Orofacial granulomatosis presenting as bilateral eyelid swelling

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Abstract

Orofacial granulomatosis (OFG) is an uncommon but increasingly recognized disease of unknown etiology. The typical presentation is chronic swelling of the perioral soft tissue, but eyelid edema can be the sole manifestation. Terminology of this disease can be confusing as it may also be referred to as granulomatous cheilitis and a monosymptomatic presentation of Melkersson–Rosenthal syndrome (MRS). Crohn’s disease and sarcoidosis should also be considered in the differential as the histopathology can be similar. Corticosteroids are the mainstay of treatment but can lack efficacy. Atypical presentations and the possibility of systemic disease involvement can further challenge the management. We describe an unusual case in which OFG manifests solely as chronic eyelid swelling. This 69-year old Asian female patient had a delayed diagnosis that responded well to intralesional corticosteroid injection with surgical skin reduction. In addition to describing this unusual presentation of OFG, we review the relevant literature and evaluate the current terminology used to describe this entity.

Keywords: Orofacial granulomatosis, Melkersson–Rosenthal syndrome, Granulomatous cheilitis, Eyelid swelling, Histopathology

Introduction

Orofacial granulomatosis is a clinicopathological diagnosis that, as the name implies, is characterized by orofacial swelling that on histopathologic analysis shows non-caseating granulomata within or in close proximity to the lymphatic vessels. 1

The term orofacial granulomatosis (OFG) was introduced in 1985 by Wiesenfeld et al. to emphasize the importance of systemic investigations, namely for Crohn’s disease as the histopathology is similar. 2 This update in nomenclature was also an attempt to unify, and be an umbrella term for other less descriptive names for this entity, namely Melkersson–Rosenthal syndrome (MRS) and granulomatous cheilitis.

MRS was named after the descriptions by Melkersson in 1928 and Rosenthal in 1931. Melkersson described the case of a 35-year old woman with facial edema and palsy and he suggested a relationship between the two findings. 3 Rosenthal later described a similar presentation but noted the additional finding of a fissured tongue and this lead to the triad to be known as Melkersson–Rosenthal syndrome. 4

In 1945, Meischer described a monosymptomatic variant of MRS that was characterized by granulomatous lip swelling and became known as cheilitis granulomatosa. 5

OFG most commonly presents with swelling of the perioral area. We describe an unusual case in which eyelid swelling is the sole manifestation of OFG.

Case report

A 69-year old Asian female presented to our oculoplastics service with a four-year history of bilateral eyelid swelling. She had seen numerous specialists over time but the diagnosis remained elusive. She had seen a dermatologist who had performed allergy testing which was negative. Her medical history was significant for diabetes mellitus, hypertension, and...
hypercholesterolemia. She also had recently seen a gastroenterologist for iron-deficiency anemia. Upper gastrointestinal tract endoscopy revealed helicobacter pylori-associated chronic gastritis. She denied any history of recent trauma, infection, or allergy.

On examination, there was non-tender, non-erythematous, firm edema of the upper eyelids (Fig. 1). There was secondary eyelash ptosis. Ocular motility was full. The remainder of the ocular exam was within normal limits. A biopsy was obtained via a debulking blepharoplasty and intralesional triamcinolone was injected.

Histopathological analysis revealed non-caseating granulomata in the eyelid dermis in perivascular and perilymphatic distributions (Fig. 2a). There were granulomata within the lumena of the lymphatic vessels (Fig. 2b). CD68 immunoreactivity confirmed the intraluminal cells as histiocytes (Fig. 2c). There was edema of the dermis and the epidermis was undisturbed. The findings were consistent with orofacial granulomatosis.

Further investigation included extensive blood work, including ACE, and showed no significant abnormalities. Abdominal CT scan and chest X-ray were unremarkable. Her previous upper endoscopy included duodenum assessment and was normal. Overall, her work-up found no systemic involvement or alternative diagnoses.

At nine-week follow-up the eyelid swelling continued to be in remission (Fig. 3).

**Discussion**

The etiology of orofacial granulomatosis (OFG) is unknown but a number of causative agents have been suggested such as microbes, food substances and additives, dental material, other contact allergens, and immunological processes.6

No clear genetic or ethnic predilection has been identified for OFG. Based on the English literature, most case series are from Europe and North America and describe Caucasian patients. Our case describes an Asian female which does not fit the usual profile. The median age of presentation is 28 years but the age range includes children and the elderly.7

In our case, there was a four-year symptomatic period before the diagnosis was made. This long duration is representative of other case reports and highlights the importance of considering OFG in the differential of chronic eyelid swelling. Other important considerations include thyroid-associated orbitopathy, blepharochalasis, and allergy.

Isolated bilateral eyelid swelling is an unusual presentation of OFG, but appears to be an increasingly recognized entity.8–14 There have also been reports of unilateral presentation.14–16 The eyelid swelling is typically painless, non-pruritic, non-pitting edema, and may fluctuate over time and involve other parts of the face.17

The terminology for this clinicopathologic entity varies in the literature. It is also referred to as a monosymptomatic variant of Melkersson–Rosenthal syndrome (MRS) and as granulomatosis cheilitis when localized to the perioral tissues. Such variations in nomenclature can be confusing and dilute the catalogue of this disease in the literature. MRS refers to the triad of findings that include facial swelling, facial palsy, and fissured tongue. Orofacial swelling is the presenting sign in 86% of cases but the complete triad is only found in a minority of patients (8–25%).10,18,19 We question the logic of referring to this type of isolated eyelid swelling, or other isolated facial swelling, as a syndrome when there are no other findings. We feel that orofacial granulomatosis is a better term to use in these instances, and the eponym Melkersson–Rosenthal syndrome is best reserved for describing the complete triad, or at least two features of the triad (oligosympto-
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motic variant). We can further simplify the nomenclature by referring to all isolated facial swelling of this nature as OFG, and granulomatosis cheilitis as a subtype classification.

As Wiesenfeld and colleagues intended in their 1985 description of OFG, the clinician must investigate for systemic involvement. Crohn’s disease may manifest as orofacial swelling and the histopathology findings can be identical to OFG. Furthermore, it is important that patients have long-term follow-up as Crohn’s disease may show systemic findings at a later time. Sarcoidosis can also have similar clinical and histopathological findings.

Biopsy is crucial in diagnosing OFG as it truly is a clinicopathological correlation. Intralymphatic granulomas are the classic histopathological findings. Descriptions of OFG without histopathology should be critically analyzed. In our case, with an atypical location of facial swelling, the diagnosis could not have been accurately determined without the necessary biopsy. This emphasizes the importance of biopsying idiopathic eyelid edema.

Treatment of OFG is challenging. Complete remissions are rare and relapses are common. Delayed diagnoses are frequent and may further compromise the treatment response. Corticosteroids (topical, intralesional, and systemic) have been the mainstay of treatment but results have been mixed. Other medications that have not been overly efficacious have included clofazimine, hydroxychloroquine, dapsone, sulphasalazine, thalidomide, danazol, and minocycline. Elimination diets and avoidance of potential allergens have also been advocated but with minimal success.

Our patient’s edematous upper eyelids were treated with intralesional steroid injection and surgical debulking. Her response was excellent despite a delay in her diagnosis of four years. We feel that local treatment such as surgical debulking and intralesional steroid injection is a logical first step in treating isolated eyelid edema and systemic treatment should be reserved for relapsing disease. Further study to elucidate the etiology of OFG will further guide rationale treatment protocols. Using consistent nomenclature will streamline future research in order to better understand this complex disease process.

References