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Palisaded neutrophilic and granulomatous dermatitis following a long-standing monoclonal gammopathy: A case report

Dorsa Zabihi-pour[1], Bahar Bahrani[2], Dalal Assaad[2] and Jensen Yeung[3]

Abstract

Background: Palisaded neutrophilic granulomatous dermatitis is a rare inflammatory dermatosis with possible underlying systemic conditions including rheumatoid arthritis, autoimmune connective tissue disease, and malignancies.

Case Summary: We report a case of an 84-year-old man presenting with a 3-week eruption of asymptomatic annular plaques on his neck, which progressed to involve his back and legs. Skin biopsies confirmed a diagnosis of palisaded neutrophilic granulomatous dermatitis, and he was treated with prednisone. Full workup related to potential underlying causes of palisaded neutrophilic granulomatous dermatitis was completed.

Conclusion: Palisaded neutrophilic granulomatous dermatitis may precede the onset of underlying systemic conditions or occur concomitantly. Following the diagnosis, clinicians should perform a comprehensive focused history, physical examination, and laboratory investigation related to the associated underlying diseases.

Keywords

Palisaded neutrophilic and granulomatous dermatitis, neutrophilic dermatoses, dermatoses with underlying systemic conditions

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Introduction

Palisaded neutrophilic granulomatous dermatitis (PNGD) is a neutrophilic skin condition and a well-reported cutaneous marker for a number of systemic associations including rheumatoid arthritis, lupus erythematosus, vasculitis,[1] lymphoproliferative disorders,[2] and drug reactions.[3] The clinical presentation of PNGD is diverse and often includes tender erythematous to violaceous papules or plaques on neck and extensor surfaces.[1] Histologically, it is characterized by neutrophilic infiltrate, vasculitis, and collagen trapping. This case report describes a patient with PNGD in an effort to illustrate the importance of following up the diagnosis of PNGD by investigating possible systemic conditions linked to this condition.

Case report

An 84-year-old man presented to the emergency department of a university hospital with a 3-week eruption of asymptomatic erythematous to violaceous edematous annular plaques with no epidermal change limited on his neck. His medical history included dyslipidemia, chronic renal failure of unknown cause, and a mild monoclonal gammopathy of undetermined significance that was diagnosed 12 years prior. He denied any new medications preceding the eruption. His review of systems was completely unremarkable. Two punch biopsies were done to determine the diagnosis. Full laboratory investigations related to connective tissue disease and lymphoproliferative disorders were done (Table 1).

A diagnosis of PNGD was made based on histopathologic features, which showed lymphocytes and neutrophils around the vessels and scattered interstitially in the presence of focal histiocytes between collagen bundles (Figure 1). Clobetasol propionate 0.05% ointment was prescribed twice daily for

[1]Schulich School of Medicine & Dentistry, London, ON, Canada
[2]Division of Dermatology, Department of Medicine, University of Toronto, Women's College Hospital, Toronto, ON, Canada
[3]Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Corresponding Author:
Dorsa Zabihi-pour, Schulich School of Medicine & Dentistry, 1151 Richmond Street, London, ON N6A 5C, Canada.
Email: dzabihipour2023@meds.uwo.ca

2 weeks, while awaiting biopsy results. At the second visit, he had developed significantly more similar lesions on his back and legs. He also reported a new onset of lethargy and lack of appetite. He denied any weight loss, fevers, and night sweats. Full workup only revealed abnormalities in his serum protein electrophoresis with mild IgG Kappa restriction, which had been chronic. The urine protein electrophoresis showed an increased protein level in the absence of free immunoglobulin light chains, consistent with his chronic renal failure. He was referred to internal medicine for a full workup for malignancy, hematologic in particular. His additional blood work and full-body computed tomography (CT) scans were unremarkable.

Following the biopsy results, prednisone 20 mg (0.3 mg/kg) PO daily was initiated. Three weeks after prednisone, his lesions almost completely resolved along with the fatigue and weakness.

Table 1. Full list of laboratory investigations ordered for the patient.

Complete blood count
Liver function tests
Kidney function tests
Electrolytes
LDH
TSH
INR
C-reactive protein (CRP)
Erythrocyte sedimentation rate (ESR)
Anti-nuclear antibody (ANA)
Extractable nuclear antigen (ENA)
C and P anti-neutrophil cytoplasmic antibody (ANCA)
C3/C4
Anti dsDNA
Rheumatoid factor (RF)
Hepatitis B and C serology
ASOT
Cryoglobulin/cold agglutinin
Cryofibrinogen
Serum protein electrophoresis (SPEP)
Urine protein electrophoresis (UPEP)
Immunofixation (IFE)
Peripheral blood cytometry
Urinalysis
Non-contrast CT scan of chest/abdominal/pelvis

LDH: lactate dehydrogenase; TSH: thyroid-stimulating hormone; INR: international normalized ratio; ASOT: Antistreptolysin O Titer; CT: computed tomography.

Discussion

PNGD is a rare inflammatory dermatologic reaction pattern, with a diverse range of clinical and histological manifestations. Typical clinical presentations include skin-colored linear cords involving the lateral trunks, skin-colored or erythematous papules with crusting, perforation, or umbilication, as well as asymptomatic, erythematous to violaceous plaques with symmetrical distribution.[4]

Histologically, PNGD lesions are dynamic and depend on the stage of this condition at the time of biopsy. Early-stage biopsies have shown lymphohistiocytic cells with leukocytoclastic vasculitis and pan-dermal infiltrate of neutrophils surrounding foci of degenerated collagen. Late-stage features include palisading granulomas, scattered leukocytes, fibrin, and degenerated collagen fibers, neutrophil debris, and ultimately fibrosis.[5] Recent studies have shown that different biopsies from multiple lesions within one patient with PNGD may present distinctively under the microscope.[2]

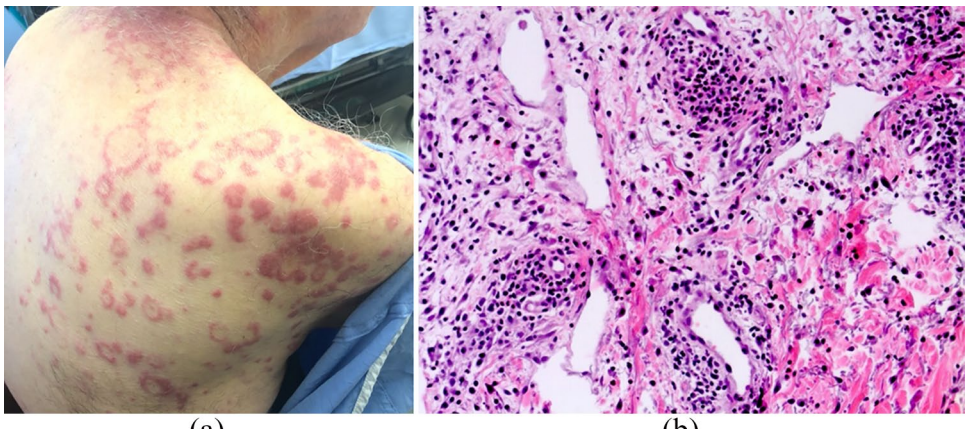

Figure 1. Palisaded neutrophilic and granulomatous dermatitis clinical presentation and biopsy: (a) clinical image and distribution of plaques. (b) Punch biopsy specimen with a mixture of lymphocytic and neutrophilic infiltrates around the vessel and scattered interstitially. Also, focal histiocytes observed between collagen bundles. (b) Hematoxylin–eosin stain; original magnification: ×100.

Table 2. List of conditions linked to PNGD.

Adult-onset Still's disease[9]
Chronic uveitis[4]
Eosinophilic granulomatosis with polyangiitis (Churg Strauss syndrome)[10]
Rheumatoid arthritis[1]
Sarcoidosis[4]
Systemic lupus erythematosus (SLE)[6]
Systemic vasculitis[10]
Takayasu arteritis[9]
Ulcerative colitis[10]
Chronic myelomonocytic leukemia[2]
Hodgkin's/non-Hodgkin's lymphoma[9]
Allopurinol[5]
Ledipasvir/Sofosbuvir[3]
Subacute bacterial endocarditis[9]

PNGD: palisaded neutrophilic granulomatous dermatitis.

Certain features from pathology may also help diagnose an underlying systemic condition associated with PNGD. A case study on PNGD linked to systemic lupus erythematosus (SLE) has noted a high concentration of infiltrated cells strongly positive for CD163 and CD68, suggesting a possible role for M2 macrophages in PNGD pathogenesis.[6] Considering the dominance of M2 macrophages in lupus nephritis,[7] clinicians should also consider a subsequent diagnosis of SLE and lupus nephritis in patients presenting with mentioned pathological characteristics.

Over the years, PNGD has been described as eosinophilic granulomatosis with polyangiitis (EGPA), cutaneous extravascular necrotizing granuloma, rheumatoid papules, and Winkelmann granuloma.[1] Moreover, due to the overlapping histological features between PNGD and interstitial granulomatous dermatitis (IGD), there has consistently been a debate in the literature to whether classify the two as one disease on a spectrum or separate entities.[8]

Although PNGD is a rare and intrinsically benign presentation, its proper diagnosis is crucial since it has repeatedly been reported to be a cutaneous marker for systemic conditions including connective tissue disease, systemic vasculitis, subacute bacterial endocarditis, and lymphoproliferative conditions (Table 2). PNGD was first discovered in patients with rheumatoid arthritis and hence primarily named rheumatoid papules and IGD with cutaneous cords and arthritis.[1] Subsequently, more clinicians observed similar features in other autoimmune conditions such as pediatric sarcoidosis,[4] Takayasu arteritis,[2] systemic lupus erythematosus, and EGPA.

PNGD has also been linked to lymphoproliferative malignancies including chronic myelomonocytic leukemia[3] (CML), non-Hodgkin's lymphoma, and less commonly Hodgkin's lymphoma.[9] In some cases, these conditions developed chronologically after the presentation of PNGD,[3] leading clinicians to consider the cutaneous lesions to be an early marker for a range of systemic disorders. The patient in our case presented with monoclonal gammopathy several years prior to the onset of the PNGD. He will continue to be monitored by internal medicine to determine if the monoclonal gammopathy will progress to a hematologic malignancy.

Rarely, PNGD has also been linked to drug reactions in literature namely, ledipasvir/sofosbuvir[3] and allopurinol.[5] In such cases, stopping the medication was sufficient to induce remission.

The treatment of PNGD is primarily directed to the underlying disease. A small proportion of patients, up to 20%, may show spontaneous resolution of the lesions. Available treatment options include topical corticosteroid, non-steroidal anti-inflammatory drugs (NSAIDs), dapsone, colchicine, prednisone, oral tacrolimus, and tumor necrosis factor (TNF) inhibitors.[10] Topical therapies for PNGD are generally less effective in comparison to systemic treatments.

The clinical course of PNGD may precede the onset of its associated systemic disease or occur concomitantly. Therefore, we recommend that after the diagnosis of PNGD, a patient should be followed up with a comprehensive and focused history, physical examination, and thorough laboratory testing to investigate the possibility for an underlying autoimmune, malignancy or infection.

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Informed consent

Patient provided consent for publication of the case report and images.

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