Acquired reactive perforating collagenosis combined with MRSA: A case report

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Abstract. Acquired reactive perforating collagenosis (ARPC) is a rare chronic skin disease associated with various internal diseases, particularly diabetes and chronic renal failure. The present study describes the case of a patient with ARPC combined with methicillin-resistant *Staphylococcus aureus* (MRSA), in an aim to broaden the current understanding of ARPC. A 75-year-old female presented with a 5-year history of pruritus and ulcerative eruptions on the trunk of her body, which became more severe within 1 year. A cutaneous examination revealed a diffuse distribution of erythema and papules, and nodules of various sizes, some of which sagged at the center and had a dark brown crust. A histopathological analysis revealed typical perforations of the collagen fibers. The patient was initially treated with topical corticosteroids and oral antihistamines for skin lesions and pruritus. Medications for glucose control were also administered. Upon the second admission, a combination of antibiotics and acitretin was added. The keratin plug shrank, and the pruritus was relieved. To date, to the best of our knowledge, this is the first reported case of concurrent ARPC and MRSA.

Introduction

Acquired reactive perforating collagenosis (ARPC) is a rare form of dermatosis. In 1989, Rapini *et al* (1) proposed the umbrella term acquired perforating dermatosis (APD), encompassing cases with an onset in adult life, and associated with diabetes mellitus and chronic renal failure, particularly in patients on dialysis. APD forms with perforating folliculitis, Kyrle's disease and elastosis perforans serpiginosa, which are forms of perforating dermatosis (2). The prevalence and incidence of ARPC remain unknown, with only a limited number of reported cases (3-6). Karpouzis *et al* (7) once reported the epidemiological features of ARPC by analyzing the diagnostic data of 101 cases, indicating that the peak onset age ranged from 50 to 59 years.

The diagnosis of ARPC is made according to a histopathological analysis, the age at onset and typical skin lesions. Faver *et al* (8) stated the criteria for ARPC as follows: The onset of lesions after the age of 18 years, umbilicated papules or nodules with a central adherent keratotic plug, and the elimination of necrotic collagen tissue within an epithelium-lined crater. Accordingly, the treatment of ARPC continues to be challenging. It usually consists of a wide range of treatment measures. Apart from the treatment of any underlying disease, systemic steroids and retinoids, as well as UVB phototherapy are well-established treatment options (9). However, in spite of various therapeutic measures, the prognosis of patients with this condition is not satisfactory. The symptoms of the majority of reported cases can only be improved rather than cured. It is worth noting that infection is a key factor affecting the efficacy of therapeutics for ARPC. The present study describes the case of a patient with ARPC combined with methicillin-resistant *Staphylococcus aureus* (MRSA), which was effectively treated by the addition of sensitive antibiotics.

Case report

On July, 2021, a 75-year-old female patient was admitted to the Department of Dermatology, Affiliated Hospital of Qingdao University of University, Qingdao, China. She had erythema and itchy papules on her back 5 years prior. The lesions gradually became exacerbated with severe pruritus, spreading all over the trunk of her body, right upper and left lower limb, part of which was covered with crust (Fig. 1). The lesions then improved by the topical administration of fluticasone; however, the disease relapsed several times. She presented with a 12-year-history of diabetes and well-controlled blood glucose level by the daily subcutaneous insulin injection and oral metformin and acarbose.

A cutaneous examination revealed diffusely distributed multiple keratotic, hyperpigmented papules on the limbs, back, chest and abdomen, and a linear distribution of the skin lesions. The diameter of the papules ranged from 2 to 8 mm, with keratotic plugs and a crust in the center.

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Laboratory examinations revealed elevated eosinophil levels ($1.24x10^9$/l). The urine analysis indicated positive leucocyte, protein and occult blood. The liver function test revealed decreased total protein (63.3 g/l) and prealbumin (150 mg/l) levels. Thyroid dysfunction was also observed in this patient. Fasting blood glucose levels reached 6.43 mmol/l. MRSA was identified from the bacterial culture.

Lesion skin biopsy samples examined using hematoxylin and eosin staining (as described below) revealed a cup-shaped depression plugged with necrotic inflammatory debris. The majority of the collagen was found in the lower part of plug, and the surrounding epidermal spinous layer was thickened. Lymphocytes, neutrophils and eosinophils infiltrated the superficial dermis vessels. Masson's staining(as described below) revealed collagen fibers penetrating the surface (Fig. 2). Masson's staining for elastin fibers was negative.

The patient was treated with topical corticosteroids, antihistamine tablets (Ebastine, oral, 10 mg, once a day) for the skin lesion and pruritus, glycyrrhizin (60 mg, intravenous, once a day) to regulate immunity, and acitretin (20 mg, oral, once a day) to regulate epithelial cell keratinization. In addition, an insulin injection (the unit was adjusted according to the blood glucose levels) together with acarbose tablets (100 mg, oral, twice a day) were applied for glucose control. At 1 week following admission, the treatment efficacy was found to be poor and the lesions continued to progress. Considering the possibility of local secondary infection, the patient was also treated with a combination polymyxin B cream and a bacterial culture examination was performed. Minocycline (100 mg, oral, once a day) was also added to the treatment regimen according to the results of the bacterial culture and drug sensitivity test, which indicated that the strain cultured at the site of infection was MRSA and was sensitive to minocycline. On the day of hospital discharge, the keratotic plug had narrowed down slightly; however, the patient noted a marked reduction in the itchiness of the lesions. Subsequently, her outpatient follow-up records were examined and her condition was found to be gradually in remission within 6 months.

Staining procedures. Under aseptic operation, two sections of skin lesion were obtained. One was stained with hematoxylin and eosin (H&E) and the other with Masson's stain. For H&E staining, the tissues were then fixed in 10% neutral phosphate-buffered formalin (ZheJiang Shitai Industrial Co., Ltd.) for 24 h at room temperature. This was followed by dehydration with ethanol. The tissue sections were then infiltrated with paraffin wax and cut into sections of a thickness of 3 μm. The tissues were washed three times with xylene for 10 min each and washing with anhydrous alcohol and diluted alcohols (95 and 70%) before washing with water. The sections were then stained with hematoxylin solution (Roche Diagnostics) for 12 min at room temperature. The unbound hematoxylin was then removed with water rinses followed by an optional differentiation step using 1% acid alcohol and bluing for 25 min. Eosin (Roche Diagnostics) was then used to stain in the cytoplasmic counterstain for 5 min at room temperature. Following dehydration with 95 and 100% alcohol, the sections were sealed with neutral gum and examined under a microscope (ECLIPSE Ci-L, Nikon Corporation).

For Masson's staining, the procedure before staining was the same as that described above H&E staining. The nuclei were stained with Weigert's iron hematoxylin (Roche Diagnostics) for 5 min at room temperature. This was followed by washing with distilled water and differentiation with 1% hydrochloric acid alcohol. Following rinsing running water for a few minutes, the sections were stained with Masson's trichrome solution (Roche Diagnostics) for 5 min at room temperature. The sections were then soaked in 2% glacial acetic acid solution for 1 min followed by differentiation with 1% phosphomolybdic acid solution for 5 min. The sections were then directly stained with aniline blue or light green liquid for 5 min at room temperature followed by soaking in 0.2% glacial acetic acid solution again for 20 sec. Subsequently, 95% alcohol was used for dehydration multiple times. Finally, dehydration was performed with anhydrous alcohol, washing with xylene and sealing with neutral gum. An ECLIPSE Ci-L microscope (Nikon Corporation) was then used to examine the sections. All stains used were supplied by Roche Diagnostics.

Discussion

Reactive perforating collagenosis (RPC) was first described in 1967 by Mehregan *et al* (10). There are two types of RPC, ARPC and inherited RPC (IRPC). IRPC, hereditary with autosomal dominant transmission, is more common in infants and children, whereas ARPC usually develops in adults. The patient in the present study, without a family history of RPC, had presented with ARPC and diabetes, which already confirmed a cause-effect association. The pathogenesis of ARPC remains unknown. It has been suggested that mild superficial trauma, sometimes in association with diabetic vasculopathy and a hypoxic state, in genetically susceptible individuals, leads to necrobiosis of papillary dermis collagen that is subsequently eliminated by a trans epidermal route (7). This hypothesis has been supported by the findings of a positive stain with periodic acid-Schiff (PAS), and the thickening of the vessel walls in the upper dermis of diabetic patients with APD (11). PAS-positive and thickened vessel walls were detected in all 8 diabetic patients in the study by Kawakami and Saito (12). Depending on all these observations, diabetic vasculopathy appears to be an underlying factor in this eruption. The condition of the patient in the present study has been speculated to develop from the chronic irritation that occurs secondary to the subcutaneous insulin injection. In addition, this patient was affected by MRSA.

Subsequent infection can be caused by colonizing bacteria or other pathogens. As regards bacteria, the skin is dominated by members of the genera *Staphylococcus aureus*, *Corynebacterium*, *Streptococcus* and *Propionibacterium* (13). Notably, it has been reported that *Staphylococcus aureus* skin colonization rates are relatively low, and abundance levels compared to other bacterial skin colonizers are barely detectable (14). The patient described herein was affected by MRSA, a variant of *Staphylococcus aureus*. In recent decades, with the application of antibiotics, some bacteria exhibit resistance, among which MRSA is resistant to all β-lactamase antibiotics, the majority of macrolides and aminoglycoside antibiotics (15). MRSA infection has become an epidemic, occurring most frequently on the skin and soft tissue (16).

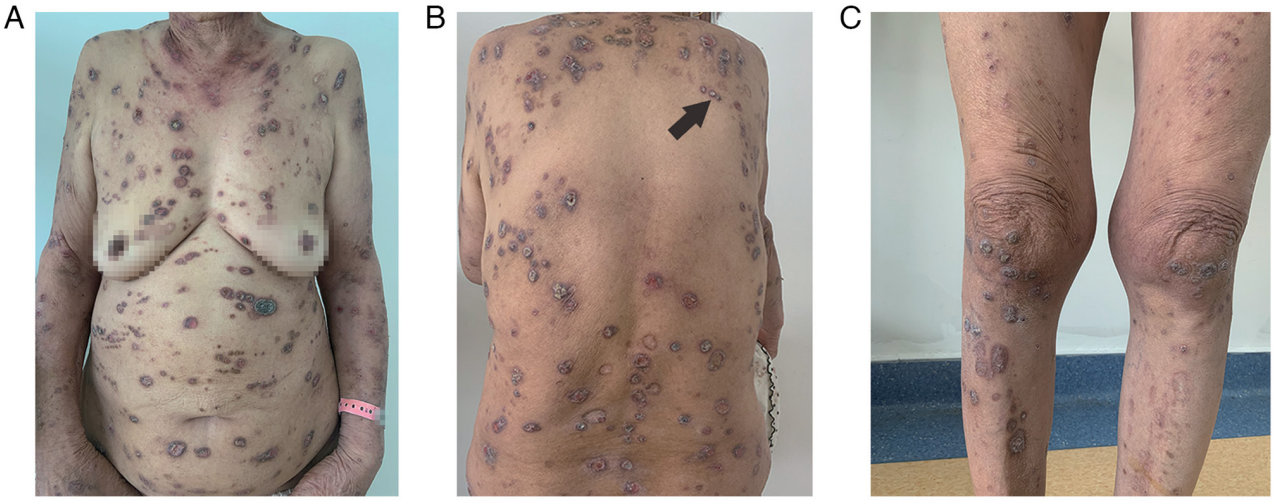

Figure 1. Skin lesion of acquired reactive perforating collagenosis. (A) The patient exhibited central keratosis with brown crusts primarily on the trunk. (B) The Koebner phenomenon was observed on the back (indicated by the black arrow). (C) Multiple non-tender erythematous papules and eschars were observed on the lower limbs.

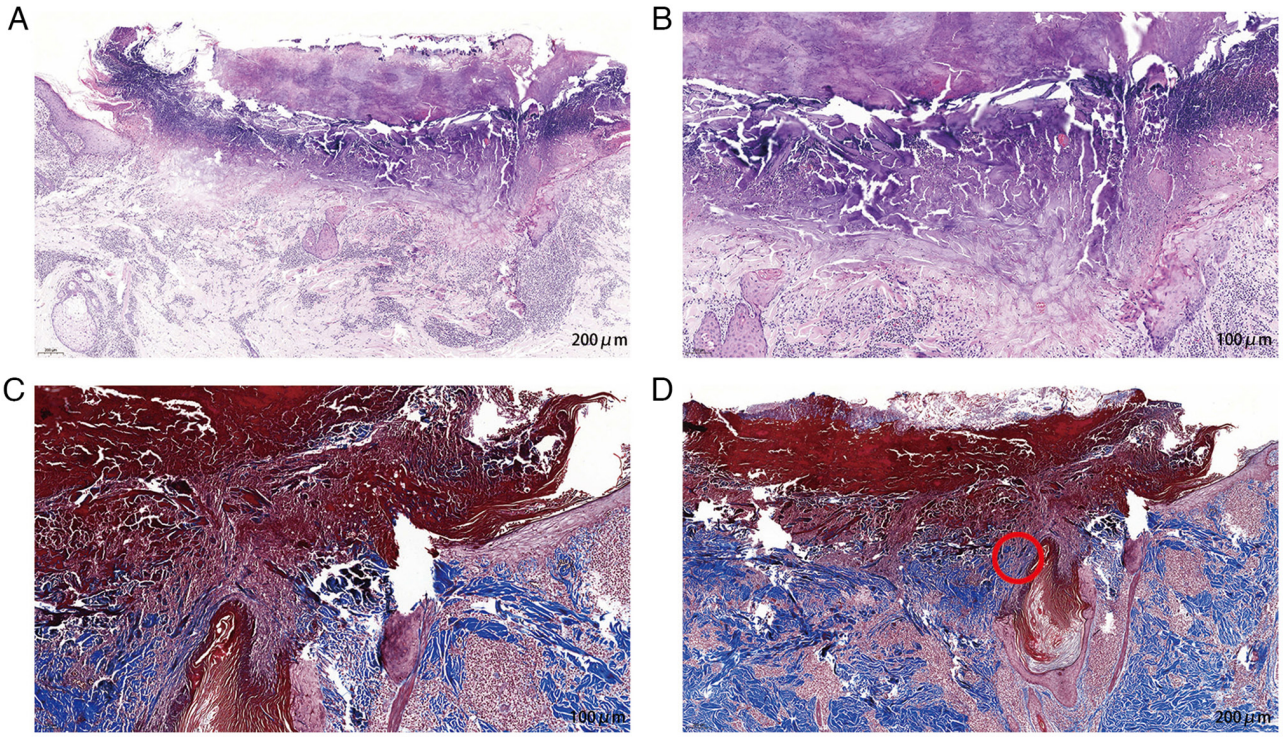

Figure 2. (A) Pathology of the skin biopsy, observed using hematoxylin and eosin staining. (B) The epidermal spinous layer was thickened. The ulceration filled with lymphocytes and eosinophils. (C) Pathology of the skin biopsy, observed using Masson's staining. (D) Necrotic collagen fibers penetrated into the surface (indicated by the red circle).

The mortality rates for patients diagnosed with ARPC may be higher in the case of a secondary infection. The study by Weiss *et al* (17) described a patient with ARPC who developed extensive cutaneous mucormycosis. The patient in that study succumbed due to progressive disease after 3 weeks of hospitalization (17). Accordingly, physicians need to be warned of the possibility and potential complications of fungal, mycobacterial, or bacterial opportunistic superinfection.

To the best of our knowledge, the present study is the first to report a case of concurrent ARPC and MRSA infection. Early treatment can be administered by conducting timely examinations to confirm the pathogen and select sensitive drugs for treatment. Apart from infection, ARPC is frequently accompanied by several systemic diseases, including malignant conditions. Thus, a thorough paraclinical exploration is necessary to reveal a possible underlying extracutaneous disease and to avoid secondary infections.

In conclusion, the present study reports a rare case of ARPC associated with MRSA. The present case report should

alert dermatologists to the possibility of secondary infection in patients with chronic ARPC.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

All authors (FH, WR, MW, XL and MP) were involved in the acquisition, analysis, or interpretation of the data. MP was involved in the conception and design of the study, and supervised the study. FH and WR were involved in the drafting of the manuscript. All authors had full access to all the study data and are responsible for the integrity of the data and the accuracy of the data analysis, confirm the authenticity of all the raw data, and have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Affiliated Hospital of Qingdao University (Qingdao, China). Written informed consent was obtained from the patient.

Patient consent for publication

Written informed consent was obtained from the patient for publication of the data and images in the present case report.

Competing interests

The authors declare that they have no competing interests.

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