Acquired reactive perforating collagenosis
A report of a typical case
Chengwen Fei, MD, Yao Wang, MD, Yu Gong, MD, Hui Xu, MD, Qian Yu, MD, Yuling Shi, MD, PhD∗

Abstract
Background: Reactive perforating collagenosis (RPC) is a rare form of transepithelial elimination, in which altered collagen is extruded through the epidermis. There are 2 types of RPC, acquired RPC (ARPC) and inherited RPC, while the latter is extremely rare. Here we report on 1 case of ARPC.

Methods: A 73-year-old female was presented with strongly itchy papules over her back and lower limbs for 3 months. She denied the history of oozing or vesiculation. A cutaneous examination showed diffusely distributed multiple well-defined keratotic papules, 4 to 10 mm in diameter, on the bilateral lower limbs and back as well as a few papules on her chest and forearm. Scratching scars were over the resolved lesions while Koebner phenomenon was negative. The patient had a history of type 2 diabetes for 15 years. Laboratory examinations showed elevated blood glucose level. Skin lesion biopsy showed a well-circumscribed area of necrosis filled with a keratotic plug. Parakeratotic cells and lymphocytic infiltration could be seen in the necrosed area. In dermis, sparse fiber bundles were seen perforating the epidermis. These degenerated fiber bundles were notarized as collagen fiber by elastic fiber stain, suggesting a diagnosis of RPC.

Results: Then a diagnosis of ARPC was made according to the onset age and the history of diabetes mellitus. She was treated with topical application of corticosteroids twice a day and oral antihistamine once a day along with compound glycyrrhizin tablets 3 times a day. And the blood glucose was controlled in a satisfying range. Two months later, a significant improvement was seen in this patient.

Conclusion: Since there is no efficient therapy to RPC, moreover, ARPC is considered to be associated with some systemic diseases, the management of the coexisting disease is quite crucial. The patient in this case received a substantial improvement due to the control of blood glucose and application of compound glycyrrhizin tablets.

Abbreviations: ARPC = acquired reactive perforating collagenosis, KD = Kyrle disease, MMP = matrix metalloproteinase, PF = perforating folliculitis, RPC = reactive perforating collagenosis, TEE = transepithelial elimination, TGF = transforming growth factor.

Keywords: acquired reactive perforating collagenosis, ARPC, reactive perforating collagenosis, RPC

1. Introduction
There are 4 classical forms of transepithelial elimination (TEE) disorders: reactive perforating collagenosis (RPC), elastosis perforans serpiginosa (EPS), perforating folliculitis (PF), and Kyrle disease (KD). These 4 diseases share common features of elimination of altered dermal components through epidermis; also they have some specific differentiating features.[1]

RPC is a rare form of TEE, in which altered collagen is genetically extruded through the epidermis.[2] There are 2 types of RPC, acquired RPC (ARPC) and inherited RPC and it is indicated that ARPC may be associated with several inflammatory or malignant systemic diseases.[3] Here, we reported a case of ARPC accompanied with diabetes mellitus.

2. Consent
This patient signed informed consent for the publication of this case report and the associated images. And this study was approved by the ethics committee of Shanghai Tenth People’s Hospital, Tongji University School of Medicine.

3. Case report
A 73-year-old female was presented to our out-patient department with strongly itchy papules over her back and bilateral lower limbs for 3 months without specific causes. The exacerbation of pruritus and lesions was presented through time. There was no history of oozing or vesiculation during the whole course of disease. Cutaneous examination revealed diffusely distributed multiple well-defined keratotic papules on the bilateral lower limbs and back, also a few papules on the chest and forearm. Those keratotic papules, 4 to 10 mm in diameter were adhered by keratotic plugs in the center. Scars caused by...
scratching could be seen over the resolved lesions (Fig. 1) and Koebner phenomenon was negative. Oral mucosa, vaginal mucosa, and cutaneous appendages were normal. Systemic examination was unremarkable. The patient had a history of type 2 diabetes for 15 years. Laboratory examinations showed elevated blood glucose level. Complete hemogram, hepatic function tests, and renal function tests were within normal ranges.

Biopsy showed a well-circumscribed area of necrosis filled with a keratotic plug. In the necrosed area, parakeratotic cells and lymphocytic infiltration could be seen. Sparse fiber bundles in dermis were seen to perforate epidermis. These degenerated fiber bundles were notarized as collagen fiber by elastic fiber stain, suggesting a diagnosis of RPC (Fig. 2). According to the onset age and the accompany disease, diabetes mellitus, we tended to make a diagnosis of ARPC.

The treatment with topical application of corticosteroids twice a day and oral antihistamine once a day along with compound glycyrrhizin tablets (manufactured by Japanese Minophagen Pharmaceutical Co (Ltd, 3F Shinjuku Mitsui Bldg #2, 3-2-11, Nishi-Shinjuku Shinjuku-ku, Tokyo 160-0023, JAPAN), containing 25 mg glycyrrhizin, 35 mg monoammonium glycyrrhizinate, 25 mg aminoacetic acid, and 25 mg methionine per tablet) 3 times per day and 2 tablets per time resulted in fair improvement over the period of 2 months. Moreover, an expert

Figure 1. Lesions of the patient presented as multiple well-defined keratotic papules on the bilateral lower limbs (A) and back (C) diffusely distributed, also few papules can be seen on the upper limbs (B).
on endocrinology was invited for a consultation to control the blood glucose.

4. Discussion

RPC is a rare skin disorder characterized by transepidermal elimination of altered collagen through the epidermis.[4] The first case was reported by Mehregan et al[5] in 1967. There are 2 patterns of RPC: inherited RPC is relatively rare and usually seen in children, while acquired RPC (ARPC) can usually be seen in adults,[2] which is sometimes accompanied by systemic diseases. ARPC is also said to be triggered by minor trauma, arthropod bites, scabies infection, and scratching.[6]

Although the pathogenesis of ARPC is unknown, over-expression of transforming growth factor-3 (TGF-β3) has been seen in many ARPC patients. TGF-β, matrix metalloproteinase-1, and tissue inhibitor of metalloproteinase-1 immunoreactivity were significantly increased in the lesions of ARPC,[7] indicating the crucial function of these factors in regulating epidermal homeostasis, postponing the re-epithelialization and remodeling, and changing extracellular matrix protein metabolism.

Moreover, some authors indicate that the genetic abnormality of the collagen causes the focal damage of RPC and leads to collagen perforation after necrolysis of the overlying epidermis. While some researches support the theory that transepidermal elimination of collagen is simply a reaction to chronic scratching or rubbing in pruritic diseases.[8]

There are 4 classical forms of TEE disorders: RPC, EPS, PF, and KD. These 4 diseases share common features of elimination of altered dermal components through epidermis and the differentiation is made according to the types of epidermal damage and the features of elimination material. The classic lesion and histopathological examination are the major distinguishing characteristics. The classic lesions of RPC are isolated papules, with keratotic plugs in the center, and are usually self-healing in 6 to 8 weeks without any therapy, but often recur. And the histopathological changes of the lesion show hyperplasia, thickening of epidermis, and widening of papillary dermis, with degenerated collagen bundles in the early period. In the later period, cup-shape invagination of epidermis can be seen, which is filled with keratotic plug, intermingled with parakeratotic cells, degenerated collagen fibers and cell fragments. Necrotic basophilic collagen fibers are eliminated to epidermis. The lesions of EPS patients are usually keratosis papules, with desquamation or atrophy in the center. Those asymptomatic or pruriginous plaques grouped in arciform or serpiginous
pattern. Lesions of PF patients are isolated papules, with white keratotic plugs in the center, curly can be seen in the keratotic plug. The lesions of KD are papules filled with conical keratotic plugs, which are always found near follicle. Histopathological examination is crucial for differential diagnosis.

We reviewed some cases of ARPC reported in the literature and tried to summarize the clinical characteristics, effective management, as well as prognosis. In general, the skin lesions of the majority were described as multiple round plaques and nodules with central hyperkeratotic plugs, usually distributing on the extremities and back, sometimes face and neck. Pruritus was common but Koebner phenomenon was not mentioned in most of the cases, not as previously reported. Of these patients, the most common associated diseases were diabetes mellitus (DM, type 1, and type 2 were both reported) and complications of DM, including chronic renal failure, cardiopathy, and retinopathy. Some autoimmune diseases were regarded to be associated as well, such as systemic lupus erythematosus, vasculitis, dermatomyositis, and Mikulicz disease (an IgG4-related disease). Moreover, some malignancies, including lymphoma, thyroid carcinoma, and breast carcinoma, were also reported as coexisting diseases.

Currently, there is no efficient therapy to RPC. Treatment is mainly aimed at controlling the symptom. In the literature, multiple treatments, including topical corticosteroids under occlusion, emollients, keratolytics retinoids, systemic antihistamines, allopurinol, isotretinoin, narrow-band ultraviolet B phototherapy, and liquid nitrogen cryotherapy, have been tried, with different degrees of improvements.

In the case of our patient, compound glycyrrhizin tablet was one of the treatments. Glycyrrhizin, an active component of liquorice roots, had a glucocorticoid-like effect and was used to manage some autoimmune diseases, such as systemic lupus erythematosus, vasculitis, and alopecia areata. However, it was the first time that CGT was reported to be used to treat ARPC to our knowledge. Moreover, since ARPC is considered to be associated with some systemic diseases, the management of the coexisting disease is also beneficial. As for this patient, who got a significant amelioration without recurrence, the control of blood glucose was quite crucial.

In conclusion, we reported a rare case of ARPC with a good prognosis. It indicated that recognition and control of associated disease and CGT therapy may help to treat ARPC.

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