Case Report

Allopurinol induced granuloma annulare in a patient of lepromatous leprosy

Satyendra Kumar Singh, Kajal Manchanda, Aakash Amar Bhayana, Anurag Verma

Department of Dermatology and Venereology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

ABSTRACT

Granuloma annulare (GA) is a benign, inflammatory dermatosis involving dermis or subcutis with unknown etiology and poorly understood pathology. GA has characteristic histological features of necrobiosis, granuloma formation and abundant mucin deposition. Various predisposing factors, systemic diseases and drugs have been implicated in the etiology. We hereby describe a case of 70 year old male who was a known case of lepromatous leprosy, taking multidrug therapy for 6 months presented with multiple discrete, annular, firm, non tender, smooth surfaced skin colored papular lesions ranging in size from 0.5-1 cm over back for 1 month. There was past history of intake of allopurinol for hyperuricemia which was started 1 year back. There was history of similar lesions 6 months back which healed within 1 month of stopping allopurinol and he started taking the drug for the past 4 months on his own without any medical advice. Histopathological examination showed superficial and deep perivascular lymphocytic infiltrate with numerous histiocytes scattered in the intersititum of reticular dermis and abundant mucin in between the histiocytes. Allopurinol was implicated as an etiological agent and dramatic improvement was seen after stopping the drug for a period of 4 weeks. Naranjo's algorithm showed a probable association with a score of 6. Thus the final diagnosis of allopurinol induced generalised interstitial granuolma annulare was made. Patient was advised to continue antileprotic drugs, low purine diet and avoid allopurinol intake.

Key words: Allopurinol, granuloma annulare, interstitial

INTRODUCTION

Granuloma annulare (GA) is benign self limited disorder with unknown etiolwogy and poorly understood pathology.[1] It was first described by Colcott- Fox in 1895 and Radcliffe-Crocker in 1902.[1] The various morphological forms that have been described include localized, generalized, subcutaneous, perforating and patch type. Generalized type comprises 8-15% of the cases, mainly affecting the adults, with trunk being a common site of involvement.[1] It is characterized by focal degeneration of collagen i.e., necrobiosis with surrounding inflammation and fibrosis.[2] A variety of predisposing events and associated systemic diseases have been reported previously but, their significance is not clear. Various drugs which have been implicated in etiology of granuloma annulare include amlodipine, gold, allopurinol, diclofenac, quinidine and intranasal calcitonin.[1,3,4] There are very few case reports establishing drugs as an etiological factor in granuloma annulare. We hereby report a case of generalized interstitial type of granuloma annulare in an elderly patient due to allopurinol, providing further evidence in support.

Access this article online	
Quick Response Code:	Website: www.jpharmacol.com
	DOI: 10.4103/0976-500X.110915

CASE REPORT

Seventy year old male presented with multiple aymptomatic red raised lesions over back for one month. He was a known

Address for correspondence:
Kajal Manchanda, Department of Dermatology and Venereology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
E-mail: kajalmanchanda@gmail.com

case of lepromatous leprosy and was on multidrug therapy for multi bacillary Hansen's disease for the past six months. There was past history of intake of allopurinol for hyperuricemia which was started one year back. There was history of similar lesions six months back which healed within one month of stopping allopurinol and he started taking the drug for the past four months on his own without any medical advice. There was no history of any other drug intake and any other associated systemic illness. On examination, there were multiple grouped but discrete, annular, firm, non tender, smooth surfaced skin colored papular lesions ranging in size from 0.5-1 cm over back [Figure 1a and b]. There was diffuse loss of touch and temperature sensations over dorsal aspect of bilateral hands and feet, with thickening of bilateral ulnar and common peroneal nerves. There was ulnar clawing in bilateral hands and blister over index finger of right hand. Based on history and clinical examination, differential diagnosis for the lesions over back included granuloma annulare (drug induced), lesions of lepromatous leprosy, sarcoidosis. On routine investigations, complete blood counts, liver and renal function tests, thyroid function tests, random blood sugar, chest radiographs were within normal limits. Enzyme linked immunosorbent assay for human immunodeficiency virus 1 and 2 was non reactive. Histo-pathological examination of biopsy sample from lesion over back showed sparse superficial and deep perivascular lymphocytic infiltrate with numerous histiocytes scattered in the intersititum of reticular dermis. Abundant mucin was present in between the histiocytes. The overlying epidermis was unaffected [Figure 2]. Thus the diagnosis of generalised interstitial granuloma annulare was confirmed. As allopurinol has previously been implicated as an etiological agent in granuloma annulare, the patient was advised to stop the drug in future. The patient was reviewed after a period of fourweeks, the lesions of granuloma annulare over his back had completely resolved [Figure 1c and d]. Naranjo's algorithm was also applied for determination of adverse drug reaction probability and the total calculated score was 6, which showed a probable association. Thus the diagnosis of allopurinol induced generalised interstitial granuloma annulare was confirmed.The patient was advised to continue with the antileprotic drugs, low purine diet and to avoid allopurinol intake.

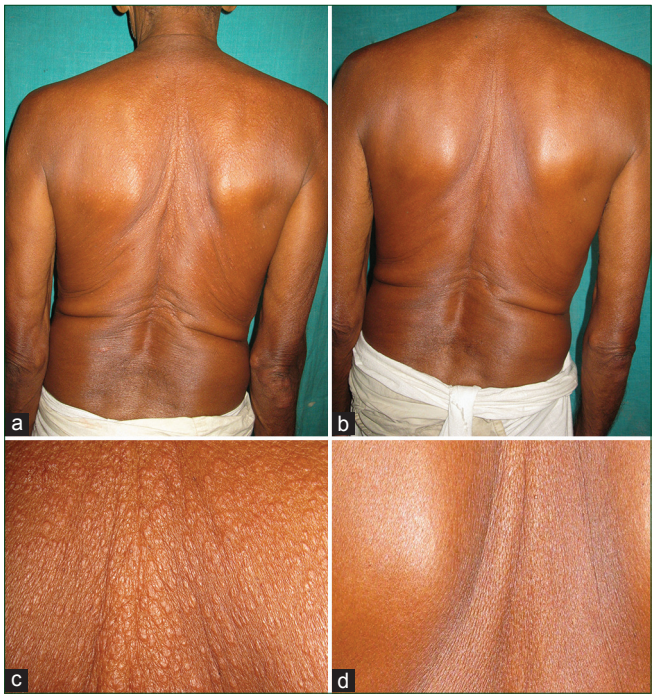

Figure 1: (a) Multiple discrete, annular, firm, smooth surfaced skin colored papular lesionsover back. (b) A closer view of the lesions over back. (c) Complete clearance of lesions after fourweeks in the same patient. (d) A closer view of back of same patient after four weeks

DISCUSSION

GA is a disease of unknown etiology, characterized by focal degeneration of collagen with surrounding areas of reactive inflammation and fibrosis.[5] GA can occur at any age, with a slight female predominance.[1] Most of the cases are sporadic, occasional familial cases have been described. The clinical variants include localized, generalized, subcutaneous, perforating, and patch type.[1] Generalised or widely disseminated GA presents clinically as predominantly annular lesions in 67% of cases and non-annular lesions in 33%.[5] The etiology is mainly unknown, it has been reported after trivial non specific trauma including cat bite, insect bite, tuberculin test, PUVA therapy. Viral infections including Epstein Barr virus, HIV, chronic hepatitis B, hepatitis C, herpes zoster have also been implicated.[1] Certain cases of GA have been reported to occur after ingestion of various drugs e.g., gold, allopurinol, diclofenac, quinidine, intranasal calcitonin, amlodipine.[1,3,4]

Association of GA with various disorders have been described previously, studies with diabetes mellitus are controversial. Other associations that have been described include thyroiditis,

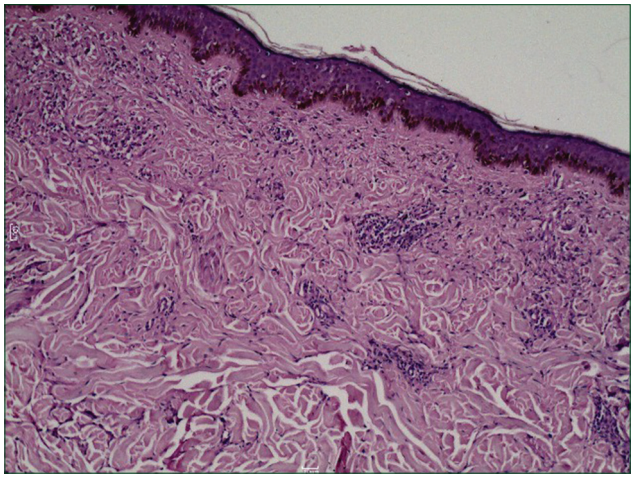

Figure 2: Numerous histiocytes scattered in the intersititum of reticular dermis with abundant mucin in between the histiocytes (H and E, ×400)

thyroid adenoma, Hodgkin and non Hodgkin lymphoma and mycosis fungoides.[1] Histopathology is characteristic, including features of necrobiosis and granuloma formation along with abundant mucin deposition. The characteristic pattern include lymphohistiocytic granuloma associated with varying degrees of connective tissue degeneration and mucin deposition.[2] The infiltrate may have a palisaded or interstitial pattern or a mixture of both. GA is rarely symptomatic and usually resolves without complications. Various treatments including X-ray therapy, cryotherapy, laser destruction, and intralesional triamcinolone injection have been used with success in various case reports and series. Systemic treatment with PUVA, pentoxifylline, nicotinamide, niacinamide, isotretinoin, salicylates, chlorpropamide, potassium iodide, thyroxine, aspirin, dipyridamole, dapsone, antimalarials, corticosteroids and chlorambucil have been reported to clear the lesions, but spontaneous resolution makes evaluations of treatments difficult.[6] This case represents a case of allopurinol induced generalized interstitial granuloma annulare as it had temporal association with drug intake and lesions healed spontaneously after withdrawal of drug. There have been previous reports supporting this but further studies are necessary to confirm allopurinol and various other drugs as etiological agents in generalized granuloma annulare.

REFERENCES

1. Prendiville SJ. Granuloma annulare. In: Fitzpatrick TB, Wolff K, Goldsmith AL, Gilchrest AB, Paller SA, Leffell JD, editors. Dermtology in General Medicine. 7th ed. New york: Mc-Graw-Hill; 2008. p. 369-72.
2. Ko CJ, Glusac EJ, Shapiro PE. Noninfectious granulomas. In: Elder DE, Elenitsas R, Johnson BL, Murphy GF, editors. Lever's Histopathology of the skin. 10th ed. Philadelphia: Lippincott Williams and Williams; 2009. p. 361-3.
3. Brechtel B, Kolde G. Granuloma annularedisseminatum as a rare side effect of allopurinol. Hautarzt 1996;47:143.
4. Goihman-Yahr M. Disseminated granuloma annulare and intranasal calcitonin (Letter). Int J Dermatol 1993;32:150.
5. Dabski K, Winkelmann RK. Generalised granuloma annulare: Clinical and laboratory findings in 100 patients. J Am AcadDermatol 1989;20:39-47.
6. Cyr PR. Diagnosis and management of granuloma annulare. Am Fam Physician 2006;74:1729-34.

How to cite this article: Singh SK, Manchanda K, Bhayana AA, Verma A. Allopurinol induced granuloma annulare in a patient of lepromatous leprosy. J Pharmacol Pharmacother 2013;4:152-4.
Source of Support: Nil, **Conflict of Interest:** None declared.