Case Report

PRURITIC RASH IN AN ELDERLY PATIENT WITH UNCONTROLLED DIABETES MELLITUS

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ABSTRACT

Objective: Acquired reactive perforating collagenosis is an uncommon skin disease that belongs to a group of dermatologic disorders characterized by transepidermal elimination of dermal material. It is highly associated with systemic disease, primarily diabetes mellitus and dialysis-dependent chronic renal failure.

Methods: A 70-year-old female with 20 years of poorly controlled type 2 diabetes mellitus presented with a 6-month history of multiple pruritic erythematous papules and nodules with central hyperkeratosis, involving her right dorsal arm. Histologic examination was consistent with acquired reactive perforating collagenosis. In addition to topical treatment of the disease, the patient was referred to endocrinology for appropriate management of her underlying diabetes mellitus.

Results: Ideal treatment should involve both the endocrinologist and dermatologist. Control of the underlying systemic disease, in this case diabetes, as well topical or systemic medications can both help to improve this condition. Our patient re-established care with her endocrinologist who adjusted her medication regimen, resulting in improved hemoglobin A1c values. Our patient additionally benefited from topical betamethasone cream, ammonium lactate, and pimecrolimus application. The combined therapy led to resolution of her pruritic rash.

Conclusion: This case highlights the importance of the skin exam by the endocrinologist, as he or she plays a unique role in identifying this rare and difficult-to-treat dermatologic disease. Early detection and prompt referral to a dermatologist are crucial in preventing progression of disease, treating the disease, and improving the patient’s quality of life. (AACE Clinical Case Rep. 2019;5:e146-e149)

INTRODUCTION

Acquired reactive perforating collagenosis (ARPC) is a unique skin disease belonging to the group of perforating dermatoses, which are characterized by transepidermal elimination of dermal material such as collagen, elastin, or fibrin (1). These perforating dermatoses may be subdivided based on the eliminated dermal material and include Kyrle disease, elastosis perforans serpiginosa, perforating folliculitis, and acquired reactive perforating collagenosis. ARPC eliminates dermal collagen and is typically associated with systemic disease, most notably diabetes mellitus, dialysis-dependent chronic kidney disease, and malignancy. This case report examines the typical presentation of ARPC and reviews its pathogenesis, relationship with associated diseases, and treatment options. Given its significant association with diabetes mellitus, the endocrinologist should be familiar with this disease. Early recognition and appropriate treatment can help slow progression of the disease and improve patient quality of life.

Abbreviation:
ARPC = acquired reactive perforating collagenosis

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CASE REPORT

Our patient was a 70-year-old African American woman who presented to the dermatology clinic for evaluation of a persistent rash on her right arm that had been present for 6 months (Fig. 1). The rash had initially begun as small, grouped pruritic red papules that spread proximally and developed a crust. She denied blisters or drainage from the sites. She had previously been evaluated by another dermatologist for this issue and been prescribed betamethasone and ammonium lactate cream with minimal improvement. The patient’s medical history was notable for poorly controlled type 2 diabetes mellitus, diagnosed 20 years previously, as well as hypertension, peripheral vascular disease, and coronary artery disease. Her most recent hemoglobin A1c, measured 4 months prior to presentation, was 11.3% (100 mmol/mol).

Physical exam showed a somewhat linear grouping of approximately 30 dome-shaped papules and nodules with keratotic cores on the dorsal right forearm. There was an area of hypopigmentation surrounding the papules and nodules, likely the result of prolonged topical steroid use. Histologic examination of a 4-mm punch biopsy taken from her right arm revealed epidermal ulceration with a dense seropurulent crust. Collagen fibers were noted within the crust and penetrating through the ulceration as well, consistent with a reactive perforating collagenosis (Figs. 2 and 3). This was further highlighted by a trichrome stain (Fig. 3).

The betamethasone cream was discontinued due to concerns over prolonged corticosteroid use. It was replaced with pimecrolimus, and the ammonium lactate cream was continued. The patient additionally re-established care with an endocrinologist. Her previous regimen of insulin aspart protamine/insulin apart (70/30) 55 U twice daily and metformin 1,000 mg twice daily was adjusted. The insulin aspart was discontinued, and she was started on insulin glargine 50 U nightly and empagliflozin 10 mg. Her metformin 1,000 mg was continued. Her hemoglobin A1c at that time was 10.6% (92 mmol/mol). Upon follow-up with the dermatology clinic 3 weeks later, the patient’s rash had significantly improved, with decreased erythema and significantly decreased pruritus. Her most recent hemoglobin A1c, taken 4 months later, was 8.1% (65 mmol/mol). By that time, her rash had almost completely resolved (Fig. 4).

DISCUSSION

ARPC is a rare disease characterized by transepidermal elimination of dermal collagen. First described by Megregan et al (2) in 1967, the disease typically presents as a group of umbilicated hyperkeratotic papules with a central adherent plug. They may coalesce to form larger lesions and are commonly located on the trunk, shoulder girdle, gluteal region, and the extensor surfaces of the extremities (3,4). Rarely, patients may develop a giant variant of ARPC with plaques up to several centimeters in diameter (3). Patients typically complain of significant pruritus that at times comes on suddenly. Pain may be present as well.

A review of 101 cases of ARPC by Karpouzis et al (4) showed a slight male predominance, with 59% of cases being reported in male patients. The age ranged from 29 to 96 years, with the majority of patients belonging to the 50 to 59 years age group.

Histologic evaluation is required for diagnosis. The majority of cases show a dome-shaped lesion with central epidermal ulceration with overlying hyperkeratotic crust. The keratotic plug extruding from the ulceration contains varying degrees of vertically oriented collagen fibers, neutrophils as well as their nuclear debris, and altered connective tissue. There may be reactive changes to the epidermis surrounding the ulceration, such as acanthosis, hypergranulosis, and hyperkeratosis (4-6).

ARPC is frequently associated with systemic disease, most notably diabetes. Of the 101 cases reviewed by Karpouzis et al (4), 62% of patients with ARPC also had diabetes mellitus with or without its complications, including peripheral vascular disease, retinopathy, and cardiomyopathy. Our patient had poorly controlled type 2 diabetes mellitus as well as its sequela of peripheral vascular disease, consistent with the typical patient who develops this dermatologic disease. Both type 1 and type 2 diabetes mellitus have a strong association with ARPC, although the exact mechanism remains unclear at this time. Dialysis-dependent chronic kidney disease has also been associated, occurring in up to 10% of patients undergoing dialysis (7), although many of these patients were additionally reported to have diabetes. While diabetes and dialysis-dependent...
chronic renal failure are the most common diseases associated with ARPC, other diseases and metabolic derangements have been reported as well, including hyperuricemia, hypothyroidism, Hodgkin disease, IgA nephropathy, hyperparathyroidism, hepatocellular carcinoma, thyroid cancer, prostate cancer, AIDS, acute leukemia, sclerosing cholangitis, and dermatomyositis (8). Pharmacologic agents such as clopidogrel (9) and erlotinib (10) have been reported as well.

The exact etiology and pathophysiology of ARPC remains unclear. It has been suggested that a disease-associated pruritus leads to scratching, which then causes microtrauma, leading to degeneration of collagen fibers, elimination of the fibers, and abnormal keratinization in genetically susceptible individuals (11,12). Support for this theory cites the location of the disease, which tends to be in areas that can be reached by the hand for scratching. Additional support is found with the presence of the Koebner phenomenon (13,14). It has also been suspected that the inappropriate glycosylation that occurs in diabetes mellitus may lead to impaired differentiation of the epidermis and dermal-epidermal junction (15).

While multiple treatment modalities have been suggested, there have been no randomized controlled trials to date to assess their efficacy. Several case reports reveal that treatment of the underlying disease could have significant benefit in the treatment of ARPC (16-19). However, upon review of the literature, there are no reported cases prior to this one showing improved rash specifically with improved glycemic control in patients with diabetes. As the vast majority of patients have associated diabetes, the endocrinologist plays a vital role in treating this

![Fig. 2. (A) The biopsy reveals epidermal ulceration with a dense seropurulent crust. Collagen fibers are noted within the debris and also penetrating through the ulceration. The underlying dermis contains chronic inflammation. (hematoxylin and eosin, 20×). (B) A Masson’s trichrome stain is used to highlight the transepidermal elimination of collagen (staining blue) through the epidermis. (Masson’s trichrome, 20×).](image1)

![Fig. 3. A Masson’s trichrome stain is used to highlight the transepidermal elimination of collagen (staining blue) through the epidermis. Arrows are used to further highlight vertically oriented collagen fibers as they exit through the dermis into the epidermis (Masson’s trichrome, 40×).](image2)

![Fig. 4. Resolved patient rash right dorsal forearm with post-inflammatory pigment changes, 5 months after topical treatment initiation with dermatologist and change in diabetes medication regimen.](image3)
dermatologic condition. In addition, referral to a dermatologist is recommended. Treatment of pruritus is essential to stop the scratch-itch-microtrauma cycle. Treatment options include: topical retinoids, topical or intralesional glucocorticoids, topical calcineurin inhibitors, keratolytics, and phototherapy. Systemic antihistamines, doxycycline, rifampin, retinoids, and allopurinol have also been shown to be effective (20). Allopurinol is hypothesized to be effective specifically in diabetic patients by blocking hyperglycemia-induced collagen cross-linking and by decreasing collagen damage by oxygen free radicals via its inhibition of xanthine oxidase (21). However, these treatment options are only suggestions based on case reports, as randomized clinical trials and further research are needed to better evaluate the efficacy of these medications.

When the endocrinologist encounters a rash that may be concerning for ARPC, the following approach is recommended: in addition to achieving glycemic control through diet and medication adjustment, prompt referral should be placed to dermatology. Topical steroids may be initiated for symptomatic relief while the patient awaits their dermatology appointment. However, it is perfectly acceptable to defer skin treatment to the dermatologist.

CONCLUSION

The endocrinologist is in a unique position to be able to identify this rare disease process and facilitate appropriate treatment. The diagnosis of reactive perforating collagenosis should be considered in any patient with diabetes who presents with a new pruritic skin lesion. Being aware of this condition can allow for early detection, initiation of treatment, and prompt referral to a dermatologist, which is crucial in preventing progression of disease, treating the symptoms, and improving the patient’s quality of life.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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