Genaralised Granuloma Annulare-Uncommon in Clinical Practice.

Islam N[1]

Abstract

Generalised granuloma annulare is a benign inflammatory dermatosis characterized by dermal papules and annular plaques. It is often clinically confused with other dermatoses particular superficial fungal infection. A man of 50 years came with multiple erythematous, mildly pruritic, firm papules and annular skin lesion over the extremites and back of trunk for the last two years. He was treated with an oral antifungul for several months under diagnosis of tinea corporis without remission. The diagnosis of Generalised Granuloma Annulare was made based on skin biopsy and histopathological examination. Oral Acitretin and topical tacrolimus (0.1%) were administered and after 1 month of follow up period the lesion were started to regress. Complete remission was found after 3 months treatment.

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Key words: Generalised Granuloma Annulare; Acitretin and topical tacrolimus.

Introduction

The latin word 'annulus' meaning ringed. Granuloma annulare (gran-u-low-muh an-u-LAR-e) is a skin condition that most commonly consist of raised, reddish or skin colored bumps (lesion) that form ring patterns. It occurs in all age groups but rare in infancy. Women are affected by Genaralised granuloma annulare twice as often as men. Localized Genaralised granuloma annulare is most commonly found in children and in adult youngers than 30 years. Genaralised granuloma annulare demonstrates a bi-modal age distribution occurring in patient younger than 10 years and patient aged 30-60 years. The frequency of Genaralised granuloma annulare is in the general population is unknown. Genaralised granuloma annulare does not favour a particular race, ethnic group or geographical race. Localized Genaralised granuloma annulare is the most common among the various sub-types. 9-15% have the generalized variant. Perforating Genaralised granuloma annulare has been reported to have a prevalence of 5% among Genaralised granuloma annulare sub-types. The precise causes is unknown proposed pathogenic mechanism for Granuloma Annulare include cell-mediated immunity (type-IV) immune complex vasculitis and abnormality of tissue monocyte. Some other possible mechanism include primary degeneration of connective tissue leading to granulomatous inflammation, lymphocyte mediated immune reaction with macrophage activation and cytokine mediated degradation of connective tissue. Granuloma Annulare is characterized clinically by dermal papules and annular plaques. Usually on your hands & feet. It may be triggered by minor skin injury, certain medication, animal or insect bites, sun exposure, PUVA therapy, infection including hepatitis, tuberculin skin test,vaccination. DM and thyroid disease are risks factor for Genaralised granuloma annulare. Most often when lesions are numerous and wide spared. Although most annular lesion will be typical of a dermotophytosis. Physicians must consider other possible diagnoses.

Generalised cases represent a major therapeutic challenge. Although systemic steroid may be very effective. In addition,

1. ***Dr. Nahida Islam***
Assistant Professor
Department of Dermatology & VD
Community Based Medical College Bangladesh

Address of correspondence
Phone: 01711156198
E-mail : nislamcb5@gmail.com

because diabetes may be present, systemic steroid may complicated the management of the diabetes. Oral retinoid, especially isotretinoin can be considered at a dose of 0.5 mg/kg or slightly more. Generalized granuloma annulare treated with short-term administration of etretinate[1]. The response of Generalised granuloma annulare to Dapsone, Doxycycline, Hydroxychloroquine$_{(2,3,4)}$. Super potent topical steroid or topical calcineurin inhibitor or imiquimod may be effective.

Case Report

A 50 years man came to us with multiple well defined, mild pruritic, firm papules and annular erythematous plaques, on extremites and back of the trunk for two years duration (Fig. 1). He had previously received different therapies such as anti-fungal, antibiotics topical drugs. None of this medication was effective. On physical examination we observed a well demarcated, regular bordered erythematous annular plaques with polycyclic lesion on the extremities and back of the trunk (Fig.1).The result of the laboratory test including a complete blood cell count, VDRL, skin scraping for fungus, Mantoux test, thyroid disorders and chest x-ray were within normal limits. But random blood glucose was 13 mmol/L. An elliptical incision was made along the border of the lesion to take the biopsy specimen. Histopathology of the lesion revealed epidermis with mild hyperkeratosis, acanthosis and increase number of melanocytes in the basal layer. Where as the dermis reveals collection of histiocytes some vacuolated cell and moderate infiltrate of lymphocytes (Fig.2). A few multinucleated giant cells including langhans type are seen(Fig.3).No malignancy seen.

A diagnosis of Genaralised granuloma annulare(GA) was made base on the cutaneous finding and this was supported by the histopathological examination. He was treated oral Acitretin & topical tacrolimus (0.1%) for three months (Fig-4). The cutaneous lesion started to regress within one month and they healed with post inflammatory hyper-pigmentation and hypo-pigmentation after three months.

Figure-1: Erythematous papules over extremity & Back before treatment.

Figure-2: Lympho-histiocytic infiltrate extending in between the collagen bundles which appeared to be separated from each other.

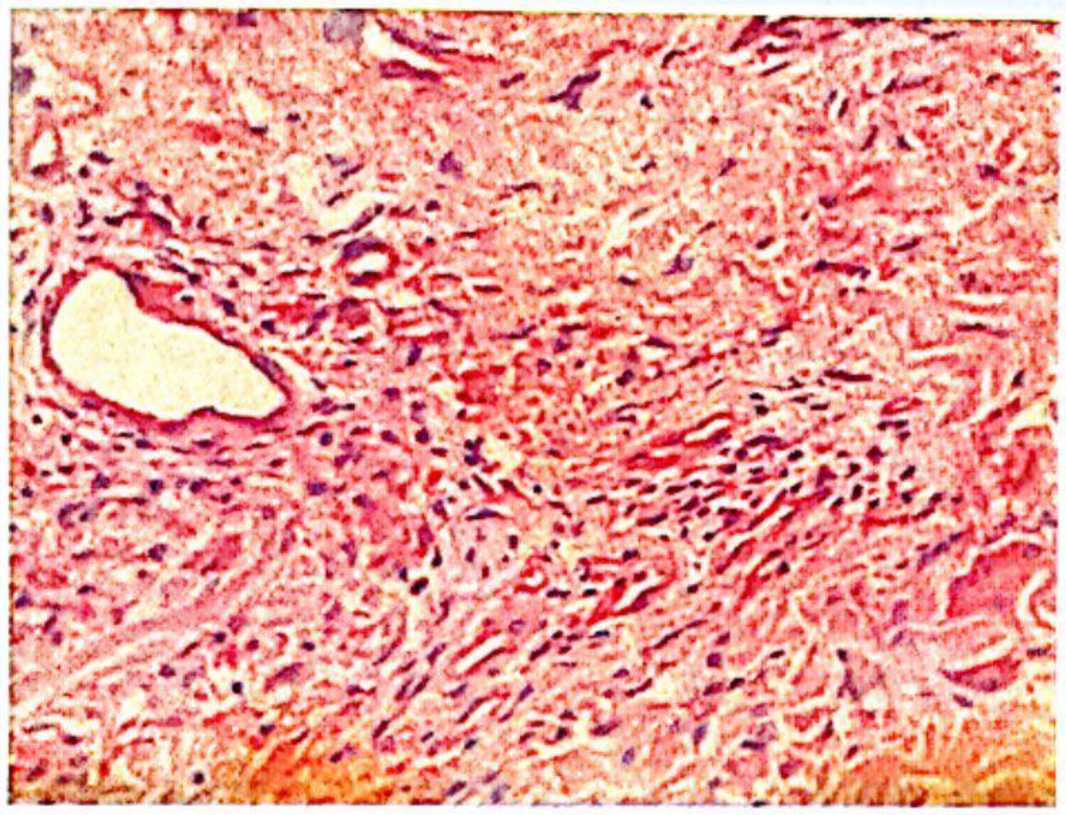

Figure-3: Inflammatory infiltrate composed of lymphocytes, histiocytes and giant cells (H&E original magnification x400).

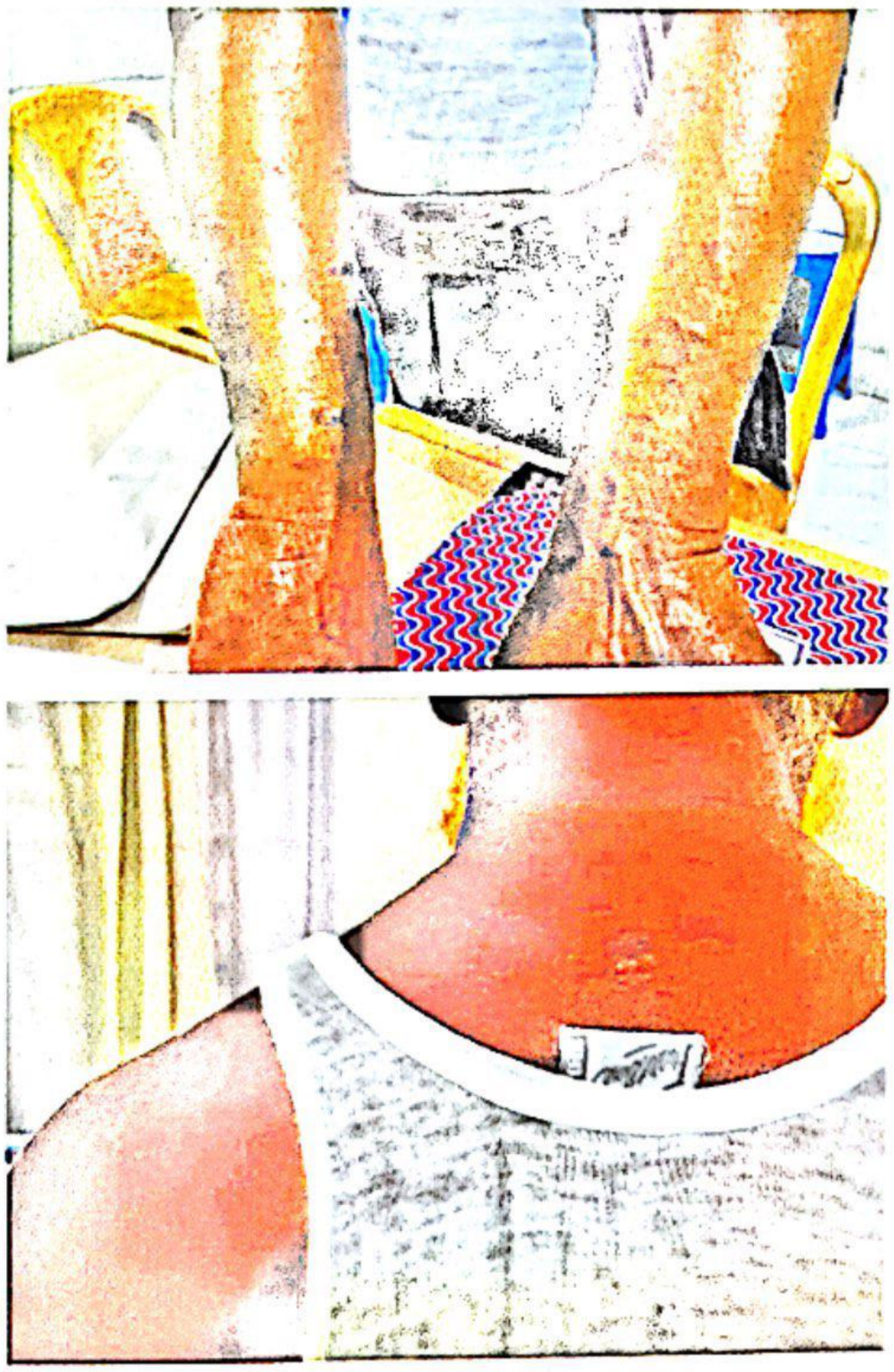

Figure-4: Erythematous papules over extremity & Back after treatment.

Discussion

The Genaralised granuloma annulare form is rarer and it's a persistent disease with a very long evolution[5].The trunk is usually involved, along with the neck and extremities. Face, scalp, palms, and soles may be affected[6]. Five morphologic variants of granuloma annulare have been described: localized, generalized, perforating, subcutaneous, and patch type[7]. Patch type granuloma annulare is a relatively recently described variant, which presents as erythematous to brown patches with or without scales, which may have annular configuration on the trunk or extremities. Female predominance has been reported, as with other forms of GA[8]. High index of suspicion and clinico-pathologic correlation is required to make a diagnosis of patch type of granuloma annulare. The clinical differential diagnosis of patch type granuloma annulare includes morphea, erythema annulare centrifugum and parapsoriasis[9]. Histologically granuloma annulare can present in three patterns, necrobiotic granuloma, interstitial or incomplete form and granuloma of sarcoidal or tuberculoid type[10]. Interstitial pattern was the most common histological pattern in a study[11]. Interstitial pattern is most often found in patients with patch type granuloma annulare, as was seen in our case. Histologically interstitial granuloma annulare shows 'busy dermis' with increased number of inflammatory cells in the dermis separated by connective tissue mucin. The infiltrate is composed of lymphocytes and histiocytes.Inflammatory cells are also noted around blood vessels and between collagen bundles without well formed area of necrobiosis[12]. Differential diagnosis of interstitial type granuloma annulare includes morphea, mycosis fungoides, xanthoma, interstitial granulomatous drug reaction and interstitial granulomatous dermatitis. Histologically morphea can be confused with interstitial type granuloma annulare but the subtle presence of histiocytes in an interstitial pattern usually allows a definitive diagnosis of granuloma annulare[13]. Increased hyalinization of collagen is a feature of morphea, which is not seen in granuloma annulare. Mycosis fungoides can have granulomatous infiltrate with a granuloma annulare like pattern. This can easily be recognized by the presence of at least some intraepidermal lymphocytes[14]. Xanthoma can be differentiated from interstitial pattern of GA on the basis of foamy

appearance of histiocytes which is completely lacking in granuloma annulare and there is also a lack of perivascular lymphocytic infiltrate in xanthomas. Interstitial granulomatous drug reaction shows predominantly eosinophils, lichenoid changes at dermo-epidermal junction while tissue necrobiosis is rarely noted. Interstitial granulomatous dermatitis shows predominance of neutrophils and neutrophil fragments.Histiocytes, lymphocytes and eosinophils are also present within palisades of histiocytes around basophilic collagen fibers. Changes may involve full thickness of dermis[15]. We also find Generalised Granuloma Annulare associated with Diabetic Mellitus (DM).

One case of generalized granuloma annulare reported in 94 year old male[16]. Two cases reported as a initial manifestation of chronic myelomonocytic leukemia[17]. Generalised granuloma annulare associated with gastrointestinal stromal tumor[18]. Genaralised granuloma annulare always mimic with tinea corporis that must be exclude for confirmation.

Conclusion

Generalised granuloma annulare is uncommon in clinical practice. Although prognosis is variable but this case tinea corporis and other dermatosis like may consider as erythema multiforme, drug reactions, vasculitis, urticarial vasculitis, secondary syphilis, cauteneous TB etc and skin biopsy is the golden tool for confirmation of diagnosis.

Reference

1. *Asano Y, et al: Generalized granuloma annulare treated with short-term administration of etretinate. J Am Aead Dermatol 2006; 54:S245.*
2. *Czarnecki DB,et al: The response of GGA to dapsone. Acta Dermatol Venereol (Stockh) 1986;66:82.*
3. *Duarte AF,et al: Generalized granuloma annulare-response to doxycycline.*
4. *Cannistraci C, et al: Treatment of Generalized granuloma annulare with hydroxychoroquine.*
5. *Penas PF, Jones-Caballero M, Fraga J, Sánchez-Pérez J, García-Díez A. Perforating granuloma annulare.Int J Dermatol 1997;36:340-8.*
6. *Prendiville JS. Granuloma annulare. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, editors. Fitzpatrick's dermatology in general medicine. 7th ed. New York: McGraw-Hill, 2008:p369-73.*
7. *Mutasim DF, Bridges AG. Patch granuloma annulare: clinic- pathologic study of 6 patients. J Am Acad Dermatol 2000; 42: 17-421.*
8. *Coelho R, Carvalho R, Rodrigues A, Afonso A,Cardoso J. Patch ype granuloma annulare. Eur J Dermatol 2009; 19: 285-286.*
9. *Jang EJ, Lee JY, Kin MK, Yoon TY. Erythematous granuloma nnulare. Ann Dermatol 2011; 23: 409-411.*
10. *Ko CJ, Glusac EJ, Shapiro PE. Non-infectious granulomas. In: ever's histopathology of the skin. Elder DE.edi. 10th edition. ippincott Williams & Wilkins, Philadelphia 2010.p 361-364.*
11. *Umbert P, Winkelmann RK. Histologic, ultrastructural and isto-chemical studies of granulomas annulare. Arch ermatol 977; 113:1681-1686.*
12. *Victor FC, Mengden S. Granuloma annulare, patch type. Dermatol nline 2008; 14: 21*
13. *Sarkany RPE, Breathnach SM, Seymour CA,Weisman K, Burns DA. etabolic and nutritional disorders. In: Rook's textbook of ermatology.Burns T, Breathnach S, Cox N, Griffiths C.editors.7th dition. Blackwell publishing,Massachusetts, USA 2004.p. 57.109- 7.119.*
14. *Su LD, Kim YH, Leboit PE, Swetter SM, Kohler S.interstitial ycosis fungoides- a variant of mycosis fungoides resembling ranulomas annulare and inflammatory morphea. J Cutan Pathol 002; 29:135.*
15. *Perrin C, Lacour JP, Castant J, Michiel JF.Interstitial ranulomatous drug reaction with a histological pattern of nterstitial granulomatous dermatitis.Am J Dermatopathol 2001; 23: 95-298.*
16. *Olympia Kovich MD and Susan Burgin MD.Generalized ranuloma nnulare Dermatol Online J 2005;11:23.*
17. *Hinckley MR, Walsh SN, Molnár I, Sheehan DJ, Sangueza OP, osipovitch G. Generalized Granuloma Annulare As an Initial Manifestation of Chronic Myelomonocytic Leukemia: A Report of 2 Cases. Am J Dermatopathol 2008;30:274-77.*
18. *Chiu ML,Tang MB. Generalized granuloma annulare associated with gastrointestinal stromal tumour: case report and review of clinical features and management. Clin. Exp Dermatol 2008;33:469-71.*