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

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ABSTRACT

Actinic granuloma is a rare granulomatous reaction that is more commonly seen in females and thought to occur as an autoimmune response to actinic damage of elastic tissue. We discuss a case of a patient with actinic granuloma presenting with concomitant temporal arteritis. Our case and review of the literature emphasize the association between actinic granuloma and temporal arteritis, a serious inflammatory condition that could lead to blindness if misdiagnosed.

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 related inflammatory conditions. We present this case and review of the literature to emphasize the 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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Table 1
Selected Studies on Actinic Granuloma.

Reference	Type of Study	Mean Age (y)	Sex	Finding	Treatment	Course of Disease	Comments
Hanke et al., 1979	Case series (five patients)	39.8 Range (31–59)	F	Clinical: Annular patches with erythematous borders and central hypopigmentation 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 elastotic 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**	**Excision; prednisone 60mg/day PO**	**Resolution of headache and scalp tenderness**	**First documented association of actinic granuloma and giant cell arteritis**
		Elderly	**M**	**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**	**Unknown**	
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	

Limas, 2004	Prospective observational study (20 patients)	31-81 (most 40–70 years old)	F > M (3:2)	Lesion location included: dorsal hands, forearms, neck, face, V of neck and trunk, upper back. Lesions were few or multiple, annular with centrifugal extension and central clearing	–	–	Diabetes mellitus was mentioned more often than any other coexisting disease Other potential eliciting factors: sun exposure, tanning bed use, high heat, intense light
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	Alcian blue & elastic van Gieson (EVG) stains (demonstrated loss of elastin in granulomatous areas) used to differentiate between granuloma annulare and actinic granuloma
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**	**Studies have demonstrated AEGCG may be unresponsive to topical steroids, methotrexate, crythotherapy, cautery; anecdotal evidence has found promising results with chloroquine, cyclosporine, systemic corticosteroids, acitretin, pentoxyfylline, isotretinoin. Treatment is best when individualized**
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	–	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
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	–	
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, tranilast, 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	4 cases of actinic granuloma of the conjunctiva reported prior to this publication occurred in females

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.

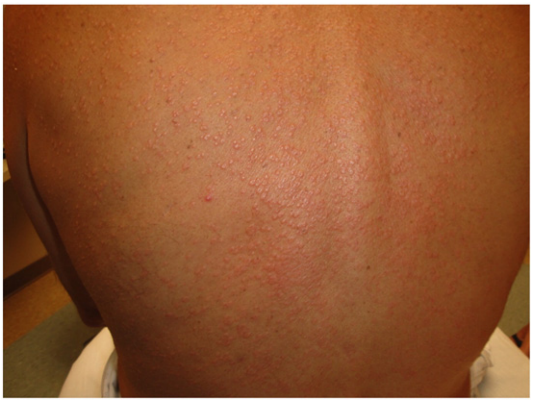

Fig. 1. Erythematous indurated papules on patient's back.

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 superficial, dermal infiltrate with more commonly palisading granulomas; reduced frequency of multinucleated giant cells; and increased mucin deposition seen in granuloma annulare (Al-Hoqail et al., 2002). Four general histologic

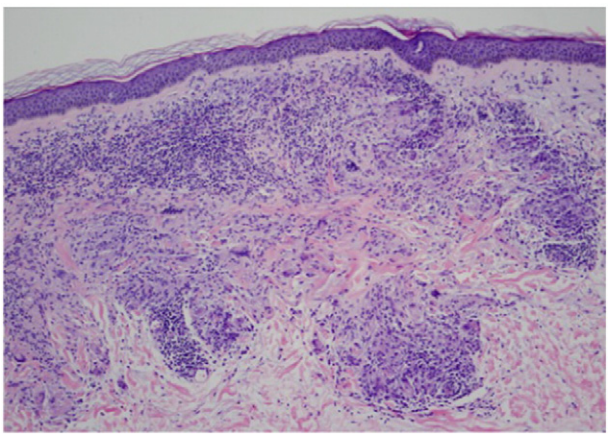

Fig. 2. Interstitial granulomatous dermal infiltrate composed of histiocytes, lymphocytes, and multinucleated giant cells (hematoxylin and eosin, 10× magnification).

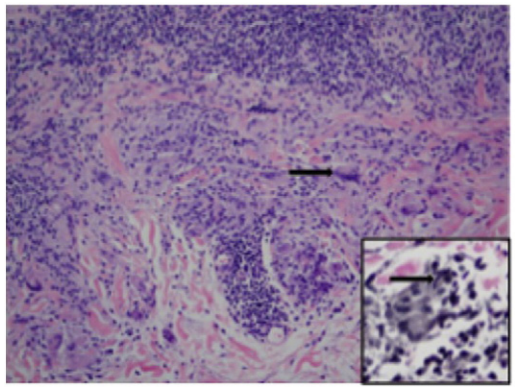

Fig. 3. Multinucleated foreign-body giant cells in the dermis (arrow; hematoxylin and eosin, 20× magnification). Giant cell containing elastic fiber fragment visualized with Verhoeff-van Gieson stain (arrow; hematoxylin and eosin, 40× magnification).

patterns of actinic granuloma have been described: histiocytic, giant cell, necrobiotic or vascular, and sarcoid (O'Brien, 1985). The histiocytic variant predominantly consists of scattered histiocytes near elastic fibers. The giant cell pattern is the original pattern, initially consisting of a small granuloma that becomes annular as it advances into elastotic tissue nearby. 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 atrophic stroma, fibrosis, 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, antimalarials, 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 pseudophakia, 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 ecchymoses, 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 McCallum, 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 finding 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 vessels (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;

Shoimer and Wismer, 2011); interestingly, all cases demonstrating the association have occurred in males, despite the higher prevalence of actinic granuloma in females. Our case supports this rarely discussed, yet serious, complication.

Of note, our patient had a unique clinical presentation that differed from previously reported cases of actinic granuloma associated with temporal arteritis. Lau et al. (1997) described two elderly gentlemen who presented with solitary lesions on the forehead, and Shoimer and Wismer (2011) described an elderly gentleman who presented with erythematous annular confluent plaques in predominantly sun-exposed locations. Our case further supports the possibility of temporal arteritis in a variety of presentations of actinic granuloma. Given the severe consequences of temporal arteritis, most notably blindness, we emphasize the importance of ruling out temporal arteritis in any patient presenting with actinic granuloma and headaches. If an associated temporal arteritis is suspected, systemic corticosteroids should be started to suppress the immune system and prevent blindness.

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