

CASE REPORT

Genital granuloma annulare of scrotum and penis with localized hand lesion: A rare presentation

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ABSTRACT

Granuloma annulare (GA) is a common chronic inflammatory condition of the dermis or subcutis of unknown etiology characterized histopathologically by collagen degeneration surrounded by palisading granulomas with mucin predominantly seen on the hands and feet in females. Penile GA is rare with only 15 cases reported so far. We report here a case of genital GA with many unusual features such as the presence of dermal nodules and typical annular plaque lesions involving the scrotum as well as the shaft of the penis along with a classical lesion on the hand in a 29-year-old Asian heterosexual male with no apparent precipitating factors.

KEY WORDS: Granuloma annulare, genital

INTRODUCTION

GA is a common chronic benign inflammatory condition of the dermis characterized by foci of altered collagen (necrobiosis) surrounded by histiocytes and lymphocytes.¹ It was first described by Colcott Fox in 1895.²

About 0.1% to 0.4% of new patients coming to dermatologists have GA. The condition is found 2.5 times more often affected in females than males.^{3,4} The onset of GA is usually in the first three decades of life in two thirds of patients, though the patients have been reported from 1 to 88 years of age.³⁻⁵ Spontaneous resolution occurs in 50% of patients within 2 years; however, the duration of lesions may range from a few weeks to several decades. About 40% of patients get recurrent lesions usually in the same sites. Palms, soles, and mucosae are rarely affected.

Clinical variants include localized, generalized (disseminated), perforating and subcutaneous forms.^{3,5} Localized GA is the most common

form followed by generalized, perforating and subcutaneous forms. Online search revealed that only 15 cases of penile GA have been reported so far.⁶⁻¹⁹ All these patients had isolated subcutaneous lesions on the penis with only one patient having perforating GA involving the scrotal skin.²⁰ None of them had associated skin lesions elsewhere on the body. We report here a male patient with nodular and annular plaque GA affecting the shaft and root of the penis, scrotum as well as his right hand.

CASE REPORT

A 29-year-old Pakistani male presented with multiple asymptomatic lesions on his scrotum, penis and dorsum of the right hand of 18-months' duration. There was no family history of similar lesions. He was married for the past 5-years and living in a monogamous relationship. He had no history of pre- or extramarital sexual exposures, or known to be suffering from any sexually

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transmitted infections or any preceding genital dermatoses such as fungal infections or scabies. There was no history of diabetes, arthritis or tuberculosis. He had not received vaccination for hepatitis B or A recently. He denied using any topical irritant or cleanser on his genitalia. The patient had been treated with mild topical corticosteroid and antifungal creams with no change in the lesions before presenting to us. His general physical and systemic examinations were normal. Cutaneous examination revealed five skin colored to erythematous 0.5 - 2.0 cm annular papules and plaques on the shaft of the penis (Fig.1). Two erythematous firm nodules, one at



Fig. 1 Nodular and annular plaque lesions of GA on shaft and root of penis and scrotum.



Fig. 2 Typical annular plaque with beaded border on dorsum of right hand.

the root of the penis and another on the scrotum were also noted (Fig. 1). A single 2.0 cm annular plaque was present on the dorsum of right hand (Fig. 2). All the plaque lesions had typical beaded borders made of coalesced papules.

His laboratory investigations consisting of complete blood counts, ESR, blood sugar, kidney, liver and thyroid function tests were all normal. Serology for syphilis (VDRL, TPHA), HIV, HBV, HCV, EBV and borrelia burgdorferi infections were negative. Thyroid and antinuclear antibodies were not detected in the blood. A skin biopsy from the hand and scrotal lesions showed foci of degenerated collagen surrounded by palisading granulomas in the mid and upper dermis (Fig. 3). The infiltrate was composed mainly of histiocytes admixed with lymphocytes and included numerous multinucleated giant cells (Fig. 4). Presence of mucin was demonstrated by Alcian blue stain. The histopathological features were consistent with the clinical diagnosis of GA. The patient was treated with topical pimecrolimus 0.1% cream application with good response over next three months.

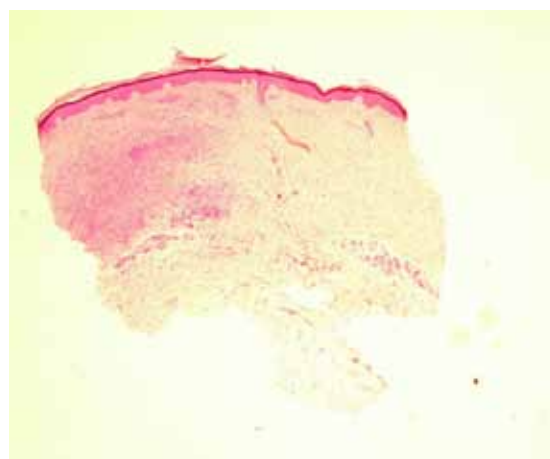


Fig. 3 Skin biopsy from scrotal lesion showing foci of collagen degeneration with palisading granulomas in mid and upper dermis. (H & E).

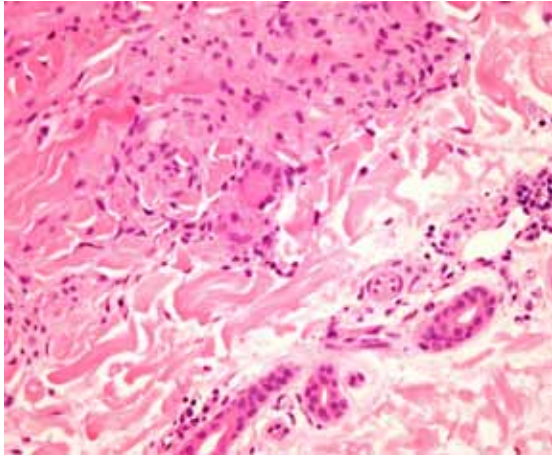


Fig. 4 The granulomatous infiltrate is formed mainly of histiocytes and included numerous multinucleated giant cells.

DISCUSSION

The exact etiology and pathogenesis of GA are unknown. It is considered to represent a reaction pattern to a variety of triggering factors. Reported triggering factors have included insect bites, scabies, bites by animals (octopus and cat), waxing-induced pseudofolliculitis, tuberculin tests, BCG vaccination, hepatitis B vaccination, chronic hepatitis B virus infection, other viral infections such as human papilloma virus, varicella/zoster virus, EBV and *Borrelia burgdorferi* infection, various forms of trauma such as occupational pressure on the fingers in a milkman and saphenectomy.^{1,3,5} GA has been reported to occur at the site healed herpes zoster, a phenomenon termed an 'isotopic' response.²¹ Among the physical factors, sun exposure has been implicated in provoking or contributing to localization of lesions in sun exposed areas in a number of cases. Disseminated GA has occurred in a patient undergoing PUVA therapy. GA has also occurred in the red pigment areas of tattoos.^{1,3,5} It has been suggested that an immunoglobulin-mediated vasculitis could be the cause of the necrobiotic granulomas however the evidence

from immunofluorescence studies is conflicting. Immunoreactants in vessel walls have been found in some but not in all the patients. Some authors favour a delayed-type hypersensitivity response to unknown triggers as the pathogenetic mechanism.¹

Clinically the lesions consist of an annular plaque having a beaded border made of coalescing papules and a depressed skin colored or hyperpigmented center. The lesions vary from 1 to several centimeters in size. Papules, nodules and subcutaneous lesions have been described. Hands and feet are the most commonly affected sites but the lesions can occur anywhere on the body.

Localized granuloma annulare is the commonest form, and typically presents as a ring of small, smooth, flesh-coloured or erythematous papules forming an annular plaque. They may be solitary or multiple, and may occur anywhere on the skin, although the dorsa of the hands and feet, and the fingers are the commonest sites. Uncommon sites for lesions of granuloma annulare are the ears, penis, palms and periocular regions. Lesions are usually asymptomatic. The other patterns of granuloma annulare may occur alone or in association with the annular lesions. In the generalized (disseminated) GA, there are numerous skin-coloured or erythematous papules, which may have an annular configuration symmetrically distributed, often coalescing lesions, on the trunk and limbs. The lesions may be violaceous or hyperpigmented in the center. Pruritus may be a prominent complaint in generalized lesions. The distribution is bimodal with two peaks, one in the children less than ten years and the second at a mean age at onset later than in the localized variety.^{1,3} The condition is usually localized in immunocompetent individuals, whereas in HIV

positive patients it is often more generalized. Perforating granuloma annulare (PGA) was named by Owens and Freeman in 1971.²¹ In this uncommon variety, some of the papules develop yellowish centres and discharge a little clear, viscous fluid. This dries to form a crust, which eventually separates, and may leave a hypo- or hyperpigmented scar. Lesions may be localized or generalized. Till now only one case of perforating GA has been reported to involve the genitalia.²⁰ Subcutaneous granuloma annulare (SGA) is the least common form of GA. It occurs predominantly in children, lesions are nodular and occur predominantly on the scalp and legs, particularly in the pretibial region, but unusual locations include periorbital, subperiosteal, palm and penis. Pustular generalized perforating granuloma annulare, and papular umbilicated form on the dorsa of the hands in children are extremely rare in occurrence.

First case of penile GA was reported by Kossard *et al* in 1990.⁶ Since then 14 more cases have been described.⁶⁻¹⁹ Seven of them were less than 30-years of age, 4 were teenagers and three patients were older than 40-years of age. The oldest patient was 61 years old. The youngest patient having penile GA was a seven year boy.¹⁶ Many of these patients have presented to urologists or venereologists prompting STI work up, however diagnosis was confirmed by biopsy only. The lesions were painful, tender in some and had caused discomfort during erection. All except one patient with penile GA had subcutaneous form of GA which is peculiar but difficult to explain. None of the patients had extragenital lesion. Only one patient had perforating nodules of GA on the scrotum.²⁰ Our patient had many unusual features. The lesions were of typical annular morphology

and superficial dermal nodules in contrast to deeper subcutaneous lesions reported by other authors. The lesions were not confined the shaft of the penis but also present on the scrotum, a site previously reported in only one patient who had perforating lesions confined exclusively to the scrotum with no involvement of shaft of the penis.²⁰ In addition our patient had typical annular extragenital lesion on the usual common acral site of dorsum of the hand, an association never reported in patients of penile GA. Lesions in some of these cases subsided after excision biopsy, or spontaneously in one or two. But persisted or even recurred after excision in others. In view of the natural history of spontaneous remission most authors did not recommend any aggressive surgical treatment for penile GA, however majority advocate biopsy of isolated subcutaneous nodular genital lesions of GA as they are clinically indistinct unlike in our patient who also had typical lesions on the genitalia as well as the hand. The nodular subcutaneous form can mimic many conditions. Differential diagnosis of penile GA include dermatophyte infection, annular lichen planus, secondary syphilis, Peyronie's disease, epidermoid cysts.

Association of localized and generalized GA has been reported with autoimmune thyroiditis but not with penile GA. Generalized GA may be a marker for diabetes mellitus, although earlier reported association of localized GA with DM has not been proven.

A number of treatments have been tried for GA, mainly with the aim of achieving quicker response than the usual expectant observed natural course of spontaneous clearance in 2-years. Intralesional steroids, given by either needle injection or jet injector appear to be more effective in the

management of localized lesions. Topical steroids although prescribed are of no benefit. Cryosurgery is also effective treatment for localized disease with clearance being achieved in 1-3 sittings in majority of the patients on applying single freeze-thaw cycle. Localized granuloma annulare has also been treated with local injections of low-dose recombinant interferon gamma, photodynamic therapy, and pulsed dye laser. PUVA therapy appears to be an effective treatment for generalized granuloma annulare. Narrowband UVB, and UVA-1 phototherapy have also been reported as effective in the treatment of GGA. Etretinate and isotretinoin have both shown to be beneficial in GGA. Isotretinoin has also improved localized and perforating granuloma annulare. There are a few reports of the use of ciclosporin in generalized granuloma annulare, with good results in most cases. Other treatments which have been used with apparent benefit in isolated cases or small numbers of patients with disseminated granuloma annulare include low-dose chlorambucil, dapsone, antimalarials, niacinamide, pentoxifylline, tranilast, fumaric acid esters, clofazimine and topical vitamin E, a combination of vitamin E and a 5-lipoxygenase inhibitor, and defibrotide. Recent reports suggest that topical imiquimod, tacrolimus and pimecrolimus may be helpful. Rapid resolution of recalcitrant disseminated lesions with infliximab and efalizumab has been reported.¹ We treated our patient with topical pimecrolimus 1% cream application twice a day as the patient did not want to apply topical or injectable steroid on his genital skin. He responded well to this treatment over next 3 months with no recurrence after further 6 months follow up suggesting role of calcineurin inhibitors as a safer treatment option for localized genital

GA avoiding the pain of intralesional injections and side effects of corticosteroids. Lesions of subcutaneous granuloma annulare should be left to resolve spontaneously as it is difficult to know the extent and depth of the lesions, and because of chances of recurrence despite excision.

CONCLUSION

GA involving genital skin is rare, but recently a number of new cases have been reported. Therefore the condition may be underreported. It may not be confined to the penile skin only and may occur over adjoining scrotal skin as seen in the present case. We believe that the term genital GA is more appropriate than penile GA to describe lesions of GA affecting shaft and root of penis and scrotum. We also recommend that a thorough examination of the pubic and genital skin is conducted in all patients of localized or generalized GA as our patient also had a typical lesion on the most commonly reported site that is dorsum of the hand.

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