Acquired Reactive Perforating Collagenosis: Case Series

Abstract

Acquired reactive perforating collagenosis (ARPC) is one of the four acquired perforating dermatoses. The condition is characterized by transepidermal elimination of altered collagen. These are rare and underdiagnosed clinical entities and a few studies are available in the Indian literature. The present study described 15 patients of ARPC with underlying comorbidities and clinical response to systemic antihistamines, doxycycline, and topical clobetasol propionate. Of total 15 patients, 10 were men and the other five were women. Except two patients, diabetes mellitus was seen in 13 patients. Three patients had mild proteinuria. Four patients were known hypertensive. Itchy, papular, nodular lesions with central keratotic plug were seen commonly on the limbs and trunk. In another five patients, lesions were seen other than limbs and trunk, on the abdomen, chest, and back. In one case, giant plaques of more than 2 cm were present on the abdomen and limbs. In another patient, psoriasis lesions were concomitantly seen with ARPC lesions. Koebner's phenomenon was observed in six patients. The histopathological features of skin lesions in all 15 patients were consistent with ARPC. In all the patients, the lesions regressed within 4-6 weeks with topical clobetasol propionate and antihistamines. In three patients, systemic doxycycline was found to hasten the regression of lesions. Recurrences were observed in six patients during the follow-up period of 3 months.

Keywords: *Acquired reactive perforating collagenosis, diabetes, doxycycline, histopathology, topical steroid creams.*

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Introduction

In recent times, the term acquired perforating dermatoses is broadly applied to all perforating dermatoses including the four traditional classic forms like Kryle's disease, reactive perforating collagenosis, perforating folliculitis, elastosis perforans serpiginosa, and others.[1] From a clinician's perspective, there are subtle clinical and histopathological differences among these four major perforating dermatoses. Acquired reactive perforating collagenosis (ARPC) is the most common prototype of these perforating dermatoses. It was first described by Mehergen in 1967 as a new and distinct clinico-pathological entity.[2] Later on, Faver[3] suggested the following criteria for ARPC: onset of lesions after the age of 18 years, lesions of umblicated papules, nodules with central adherent keratotic plugs, and histopathological findings of elimination of necrotic, basophilic collagen bundles into a cup-shaped epidermal depression.

We described 15 patients with ARPC who met the above criteria and discussed the etiology, particularly its relationship with diabetes and other systemic diseases, diagnosis, and management of this rare clinical condition. The patients with other perforating conditions like Kryle's disease were not included in the study.

Cases

We studied 15 patients of ARPC with proven histopathological features who attended to our center during the period 2019-2021. Complete clinical and demographic data were obtained from all the patients. An informed and written consent was obtained from all the patients. All the relevant hematological, biochemical, and serological tests were done in addition to lesional skin biopsies for histopathological examination. Special stains like Masson's trichome and Van Gieson stains were done to highlight collagen and elastin.

Table 1 summarizes the clinical and demographic data of all 15 patients. Men were 10 and the other five were women. Their age ranged from 41-86 years (mean age: 58.4 years). Of these 15 patients, 13 had associated diabetes and two were

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Table 1: Case details

Patient No.	Age(yrs)/ Gender	Type of lesion/ duration(months)	Distribution of skin lesions	Pruritus	DM duration (yrs)	Chronic kidney disease	Other disorders
1	65 yr /M	Papules/ (4)	Limbs	+++	Yes/(20)	Mild proteinuria	-
2	69 yr/M	Papules, nodules / (3)	Limbs, trunk	+++, Koebner's present	Yes/(10)	-	-
3	45 yr/F	Papules, linear lesions/ (5)	Limbs, trunk	++	Yes/(5)	-	-
4	53 yr/M	Papules/ (4)	Limbs, trunk	+++ Koebner's present	Yes/(6)	-	-
5	43 yr/M	Nodules, linear papules/ (2)	Thighs, buttocks, Lower limbs	++	Yes/(7)	-	-
6	56 yr/F	Papules/ (4)	Limbs, trunk	+++ Koebner's present	Yes/(30)	-	Peripheral neuropathy
7	58 yr/F	Papules, crusted plaques, giant lesions /(2)	Limbs, trunk, arms, chest, scalp	+++ Koebner's present	Yes/(8)	Mild proteinuria	-
8	62 yr/M	Annular lesions/(3)	Lower limbs	++	No	-	Psoriasis, hypertensive
9	70 yr/M	Papules, annular/(2)	Limbs	+++ Koebner's present	Yes/(5)	-	Hypertensive
10	52 yr/F	Nodules, linear papules/(2)	Limbs	+++	Yes/(4)	-	-
11	86 yr/M	Crusted papules, plaques/(2 wks)	Thighs, trunk	++	Yes/(15)	Mild proteinuria	Hypertensive
12	67 yr/M	Keratotic papules/(2 wks)	Lower limbs	++	Yes/(30)	-	Hypertensive
13	45 yr/F	Linear, keratotic papules/(4)	Lower limbs	+++	No	-	-
14	41 yr/M	Papules, linear, crusted lesions/ (2)	All over the body including scalp, face	++++ Koebner's present	Yes/(2)	-	-
15	64 yr/M	Papules/(2)	Limbs	++	Yes/(20)	-	-

nondiabetic. Patients 1, 7, and 11 had altered renal profile with mild proteinuria. Patients 8, 9, 11, and 12 were known hypertensives. Patient 6 had a long history of poorly controlled diabetes with peripheral neuropathy. Patient 8 was nondiabetic but a known case of psoriasis.

All patients presented with intensely pruritic lesions and Koebner's phenomenon was observed in six cases. We did not observe any correlation between severity of itching and proteinuria and severity of diabetes. The duration of the skin lesions ranged from two weeks to four months. The lesions were predominantly on the lower limbs, buttocks, and trunk. One patient (Patient 14) had generalized lesions all over the body including scalp, palms, and soles. Majority of our patients had multiple, umblicated papules with central keratin plug, some are distributed in linear and annular patterns [Figure 1a, 1b]. Patient 7 had multiple, giant, crusted plaques of varying sizes all over the abdomen, trunk, chest, thighs, and limbs [Figure 2a, 2b]. Patient 8 had typical ARPC lesions adjacent to psoriatic lesions on the lower limbs [Figure 3a, 3b]. The histopathological features of skin lesions in all 15 patients were consistent with ARPC: cup-shaped epidermal depression with a central crater extending from epidermis to the dermis and containing neutrophils, basophilic debri, parakeratotic horny material, and degenerated collagen in vertical strands [Figure 4a, 4b]. The epidermis was thin or absent at the base of the crater where the collagen was being extruded. Masons trichome stain revealed vertically oriented collagen bundles [Figure 5] and Van Gieson stain failed to stain elastin fibers.

All the patients were treated with a combination of systemic antihistamines and topical clobetasol 0.05% cream for 4-6 weeks depending upon the individual's clinical lesions. In majority of patients, pruritus subsided within 2-4 weeks, but the regression of clinical lesions took 4-6 weeks. Three patients with extensive lesions were managed with systemic doxycycline 100 mg twice daily for 15 days in addition to the above. Doxycycline was found to be useful in getting rapid clearance of lesions. Recurrences were observed in six patients during the follow-up period of 3 months. In two patients, recurrences were observed within 2 weeks after stopping the treatment.

Discussion

Reactive perforating collagenosis (RPC) is a rare skin disorder characterized by transepidermal elimination of

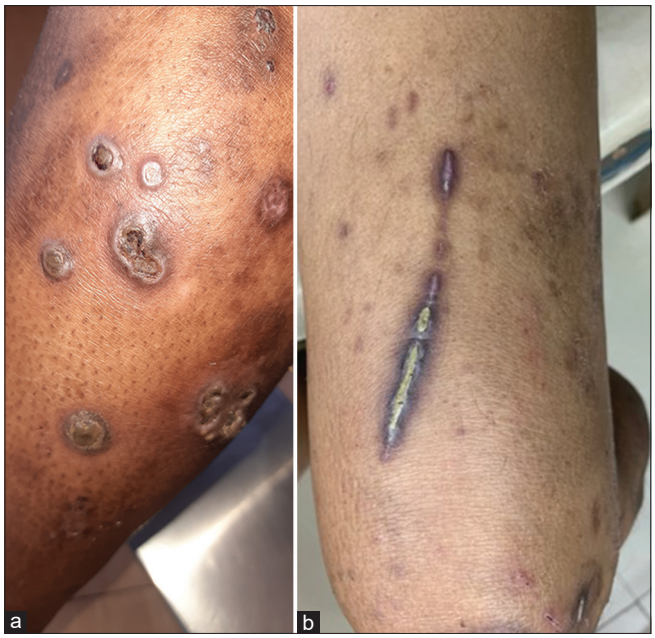

Figure 1: (a): Umblicated papules with central keratin plug. (b): Koebner's phenomenon

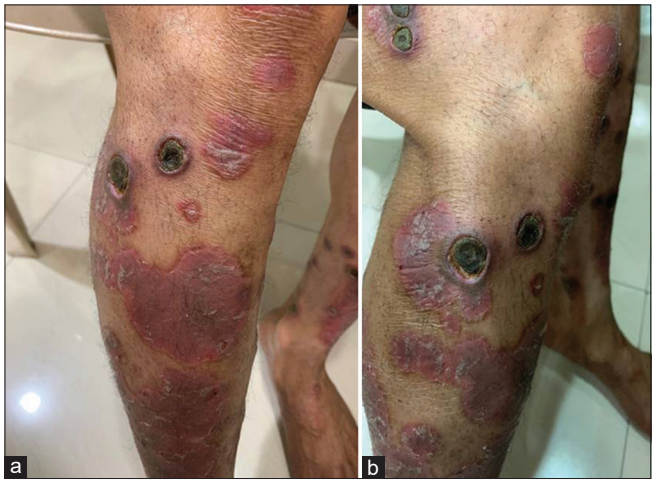

Figure 3: (a&b): Umblicated papules with central keratin plug with psoriatic lesions on lower limbs

altered collagen through epidermis. There are two patterns of RPC: inherited RPC is relatively rare and usually seen in children, whereas acquired RPC can usually be seen in adults which are sometimes accompanied by systemic diseases like diabetes mellitus and many other conditions.[2] ARPC is essentially a pruritic disease and said to be triggered by minor trauma, arthropod bites, scabies, and subsequent scratching. Although the pathogenesis of ARPC is unknown, it has been suggested that mild superficial trauma in genetically susceptible individuals leads to necrobiosis of papillary dermal collagen that is subsequently eliminated by a transepidermal route. Recently, overexpression of transforming growth factor-3 (TGF-β3) and extracellular matrix proteins were found to be significantly increased in the lesions of ARPC,[4]

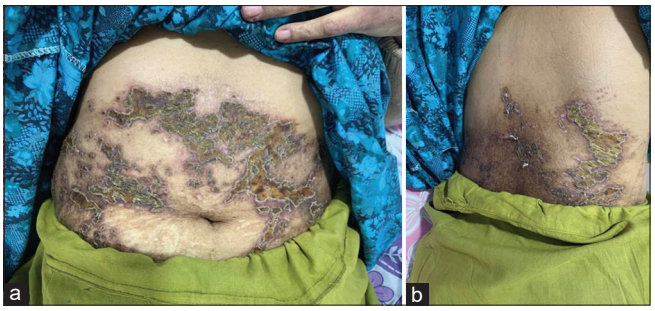

Figure 2: (a&b): Multiple, giant, crusted plaques of varying sizes all over the abdomen and trunk

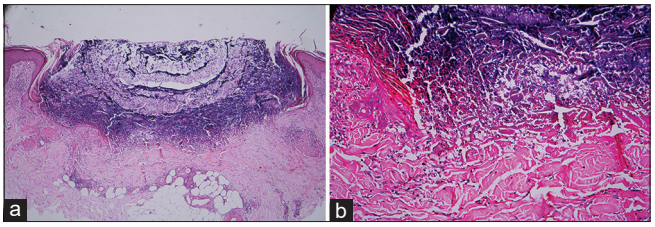

Figure 4: (a): Cup-shaped epidermal depression with a central crater containing neutrophils, basophilic debri, parakeratotic horny material and degenerated collagen in vertical strands (H&E x50). (b): High-power view highlighting the degenerating collagen bundles, vertically oriented, and the basophilic debris within the crater (H&E x200)

indicating the crucial function of these factors in regulating epidermal homeostasis, postponing the re-epithelization, and remodeling and changing extracellular matrix protein metabolism. Moreover, some authors indicate that the genetic abnormality of the collagen causes the focal damage and leads to collagen perforation after necrolysis of the overlying epidermis in RPC. Some researchers support the original Mehergan's theory that transepidermal elimination of collagen is slightly a reaction to chronic rubbing or scratching in pruritic disease.[5]

Our study in addition to various previous studies[6-8] showed that there is a strong relationship between ARPC and diabetes. The reasons for this association are exactly not known. Akoglu[9] *et al*. have suggested that diabetic patients are predisposed to ARPC. In diabetic patients, increased oxidative stress and glycosylated end products cause cross-linking of collagen. Trauma and scratching associated with poor blood supply (diabetic vasculopathy) may also lead to dermal necrosis and alteration of connective tissue.[8,10] There is evidence that the eliminated collagen is type IV collagen and elevated levels of serum and tissue fibronectin, possibly by transforming growth factor beta (TGF-β) or platelet-derived growth factor may incite an increased epithelial migration and proliferation and finally results in perforation.[11,12]

ARPC has also been commonly associated with chronic renal failure with or without dialysis and it was the third common skin complaint in the dialysis population studied. In our series, only three patients had mild proteinuria with normal renal parameters. In addition to diabetes and renal failure, ARPC has also been reported in association

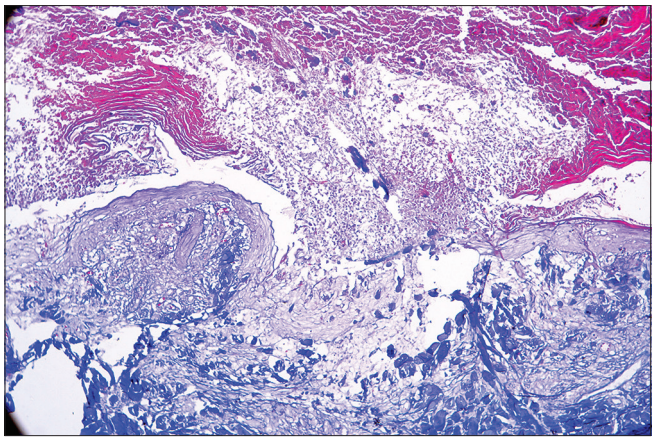

Figure 5: Masson's trichome stain revealing vertically oriented collagen bundles (400x)

with hypertension, chronic venous insufficiency, heart diseases, lymphoma, AIDS, hypothyroid, hyperparathyroid, liver dysfuction, atopic eczema, and malignancy. Another proposed mechanism involves epidermal and dermal abnormalities associated with metabolic disorders and dermal micro deposits (e.g., calcium) in patients with chronic renal failure. Vasculopathy underlying chronic venous insufficiency or hypertension is another potential mechanism involved in the pathogenesis of ARPC.[2,10]

In our study, a known psoriatic patient developed multiple annular necrotic lesions with keratotic plug on the lower limbs adjacent to active psoriatic patches. This showed that ARPC can develop in pre-existing psoriatic lesions. In this particular case, it maybe a coincidental or concomitant existence of both psoriasis and ARPC.

ARPC presents as itchy papules, or nodules, umblicated hyperkeratotic lesions commonly on the trunk and lower limbs. They may occur uncommonly on the back, chest, face, and scalp. Rarely, giant hyperpigmented hyperkeratotic plaques of more than 2 cm in diameter were reported.[13,14] In our series of 15 cases, one patient had large crusted hyperkeratotic giant plaques over the abdomen, trunk, lower, and upper limbs. One had eruptions all over the body including face and scalp; such generalized lesions are uncommon. Almost always the lesions are pruritic and new lesions appear followed by Koebner's phenomenon. The lesions heal with hyperpigmentation. In this study, pruritus was observed in all cases and Koebner's phenomenon was seen in six cases.

Various treatments have been tried with ARPC. These include topical and systemic steroids, topical and systemic retinoids, antibiotics, NBUVB (Narrow band ultra violet B) therapy, methotrexate, and allopurinol.[13,14] In our series, majority of the patients have had a significant improvement with topical potent steroid cream with antihistamines and proper management of diabetes mellitus. Oral doxycycline 100 mg BD for 15 days was given in addition to above treatment in 3 patients. There was a rapid clearance of lesions with doxycycline in these patients. Doxycycline may act as immunomodulator, anti-inflammatory and may inhibit interstitial collagen loss potently by inhibiting matrix metalloproteinase.[15,16]

Our report of 15 cases of ARPC further establishes that ARPC is another cutaneous marker for underlying diabetes. In addition to localized lesions, generalized giant forms mimicking various dermatoses can occur and skin biopsy is mandatory to confirm the diagnosis. ARPC lesions can concomitantly occur with other skin diseases like psoriasis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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