Rheumatoid Neutrophilic Dermatitis

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Rheumatoid neutrophilic dermatitis (RND) is an infrequent cutaneous manifestation of rheumatoid arthritis (RA). This condition is seen in patients who are both positive and negative for a circulating rheumatoid factor. Histologically, it presents with a neutrophilic dermatosis, characterized by a heavy dermal infiltrate of neutrophils with variable degrees of leukocytoclasis but no vasculitis. We describe the case of a young female with seronegative RA who had concomitant lesions of RND over both elbows. Her lesions appeared as nodules, but RND has been reported as papules and plaques, sometimes with an urticarialike appearance or ulcerations. They are often symmetric. The possibility of RND should be considered in the differential of unusual skin lesions in all patients with RA, as the presentation is quite varied.

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Case Report

A 22-year-old woman presented in September 2003 with a 6-year history of nodules on her elbows. The lesions disappeared when she took oral prednisone for her rheumatoid arthritis (RA) flares, but they returned immediately after cessation of the steroids. The lesions were otherwise persistent and asymptomatic. The patient also complained of occasional purple macules on her fingertips. She was diagnosed with seronegative RA in March 2003 but was otherwise healthy. Her medications included hydroxychloroquine sulfate 200 mg twice daily (starting in August 2003), prednisone 10 mg once daily as needed (last taken July 2003), and celecoxib 200 mg once daily.

On physical examination, firm nodules were observed over both elbows (Figure 1). These lesions were flesh colored or hypopigmented and ranged in size from 4 to 8 mm. Several lesions had a faint ring of erythema. Central umbilication was observed on one lesion, while others had overlying crust. In addition, there were 1- to 2-mm tender reddish-purple papules on a few fingertips (Figure 2). The nails and mouth were clear of lesions, and no similar lesions were noted elsewhere on the body.

The patient's erythrocyte sedimentation rate was elevated at 50. Extractable nuclear antigen antibody SSA/anti-Ro was strongly positive, and the extractable nuclear antigen anti-Smith antibody was mildly positive. However, her rheumatoid factor was negative as well as her antinuclear antibody screen. Cryoglobulins and antineutrophil cytoplasmic antibodies against both proteinase-3 and myeloperoxidase were negative. Antiribonucleoprotein, anti-SSB, and anti-Scl-70 antibodies also were negative. A hepatitis panel was negative for types B and C immunoglobulin G (IgG) antibodies.

A 4-mm punch biopsy was taken from the left elbow. It showed a dense neutrophilic infiltrate throughout the dermis. There was a mild infiltrate predominance in the upper and middle levels of the dermis (Figure 3). Microabscesses of neutrophils were noted in the papillary dermis, similar to those observed in dermatitis herpetiformis (DH) (Figure 4). The deeper dermis revealed a perivascular mixed infiltrate, in which neutrophils also were the predominant cell type. Scattered histiocytes, lymphocytes, and eosinophils were seen. The dermal blood vessels appeared unaffected with no evidence of vasculitis or vasculopathy. The findings were deemed histologically most consistent with rheumatoid neutrophilic dermatitis (RND). Biopsy was not performed on the fingertip lesions, but they were clinically compatible with Bywater lesions. The patient's rheumatologist represcribed prednisone for her arthralgias, which caused the skin lesions to resolve.

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The views expressed in this article are those of the authors and do not reflect the official policy or position of the US Department of the Navy, US Department of Defense, or the US Government.

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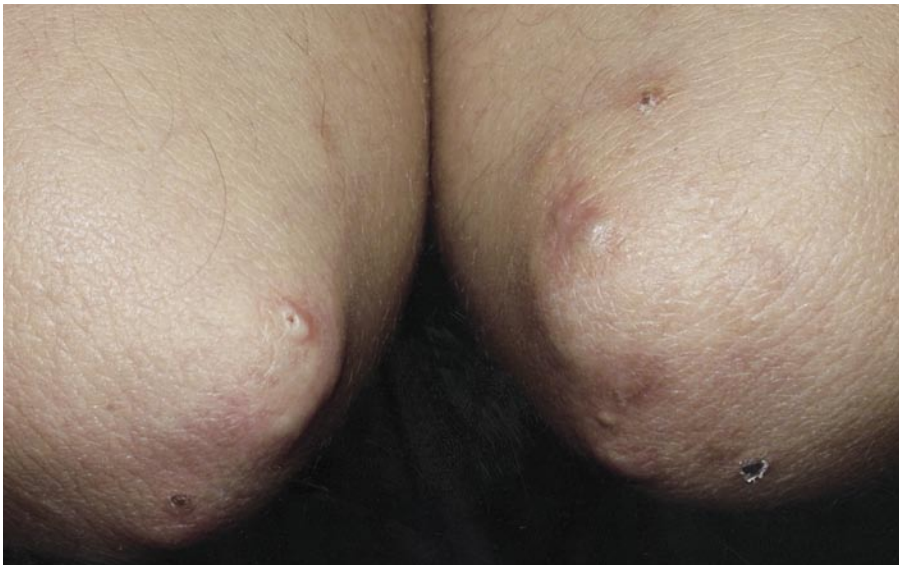

Figure 1. Patient with multiple, firm, 4- to 8-mm nodules over both elbows. Several lesions had central umbilication or overlying crust.

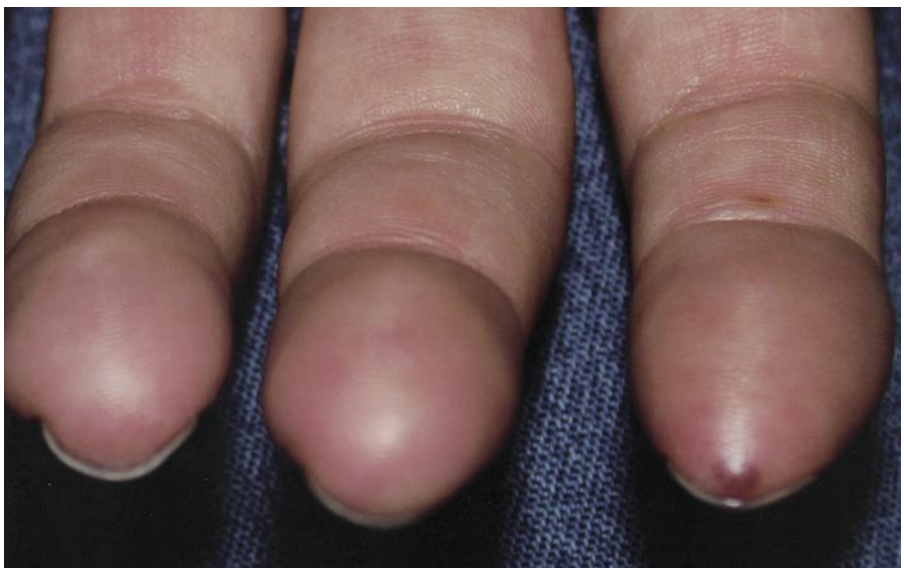

Figure 2. Reddish-purple tender papules were noted on a few fingertips and were consistent with Bywater lesions.

Comment

RND was first described by Ackerman[1] in 1978. It is one of a number of dermatologic manifestations of RA in which neutrophilic or histiocytic infiltrates predominate or contain evidence of vasculitis. These manisfestations include rheumatoid nodules, rheumatoid vasculitis to include type 2 cryoglobulinemia and Bywater lesions, and pyoderma gangrenosum.[2] Evanescent nonpruritic salmon-pink macules and papules that usually appear with fever are indicative of juvenile RA (Still disease), which also has been reported to have an adult onset.[3] Additionally, RA may be associated with Sweet syndrome or interstitial granulomatous dermatitis with cutaneous cords.[4,5]

RND is an uncommon extra-articular manifestation of RA. Its morphology is quite varied, which hinders its immediate recognition. Some patients have presented with asymptomatic, nonpruritic, urticarialike plaques localized solely to the back.[6] Other cases have presented with 0.5 to 1.2 cm annular, yellow, and erythematous papules and plaques localized to the lateral neck, or symmetrical yellow papules and plaques on the extensor surface of the upper extremities, elbows, chest, buttocks, and thighs.[7] In general, lesions tend to be symmetrically distributed, with a predilection for the dorsum of the arms and hands.[8] Rarely, vesicles or ulcerations may be seen. While lesions often heal without scarring, atrophic scars from healed lesions have been reported.[9]

A positive rheumatoid factor is seen in 70% of all patients with RA.[10] Originally, all described

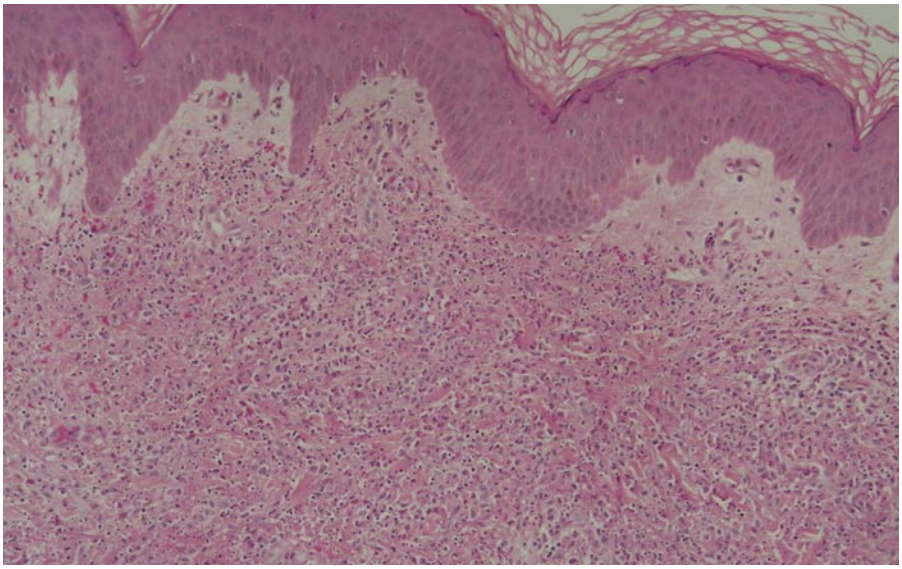

Figure 3. Biopsy specimen revealed a dense dermal neutrophilic infiltrate. Scattered histiocytes, lymphocytes, and eosinophils were present. There was no evidence of vasculitis (H&E, original magnification ×100).

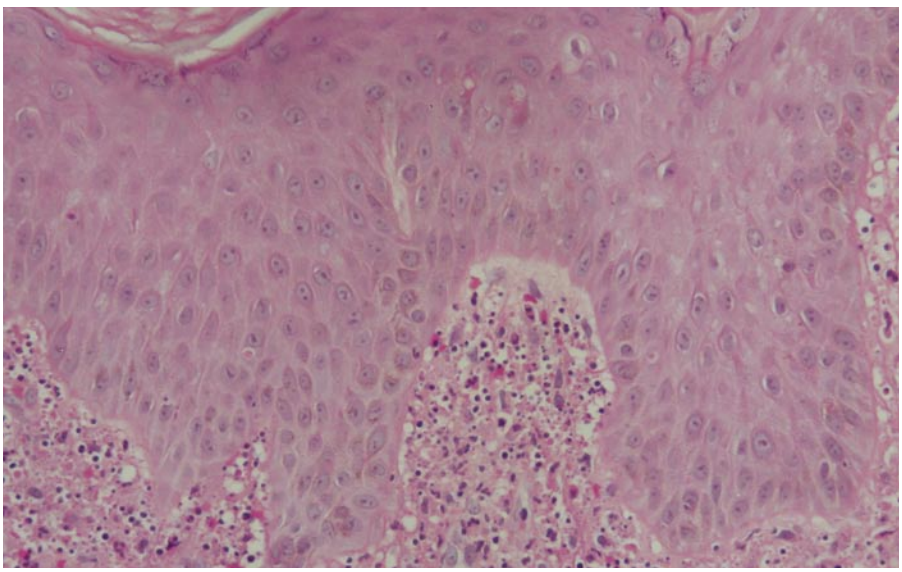

Figure 4. Collections of neutrophils in the papillary dermis, forming microabscesses similar to those observed in dermatitis herpetiformis (H&E, original magnification ×400).

cases of RND occurred in those with a positive rheumatoid factor; however, more recent literature has shown that this correlation is not complete. Brown et al[11] described a case report of RND in a woman with seronegative RA. The researchers found this case to be the first reporting on this association, an association that subsequently has been confirmed by other researchers.[8] Our patient also manifested RND while exhibiting rheumatoid factor negativity.

The histopathologic picture of RND reported in the literature is remarkably similar to our patient.[12,13] Biopsy results typically reveal a dense neutrophilic infiltrate, primarily in the mid to upper dermis but occasionally extending into the subcutis. Papillary dermal microabscesses often are seen and may be preliminarily confused with DH. However, direct immunofluorescence reveals granular IgA deposits within the dermal papilla of DH. By contrast, immunofluorescence of RND has been negative for IgG, IgM, and C3, and IgA.[12,13] Biopsy results have shown no evidence of vasculitis, though mild to marked leukocytoclasis has been reported by Lowe et al[14] and later confirmed by Mashek et al.[7]

The skin lesions of RND most closely resemble Sweet syndrome histologically and also can be confused with Sweet clinically. However, lesions of Sweet syndrome most commonly occur on the face and extremities, often following an upper respiratory or gastrointestinal disorder. Sweet syndrome also may be seen with malignancies, specifically myelogenous disorders, as well as with medications

such as granulocyte-macrophage colony-stimulating factor or tretinoin. Fever, malaise, and conjunctivitis often accompany the onset of Sweet syndrome but are not seen in patients with RND. Other neutrophilic dermatoses must be included in the differential diagnosis, including pyoderma gangrenosum; bowel-associated dermatitis-arthritis syndrome; Behçet syndrome; and erythema elevatum diutinum, which invariably shows vasculitis on pathology. Other conditions usually can be ruled out on clinical appearance or evidence of other findings.

Treatment of RND obviously is limited in definitiveness because of the small number of reported cases. Some researchers feel that dapsone is the treatment of choice,[11] though other researchers have reported on the failure of dapsone in their patients.[7] Topical clobetasol has been successfully used as well as hydroxychloroquine.[13] Several patients have exhibited an eruption of RND lesions with an RA flare or as medications such as oral steroids were tapered.[11] Our patient had worsening lesions after her prednisone was discontinued and subsequently had resolution of her RND with the resumption of prednisone. Recalcitrant lesions also have responded to cyclophosphamide.[7]

REFERENCES

1. Ackerman AB, ed. Histologic diagnosis of inflammatory skin diseases: a method by pattern analysis. Philadelphia, Pa: Lea & Febiger; 1978.
2. Jorizzo JL, Daniels JC. Dermatologic conditions reported in patients with rheumatoid arthritis. *J Am Acad Dermatol*. 1983;8:439-457.
3. Elinav H, Maly A, Ilan Y, et al. The coexistence of Sweet's syndrome and Still's disease—is it merely a coincidence? *J Am Acad Dermatol*. 2004;50(suppl 5):S90-S92.
4. Gay-Crosier F, Dayer JM, Chavaz P, et al. Rheumatoid neutrophilic dermatitis/sweet's syndrome in a patient with seronegative rheumatoid arthritis. *Dermatology*. 2000;201:185-187.
5. Gottlieb GJ, Dove RS, Ackerman AB. Interstitial granulomatous dermatitis with cutaneous cords and arthritis: linear subcutaneous bands in rheumatoid arthritis revisited. *Dermatopathol Practical Conceptual*. 1995;1:3-6.
6. Hirota TK, Keough GC, David-Bajar K, et al. Rheumatoid neutrophilic dermatitis. *Cutis*. 1997;60:203-205.
7. Mashek HA, Pham CT, Helm TN, et al. Rheumatoid neutrophilic dermatitis. *Arch Dermatol*. 1997;133:757-760.
8. Yamamoto T, Matsunaga T, Nishioka K. Rheumatoid neutrophilic dermatitis, rheumatoid papules, and rheumatoid nodules in a patient with seronegative rheumatoid arthritis. *J Am Acad Dermatol*. 2003;48:634-635.
9. Hassab-El-Naby HM, Alsaleh QA, Khalifa MA. Rheumatoid neutrophilic dermatitis. *Int J Dermatol*. 1996;35:207-208.
10. Specter TD. Rheumatoid arthritis. *Rheum Dis Clin North Am*. 1990;16:513-537.
11. Brown TS, Fearneyhough PK, Burruss JB, et al. Rheumatoid neutrophilic dermatitis in a woman with seronegative rheumatoid arthritis. *J Am Acad Dermatol*. 2001;45:596-600.
12. Scherbenske JM, Benson PM, Lupton GP, et al. Rheumatoid neutrophilic dermatitis. *Arch Dermatol*. 1989;125:1105-1108.
13. Sanchez JL, Cruz A. Rheumatoid neutrophilic dermatitis. *J Am Acad Dermatol*. 1990;22:922-925.
14. Lowe L, Kornfeld B, Clayman J, et al. Rheumatoid neutrophilic dermatitis. *J Cutan Pathol*. 1992;19:48-53.