Infiltrated papules on the trunk and headaches: A case of actinic granuloma and a review of the literature

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Introduction

Actinic granuloma is an uncommon granulomatous reaction hypothesized to be an autoimmune response to actinic damage to elastic tissue (O’Brien, 1978). It is more commonly seen in women, with a female–male ratio ranging from 1.2:1 to 2:1 (Gutierrez-Gonzalez et al., 2013; Limas, 2004; O’Brien, 1975; Ragaz and Ackerman, 1979). Case studies and observational studies suggest that factors associated with this condition include diabetes mellitus and exposure to sun, radiation, intense light, tanning beds, and high heat (Table 1). Actinic granuloma classically presents as an annular plaque, most commonly on sun-exposed areas of the head, neck, and upper extremities, with an atrophic or hypopigmented center and elevated erythematous borders. There is also an ocular variant of actinic granuloma, which has been reported to occur as a yellow to pink plaque on the conjunctiva (Konar et al., 2014; Mittal et al., 2013). Few reports have detailed an association between actinic granuloma and temporal arteritis, a serious inflammatory condition that could lead to blindness if misdiagnosed.

Case report

A 62-year-old Caucasian male presented during the summer with a 3-month history of asymptomatic papules on the arms, legs, and trunk. The patient was previously treated with a course of methylprednisolone, which resulted in some improvement. Review of systems was positive for fatigue, fever, and headache. Physical examination revealed multiple tan-to-pink infiltrated annular papules on the chest, back, upper arms, and legs. Some appeared to show linear koebnerization (Fig. 1).

Microscopic findings and clinical course

Laboratory studies showed a normal complete blood count, normal Lyme and Anaplasma titers, and negative Hepatitis B and C serologies. Liver function testing showed Aspartate aminotransferase (AST) of 57 and Alanine aminotransferase (ALT) of 79. Erythrocyte sedimentation rate (ESR) was elevated to 104 mm/hr. Histopathologic examination showed an interstitial granulomatous infiltrate in the superficial and mid-dermis composed of histiocytes, lymphocytes, occasional eosinophils, and numerous multinucleated giant cells (Fig. 2). The papillary dermis demonstrated solar elastosis. Verhoeff-van Gieson stain showed fragmented elastin fibers within the cytoplasm of occasional multinucleated giant cells (Fig. 3). Periodic acid–Schiff stain (PAS), Acid-fast bacillus (AFB), and Fite stains were negative. No additional stains were performed. Differential diagnosis based on histopathology included actinic granuloma, interstitial granulomatous dermatitis, interstitial granulomatous drug reaction, and granuloma annulare. Given the presence of numerous multinucleated giant cells, findings on the Verhoeff-van Gieson stain, and solar elastosis with the time of presentation during summer, the patient was diagnosed with actinic granuloma.

Although the patient’s headaches were not classic enough to prompt an earlier workup for temporal arteritis, temporal artery biopsy was

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| Reference            | Type of Study | Mean Age (y) | Sex   | Finding                                                                 | Treatment                                                                 | Course of Disease                                                                 | Comments                                                                 |
|----------------------|---------------|--------------|-------|-------------------------------------------------------------------------|---------------------------------------------------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Hanke et al., 1979   | Case series   | 39.8         | F     | Clinical: Annular patches with erythematous borders and central hypo pigmentation on the face, scalp, and exposed surfaces Histopathology: Multinucleated giant cells, histiocytes, lymphocytes, scattered epithelioid cells, total lysis of elastic tissue, absence of mucin and lipids, and no evidence of necrobiosis | Case 1: PUVA Case 2: Hydroxychloroquine sulfate started at 200 mg daily then increased to 400 mg daily Case 3: Topical steroids, hydroxychloroquine sulfate × 4 months, IL triamcinolone acetonide Case 4: Hydroxychloroquine sulfate, 200 mg daily × 24 months; topical steroids Case 5: Not discussed | Case 1: No apparent improvement until after discontinuation of treatment and tan faded Case 2: Active borders faded and flattened, recurrences occurred but treated successfully with IL triamcinolone acetonide Case 3: Improvement only with IL triamcinolone acetonide, recurrence treated with IL triamcinolone acetonide, and intermittent hydroxychloroquine sulfate 250 mg daily used for exacerbations Case 4: No improvement | Confirmed the distinction of GA and AG First proposal of term “annular elastolytic giant cell granuloma,” purely based on morphology |
| O’Brien and Argyle, 1981 | Comparative study (of histologic specimen of 40 females and 16 males) | N/A | N/A | Note of subclinical findings of actinic granuloma and temporal arteritis in a patient with polymyalgia. Histologic description reads, “Active elastolysis occurring in skin of temple. Note tuberculoid (‘sarcoid’) infiltrate and giant cell containing fragments of what appears to be resorbing elastic fibers.” | – | – | – |
| Fukai et al., 1990   | Case report   | 79           | M     | 3-month history of numerous asymptomatic erythematous papules on trunk and extremities; 4 months later, developed headache and loss of vision from temporal arteritis | PO prednisone 60 mg daily | Headache resolved, visual acuity returned to normal | At time of publication, was thought to be a case of generalized granuloma annulare; closer examination of histology demonstrated that the condition was more consistent with AEGCG and did not support granuloma annulare (O’Brien and Regan, 1999). |
| Lau et al., 1997     | Case report   | 76           | M     | Clinical: Pt 1: Forehead lesion + bi-temporal headaches and scalp tenderness x 12 months Pt 2: Farmer, forehead lesion Histopathology: Granulomatous process in dermis, basophilic degeneration of dermal elastic tissue, admixture of lymphocytes, lack of palisading arrangement seen in GA, Similar chronic inflammatory and granulomatous reaction in vessel walls of small arteritis in subcutis. Giant cells in dermis and vessel walls demonstrate phagocytosis of elastic fibers | Excision; prednisone 60mg/day PO Excision | Resolution of headache and scalp tenderness Unknown | First documented association of actinic granuloma and giant cell arteritis |
| Davies and Newman, 1997 | Case Report | 33           | F     | Presented with a 9-month hx of two nodular lesions (cheek and forehead); 4 year hx of chronic tanning bed use with large exposure to UVA | No treatment methods discussed other than stopping attendance at tanning parlor | No further lesions developed | |
| Author, Year | Study Type                  | Participants | Sex Ratio | Lesion Location                          | Treatment                                                                 | Outcome                                                                 |
|-------------|-----------------------------|--------------|-----------|------------------------------------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Limas, 2004 | Prospective observational study (20 patients) | 31-81 (most 40–70 years old) | F > M (3:2) | Dorsal hands, forearms, neck, face, V of neck and trunk, upper back | –                                                                         | Diabetes mellitus was mentioned more often than any other coexisting disease |
| Delgado-Jimenez et al., 2006 | Case report | 74 | F | Pruritis, erythema and alopecia of scalp, extending centrifugally; annular border composed of small erythematous papules with slight central atrophy | Topical diflucortolone 0.1% twice daily | Resolution of lesion 3 months later with hair regrowth |
| Patel and Rogers, 2010 | Case report | 58 | F | Dry, crusty annular lesion on upper lip with central pale skin | Intralesional steroid injection (methylprednisolone acetate 40 mg/ml about every 4 months) | Partial improvement |
| Shoimer and Wismer, 2011 | Case report | 71 | M | Erythematous plaques in predominantly sun-exposed locations + conjunctival injection. Clinical and histologic diagnosis of AEGCG. Developed temporal arteritis while tapering steroid treatment that lead to blindness in right eye | Oral prednisone 50 mg daily × 1 week, then tapered to 25 mg and betamethasone 0.1% cream × 1 week | 2 weeks later: modest improvement. 2 mo. f/u: continued oral prednisone at 20 mg daily × 1 week, then tapered by 2.5 mg q weekly until off; started azathioprine 100 mg daily + clobetasol propionate cream. 4 mo. f/u: azathioprine held, prednisone maintained at 7.5 mg daily due to recurrence of lesions. 5/6 mo. f/u: developed headaches; elevated ESR and C-reactive protein; progressive visual loss; patient had stopped the prednisone without supervision 2 weeks prior to visual loss |
| Matsuzaki et al., 2011 | Case report | 73 | F | Annular plaques on right forearm with depigmented and telangiectatic atrophic centers; painful erythematous lesions on right lower leg; diagnosed with actinic granuloma and erythema nodosum | Actinic granuloma lesions failed to respond to topical corticosteroids | –                                                                         |
| Mittal et al., 2013 | Retrospective case series (3 patients) | 22.5 | F | Painless red masses of conjunctiva, histologically dx’ed as actinic granuloma | 1 patient received 1 week topical steroids with no improvement; all 3 received excisional biopsy and excision | Discussion of the possible hypothesis that actinic granuloma and cutaneous sarcoidosis are within the same spectrum of non-caseating granulomatosis given the association of sarcoidosis with EN |
| Gutierrez-Gonzalez et al., 2013 | Single-center retrospective study (20 patients) | 58 | 55% F | Most common presentation: annular plaques with central clearing. Giant cell and necrobiotic histologic patterns were more common in F than M | Suggests the use of: spontaneous resolution, topical/intralesional/systemic corticosteroids, chloroquine, hydroxychloroquine, tranila, topical pimecrolimus, cyclosporine, UVA/UVB sunscreens, fumaric acid esters | Sometimes spontaneous |
| Berliner et al., 2013 | Case report | 59 | F | Annular plaque on forehead with erythematous scaly raised border and subtly central atrophy | –                                                                         | –                                                                         |
| Konar et al., 2014 | Case Report | 70 | M | 14 mm × 7 mm fleshy mass on right lower bulbar conjunctiva | Surgical excision | 2 year follow up demonstrated no further recurrence of disease |

Abbreviations: M: Male; F: Female; N/A: not available; GA: granuloma annulare; AEGCG: annular elastolytic giant cell granuloma; AG: actinic granuloma; GCA: giant cell arteritis; EN: erythema nodosum; ESR: erythrocyte sedimentation rate; UVA: ultraviolet A; UVB: ultraviolet B; IL: intralesional; PUVA: psoralen + ultraviolet A. Bolded studies discuss the association of AG and GCA.
performed because the patient complained of headaches and had an elevated ESR. Biopsy results revealed giant cell arteritis of the right temporal artery, and Verhoeff-van Gieson stain revealed focal disruption in the temporal artery internal elastic lamina. The patient was started on hydroxychloroquine 200 mg orally BID and prednisone 2.5 mg daily for his temporal arteritis, with partial clearance of his skin lesions. Though his skin lesions drastically improved on this regimen, persistent ESR elevation required an increase in prednisone to 40 mg PO daily and the addition of methotrexate.

Discussion

The term actinic granuloma was first proposed by John O’Brien in 1975 after he observed histologic similarities in patients with annular lesions. Because of its clinically similar appearance to granuloma annulare, some critics have questioned whether the condition should be classified as a separate entity or simply as granuloma annulare occurring in sun-damaged skin (Ragaz and Ackerman, 1979). Others have accepted the distinction but have reclassified the lesions morphologically as annular elastolytic giant cell granuloma (Hanke et al., 1979). Both of these terms, however, are descriptive only, while actinic granuloma offers an etiologic implication (Limas, 2004).

Histopathologic examination of actinic granuloma shows an inflammatory process limited to the superficial dermis, with usually nonpalisading granulomas, greater frequency of multinucleated giant cells, solar elastosis, and no increase in mucin (Al-Hoqail et al., 2002). This is in contrast to the deep, as well as superfi- cial, dermal in- flammatory reaction. Of the four histologic patterns, the histiocytic, giant cell, necrobiotic or vascular, and sarcoid (O’Brien, 1985). The histiocytic variant predominantly consists of scattered histiocytes near elastic fi bers. The giant cell pattern is the original pattern, initially consisting of a small granuloma that becomes annular as it advances into elastic tissue near- by. The necrobiotic variant, also known as the vascular variant, consists of areas of ischemic necrosis in the advancing granulomatous edge. Lastly, the sarcoid variant often demonstrates atrophie scar, fi brosis, and a persistent inflammatory reaction. Of the four histologic patterns, the giant cell and necrobiotic histologic patterns appear to be more common patterns in females than males (Gutierrez-Gonzalez et al., 2013).

In general, treatment for actinic granuloma includes topical and intralesional corticosteroids, psoralen ultraviolet A therapy, antimalar-ials, cyclosporine, methotrexate, and cryotherapy (Reisenauer et al., 2012). Case reports and observational studies have demonstrated variable results with these treatment modalities (Table 1).

Temporal arteritis, also known as giant cell arteritis (GCA), is a form of medium-to-large-vessel vasculitis with the possible complication of vision loss if left untreated (Smith and Swanson, 2014). Criteria for diagnosis include the presence of three or more of the following: age of 50 years or older, new headache, a clinically abnormal temporal artery, an ESR greater than 50 mm/hr, and an abnormal temporal artery biopsy (Smith and Swanson, 2014). Interestingly, temporal arteritis occurs preferentially in women (Smith and Swanson, 2014). Giant cell arteritis has been most notably associated with polymyalgia rheumatica (Smith and Swanson, 2014). Comorbidities in addition to polymyalgia rheumatic in GCA include osteoporosis, cardiovascular conditions, diabetes mellitus, hypokalemia, and pseudohypoparathyroidism, all conditions that appear to have a high burden in the populations affected by GCA (Petri et al., 2015). Temporal arteritis has also been associated with extreme ear pain (Aui-Aree et al., 2010). Other cutaneous conditions and manifestations with which temporal arteritis has had rare associations include psoriatic arthritis, scalp abscess, scalp ulceration with necrosis, butterfly rash of the face, tongue changes, gangrene or ulcers of the leg, purpura and ec- chymoses, urticaria, edema, lividity, tender nodules, hyperpigmentation, tortuous arteries, and supravascular pallor (Aui-Aree et al., 2010; Baum et al., 1982; Corli et al., 2015; Kinmont and McCullum, 1964).

The association between actinic granuloma and temporal arteritis was first postulated in 1978 by John O’Brien (see also Lau et al., 1997). A few years later, the same author noted a histologic fi nding of actinic arteritis in a small vessel within the dermis of a polymyalgia patient (Lau et al., 1997; O’Brien and Argyle, 1981). The underlying basis of this association is thought to be related to actinic degeneration of elastic tissue not only of the skin, but also of the internal elastic lamina of ves- sels (Gutierrez-Gonzalez et al., 2013; O’Brien and Regan, 1999). Since then, few reports in the literature have demonstrated the association between actinic granuloma and temporal arteritis (Lau et al., 1997;
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