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A Case of Rheumatoid Neutrophilic Dermatitis with Annular Bullae Treated with Prednisone and Colchicine Combination Therapy

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Abstract

This report describes a 73-year-old female with rheumatoid neutrophilic dermatitis (RND), a distinct cutaneous manifestation associated with rheumatoid arthritis (RA), characterized by persistent annular blisters. Over six months, the patient developed erythematous plaques and annular blisters on the upper and lower limbs. She had a known history of RA and interstitial pneumonia. Serological tests revealed markedly elevated rheumatoid factor (RF,1260 IU/mL) and anti-cyclic citrullinated peptide (anti-CCP) antibody (>500 U/mL). Histopathological analysis demonstrated marked hyperkeratosis accompanied by neutrophilic aggregates in the stratum corneum, subepidermal blister formation, and dense neutrophilic infiltrates mixed with lymphocytes and eosinophils in the papillary to mid-dermis, while DIF was negative. The patient was treated with a combination of prednisone (30 mg qd) and colchicine (0.5 mg tid). After nearly one month of treatment, she experienced significant clinical improvement, with a marked reduction in RF-associated antibody levels and near-complete resolution of skin lesions.

Keywords

Rheumatoid Neutrophilic Dermatitis, Annular Bullae, Neutrophilic Dermatosis, Autoimmune Blistering Disease, Case Report

1. Introduction

Rheumatoid neutrophilic dermatitis (RND) is a rare cutaneous disorder closely associated with rheumatoid arthritis (RA), belonging to the category of neutrophilic dermatoses [1]. The condition was first described in 1978 and is predominantly observed in seropositive RA patients, though rare cases have also been re-

ported in seronegative individuals [2]. Clinically, RND typically presents as symmetrical erythematous papules, nodules, and plaques on extensor surfaces, whereas annular vesicles, pustules, or ulcerations are uncommon; lesions mainly affect the extremities [3]. Histopathologically, RND is characterized by dense neutrophilic infiltrates in the dermis without vasculitis. Direct immunofluorescence (DIF) is typically negative. The exact pathogenesis of RND remains unclear, though it is believed to represent a cutaneous manifestation of RA-associated systemic immune dysregulation, possibly involving immune complex deposition and abnormal cytokine activity, particularly IL-6 and IL-8 [4]. RND should be differentiated from other neutrophilic dermatoses. The condition may resolve spontaneously or improve with RA treatment. Therapeutic strategies include topical or systemic corticosteroids, colchicine, dapsone, hydroxychloroquine, and biologic agents [5]. Given its rarity, we report a rare case of RND with annular vesicles managed at our institution.

2. Case Report

2.1. History of Present Illness

A 73-year-old woman presented to our dermatology department on October 20, 2024, with a six-month history of recurrent erythematous plaques and annular blisters on her extremities. The lesions initially appeared as asymptomatic blisters on both shins without an identifiable trigger. Initial treatment with topical halometasone resulted in transient resolution within three days. However, two weeks later, the vesicles reappeared, increasing in number and extending to both feet, thighs, and upper limbs. Continued use of topical halometasone proved ineffective. One month prior to admission, the patient developed mild pain in the lower extremity lesions, along with significant swelling and tenderness of the heels. The patient sought further treatment at our hospital and was admitted with a provisional diagnosis of "dermatitis herpetiformis?". Throughout the illness, the patient denied any systemic symptoms, such as fever or abdominal pain.

2.2. Past Medical History

Her medical history included seropositive rheumatoid arthritis (RA) with associated connective tissue disease-related interstitial lung disease. In June 2024, the patient presented with a cough and sputum production. A chest CT performed at an external hospital revealed interstitial lung changes. Laboratory data were significant for CRP 45.42 mg/L, ESR 112 mm/h, RF 808.9 IU/mL, and anti-CCP 78,040 U/mL, indicating active RA and concurrent interstitial lung disease. The patient was initially given prednisone 5 mg /d, with a monthly taper of 5 mg, and was currently maintained on prednisone 5 mg /d. She also had knee osteoarthritis, treated with imrecoxib and Wangbi tablets. She denied any history of hypertension, diabetes, coronary artery disease, or gluten-sensitive enteropathy.

2.3. Physical Examination

On physical examination, no obvious deformities were noted in the small and medium joints of the extremities, and there was no redness, swelling, tenderness, or restriction of movement. Both knee joints showed tenderness (+) and limited range of motion. Dermatological examinations revealed annular, tense bullae (0.2 - 1 cm) with central necrosis observed on the lower extremities (Figure 1(a)), along with hyperkeratotic plaques on the soles and subcutaneous blisters on the left ulnar hand. Some erythematous blisters subside, leaving pigmentation, while others show central necrosis, erosion, and brown crusting (Figure 1(b)). There was no mucosal or truncal involvement, and the Nikolsky sign was negative.

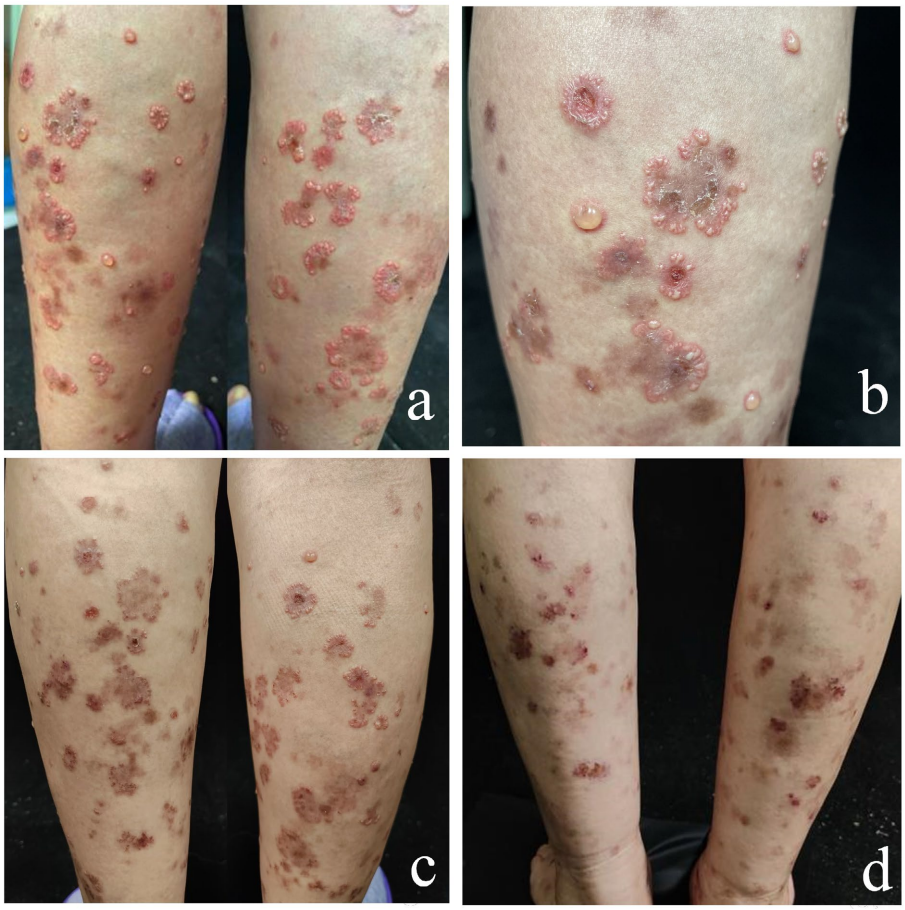

Figure 1. Clinical photos showing. (a) The lower legs and left forearm show erythema, ring-shaped blisters (0.2 - 1 cm), and pustules (0.2 - 1 cm); (b) Some erythematous blisters subside, leaving pigmentation, while others show central necrosis, erosion, and brown crusting; (c) After 7 days of treatment, there were no new blisters, the original erythema and blisters dried up and subsided, and the patient was discharged; (d) After one month of treatment, the blisters and pustules have mostly resolved, leaving pigmentation.

2.4. Laboratory and Imaging Studies

Laboratory examinations in the hospital outside showed continuous elevation of inflammatory markers (CRP: 45.42 - 47.25 mg/L; ESR: 97 - 112 mm/h) and ex-

tremely high autoantibodies (RF: 719.1 - 808.9 IU/mL; anti-CCP: >500 U/mL). After admission, laboratory examinations showed RF 1260 IU/mL, anti-CCP >500 U/mL, DD 3.94 mg/L, IgA 5.7 g/L (0.7 - 4 g/L). ANA, ANCA, anti-phospholipid antibodies, and immunofixed electrophoresis are all within the normal range. Serological examination of autoimmune vesicular diseases BP180, BP230, Dsg1, and Dsg3 antibodies were all negative. Both hands DR orthophone and magnetic resonance of both hands both indicate degenerative changes in both hands and abnormal signals of wrist bones in both hands. Skin histopathology showed subepidermal blister formation, neutrophilic microabscesses in the stratum corneum (Figure 2(a)), and dense dermal infiltrates consisting of neutrophils, lymphocytes, and eosinophils (Figure 2(b)). DIF was negative for IgG, IgA, IgM, and C3.

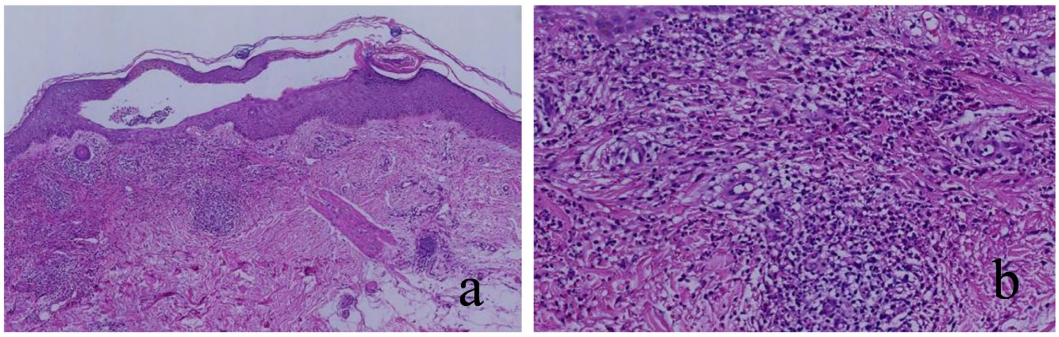

Figure 2. Histopathological findings. (a) subepidermal blister formation, neutrophilic microabscesses in the stratum corneum (Haematoxylin and eosin,original magnification × 5); (b) dense dermal infiltrates consisting of neutrophils, lymphocytes, and eosinophils (Haematoxylin and eosin, original magnification × 10).

2.5. Diagnosis and Treatment

Based on the patient's medical history, cutaneous manifestations, laboratory findings, and histopathological features, a diagnosis of rheumatoid neutrophilic dermatitis (RND) was confirmed. Dapsone (DDS) was initially considered for treatment. To prevent DDS-related adverse reactions, particularly dapsone hypersensitivity syndrome (DHS) and G6PD deficiency-associated hemolytic anemia, pretreatment screening for HLA-B*13:01 and G6PD activity was performed. As genetic testing requires approximately one week for results, a temporary treatment regimen was initiated on October 24, 2024, consisting of prednisone acetate (30 mg/d) combined with colchicine (0.5 mg/d). Due to persistent blistering, colchicine was increased to 0.5 mg twice daily on day 4. By day 7, the erythema and blisters on the limbs had significantly dried up and subsided, leaving pigmentation, and no new blisters had appeared (Figure 1(c)), alongside a parallel decline in RF levels (1260 to 1100 IU/mL). At the 20-day follow-up, disease activity further subsided (RF 401 IU/mL, Figure 3), the blisters and pustules have mostly resolved, leaving pigmentation (Figure 1(d)), allowing a prednisone taper to 15 mg daily while maintaining colchicine at 0.5 mg twice daily. No new lesions appeared during follow-up, though residual post-inflammatory hyperpigmentation remained. The patient continues to be monitored. Dapsone-related genetic

screening indicated a low risk for dapsone hypersensitivity. If disease control remains suboptimal, dapsone therapy may be considered.

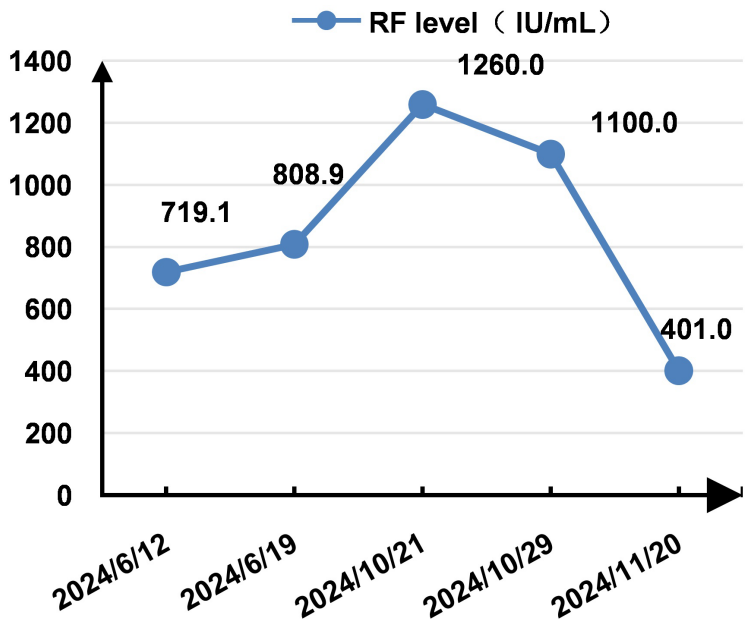

Figure 3. Variation in the level of RF during the onset and treatment of the patient.

3. Discussion

Rheumatoid neutrophilic dermatitis (RND) is a rare neutrophilic dermatosis that represents a cutaneous manifestation of severe rheumatoid arthritis (RA) [6]. It falls within the spectrum of neutrophilic dermatoses and predominantly affects middle-aged females. RND is closely associated with RA disease activity and systemic inflammation, typically occurring during active RA phases or in patients presenting with systemic symptoms. Serologic markers such as rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies are often strongly positive [2]. RND typically presents with symmetrical skin lesions affecting the extensor surfaces of the extremities, trunk, and buttocks. The lesions may appear as erythematous or violaceous papules, plaques, nodules, urticarial lesions, or ulcers. Bullae, pustules, annular lesions, petechiae, and purpura may also be observed. The condition is generally asymptomatic, though some patients experience mild pruritus or pain [7]. Associated symptoms, including joint swelling, morning stiffness, and restricted mobility, are reflective of underlying RA activity.

The exact pathogenesis of RND remains incompletely understood, but it is believed to involve multiple mechanisms. First, RND predominantly occurs in patients with active or severe RA, a systemic autoimmune disease characterized by chronic inflammation and tissue damage [8]. This inflammatory milieu may directly or indirectly contribute to cutaneous involvement. Second, a hallmark of RND is the presence of dense dermal neutrophilic infiltrates without vasculitis, suggesting that excessive neutrophil recruitment, activation, and chemotaxis play

a key role in disease pathogenesis. Third, RA is associated with immune complex formation and deposition, which may trigger localized inflammatory responses. In RND, immune complexes may accumulate within the dermis, leading to neutrophil recruitment and activation. Finally, the inflammatory environment in RA is rich in cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-8 (IL-8), which can enhance neutrophil activity and stimulate cutaneous cells to release additional inflammatory mediators, contributing to RND pathogenesis [1]. Although the pathophysiology of RND is complex, it is ultimately considered a specific cutaneous manifestation of the systemic immune dysregulation seen in RA.

Due to the rarity of RND, standardized diagnostic guidelines are lacking, and diagnosis is based on a combination of clinical, laboratory, and histopathological findings. RND should be suspected in patients with seropositive RA who develop characteristic cutaneous lesions during active disease phases. Laboratory findings often show elevated RF and anti-CCP antibody titers. Inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) may be elevated, reflecting active systemic inflammation. Peripheral blood neutrophilia may also be present. The gold standard for diagnosis is histopathology, which reveals dense neutrophilic infiltration in the dermis without evidence of leukocytoclastic vasculitis. DIF is typically negative, which helps differentiate RND from immune complex-mediated vasculitides and autoimmune blistering diseases.

Additionally, conditions such as pyoderma gangrenosum (PG), Sweet syndrome, Behcet's disease, and erythema elevatum diutinum (EED) must be ruled out [9]. RND lacks pathognomonic cutaneous or histological features, necessitating differentiation from other neutrophilic dermatoses. EED is characterized by symmetrically distributed violaceous plaques and nodules on extensor surfaces, with histopathology showing lymphocytic infiltration and leukocytoclastic vasculitis [10]. The absence of vasculitis in this case excludes EED. PG begins with inflammatory papules, pustules, or nodules that rapidly progress to painful ulcers, primarily on the lower extremities [11]. Histopathology reveals dermal neutrophilic infiltrates, abscess formation, vasculitis, and necrosis, with DIF showing local immune complex deposition. The absence of ulcerative lesions and vasculitis in this patient excludes pyoderma gangrenosum. Sweet syndrome presents as painful erythematous plaques or nodules, often with systemic symptoms such as fever and arthralgia [12]. Histopathology reveals dense neutrophilic infiltrates in the dermis, and DIF is negative. This patient's lack of fever and systemic symptoms rules out Sweet syndrome. Behcet's disease is characterized by recurrent oral and genital ulcers, uveitis, and neutrophilic skin lesions such as pustules and nodular erythema [13]. Histopathology shows perivascular lymphocytic infiltration with vasculitis, and DIF demonstrates granular IgA deposition at the dermoepidermal junction. The absence of systemic mucocutaneous involvement excludes Behçet's disease.

Given the presence of annular bullous lesions in this patient, differentiation

from autoimmune blistering disorders is crucial [14]. Bullous pemphigoid (BP) typically presents with tense bullae on erythematous or urticarial plaques, associated with severe pruritus [15]. Histopathology shows subepidermal bullae with eosinophilic infiltration, and DIF reveals linear IgG and C3 deposition along the basement membrane. This patient's negative BP180 and BP230 antibodies and DIF findings exclude BP. Dermatitis herpetiformis is characterized by grouped, pruritic vesicles and papules predominantly on extensor surfaces, often associated with gluten-sensitive enteropathy [16]. Histopathology shows subepidermal vesicles with neutrophilic microabscesses, and DIF demonstrates granular IgA deposition in dermal papillae. The absence of pruritus, gastrointestinal symptoms, and IgA deposition rules out dermatitis herpetiformis. Linear IgA bullous dermatosis (LABD) presents as clustered bullae in a "string of pearls" arrangement, frequently occurring in flexural areas. Histopathology reveals subepidermal blisters with neutrophilic infiltration, and DIF shows linear IgA deposition at the basement membrane [17]. This patient's negative linear IgA antibody and DIF findings exclude this diagnosis.

There are no standardized treatment guidelines for RND, and management primarily focuses on controlling the underlying RA-related systemic inflammation. Glucocorticoids, such as prednisone (30 - 60 mg/d), provide rapid symptom relief. Immunosuppressive agents, including methotrexate, cyclophosphamide, hydroxychloroquine, leflunomide, and tripterygium wilfordii (thunder god vine), may be used in refractory cases [1]. Biologics such as rituximab and TNF-α inhibitors (e.g., etanercept) may be considered for severe or recurrent cases [18]. Unlike classic RND, bullous RND is characterized by dense neutrophilic infiltrates within both the upper and mid-dermis beneath bullae, indicating a key role of neutrophils in the pathogenesis of the bullous variant. Bullous RND shows a superior response to dapsone or colchicine, which may be considered as first-line treatment [19]. However, dapsone carries a high risk of severe adverse effects, such as hemolytic anemia, agranulocytosis, and dapsone hypersensitivity syndrome (DHS), necessitating pre-treatment genetic screening for HLA-B*13:01 and G6PD deficiency to prevent complications [20]. In contrast, colchicine is a safer alternative with proven efficacy, mild side effects, and affordability, and has shown therapeutic benefits in neutrophilic dermatoses such as Sweet syndrome and palmoplantar pustulosis. Its anti-inflammatory mechanism primarily involves inhibition of neutrophil activation and chemotaxis, making it a suitable alternative for patients intolerant to dapsone [21].

This case highlights the diagnostic challenges of RND, particularly when bullous lesions are present, which can mimic other dermatologic conditions. The patient's history of RA and interstitial pneumonia, along with high-titer RF and anti-CCP positivity, underscores the importance of correlating cutaneous findings with systemic disease. For dermatologists, recognizing RND as a cutaneous manifestation of RA can prevent misdiagnosis and ensure timely treatment, ultimately improving patient outcomes.

4. Conclusion

Rheumatoid neutrophilic dermatitis (RND) is a rare cutaneous manifestation primarily that primarily affects patients with active or severe rheumatoid arthritis (RA). Histopathological examination remains the diagnostic gold standard. As a diagnosis of exclusion, RND must be distinguished from other neutrophilic dermatoses and autoimmune bullous disorders. Management options include topical or systemic glucocorticoids, neutrophil-targeting agents such as dapsone and colchicine, as well as immunosuppressants and biologics. The choice of treatment depends on the severity of the disease and systemic involvement. For dermatologists, recognizing RND as a cutaneous manifestation of RA is crucial to prevent misdiagnosis and ensure timely treatment, ultimately improving patient outcomes.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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