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Granuloma Annulare:

Not as simple as it seems

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Granuloma annulare (GA), the ringed eruption, has also been termed lichen annularis and heloderma simplex et annularis, just to recount a few of the names for this “deeply seated nodule or a ring of closely grouped nodules of firm consistency, elevated, sharply circumscribed, whitish, pinkish, reddish, purplish or bluish-red in color.” This is a description, presented by Ormsby and Montgomery in their definitive text of over a half century ago. [1] When first delineated in 1895 by T. Colcott Fox in London as a ringed eruption, GA was considered either of unknown cause or due to a tubercular infection. [2] Despite decades of investigations, its etiology continues to remain obscure, even today.

Our reasons for discussing this morphologically distinct entity with vague etiology and pathogenesis are due to some recent unusual findings. A discussion of the traditional differential diagnoses of erythema elevatum diutinum and necrobiosis lipoidica diabetorum would add little to our knowledge; however, a middle-aged man with stasis dermatitis and even elephantiasis raised our curiosity, when a cutaneous biopsy demonstrated GA among the areas, manifesting diffuse redness and thickening. Was this a coincidence or part of a dermatitis (figure 1)? Could the diffuse presentation represent a Koebner phenomenon.?

Granuloma Annulare and Other Diseases

GA has been linked with a number of diseases. For example, there are case reports of its association with prostate carcinoma, breast malignancies, pulmonary adenocarcinoma, and cervical adenocarcinoma. [3] GA has been found in patients with lymphomas, including Hodgkin’s disease, mycosis fungoides, and lymphoepithelioid cell lymphoma (Lennert’s lymphoma). Concerning Lennert’s lymphoma, the similarities with GA were raised because of the initial granulomatous presentation. Twenty per cent of patients with lymphomas other than mycosis fungoides have been found to have a number of

cutaneous signs, ranging from erythema nodosum to urticaria, so that a granulomatous picture might not be so strange. [4]

There are patients with morphea and systemic scleroderma who have coexisting GA. Both diseases have vascular injuries, altered collagen, and lymphohistiocytic infiltrates. Whereas GA has fragmented collagen bundles and inflammation, characterized by necrobiosis and granulomatous formation, morphea has dermal fibroblasts in excess. [5]

GA has been found following trauma, ultraviolet light exposure, insect bites, herpes zoster infection, mycobacterial infection, and even pressure applied to the hands. The list goes on and on with little documentation to prove a cause and effect. [6] GA has been found in infants as young as 68 days [7], while senior citizens infrequently are afflicted.

Additional Considerations

What is the pathogenesis of GA? No infectious origin has ever been confirmed. Periodically, the question of its being an inherited disease is raised. Some have suggested that allergic contact dermatitis reactions might precipitate GA. [8] Fortunately, GA seems to have escaped the strange fables of etiology that have plagued sarcoidosis – pine tree pollen.

Categorizing GA into various types: localized, (figure 2) generalized, (figure 3) papular, subcutaneous, or even granuloma multiforme contributes little to the understanding of this condition. There are no internal manifestations, and rarely does it involve the face. A review of the histopathologic picture of palisading granulomas and necrobiosis does not make the background of this ringed eruption any clearer. [9]

Various treatments have been suggested but none can give positive results for a pharmacologic proof. These might be considered in the eras in which they were proposed: arsenic administered by mouth, salicylic acid ointment, tuberculin injections, carbon dioxide snow, and radiation. A more contemporary approach would include topical corticosteroids, intralesional corticosteroids, oral antihistamines, PUVA, cyclosporine, pentoxifylline, isotretinoin, fumaric acid, and topical immunomodulators. To add to the muddle, performing a biopsy sometimes results in clearing of the lesions.

Conclusions

GA continues to remain an enigma with revelations lacking about its cause and more importantly, effective treatment. The patient can be reassured that the disease is self-limiting, but GA has been known to last at least 34 years.

As to its association with stasis dermatitis, it is most likely a coincidence. The facts remain that patients with granuloma annulare usually do not have other strange diseases. [6]

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Figure 1: 47 year old man developed dermatitis on both legs. While the stasis diagnosis seemed a reasonable clinical diagnosis, the dermatopathology revealed granuloma annulare.

Figure 2: The erythematous ringed lesion of GA can appear alone.

Figure 3: Generalized GA of several years' duration in a middle aged woman.