

BRIEF ARTICLES

Extensive Palisaded Neutrophilic Granulomatous Dermatitis with Systemic Lupus Erythematosus

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ABSTRACT

Systemic lupus erythematosus (SLE) is a multi-system disease with a myriad of mucocutaneous and systemic findings. One of the atypical cutaneous manifestations is palisaded neutrophilic granulomatous dermatitis (PNGD). This uncommon condition presents as tender or asymptomatic, flesh-colored, red to violaceous subcutaneous nodules. The diagnosis may be suspected clinically but is confirmed by biopsy. The impact of the disease may be the direct result of pain, psychosocial, cosmetic concerns, or be the initial presentation of an underlying systemic disease. We present a patient with known SLE who developed PNGD. We also review similar clinical and microscopic disease entities with a summative comparison of neutrophilic dermatoses in patients with autoimmune connective tissue diseases.

INTRODUCTION

Palisaded neutrophilic granulomatous dermatitis (PNGD) is a neutrophilic dermatosis associated with a characteristic phenotype of characteristic subcutaneous nodules overlying extensor surfaces, knuckles, and extremities.¹ PNGD may be seen in association with lymphoproliferative disorders, inflammatory bowel diseases, medications, and autoimmune connective tissue diseases.

Although rheumatoid arthritis is the most common underlying disease, systemic lupus erythematosus (SLE) has also been encountered. We present a patient with

known SLE who developed multiple tender, violaceous, subcutaneous nodules, and was subsequently diagnosed with PNGD. The patient reported allergy and intolerance certain first-line therapies, but oral corticosteroids led to the improvement of symptoms and over a period of months improvement of skin lesions.

CASE

A middle-age African American woman was sent to our outpatient dermatology office through an internal referral from rheumatology within a large multidisciplinary private practice. The patient's chief complaint was swollen red hands and

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generalized nodules that were progressing over a 7-month duration (Figure 1). Her medical history was significant for systemic lupus erythematosus, for which she was maintained on prednisone 5mg daily. Physical exam revealed multiple erythematous, tender subcutaneous nodules involving primarily her thighs and forearms with additional lesions on her face and trunk. Initial laboratory studies revealed serum complement C3, complement C4, anti-dsDNA, creatine kinase, and erythrocyte sedimentation rate all within normal limits. A biopsy of a lesion revealed palisading histiocytes with lymphocytes and sparse neutrophils. Stains were negative for increased mucin. Clinical and histologic findings are consistent with palisaded neutrophilic and granulomatous dermatitis (PNGD).

Figure 1. Multiple dusky, erythematous, hyperpigmented nodules on the proximal right thigh



When discussing treatment, the patient reported a severe allergy to hydroxychloroquine, as well as intolerance to dapsone, and was therefore prescribed oral prednisone 40mg daily for two weeks followed by a slow taper over two months while using topical clobetasol. Along with initial symptomatic improvement, the patient's lesions stabilized with tapering of

corticosteroids and continued to improve over a period of months.

DISCUSSION

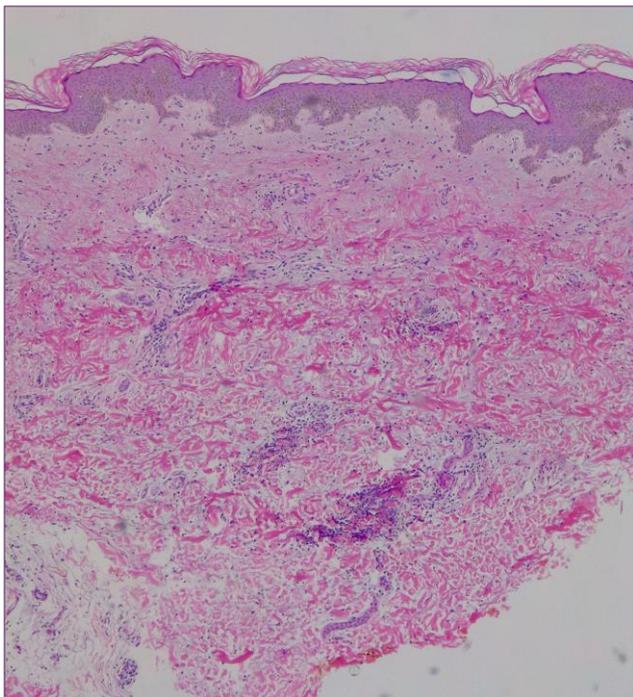
Palisaded neutrophilic granulomatous dermatitis is a rare cutaneous condition. Although the pathogenesis is not completely understood it is classically associated with underlying systemic disease. Causes are multiple and include inflammatory bowel disease, infections, lymphoproliferative disorders, and most commonly, connective tissue diseases. Also, medications such as ACE inhibitors, diuretics, tumor necrosis factor-alpha inhibitors, and soy products may cause a similar clinical and histological presentation. PNGD presents clinically as variably tender, symmetric, flesh-colored, erythematous to violaceous, umbilicated papules, nodules, and plaques that occur maximally on the extremities.¹ Most commonly, the elbows, knuckles, and knees are affected. Histologically, early lesions of PNGD reveal leukocytoclastic vasculitis with neutrophilic infiltrates throughout the dermis and late lesions reveal palisaded granulomas, collagen degeneration, neutrophilic debris, and eventually dermal fibrosis (Figure 2).²⁻⁴

Distinguishing the lesions of PNGD from similar appearing clinical or histologic entities is essential. Tumid lupus, erythema nodosum, and Sweet's syndrome may have a similar clinical appearance. The cutaneous lesions of lupus erythematosus tumidus appear as dermal, subcutaneous nodules, with little to no epidermal change. However, lupus erythematosus tumidus has a predilection for the face and trunk, and histopathology shows increased mucin.⁵

Erythema nodosum classically presents as notably painful subcutaneous nodules. Lesions of erythema nodosum are most

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Figure 2. Hematoxylin and eosin at 5x demonstrating palisading histiocytes with lymphocytes and sparse neutrophils



commonly located on the legs and symmetric upper, and lower extremity involvement is unlikely. Additionally, histopathology reveals prominent septal panniculitis with neutrophils admixed with eosinophils.⁶ Sweet syndrome is a neutrophilic dermatosis associated with underlying infections, malignancy, or autoimmune conditions. Sweet syndrome is heralded by the presence of fever, constitutional symptoms, and cutaneous lesions that present as painful vivid erythematous papules, nodules, and plaques. Histologically a dense neutrophilic infiltrate without the presence of leukocytoclastic vasculitis is an additional major diagnostic criteria.⁷ Granuloma annulare is more clinically distinct with localized or diffuse papules, nodules, or annular plaques with minimal epidermal change. Granuloma annulare, however, may have similar-appearing histologic findings with an interstitial or palisading infiltrate, but

unlike PNGD, increased mucin is a prominent finding.⁸ The association of various neutrophilic dermatoses and underlying systemic diseases, infections, medications, and autoimmune conditions is extensive. Neutrophilic dermatoses associated with autoimmune conditions include Sweet's syndrome, pyoderma gangrenosum, rheumatoid neutrophilic dermatitis, neutrophilic panniculitis, subcorneal pustular dermatosis, erythema elevatum diutinum, and as demonstrated with our case, palisaded neutrophilic granulomatous dermatitis.¹⁰ The clinical features, associations, and histologic findings are summarized in Table 1.

When treating PNGD, dapsone has demonstrated the greatest success, but cyclosporine, hydroxychloroquine, methotrexate, and prednisone are additional treatment options. If PNGD is secondary to an underlying condition, treatment of the underlying disease may result in resolution of cutaneous findings. In patients with ulcerative colitis colchicine, minocycline, and high-potency topical steroids have shown improvement in patients with secondary PNGD.³

CONCLUSION

PNGD is a cutaneous manifestation of multiple underlying disease states but can be encountered in patients with lupus erythematosus. Although the presence of PNGD in patients with SLE has an uncertain relationship to prognosis, may be associated with an increase in active lupus nephritis.⁹ Additionally, the cutaneous lesions may be extensive be a source of great distress for patients. This case provides classic and histologic correlates as well as emphasizes a dermatologist's role in the team-based healthcare model.

Table 1. Neutrophilic dermatoses and associated autoimmune and connective tissue diseases¹⁰

Neutrophilic Dermatoses	Clinical Findings	Histopathologic Findings	Associated Systemic Conditions
Palisaded neutrophilic granulomatous dermatitis	<ul style="list-style-type: none"> Erythematous papules, plaques, and nodules Minimal tenderness 	Sparse perivascular infiltrate with neutrophils, lymphocytes, and histiocytes	RA SLE SS IBD
Sweet's syndrome	<ul style="list-style-type: none"> Erythematous papules, plaques, and nodules Fever Malaise Neutrophilia Tender 	Diffuse neutrophilic infiltrate Papillary dermal edema Minimal to absent leukocytoclastic vasculitis	RA SLE IBD
Pyoderma gangrenosum	<ul style="list-style-type: none"> Ulcerative lesions with violaceous undermined borders 	Non-specific	SLE RA Juvenile RA IBD
Rheumatoid neutrophilic dermatitis	<ul style="list-style-type: none"> Urticarial papules, plaques, and nodules Overlie joints Often symmetric 	Dense neutrophilic infiltration of the dermis and may involve subcutis	RA
Subcorneal pustular dermatosis	<ul style="list-style-type: none"> Flaccid, annular, grouped pustules Involve trunk and intertriginous areas 	Neutrophilic pustules in the upper epidermis	RA SLE SJO
Erythema elevatum diutinum	<ul style="list-style-type: none"> Violaceous papules and nodules Extensor extremities 	Leukocytoclastic vasculitis with mixed infiltrate	RA
Neutrophilic urticaria (Non-bullous neutrophilic dermatosis)	<ul style="list-style-type: none"> Urticarial like lesions Pruritic 	<ul style="list-style-type: none"> Interstitial and perivascular neutrophilic infiltrate Leukocytoclasia Vacuolar interface dermatitis 	SLE RA SJO

Abbreviations: RA; rheumatoid arthritis, SLE; systemic lupus erythematosus, SS; systemic sclerosis, IBD; inflammatory bowel disease, SJO; Sjögren syndrome

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