

DERMATOPATHOLOGY UNIT

UPP | Department of Dermatology

UPMC Dermatopathology "Case of the Month" Presentations

UPP - Department of Dermatology, Dermatopathology Unit

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Case Authors: P.C.Parham-Vetter, MD,MPH Douglas Kress, MD

MARCH 2004 CASE OF THE MONTH

FINDINGS

History:

A 54 year old Hispanic female presented with a 2 month history of annular skin lesions. The lesions had started on her arms and had recently began developing on her chest, neck, and upper back. The patient reported that the lesions were mildly pruritic, but she was most concerned about their appearance. She had been using over-the-counter hydrocortisone cream without improvement.

The patient was taking aspirin for her heart but no other prescription, over-the-counter, or herbal medications. She had no known medication allergies. She had no history of significant medical illness other than mild hypertension controlled by diet. She had a family history of diabetes and breast cancer.

Social history included a 25 year history of smoking ½ ppd. She worked part-time as a pet groomer and had frequent contact with pets. She also had frequent contact with several grandchildren who were elementary school age. She had no history of STDs, although she did have a history of multiple sex partners before marrying.

The patient reported a frequent cough, but otherwise the review of systems was unremarkable.

Exam:

Physical exam revealed annular and circinate lesions ranging in size from 2 cm in diameter to 8 cm in diameter. The lesions consisted of multiple 1-3 mm slightly erythematous papules and were located on the dorsum of both arms and hands, the anterior neck, chest and upper back.

The skin and mucosal exam was otherwise unremarkable.

Based upon the physical exam, the clinical differential diagnosis included tinea corporis, granuloma annulare, cutaneous T-cell lymphoma, annular lichen planus, sarcoidosis, secondary or tertiary syphilis.

Laboratory Tests:

Laboratory tests ordered by her primary care physician two weeks after the lesions appeared included a CBC, electrolytes, lipid profile, hepatic profile, VDRL, ?Hcg, and fasting glucose. These tests were all normal. A KOH preparation performed in our office was negative.

Histopathology:

A punch biopsy was performed with a 4mm trephine on a newly developed lesion on the patient's left forearm. The path findings are discussed in the figure and image review page:

[**GO TO FIGURE AND IMAGE REVIEW PAGE**](#)

[**GO TO DISCUSSION AND DIAGNOSIS PAGE**](#)

[**Dermatopathology Homepage**](#)



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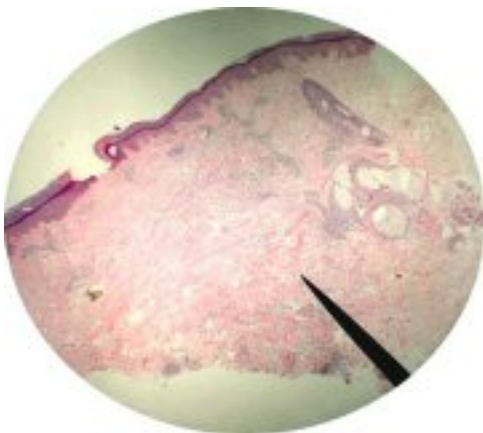
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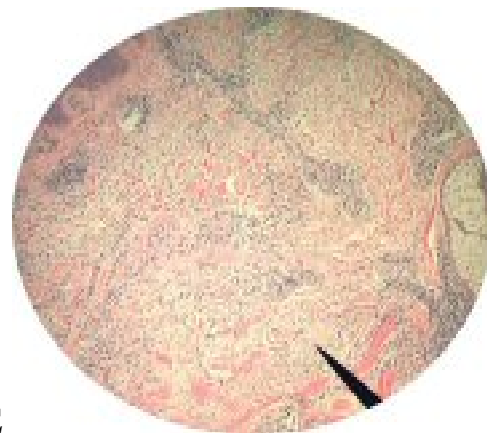
Figures & Images

1. Click on the Figure number you wish to review.
2. Click on the image to enlarge

- **Histologic examination:**



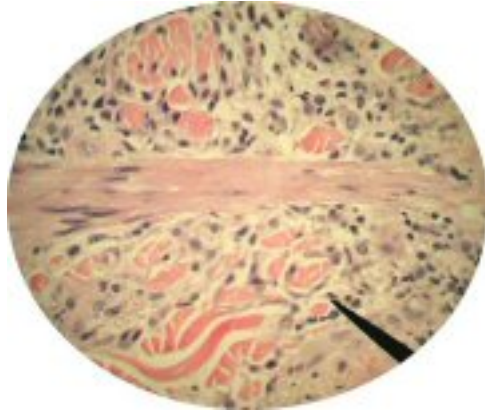
Low Mag. H&E
H&E



Medium Mag.

Low power and medium power examination of the H&E preparation showed a normal epidermis with a lymphohistiocytic infiltrate both perivascularly in the upper and mid dermis as well as interstitially. Initial histopathological differential diagnosis included interstitial granuloma annulare, the inflammatory stage of morphea, cutaneous T-cell

lymphoma, and xanthoma.



High Magnification H&E

High power examination of the H&E preparation showed basophilic histiocytes splayed between collagen bundles with an increase in feathery bluish mucin around the cells. There was minimal collagen degeneration. There was no evidence of epidermotropism, vasculitis, plasma cells or foamy cells.

[Go to Discussion Page](#)

Discus
Page

[Return to Clinical Findings](#)

Clinical
Findings

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DISCUSSION & DIAGNOSIS

DIAGNOSIS

Given these findings a diagnosis of interstitial granuloma annulare was made.

DISCUSSION

Granuloma annulare (GA) is a self-limited, benign process. In a small subset of patients it is associated with glucose intolerance. The two most common types are localized GA and generalized GA. Localized GA is the most common type and typically presents with large annular and arcuate lesions typically isolated to the hands and arms or legs and feet. It usually occurs in people younger than 30 years old, and occurs twice as often in women compared to men. Generalized GA comprises 15% of all cases and characteristically occurs in children younger than 10 and adults older than 40. The annular plaques in this variant are typically only 1-2 cm in size with a widespread distribution involving the trunk, neck, forearms and legs. In this case the age at presentation and distribution of the lesions were typical of generalized GA; however, the large size of the plaques was more characteristic of localized GA.

The exact etiology of GA is unknown. Proposed inciting factors include trauma, insect bite, TB skin testing, sun exposure, and viral infections. It is considered by many to be a delayed-type hypersensitivity reaction to an unknown antigen and it appears to be a Th1 mediated inflammatory reaction with lymphocytes producing interferon-gamma that results in dermal matrix degradation. Laboratory tests in the research setting have shown an increase in heparin precipitable cryofibrinogen, fibronectin, serum lysozyme, and benzylamine monoamine oxidase. Electron microscopy shows degeneration of both collagen and elastic fibers. Histiocytes have a high content of primary liposomes with release of lysozymes into the extracellular space. Increased levels of interstitial heparin sulfate have also been postulated to play a role.

Histopathologically granuloma annulare can present in three patterns. The interstitial pattern is the most common, comprising 70% of all cases. As in this case, this pattern presents as scattered histiocytic infiltrate between collagen bundles with a variable amount of mucin and an inflammatory infiltrate. Occasionally Giant cells may be seen. , Another common pattern is the palisaded granuloma pattern. This appears as a focal degeneration of collagen and elastic fibers with feathery blue mucin deposition surrounded by a palisade of histiocytes. A perivascular and interstitial lymphohistiocytic infiltrate in the upper and mid dermis is also seen. , Both of these two patterns have variable vascular changes of fibrinoid deposition in vessel walls and occasionally vascular lumina with immunofluorescence showing perivascular deposition of IgM, C3, and fibrinogen. , The third pattern, epithelioid histiocytic nodular pattern, is quite rare.

Fifty percent of cases will spontaneously resolve within two years; however, there is a 40% recurrence rate. Numerous topical therapies have been reported as beneficial including topical corticosteroids, intralesional steroid injections with or without interferon-gamma, topical vitamin E, topical imiquimod, cryotherapy, PUVA, and UVA-1 therapy. Systemic therapies that have been used include nicotinamide, niacinamide, isotretinoin, anti-malarials, cyclosporine, chlorambucil, dapsone, potassium iodide, thyroxine, dipyridamole, and pentoxifylline. -

Initially, our patient was prescribed a moderate potency topical steroid cream for one month, but showed no response. A high potency topical steroid was also used for one month, again showing no response. The number of lesions precluded the use of cryotherapy and intralesional steroid injections. Additionally, the patient lived in a rural area and was unable to travel several times a week for light therapy. The patient was anxious to have improvement of the skin but did not want to take oral medications with potentially harmful side effects. Based upon the above factors a regimen was prescribed to include Nicamide 500 mg per day combined with topical Elidel cream in the morning and Tazorac cream at night. The patient reported some initial irritation from the Tazorac but after one month showed no further development of plaques and partial resolution of the lesions on the neck, chest and arms. The patient was asked to return to clinic if the lesions persisted or new ones developed. As of nine months later, she had not returned with new or persistent lesions.

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[Return to Clinical Findings](#) Discuss
Page

[Return to Figures & Images](#) Figures
and