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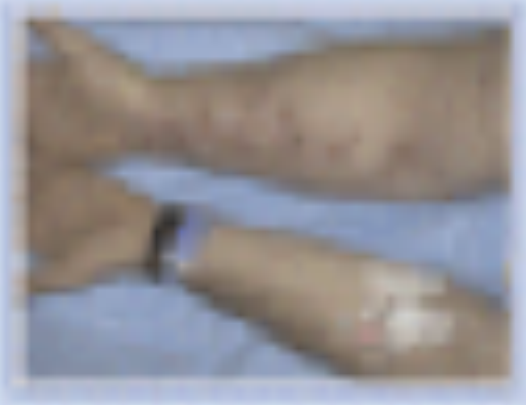

Interstitial granulomatous drug reaction to anakinra

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Interstitial granulomatous drug reactions are an uncommon entity presenting as asymptomatic, annular, erythematous to violaceous plaques. The incidence of such reactions has been increasing with the use of biologic agents. We report, to the best of our knowledge, the first such reaction to the interleukin (IL)-1 inhibitor anakinra. Our patient presented with pink dermal plaques and nodules in the periaxillary region which resolved with discontinuation of anakinra and recurred upon restarting anakinra. Biopsy revealed a diffuse dermal infiltrate of lymphocytes and histiocytes with interspersed neutrophils and eosinophils. Fragmentation and degeneration of collagen and elastic fibers was also present. Withdrawal of anakinra led to complete resolution of the lesions. Interstitial granulomatous drug reactions are increasing in frequency and we add anakinra to the list of causative agents. (J Am Acad Dermatol 2008;59:S25-7.)

Cutaneous drug reactions can exhibit a wide variety of histopathologic features. In 1998, Magro et al[1] first described interstitial granulomatous drug reactions (IGDRs) as asymptomatic, annular, erythematous to violaceous plaques with a predilection for intertriginous areas, medial thighs, and inner aspects of the arms. This reaction has been reported to sennoside, angiotension-converting enzyme inhibitors, lipid-lowering agents, calcium channel blockers, antihistamines, anticonvulsants, diuretics, antidepressants, and herbal medications.[1-3] Recently, the increasing use of biologic agents has resulted in additional adverse drug reactions. We report, to the best of our knowledge, the first case of interstitial granulomatous drug reaction to anakinra.

CASE REPORT

A 52-year-old female with rheumatoid arthritis who had been treated with the interleukin (IL)-1 receptor antagonist anakinra for 21 months presented with a 1-month history of pink dermal papules and nodules in both axillae. Histologic examination of a biopsy specimen showed a diffuse dermal infiltrate composed of neutrophils, lymphocytes, and histiocytes and rare eosinophils associated with fragmented and degenerating collagen and elastic fibers. Occasional large, "transformed-appearing" mononuclear cells with hyperchromatic, convoluted nuclei were present. Immunohistochemistry for CD68 and myeloperoxidase highlighted numerous macrophages and the dense neutrophilic infiltrate. The majority of the lymphocytes were $CD3^+$ T cells, with rare $CD20^+$ B cells also present. There was polytypic expression of kappa and lambda light chains. The interstitial pattern of the myeloid infiltrate prompted a systemic workup for leukemia. All lesions cleared following discontinuation of anakinra.

One month later, anakinra was restarted. Three months into this second treatment, the patient noted recurrence of the previous rash. She presented to our clinic with indurated pink papules and plaques in both axillae (Fig 1). The lesion was again biopsied from the left axilla. Histologic examination showed a superficial and deep perivascular and interstitial infiltrate of numerous mononuclear cells, lymphocytes, and a few interspersed neutrophils and eosinophils (Fig 2). The histiocytic-appearing cells surrounded and entrapped collagen bundles. These findings were characteristic for an interstitial granulomatous drug reaction. Skin lesions once again resolved with discontinuation of anakinra.

DISCUSSION

IGDRs may have variable histologic presentations. Microscopically, they typically exhibit a diffuse interstitial infiltrate of lymphocytes and histiocytes with collagen fragmentation and vacuolar interface dermatitis. Atypical lymphocytes may also be present. Clinically, IGDR typically presents with

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