

Case 3

An 86-year-old Thai woman from Bangkok

Chief complaint: Multiple scaly erythematous rashes on left leg for 2 months



Present illness:

The patient presented with slowly progressive itchy erythematous rashes that developed on the left leg for 2 months. There was no history of topical products used prior to the onset of skin lesions.

Past history:

Her underlying diseases were severe rheumatoid arthritis, hypertension, dyslipidemia and old cerebrovascular disease

Physical examination:

HEENT: Mildly pale conjunctivae, anicteric sclerae

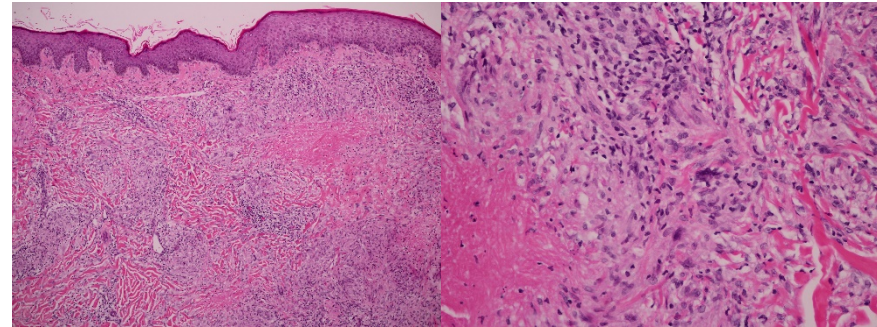
Lymph node: Not palpable

Extremities: Swelling of left thigh

Dermatologic examination:

- Multiple scaly erythematous to brownish papules and plaques on the left lower leg and thigh.

Histopathology: (S16-12139A, left leg)



- Nodular and palisaded infiltrate of lymphocytes, histiocytes, and a few multinucleated giant cell in the upper and mid dermis
- Palisaded granuloma around central foci, composed of eosinophils, degeneration of collagen bundles, neutrophils, and nuclear dust, and vasculitis with fibrinous necrosis of small blood vessels
- All special stains are negative for organisms

Diagnosis: Palisaded neutrophilic and granulomatous dermatitis with active rheumatoid arthritis

Investigations:

- CBC: Hb 10 g/dl, Hct 31%, WBC 4140/cumm (N 56, L 27%, Mo 10%, Eo 6%, Ba 1%), platelet 209,000/cumm
- ESR 84 mm/hr
- LFT: AST 54 U/L, ALT 59 U/L, ALP 330 U/L, GGT 292 U/L, TP 63.5 g/L, Alb 32.5 g/L, TB 1 mg/dl, DB 0.5 mg/dl
- BUN 11 mg/dl, Cr 0.49 mg/dl
- ANA: Negative
- P-ANCA: Negative, C-ANCA: Negative
- Chest X-ray: No active disease

- Ultrasound Doppler left leg: No DVT

Treatment:

- 0.05% Clobetasol cream apply lesion bid.
- Hydroxychloroquine 200 mg/day
- Cyclosporine 150 mg/day

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Discussion:

Rheumatoid arthritis (RA) is a chronic multisystem disease of unknown origin characterized by polyarthritis and a broad spectrum of extraarticular manifestations. Among dermatologic involvement in RA, rheumatoid nodules are most frequently observed. A rather uncommon cutaneous manifestation; however, is the development of palisaded neutrophilic granulomatous dermatitis (PNGD) that shows a broad clinical and histopathological spectrum.¹

PNGD is an unusual entity with variable clinical manifestations and histopathological features. Systemic triggers include connective tissue diseases (lupus, vasculitis, other), arthritides (rheumatoid arthritis, other inflammatory and reactive arthritides), malignancy (especially hematologic malignancy), and medications.²

PNGD was first described in 1965 by Dykman et al.⁽³⁾ They reported 2 cases of patients with RA who developed linear cords on the lateral trunk. Later several authors described this entity in many terms including Churg–Strauss granuloma, cutaneous extravascular necrotizing granuloma, rheumatoid papules, Winkelmann granuloma, interstitial granulomatous dermatitis with arthritis.

In 1994 Chu et al⁴ postulated the spectrum of changes found in this disease represented merely an evolution of immune complex–mediated changes from leukocytoclastic vasculitis in early lesions, to palisaded granulomas in fully developed lesions, and finally to fibrosis in late lesions. They proposed the unifying term PNGD to encompass this continuum.

Patients of all ages may develop PNGD, although reports in childhood are rare.^{5,6,7} Women are affected more frequently (approximately 3:1 ratio), likely owing to the associated systemic diseases.⁵

The lesions are usually symmetrically distributed on the extremities with smooth, ulcerated, or umbilicated surfaces.⁸ However, PNGD can present as pink to violaceous papules, plaques, nodules or linear bands, some of which can have urticarial or annular configurations.⁹ Early lesions are urticaria-like annular plaques, or may have a livedoid appearance. In later stages, the lesions are more infiltrative and pleomorphic (e.g. violaceous annular plaques, waxy papules, painful subcutaneous nodules, indurated linear bands etc.).⁹ Finally, fibrosis was observed.

The etiology of the disease is unknown. Theories include abnormal neutrophil activation, circulating immune complex deposition^{2,10}, a delayed-type hypersensitivity reaction¹¹, or a low grade small vessel vasculitis.¹²

The histologic findings of PNGD may be varied, possibly depending on the lesion's age or associated underlying disease. Early lesions may display intense neutrophilic inflammation, karyorrhectic debris, and frank leukocytoclastic vasculitis. There are typically more neutrophils, nuclear dust, and fibrinoid change than in pure vasculitis. As the lesions evolve, there are piecemeal areas of collagen degeneration and palisades of histiocytes and small granulomas, eventually accompanied by areas of fibrosis. The presence of vasculitis is felt to distinguish PNGD from interstitial granulomatous dermatitis (IGD). PNGD generally contains less

mucin and more intense neutrophilic infiltrate and nuclear debris than granuloma annulare.^{4,9,13,14}

Patients with PNGD should be evaluated for underlying internal systemic diseases. The recurrence or presence of PNGD usually coincided with the aggravation of underlying diseases

All patients warrant serologic testing, including antinuclear antibody, antineutrophilic cytoplasmic antibodies, rheumatoid factor, cyclic citrullinated peptide, complete blood count with differential, chest radiography.

Approximately 20% of cases may resolve spontaneously. The main principle of PNGD management is to identify the underlying disease and target therapy to control that disorder. Most treatments reported in the literature are aimed at controlling the underlying systemic diseases (e.g., nonsteroidal anti-inflammatory drugs, colchicine, hydroxychloroquine, methotrexate, cyclosporine, cyclophosphamide, systemic corticosteroids, etanercept, infliximab, etc.).^{11,15}

PNGD-specific treatments include intralesional triamcinolone, dapsone and systemic corticosteroids.^{5,16,17} Topical medications are not effective generally, although rare reports note improvement.⁽¹⁸⁾

In conclusion, the differential diagnosis of PNGD should be considered in all patients with a history of collagen vascular disease and/or autoimmune disorders who present with papular eruptions on the extremities. If the rash persists, a biopsy should be taken to confirm the presumptive diagnosis.

References

1. Sanguenza OP, Caudell MD, Mengesha YM. Palisaded neutrophilic dermatitis in rheumatoid arthritis. *J Am Acad Dermatol* 2002;47:251–257.
2. Finan MC, Winkelmann RK. The cutaneous extravascular necrotizing granuloma (Churg-Strauss granuloma) and

systemic disease: a review of 27 cases. *Medicine (Baltimore)* 1983;62:142–58.

3. Dykman CJ, Galens GJ, Good AE. Linear subcutaneous bands in rheumatoid arthritis: an unusual form of rheumatoid granuloma. *Ann Intern Med* 1965;63:134–40.
4. Chu P, Connolly MK, LeBoit PE. The histopathologic spectrum of palisaded neutrophilic and granulomatous dermatitis in patients with collagen vascular disease. *Arch Dermatol* 1994;130:1278–83.
5. Hantash BM, Chiang D, Kohler S, et al. Palisaded neutrophilic and granulomatous dermatitis associated with limited systemic sclerosis. *J Am Acad Dermatol* 2008;58:661–4.
6. Hunt RD, Hartman RD, Molho-Pessach V, et al. Palisaded neutrophilic and granulomatous dermatitis in an adolescent girl with perinuclear antineutrophil cytoplasmic antibody-positive pauci-immune glomerulonephritis and arthritis. *J Am Acad Dermatol* 2012;67:e164–6.
7. Kwon EJ, Hivnor CM, Yan AC, Forbes B, Elenitsas R, Albert D, Pawel B, Honig P, Pessler F. Interstitial granulomatous lesions as part of the spectrum of presenting cutaneous signs in pediatric sarcoidosis. *Pediatr Dermatol* 2007;24:517–24.
8. Brecher A. Palisaded neutrophilic and granulomatous dermatitis. *Dermatol Online J* 2003;9:1.
9. Stephenson SR, Campbell SM, Drew GS, Magro CM. Palisaded neutrophilic and granulomatous dermatitis presenting in a patient with rheumatoid arthritis on adalimumab. *J Cutan Pathol* 2011;38:644–8.
10. Misago N, Shinoda Y, Tago M, Narisawa Y. Palisaded neutrophilic granulomatous dermatitis with leukocytoclastic vasculitis in a patient without any underlying systemic disease detected to date. *J Cutan Pathol* 2010;37:1092–7.

11. Kim SK, Park CK, Park YW. Palisaded neutrophilic granulomatous dermatitis presenting as an unusual skin manifestation in a patient with Behcet's disease. *Scand J Rheumatol* 2005;34:324–7.
12. Al-Daraji WI, Coulson IH, Howat AJ. Palisaded neutrophilic and granulomatous dermatitis. *Clin Exp Dermatol* 2005;30:578–9.
13. Rosenbach M, English JC 3rd. Reactive Granulomatous Dermatitis: A Review of Palisaded Neutrophilic and Granulomatous Dermatitis, Interstitial Granulomatous Dermatitis, Interstitial Granulomatous Drug Reaction, and a Proposed Reclassification. *Dermatol Clin* 2015;33:373-87.
14. Bremner R, Simpson E, White CR, Morrison L, Deodhar A. Palisaded neutrophilic and granulomatous dermatitis: an unusual cutaneous manifestation of immunemediated disorders. *Semin Arthritis Rheum* 2004;34:610–6.
15. Paštar Z, Radoš J, Pavić I, Kovačević S, Vukasović A, Milavec-Puretić V, Lipozenčić J. Palisaded neutrophilic and granulomatous dermatitis in association with subcutaneous nodular and systemic sarcoidosis. *Acta Dermatovenerol Croat* 2013;21:245–9.
16. He Y, Maverakis E, Ramirez-Maverakis D. Combination therapy with intralesional triamcinolone and oral dapsone for management of palisaded neutrophilic and granulomatous dermatitis. *Dermatol Online J* 2013;19:17.
17. Fett N, Kovarik C, Bennett D. Palisaded neutrophilic granulomatous dermatitis without a definable underlying disorder treated with dapsone. *J Am Acad Dermatol* 2011;65:92–3.
18. Collaris EJ, van Marion AM, Frank J, Poblete-Gutiérrez P. Cutaneous granulomas in rheumatoid arthritis. *Int J Dermatol* 2007;46:33–5.