

Case reports

Generalized granuloma annulare and giant cell arteritis

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ABSTRACT

Granuloma annulare (Gan) and giant cell arteritis (GCA) share common histologic features. In Gan, a disease characterized by the presence of palisading granulomas usually in the dermis, the main alteration is the presence of elastic fiber degeneration and it strongly suggests that the primary target leading to the development of this disorder is the injury to the elastic tissue. On the other hand, in giant cell arteritis (GCA), a vasculitis involving large and middle-sized blood vessels, the main histologic features are the disruption of the internal elastic lamina and the nonsuppurative granulomatous giant cell infiltrate, which seems to be focused around the disintegrated elastic fibers. Due to this, these two conditions appear to be related. However, to the best of our knowledge, only one case of association of generalized Gan and GCA is described in the literature. We herein report a new case of generalized Gan in a patient previously diagnosed with biopsy-proven GCA. Both diseases were successfully treated by oral prednisone. Although the etiology of generalized Gan and GCA remains still unknown, they seem to be immunologically mediated conditions showing predominance of T-cells in the inflammatory infiltrate.

Introduction

Granuloma annulare (Gan) is a dermatosis of unknown etiology characterized by the presence of necrobiotic granulomas. The generalized form of Gan occurs primarily in adults and accounts for 10% to 15% of all cases (1, 2). It usually localizes in the trunk and is the most protracted type of Gan. In patients with this condition, ultrastructural examinations have demonstrated the presence of degenerated elastic fibers with loss of peripheral microfibrils

and abnormal elastic matrix (3). These degenerated elastic fibers are surrounded by intact collagen fibers. All these findings indicate that the main alteration in Gan is elastic fiber degeneration and they strongly suggest that the primary target leading to the development of this disorder is the injury to the elastic tissue (3).

Giant cell (temporal) arteritis (GCA) is the most common type of systemic vasculitis affecting white individuals over 50 years (4, 5). It is characterized by the granulomatous involvement of large and medium-sized blood vessels of the aorta with predilection for the extracranial arteries of the carotid artery (6, 7). In GCA, the main histologic features are the disruption of the internal elastic lamina and the nonsuppurative granulomatous giant cell infiltrate, which seems to be focused around the disintegrated elastic fibers (5, 7).

Due to the pathologic similarities described above, Gan and GCA appear to be related conditions. However, the association of generalized Gan with GCA has rarely been reported. In this regard, to the best of our knowledge, only one case of association of both conditions has been previously described in the literature (8).

We herein report a new case of generalized Gan associated with biopsy-proven GCA.

Case report

A 69-year-old woman diagnosed with biopsy-proven GCA 3 years before (Fig. 1), presented at the emergency service because of a 2-month history of non-itchy erythematous papules that initially began on her face and suddenly spread to her upper back, V of the neck and extremities. The patient attributed the onset of the eruption to sun exposure. Her general health was good, with no previous history of skin

Competing interests: none declared.

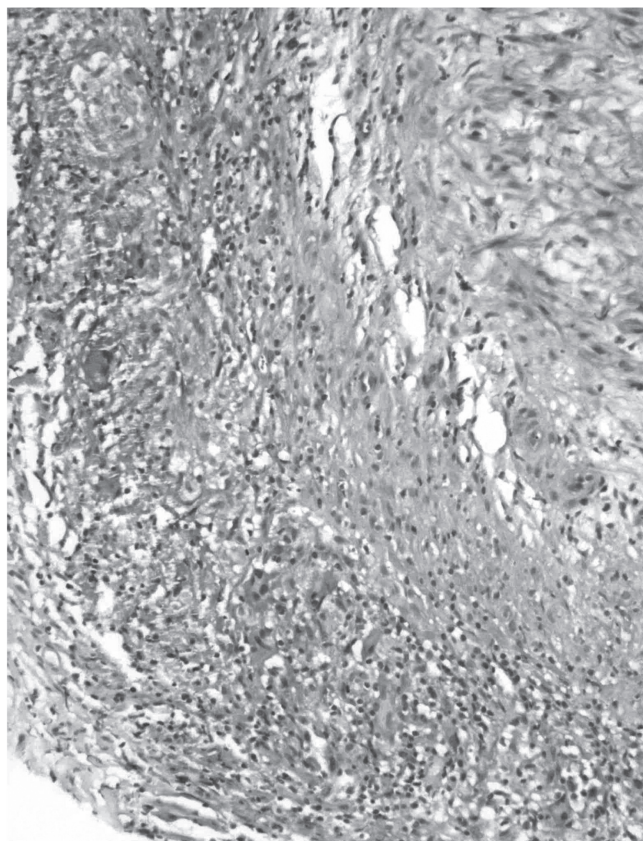


Fig. 1. Temporal artery biopsy showing a biopsy-proven giant cell arteritis. The vessel shows fibrous intimal proliferation, a mixed cellular infiltrate lymphomononuclear in the media along with multinucleated giant cells in the intima-media junction at close proximity to the internal elastic lamina (Masson trichrome).

ailments. At the time of admission she was taking prednisone (5 mg/day), di-basic calcium phosphate, vitamin D, and low-dose aspirin (100 mg/day). Apart from GCA, she did not have a medical history of diabetes mellitus, thyroid disease, risk factors for HIV infection, malignant tumor or any other serious illness. Her family history was also unremarkable.

Physical examination revealed numerous and widely distributed pink, small

papules, each 3-4 mm in diameter. The lesions were more densely grouped on her face, predominantly on the forehead, and coalescing in annular plaques with central clearing (Fig. 2). The papules clustered on the back where were non-coalescent and showed a linear arrangement suggesting the isomorphic Koebner phenomenon (Fig. 3). Fewer lesions were also observed on the V of the neck and extremities.

Full blood cell count, erythrocyte

sedimentation rate, blood levels of glucose, lipid profile, hepatic and renal function tests, calcium and angiotensin converting enzyme levels were normal. Serum IgG was slightly increased (1550 mg/dL) with normal IgA and IgM. Serum C3 and C4 complement and thyroid hormone levels were normal. Antinuclear and antithyroid (antithyroglobulin and antimicrosomal-antiperoxidase) antibodies, rheumatoid factor and syphilis and hepatitis B and C virus serologies were negative. A chest radiograph was normal and a tuberculin skin test was negative.

A skin biopsy of one papule of the back revealed interstitial (incomplete) granulomas in the dermis. The upper dermis showed an increased number of inflammatory cells, mainly macrophages and lymphocytes. They were arranged about vessels and between collagen bundles, which were separated by increased connective tissue mucin (Fig. 4). Occasional multinucleated giant cells were seen. Based on the clinicopathological findings a diagnosis of generalized Gan was made. The oral daily dose of prednisone was increased to 30 mg/day. Following this increase of prednisone dose clinical improvement of the cutaneous lesions was achieved within 1 month. The skin rash resolved completely over the following 4 months. Prednisone dose was progressively tapered up to complete discontinuation 6 months after the diagnosis of generalized Gan. No clinical data suggesting the presence of a relapse of GCA or new flares of cutaneous lesions have been observed over



Fig. 2. Generalized granuloma annulare. Individual coalescing papules on the forehead.

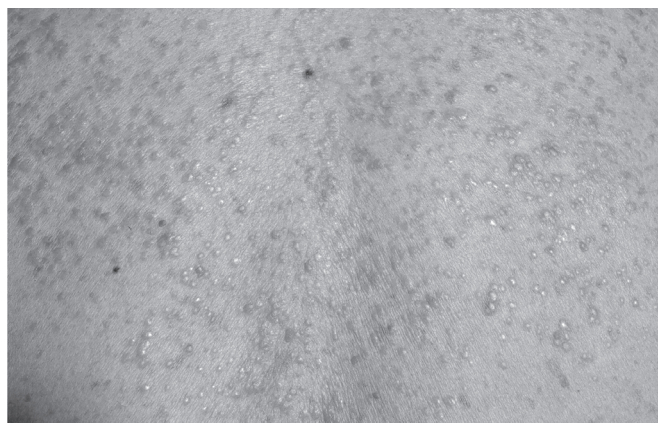


Fig. 3. Generalized granuloma annulare. Discrete papules covering large areas of the back.

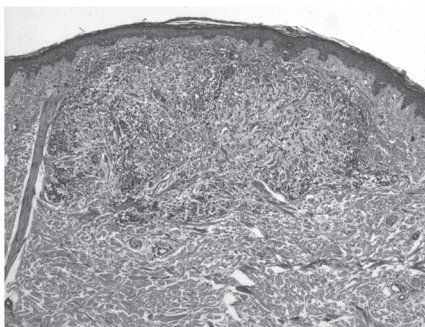


Fig. 4. Granuloma annulare. Pathologic findings: The dermis is hypercellular and there is an increased amount of interstitial mucin (Hematoxylin-eosin stain).

the following 3 years after the diagnosis of generalized Gan.

Discussion

Generalized Gan is usually considered a disseminated form of Gan. However, it differs from the localized form by a later age of onset, protracted course, and worse response to therapy with only rare cases showing spontaneous resolution (9). Generalized Gan has also been found to be associated to different conditions such as diabetes mellitus, thyroid disease and malignancies (9). Fukai *et al.* (8) described a case of generalized Gan in a 79-year-old man with GCA. To the best of our knowledge, in the present report we describe the second case of association of both diseases. In the case reported by Fukai *et al.* generalized Gan occurred before than GCA (8). In contrast, in our patient GCA pre-

ceded the development of generalized Gan. However, in both patients generalized Gan and GCA were successfully treated by oral corticosteroids. In this regard, corticosteroids are the mainstay of treatment for GCA and prolonged corticosteroid therapy is often necessary in patients with this vasculitis (10).

The association between generalized Gan and GCA may be coincidental. However, this concurrent occurrence should not be exceptional as both entities share similar characteristics. Both conditions have elastic tissue damage, displaying granulomatous inflammation and a predominance of T-cells in the inflammatory infiltrate (2, 3, 7, 11). Also, a similar MHC-class I association has been found in both conditions. In this regard, a significantly increased frequency of the HLA-B*15 allele has been described in both Gan (12) and biopsy-proven GCA patients compared to matched controls (13).

In conclusion, although generalized Gan and GCA may be coincidental conditions they share common immunogenetic and pathologic features that should be considered by clinicians who see patients with GCA.

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