Asymptomatic plaques and papules on the hands, wrists and forearms

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What is the cause of this patient's rash and what treatment options are available to her?

Case history

A 50-year-old woman presented with a four-year history of asymptomatic, smooth red papules and plaques, many of which were annular in appearance. For the first three years, the lesions had been scattered over the dorsal aspect of her hands, wrists and forearms, but during the fourth year many more had developed on these sites. The annular plaques were mainly on her hands and fingers (Figure 1a); papular lesions were the predominant type on her forearms (Figure 1b). Results of a fasting glucose test were normal. The patient was mainly concerned about the appearance of the lesions, and particularly whether they might start to appear on her face.

Diagnosis

A diagnosis of generalised granuloma annulare was made. Although this patient had more lesions than most sufferers, her rash was typical of the condition. A skin biopsy was not performed.

Treatment

Mometasone furoate ointment was applied twice daily, under plastic wrap at night during the first three weeks, but no useful response occurred after six weeks. Due to the large number of plaques, intralesional corticosteroid treatment was not practical. A combination of aspirin (300 mg daily) and nicotinamide (1.5 g daily), was then tried for two months, without success. The patient decided not to try other treatments and, at her last review visit, no lesions had appeared on her face.

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Figure 1a. Annular plaques on the patient's hand and fingers.

Figure 1b. Papular lesions on her forearms.

Comment

Granuloma annulare may be localised or generalised; there is also a rare subcutaneous form. It is more than twice as common in women compared with men. The age of onset is under 30 years in 70% of patients, but the generalised form is more often seen in older adults. In a study of 208 cases of granuloma annulare, over half had resolved by two years but 40% had a later recurrence.[1]

In the localised form, which is the more common, a small to moderate number of lesions occur, usually on the fingers, dorsal aspect of the hands, forearms, elbows, dorsal aspect of the feet, ankles and legs. In the generalised form, there are many lesions on the trunk and/or limbs. It is uncommon for granuloma annulare to affect the face.

The lesions can be rubbery, smooth, annular plaques; smaller papules or violaceous macules; or subtle plaques with thickening (particularly at the edge) that vary in size and can be quite large.

The annular lesions may not be complete rings – they may be partial, joined or more geographic in outline – and may slowly enlarge. Subcutaneous nodules occur uncommonly. The colour of the plaques and papules varies from pale or skin coloured to red or violaceous. Usually, the rash is smooth because the epidermis is not involved – the exception is granulomas that 'perforate' the epidermis, leading to scaly or crusted areas within a plaque (which may be caused by scratching). Granuloma annulare is most often asymptomatic, but the rash can itch or be tender.

Aetiology

The cause of granuloma annulare is unknown. Histopathology shows some defined patterns of dermal granulomas around mucin and collagen, but no specific immunological target has been identified. The pathology can share some features of necrobiosis lipoidica or sarcoidosis, but these are distinct conditions with definable differences in their pathology. Limited evidence suggests a pathogenic role of circulating immune complexes and microangiopathy.

Diabetes mellitus has been associated with both the generalised and localised forms of granuloma annulare. One author found no relationship in an initial study,[2] but did in a larger study (diabetes was found in 21% of 100 patients with generalised granuloma annulare and 10% of 1350 patients with the localised form).[3]

Differential diagnosis

Patients with less typical lesions may need a skin biopsy to exclude other conditions. These include:

- **Cutaneous sarcoidosis.** Distinguishing between cutaneous sarcoidosis and granuloma annulare can be difficult, but the former is not usually annular. It is more common on the face but can occur on a variety of sites. Systemic involvement may occur.
- **Necrobiosis lipoidica.** Most commonly, necrobiosis lipoidica affects the legs, with plaques developing a yellowish hue and being prone to ulcerate or perforate. About 70% of patients with necrobiosis lipoidica have diabetes at diagnosis; about half of those who don't will develop diabetes later.
- **Lichen planus.** Usually, lichen planus is not annular and is often quite itchy. The characteristic lesion is a papule, red to violaceous in colour and often with subtle white lines (Wickham's striae). The papules may coalesce into plaques or nodules, particularly in the hypertrophic form often seen on the lower limbs.
- **Cutaneous lymphomas and pseudolymphomas.** Various types of cutaneous lymphomas and pseudolymphomas cause red to violaceous plaques or nodules. They are occasionally annular (especially Jessner's lymphocytic infiltrate) and tend not to be localised to sites seen commonly for granuloma annulare.
- **Leprosy.** Although it is now rarely seen in Australia, leprosy should be considered, particularly in travellers or immigrants from endemic areas. The face, trunk or limbs can be affected. The type of lesion depends on the level of the immune response to the mycobacteria. At the tuberculoid end of the spectrum (high cell mediated immunity), there is a small number of anaesthetic plaques; hypohidrosis is present and may be a slight scaliness of the skin. At the lepromatous end of the spectrum (low cell mediated immunity), there are many plaques, which become anaesthetic later; hypopigmentation may be present. Intermediate forms are common.

Management

Localised granuloma annulare

As granuloma annulare is benign, reassurance may suffice. If treatment is required, the localised form and rare subcutaneous form are best treated with corticosteroid injected into the thicker parts of each plaque or nodule – the usual preparations used are triamcinolone acetonide (Kenacort, diluted to 5 mg/mL) or betamethasone (Celestone Chronodose, as a 50% dilution). However, these injections may not clear the erythema, can lead to dermal atrophy and do not stop the formation of lesions in new areas.

For patients who do not want injections, a less reliable option is a potent topical corticosteroid like mometasone furoate (Elocon, Novasone) or betamethasone dipropionate (Diprosone, Eleuphrat). These are more efficient when used with occlusion at night to enhance penetration into the dermis – this, however, increases the risk of superficial atrophy and telangiectasiae, so I limit the duration of plastic occlusion to around three weeks.

Cryotherapy with a freeze–thaw cycle of 5 to 10 seconds can help, but risks hypopigmentation and atrophic scarring at the site.[4] Repeated treatments every month may be needed for best results. Other treatments that have been reported to be successful in isolated case reports include topical tacrolimus and topical imiquimod, but these are generally too expensive to use in more extensive cases.

Generalised granuloma annulare

The generalised form of granuloma annulare is difficult to treat, and there are few good trials to guide treatment. Usually too many plaques are present to make intralesional therapy practical. Topical treatment should be tried first, but often is not successful.

There are simple options that can be tried next – these have a low chance of working but a low risk of side effects, and should be ceased if there is no improvement after three months:

- nicotinamide, starting at 500 mg daily and slowly increasing to 1.5 g daily, and/or

- aspirin, 300 mg/day, and dipyridamole (Persantin), 75 mg/day.

There are other treatments that may have a higher chance of success but a higher risk of side effects. Each of the following has a significant chance of relapse if treatment is successful and then stopped:

- hydroxychloroquine (Plaquenil), 200 to 400 mg/day[5]
- dapsone, 100 mg/day – the response, if it occurs, is usually within three months (glucose-6-phosphate dehydrogenase [G6PD] activity must be checked before starting treatment and a full blood examination and liver function tests must be performed regularly)[6,7]
- PUVA (psoralen and ultraviolet A) phototherapy, three times a week for at least three months;[8] photodamage, photocarcinogenesis and nausea from the psoralen tablet are the main side effects
- oxpentifylline (Trental), 300 mg three times daily for three to six months, may help.

Other treatments that have been suggested to offer benefit in small studies and case reports include isotretinoin (GenRx Isotretinoin, Isohexal, Oratane, Roaccutane), acitretin (Neotigason), clofazimine (Lamprene), potassium iodide and cyclosporin (Cicloral, Cysporin, Neoral, Sandimmun). MT

References

1. Wells RS, Smith MA. The natural history of granuloma annulare. Br J Dermatol 1963; 75: 199.
2. Dicken CH, Carrington SG, Winkelmann RK. Generalized granuloma annulare. Arch Dermatol 1969; 99: 556-563.
3. Dabski K, Winkelmann RK. Generalized granuloma annulare: clinical and laboratory findings in 100 patients. J Am Acad Dermatol 1989; 20: 39-47.
4. Blume-Peytavi U, Zouboulis CC, Jacobi H, Scholz A, Bisson S, Orfanos CE. Successful outcome of cryosurgery in patients with granuloma annulare. Br J Dermatol 1994; 130: 494-497.
5. Simon M Jr, von den Driesch P. Antimalarials for control of disseminated granuloma annulare in children. J Am Acad Dermatol 1994; 31: 1064-1065.
6. Czarnecki DB, Gin D. The response of generalized granuloma annulare to dapsone. Acta Derm Venereol 1986; 66: 82-84.
7. Steiner A, Pehamberger H, Wolff K. Sulfone treatment of granuloma annulare. J Am Acad Dermatol 1985; 13: 1004-1008.
8. Kerker BJ, Huang CP, Morison WL. Photochemotherapy of generalized granuloma annulare. Arch Dermatol 1990; 126: 359-361.

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