



Case report

An unusual orbital tumor in an adult: Granuloma annulare

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ABSTRACT

Purpose: Granuloma annulare (GA) is a rare clinical entity that does not classically arise from the peri-orbital area in adults. The purpose of this case report is to present a 69-year-old female with GA of the orbit. As well, the pathological and immunohistochemical features of these tumors will be discussed.

Observations: One case of GA of the orbit was identified from a tertiary ophthalmology referral centre. Clinical and histopathological features of the case were reviewed. Other cases of GA were also retrieved from the literature and addressed in this report.

Conclusion and importance: Granuloma annulare is a rare orbital lesion in adults. It is known to typically arise on the hands and feet of children. This lesion must be distinguished from necrobiotic xanthogranuloma (NXG), which is a progressive peri-orbital dermatosis seen in middle age men and women. GA is thought to be a benign, often self-resolving condition, whereas NXG tends to be linked to other systemic conditions and may have a poorer prognosis.

Differentiating this rare orbital tumor from necrobiotic xanthogranuloma (NXG) is essential, as both a systemic work-up and follow-up must be appropriately arranged. A comprehensive description of pathognomonic microscopic features of GA and NXG is reviewed to achieve the correct diagnosis.

1. Introduction

Granuloma annulare (GA) of the orbit, a form of necrobiotic granuloma, is a rare diagnosis in adults. To the best of our knowledge, there is presently one published case discussing this entity in the English literature.¹ Clinically, it is characterised by the development of non-itchy, raised annular papules on the skin, that tend to occur on the extremities or other bony prominences.^{2,3} These lesions typically arise on the hands and feet of children or young adults. It is more common in females, with a peak incidence in the first 3 decades of life.^{1,2}

Granuloma annulare must be distinguished from necrobiotic xanthogranuloma (NXG), which is a chronic and progressive peri-orbital dermatosis seen in middle age men and women.⁴ GA is thought to be a benign, often self-resolving condition, whereas NXG tends to be linked to other systemic conditions and altogether may have a poorer prognosis.^{3,4} An accurate diagnosis, work-up and management of the lesion is crucial in ensuring proper patient care.

This is the case of a common cutaneous lesion in children,

granuloma annulare, manifesting in an unusual location in an adult.

2. Case

This is the case of a 69-year-old female who first presented to the ophthalmology service due to symptoms consistent with chronic scleritis, epiphora and left upper eyelid ptosis. The patient was treated with oral NSAIDs with resolution of the scleritis symptoms. She was referred for oculoplastic evaluation of the epiphora and ptosis.

After evaluation by the oculoplastic service, the left-sided ptosis and nasal lacrimal duct obstruction were confirmed. Subsequently, a left levator resection was planned. Once healed, the patient underwent a left dacryocystorhinostomy (DCR). Approximately one month after DCR surgery, the patient presented to the clinic due to a focal area of induration, mild erythema and minimal sensitivity to palpation below the left lower lid. She was treated for focal post-operative cellulitis. Upon completion of the antibiotic course, the firm area below the left eye was still present. Due to concern for resistance, another antibiotic was

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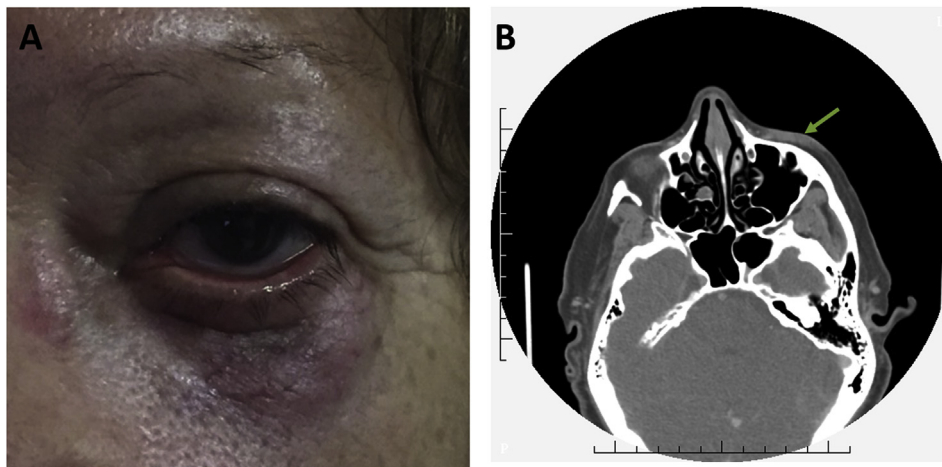


Fig. 1. Clinical Picture and CT Scan a) Post-biopsy clinical picture showing an elevated and indurated area, b) A post-operative CT scan showing soft tissue thickening involving the anterior-inferior orbital rim and inferior eyelid (arrow).

prescribed for a ten-day course, with symptomatic improvement.

Three months later, the painless mass along the inferior orbital rim persisted, though had not significantly enlarged (Fig. 1). The decision was taken to undergo biopsy for histopathological correlation. Intra-operative frozen sections confirmed the presence of granulomatous inflammation.

The final pathology report revealed granulomatous inflammation with necrobiosis and extensive areas of mucin production (Alcian Blue positive) with multinucleated giant cells (Fig. 2). There was no sign of malignancy noted. Bacterial and fungal stains (Ziehl-Neelsen and Grocott, respectively) were negative. These histopathological features are

consistent with granuloma annulare of the orbit.

Due to the unusual nature of this lesion in the orbit, the internal medicine team was involved so as to rule out systemic disease. The patient underwent a CT scan of the orbits that demonstrated non-specific skin and subcutaneous soft tissue thickening. The possibility was raised that these changes may be inflammatory in origin. There was no extension into surrounding structures, nor bony invasion noted.

Due to the absence of hematologic abnormalities, including absence of paraproteinemia, the decision was made to treat the lesion locally with topical steroid cream.

3. Discussion

Necrobiotic granuloma refers to a pathological condition for which there is formation of a granuloma around a central area of altered collagen and elastic fibers. The degraded fibers will adopt a new histopathological staining pattern, being either basophilic ('blue' granuloma) or eosinophilic ('red' granuloma).³ The blue granuloma is generally recognized by its mucinous centre or the abundance of neutrophils, as well as palisade formation around the degraded collagen. One example of this subtype is granuloma annulare. The red form of necrobiotic granuloma is associated to hyalinized collagen, fibrin deposition and/or eosinophils degranulation, such as seen in necrobiotic xanthogranuloma.^{3,4}

Typically, orbital necrobiosis in adults is associated with NXG, rather than GA. Due to the deep nature of the lesion, the orbital location and the age of the patient, GA is not systematically considered as a differential diagnosis. However, in the present case, histopathology revealed features consistent with the blue type of granuloma.

Histopathologically, GA can adopt two different patterns: palisading or interstitial histiocytic. Clinically, GA lesions may be in the dermis as a single (localized GA) or multiple lesions (generalized GA), or they can be located deep in the hypodermis (subcutaneous GA). Deep GA is believed to be seen only in young children.⁵ Rarely, GA lesions may be accompanied by ulcerated, parakeratotic epidermis (perforating GA).

The histopathology of granuloma annulare can be different depending on its subtype. The palisading pattern of GA is characterised by well-defined areas of necrobiosis with perivascular lymphocytic infiltrates. The granulomatous centre is rich in hyaluronic acid and mucin. Mitotic figures may be reported. Alternatively, as presented in this case, an interstitial pattern and mucin within the areas of necrobiosis in a poorly defined fashion and with an incomplete granulomatous rim is seen. Subcutaneous GA is more likely to have eosinophils as part of the inflammatory infiltrate,⁶ hence the possible confusion with NXG. This can be especially true with an atypical diagnosis, such as GA

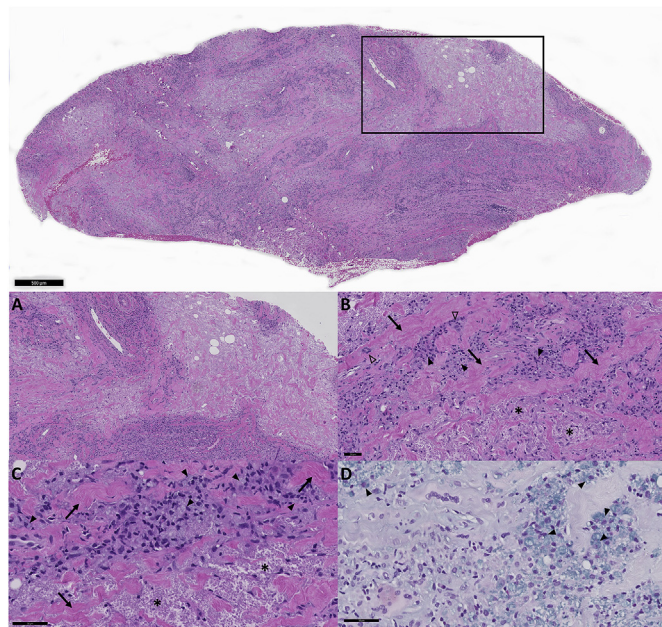


Fig. 2. Microscopic Findings: H&E photomicrograph. a) low magnification of the selected area from the top panel showing deep irregular granuloma formation surrounding areas of necrobiosis with partial palisading of the degraded collagen b) higher magnification showing typical interstitial pattern with histiocytic infiltration (arrowheads) between collagen bundles (arrows) with scant multinucleated giant cells (open arrowhead) and necrobiotic areas (asterisk) c-d) high power magnification showing degraded collagen (arrow), mucinous necrobiotic area (asterisk) and mucin-laden macrophages (arrowheads), d) Alcian-Blue stain confirms the presence of mucin in the histiocytes. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Reported cases of orbital and peri-ocular granuloma annulare in adults.

Author	Age	Sex	Area Affected	Type	Size	Comments
Cousin (1991) ²	31	F	supraorbital rim, forehead	subcutaneous	40 × 10 × 0mm largest (multiple)	multiple lesion causing discomfort. Insulin-dependent diabetic
Buchi (1995) ¹²	33	F	lateral upper lid			
Buchi (1995) ¹²	36	M	right upper lid			
Moegelin (1995) ¹³	37	F			several nodules. 4mm largest	
Buchi (1995) ¹²	40	F	below right canthus			reactive epidermis, hyperparakeratosis
Mc Farland (1982) ¹⁴	40	F	upper and lower lids (OU)	papular	several 1–3mm papules	axillae eruptions. Negative systemic workup
Kang (2013) ⁹	51	F	supraorbital rim		19 × 13 × 16mm	systemic workup revealed sarcoidosis
Buchi (1995) ¹²	66	M	right lower lid	generalized	several nodules	
Barret (2016) ¹	86	M	right orbital			Cholesterol cleft, eosin (red granuloma-like features)

in an adult patient.

On the other hand, granulomatous centres in NXG are more eosinophilic; hyalinized collagen, fibrin and Touton or bizarre foreign-body type giant cells are common. A defining histopathological feature of NXG is the presence of lymphoid nodules as well as cholesterol clefts within the lesion. None of the aforementioned features were seen in this case. A lack of xanthogranulomatous-like arrangement is identified, thereby strengthening the diagnosis of granuloma annulare.

The interstitial pattern and the abundance of mucin in the granulomatous centre are undeniable features of GA. Moreover, the overall basophilia of the tissue and the absence of cholesterol clefts weigh against a diagnosis of NXG. These histopathological identifiers further solidify the diagnosis of GA, despite the unlikely location of the mass.

In both GA and NXG, the pathogenesis is poorly understood. It is suggested that GA is a delayed-type immune response leading to collagen degradation, whereas NXG is linked to formation of immunoglobulins-lipid complexed triggering a foreign-body type granulomatous inflammation.³ Therefore, NXG is often linked to paraproteinemia like multiple myeloma. It has been also associated to other pathologies such as sarcoidosis. In periocular areas⁴ and even on the skin,⁷ its presence may lead to more serious inflammatory complications, such as scleritis and uveitis.⁸

It has been previously reported that subcutaneous GA was seen exclusively in children. Extensive follow-up of 34 pediatric cases showed no relationship to other systemic disease, despite frequent recurrence of the lesions.⁵ After an extensive review of the literature, 9 peri-orbital GA in adult patients were found, and one GA of the orbit. Interestingly, the histopathological features of the orbital lesion reported by Barret et al. demonstrated overlapping morphological features of NXG, namely cholesterol clefts and eosinophilic staining. These articles are summarized in Table 1.

One case of GA in a 51-year-old woman, reported by Kang et al.,⁹ shows a histologically confirmed lesion of granuloma annulare. After further systemic workup was undertaken, an underlying diagnosis of sarcoidosis was revealed. This manifestation of GA with overlapping features of other granulomatous process represents a low-likelihood situation in which the histopathological findings without systemic workup may lead to a wrong clinical diagnosis.^{9–11} Analogously, a previous case report suggests that GA lesions in adults can possibly evolve to NXG with paraproteinemia.¹¹ In the aforementioned case, a systemic workup at the time of initial diagnosis of GA would have been of benefit to the patient.

To the best of our knowledge, this is the first reported case of a typical-appearing, deep, subcutaneous GA presenting in the orbit of an elderly patient. A thorough systemic evaluation was completed in conjunction with the internal medicine service, and no underlying systemic disease or hematological abnormality, including paraproteinemia, were discovered.

4. Conclusion

This is the case of a 69-year-old female with clinical and histopathological features of an orbital mass consistent with granuloma annulare. Due to the infrequent occurrence of GA in the orbit, prompt referral to an internist to rule out underlying systemic disease should be considered. As well, with atypical or prolonged scleritis cases, in addition to the typical uveitis work-up, inclusion of investigation for a primary GA may be warranted. Furthermore, both GA and NXG should be considered in the differential diagnosis for atypical orbital lesions.

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Patient consent

Authorization for use of tissues for purposes of research has been obtained from the patient according to the Hospital's 'CONSENT TO: Surgery, Anesthesia, Diagnostic or Therapeutic Procedure' prior to surgical removal of the lesion.

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Conflict of interest

Authors have no conflict of interest to declare.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajoc.2018.11.013>.

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