CLINICAL VIGNETTE

Subcutaneous Nodules in a Patient with Hodgkin Lymphoma

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Introduction

Granuloma annulare is a benign condition that classically presents as annular plaques in an acral distribution. However, many clinical variants of granuloma annulare exist, which can pose diagnostic dilemmas. Subcutaneous granuloma annulare is a rare variant, and this entity must be considered in patients with known or suspected underlying malignancy. We describe the clinical features of a woman with Hodgkin lymphoma whose lower extremity subcutaneous nodules were diagnosed as subcutaneous granuloma annulare.

Case Synopsis

A 41-year-old female with nodular lymphocyte-predominant Hodgkin lymphoma presented to dermatology for evaluation of nodules on the legs that had been present for five days. Physical examination revealed multiple slightly tender, skin-colored subcutaneous nodules on bilateral lower legs. The nodules were poorly visualized but easily palpable, since there was no overlying erythema or epidermal change.

The patient denied recent medication change, exposure, infection, or illness. However, it was notable that the patient had refused her oncologist's recent suggestion to initiate chemotherapy for lymphoma. Panniculitis was initially favored, but the clinical differential diagnosis included rheumatoid nodules, subcutaneous lymphoma, subcutaneous sarcoidosis, infectious granuloma, and deep morphea. The patient was scheduled to follow-up in three weeks for clinical monitoring.

Upon her return, more subcutaneous nodules were palpated on her lower extremities. Two punch biopsies were performed, and the specimens were sent for histology and tissue culture. Histology revealed deep granulomatous inflammation with marked collagen necrosis and a mixed inflammatory infiltrate. Alcian blue and colloidal iron highlighted patchy increase in dermal mucin. Tissue cultures for bacteria, fungus, and atypical mycobacteria were negative. Lab testing, including rheumatoid factor and anti-cyclic citrullinated peptide antibodies, was noncontributory.

Based on clinical-pathologic correlation, the patient was diagnosed with subcutaneous granuloma annulare. The patient was offered intralesional steroid, but she deferred treatment. However, soon after visiting dermatology, she did agree to pursue chemotherapy for Hodgkin lymphoma and completed six cycles of bendamustine/rituximab. Her subcutaneous nodules totally resolved and have not reoccurred.

Case Discussion

Granuloma annulare is a benign, often self-limited condition and many clinical subtypes have been described: localized, generalized, micropapular, nodular, perforating, patch, and subcutaneous. Additionally, granuloma annulare has been reported to present as a paraneoplastic reaction to solid organ tumors, Hodgkin lymphoma, and non-Hodgkin lymphoma.[1] Subcutaneous granuloma annulare is rare and is characterized by painless skin-colored subcutaneous nodules on the hands, feet, ankles, tibial surfaces, buttocks, and scalp.[1,2] This variant has also been referred to as pseudo-rheumatoid nodule, deep granuloma annulare, and palisading granuloma.[2] Subcutaneous granuloma annulare is most often seen in children and young adults, and are more common in women when diagnosed in adults.[2,3]

The pathogenesis of subcutaneous granuloma annulare is uncertain. However, insect bites, trauma, PUVA-therapy, several drugs, acute phlebitis, post-surgery sepsis, and various infections have been reported as inciting events.[1] Subcutaneous granuloma annulare has not been correlated with diabetes mellitus, sarcoidosis, or autoimmune diseases.[2]

Subcutaneous granuloma annulare is a panniculitic process without dermal involvement. The diagnosis is established by histopathologic changes displaying basophilic degeneration of collagen bundles and peripherally palisading granulomas containing mucin involving the connective tissue septa of the subcutis.[4] However, 25% of patients with subcutaneous granuloma annulare also display classic findings of granuloma annulare in the dermis.[5] Rarely, subcutaneous granuloma annulare extends into deeper soft tissues.[6] Biopsy is necessary to distinguish this condition from rheumatoid nodule. Staining with Alcian Blue or colloidal iron is helpful, as mucin is characteristic of subcutaneous granuloma annulare but not rheumatoid nodule.[1] In our patient, Alcian blue and colloidal iron highlighted patchy increase in mucin, while her rheumatoid factor and anti-cyclic citrullinated peptide antibodies were negative.

Subcutaneous granuloma annulare has an unpredictable course; nodules may remain stable for months, progressively enlarge,

or spontaneously regress.[2] Intralesional injection of high potency steroids is first-line therapy.[4] Other therapies that have achieved some degree of success include cryosurgery, CO2 laser, low dose injections of recombinant human interferon gamma, and systemic medications including dapsone, chlorambucil, isotretinoin, and potassium iodide.[7-9]

Subcutaneous granuloma annulare associated with Hodgkin lymphoma is rare, as only two prior cases have been reported.[10] The diagnosis should be considered in patients with subcutaneous nodules or plaques in the context of suspected or known malignancy. A thorough evaluation and review of systems is necessary when assessing patients with uncommon subtypes of granuloma annulare.

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