforating collagenosis: four patients with a giant variant treated with allopurinol. *Br J Dermatol* 2006; 154:759-62.
5. Munch M, Balsev E, Jemec GBE. Treatment of perforating collagenoses of diabetes and renal failure with allopurinol. *Clin Exp Dermatol* 2000; 25:615-6.
6. Crowson AN, Mihm MC Jr, Magro CM. Cutaneous vasculitis: a review. *J Cutan Pathol* 2003; 30:161-73.
7. Golusin Z, Poljacki M, Matovic L, Tasic S, Vuckovic N. Kyrles's disease. *Med Pregl* 2002; 55:47-50.
8. Gilaberte Y, Coscojuela C, Vázquez C, Roselló R, Vera J. Perforating folliculitis associated with tumour necrosis factor alpha inhibitors administered for rheumatoid arthritis. *Br J Dermatol* 2007; 156:368-71.
9. Langeveld-Wildschut EG, Toonstra J, van Vloten WA, Beemer FA. Familial elastosis perforans serpiginosa. *Arch Dermatol* 1993; 129:205-7.