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Case Report

Amicrobial pustulosis of the folds associated with autoimmune disorders: report a new case of Sjogren's syndrome

與自身免疫性疾病相關的褶皺位無菌性膿皰病：一宗乾燥症候群新病例報告

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Amicrobial pustulosis of the folds is a relatively new entity, characterised by recurring aseptic pustular lesions, predominantly involving the cutaneous folds and occurring in patients with autoimmune disorders. Few cases have been reported in the literature. We present a case of amicrobial pustulosis of the folds in a woman with Sjogren's syndrome.

褶皺位無菌性膿皰病是一個相對較新的病，其特徵是複發性無菌性膿皰病變，主要累及皮膚褶皺位及在自身免疫性疾病患者中發生。文獻中報導的病例很少。我們報告了一個患有褶皺位無菌性膿皰病的乾燥症候群女性患者病例。

Keywords: Amicrobial pustulosis of the folds, Sjogren's syndrome, sterile pustule

關鍵詞：褶皺位無菌性膿皰病、乾燥症候群、無菌膿皰

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Introduction

Amicrobial pustulosis of the folds (APF) is a rare entity characterised by a relapsing aseptic, papulopustular eruption of sudden onset.[1] It predominantly affects the cutaneous folds, external auditory canal, scalp and genital area. Patients exhibit a wide spectrum of autoimmune abnormalities including elevated serum autoantibodies alone or immunological disease such as systemic lupus erythematosus. Since its initial description in 1991 by Crickx et al,[2] very few cases have been reported in the literature. Herein, we report a case of this unusual entity

with clinicopathological features and laboratory findings.

Case report

A 34-year-old female patient was admitted with a pustular, erythematous eruption affecting the skinfolds. She had been treated with hydroxychloroquine for 12 years with the diagnosis of undifferentiated connective tissue disease based on the presence of photosensitivity and antinuclear antibody positivity. She had not taken any medications prior to the eruption. On dermatological examination, there were pustules, some of which were confluent on erythematous skin and eroded plaques, predominantly affecting the axilla, submammary folds, intergluteal folds, pubic region, gluteal region and external ear canal (Figure 1). Blood tests revealed increased neutrophils (neutrophils: 82.2%, lymphocytes: 9.4%, monocytes: 6.9%, eosinophils: 1.2%, basophils: 0.3%) and elevated C-reactive protein of 3.37 (normal range, 0-0.5). Further test results were positive for speckled (granular) pattern antinuclear antibodies with a titre of 1/5120 with presence of

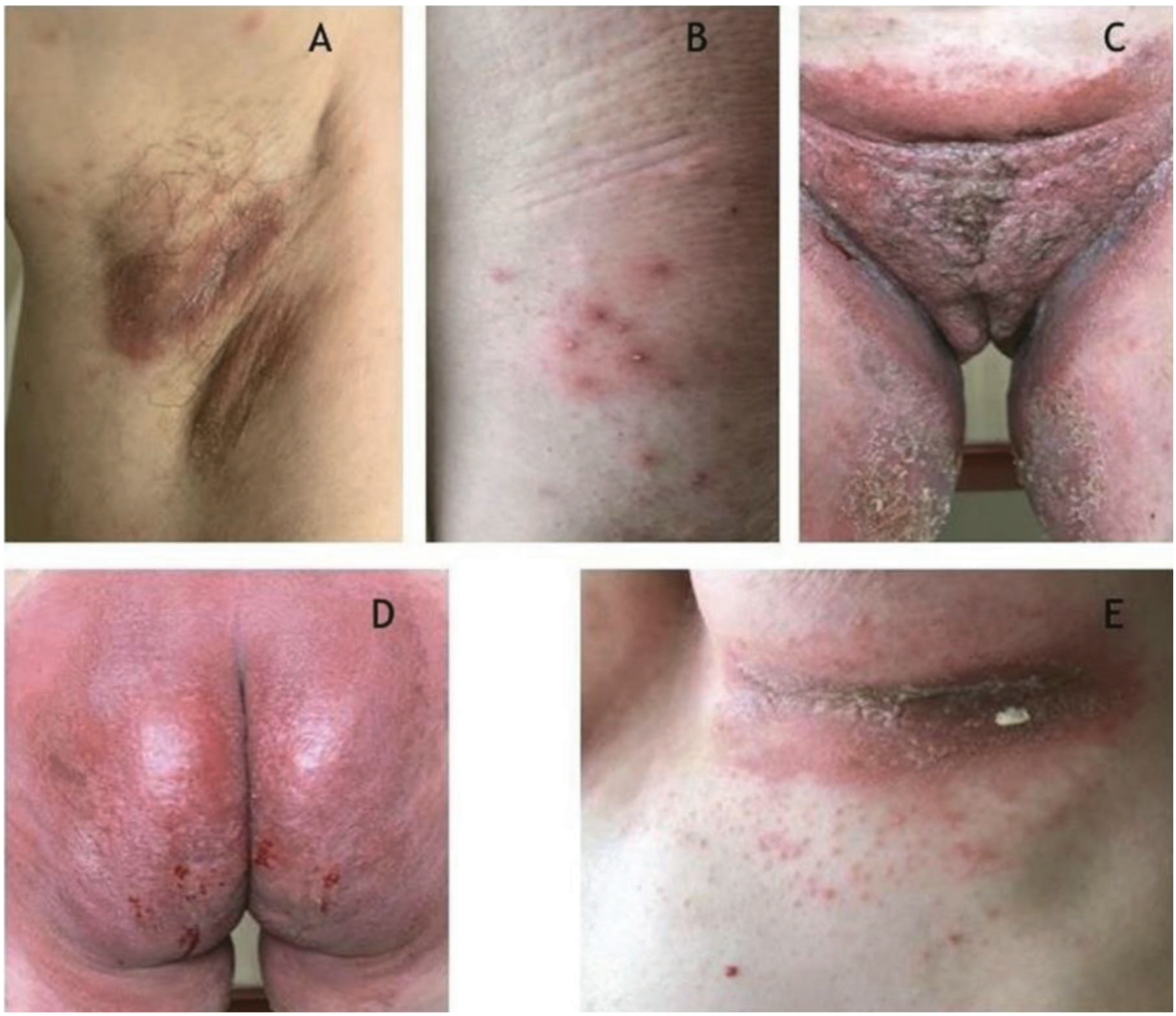

Figure 1. (A) Scaly erythematous lesions with isolated pustules and eroded plaques in axilla, (B) posterior femoral area, (C) pubic region, (D) gluteal region, and (E) submammary folds.

anti-SSB, Ro-52, and anti-SSA antibodies. Serum zinc level was low. Liver, kidney and thyroid function tests, erythrocyte sedimentation rate, autoimmune liver tests, antineutrophil cytoplasmic antibodies, serum immunoglobulins level, complement C3-C4, rheumatoid factor value were within normal limits or negative. Bacterial and mycological cultures were negative. Antibiotic and antiseptic treatment provided partial improvement. No pathology was found on the pelvic plain radiography. Skin biopsy from the gluteal region and inguinal region both showed intracorneal pustular formation and intraepidermal intense polymorphonuclear leukocyte exocytosis. In addition, irregular hyperplasia in the epidermis and perivascular intense inflammatory cell infiltrations were observed in the superficial dermis (Figures 2 & 3). No bacterial or fungal elements were detected on Gram, PAS and silver stain.

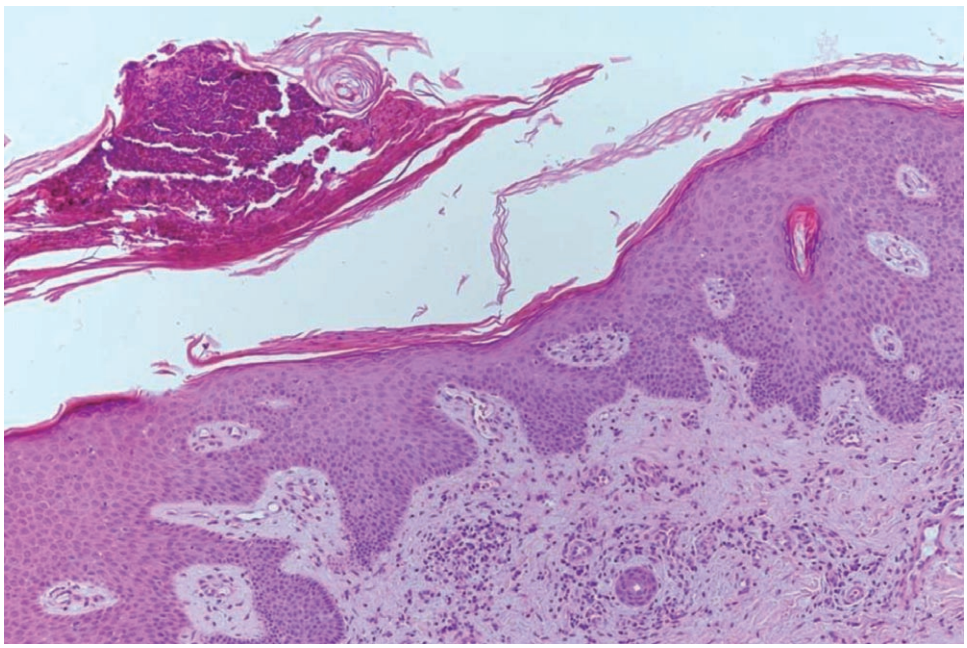

Figure 2. Intacorneal pustule formation (H & E x100).

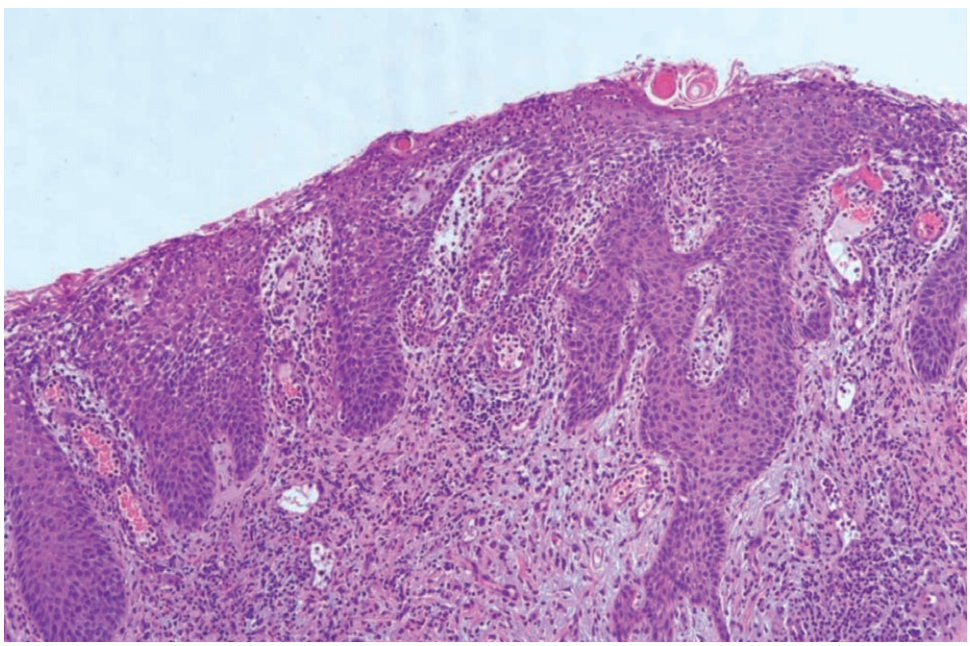

Figure 3. Intraepidermal widespread polymorphic leukocyte infiltration (H & E x100).

The rheumatology team was consulted and Sjogren's syndrome was diagnosed based on elevated serum autoantibodies, clinical and laboratory findings. Treatment was initiated with high dose oral methylprednisolone (80 mg/d for a day, subsequently tapered). Then, mycophenolate mofetil was added at the dose of 2000 mg/day during the steroid dose reduction. With this treatment regimen, the lesions improved significantly. Mycophenolate mofetil was tapered and eventually stopped. At one-month follow-up, the patient was stable with dose of the 4 mg methylprednisolone and did not recur.

Discussion

APF is a rare clinic entity most commonly seen in young women. It has an acute onset and recurring course. Typical clinical features consist of scaly erythematous and erosive plaques with follicular or non-follicular small coalescent pustules, eventually leading to crusting and impetiginisation. The clinical presentation of APF typically involves the intertriginous sites.[3] Affected skin folds of our patient included axilla, submammary folds, intergluteal folds, pubic region, gluteal region and external ear canal. Bacterial and mycological cultures from active pustules are usually negative. However, older lesions may be colonised with various bacterial species. Histopathological examination typically reveals intraepidermal spongiform pustules and neutrophilic infiltrates in the dermis.

APF has been reported to be associated with autoimmune disease and/or immunological abnormalities.[4] The most common autoimmune disease in these cases was systemic lupus erythematosus. Less frequently, mixed connective tissue disease, discoid and subacute cutaneous lupus erythematosus, rheumatoid arthritis, celiac disease, idiopathic thrombocytopenic purpura, myasthenia gravis, erythroblastic anaemia, Sjogren's syndrome, IgA nephropathy, rheumatoid arthritis, Hashimato's thyroiditis, Crohn's disease and autoimmune hepatitis association was determined.[1,3-6] In our patient associated Sjogren's syndrome and elevated ANA titres of 1/5120 were present.

APF is a diagnosis based on the combined assessment of clinical features, histopathological findings and comorbidities. Marzano et al proposed the following mandatory criteria: pustulosis affecting one or more major folds or one or more the minor folds and also anogenital fold; histological findings of intraepidermal spongiform pustulosis with neutrophil infiltrate in the dermis; and aseptic pustules. Their minor criteria include the association with one or more autoimmune disorders; elevated ANA titres of 1:160 or more; and the presence of additional autoantibodies.[1] Our case has all the criteria. The exact aetiology of APF is unclear, although neutrophil dysfunction has been suggested as a triggering factor.[7]

Due to rarity of APF, treatment regimens are not standardised. Systemic corticosteroids have been applied with good results (6-10) but are not always effective.[2,3] Systemic antibiotics are not effective in treating this disease if there is no secondary impetiginisation in the lesions. Several other treatments have been tried such as colchicine,[6] chloroquine,[8] dapsone,[9] cyclosporine,[9] cimetidine,[10] and zinc,[3] with varying results. Recently, APF cases with inflammatory bowel disease were treated with anakinra (IL-1 receptor antagonist) and ustekinumab (IL-12 / IL-23 receptor antagonist), with variable results.[11,12] In our case, a dramatic response to systemic methylprednisolone treatment was obtained and mycophenolate mofetil was added at a dose of 2000 mg/day during steroid dose reduction. Mycophenolate mofetil dose was progressively reduced after resolution of the skin lesions and eventually stopped. At one-month follow-up, the patient skin condition was in remission while using daily dosage of methylprednisolone 4 mg.

References

1. Marzano AV, Ramoni S, Caputo R. Amicrobial pustulosis of the folds. Report of 6 cases and a literature review. Dermatology 2008;216:305-11.
2. Crickx B, Diego ML, Guillevin L, Picard C, Grossins M, Belaïch S. Pustulose amicrobienne et lupus érythémateux systémique. Communication no.11. Journées Dermatologiques de Paris. París,1991.
3. Bénéton N, Wolkenstein P, Bagot M, Cosnes A, Wechsler J, Roujeau JC, et al. Amicrobial pustulosis associated with autoimmune diseases: healing with zinc supplementation. Br J Dermatol 2000;143:1306-10.
4. Wang MZ, Camilleri MJ, Guo R, Wieland CN. Amicrobial pustulosis of the folds: Report of 4 cases. J Cutan Pathol 2017;44:367-72.
5. Natsuga K, Sawamura D, Homma E, Nomura T, Abe M, Muramatsu R, et al. Amicrobial pustulosis associated with IgA nephropathy and Sjögren's syndrome. J Am Acad Dermatol 2007;57:523-6.
6. Kerl K, Masouye I, Lesavre P, Saurat JH, Borradori L. A case of amicrobial pustulosis of the folds associated with neutrophilic gastrointestinal involvement in systemic lupus erythematosus. Dermatology 2005;211: 356-9.
7. Antille C, Frei M, Sorg O, Tran C, Kaya G, Masouyé I, et al. Amicrobial pustulosis of the folds associated with auto-immune disorders. A case report with an analysis of cytokine expression profile in skin lesions of cutaneous neutrophilic lupus. Dermatology 2008;216:324-9.
8. Stefanidou MP, Kanavaros PE, Stefanaki KS, Tosca AD. Amicrobial pustulosis of the folds: a cutaneous manifestation associated with connective tissue disease. Dermatology 1998;197:394-6.
9. Kuyama M, Fujimoto W, Kambara H, Egusa M, Saitoh M, Yamasaki O, et al. Amicrobial pustular dermatosis in two patients with immunological abnormalities. Clin Exp Dermatol 2002;27:286-9.
10. Marzano AV, Capsoni F, Berti E, Gasparini G, Bottelli S, Caputo R. Amicrobial pustular dermatosis of cutaneous folds associated with autoimmune disorders: a new entity? Dermatology 1996;193:88-93.
11. Al-Raddadi R, Frances C, Moguelet P, Bachmeyer C, Guégan S. Ustekinumab as Effective Treatment for Refractory Amicrobial Pustulosis of the Folds Associated with Crohn's Disease. Acta Derm Venereol 2017;97: 389-90.
12. Amazan E, Ezzedine K, Mossalayi MD, Taieb A, Boniface K, Seneschal J. Expression of interleukin-1 alpha in amicrobial pustulosis of the skin folds with complete response to anakinra. J Am Acad Dermatol 2014;71: e53-6.