

# Primary Periocular Orofacial Granulomatosis

## Large Case Series and Systematic Review

Plemel D<sup>a</sup>, Weis E<sup>a</sup>, Punja K<sup>a</sup>, Ashenhurst M<sup>a</sup>, Kulaga A<sup>b</sup>

<sup>a</sup>Section of Ophthalmology, Department of Surgery, University of Calgary  
<sup>b</sup>Department of Pathology and Laboratory Medicine, University of Calgary

### Background

The skin has 3 basic layers: epidermis, dermis and subcutaneous fat. The dermis layer contains lymphatic channels.

Orofacial granulomatosis (OFG) occurs when inflammation clogs the lymphatic system, the lymph channels become engorged and the hydrostatic pressure swells the surrounding dermis. OFG presents with edematous skin. On a microscopic level, there is mixed perivascular inflammation with histiocytes often forming non-caseating granulomas that may be seen as intralymphatic granulomas within the dilated lymphatic channels.

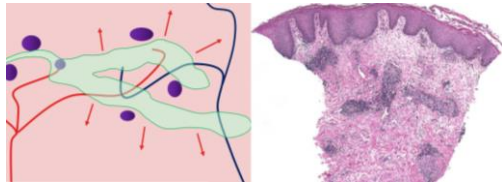


Fig 1. Cartoon representation of perivascular inflammation causing engorgement of lymphatics and hydrostatic inflation of the surrounding dermis (left). Histopathology slide showing the same in orofacial granulomatosis (right).

OFG is an umbrella term that encompasses primary and secondary causes of this histopathologic finding.

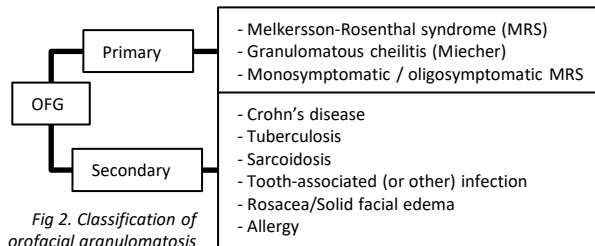


Fig 2. Classification of orofacial granulomatosis

### Purpose

To determine the optimal treatment for primary periocular OFG.

### Methods

Systematic review with case series.

- **Case series:** Patients with a clinicopathologic diagnosis of Melkersson-Rosenthal Syndrome from a periocular biopsy between 2011-2020 in Calgary, Alberta, were reviewed.



Figure 3. Photograph of primary periocular orofacial granulomatosis

- **Systematic review:** PRISMA guided PubMed search of “Melkersson-Rosenthal Syndrome” and “Orofacial Granulomatosis” using limits of English language articles.

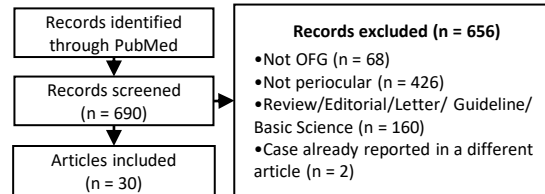


Figure 4. Flow diagram of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) review methodology

### Results

There are 44 published cases of primary periocular OFG. There were 11 unpublished cases in Calgary between 2011-2020. These 55 cases were compiled and analyzed together.

Treatment	Has a Reported Outcome	Reported Outcome	
		Improvement	No Improvement
<u>Intralesional steroids</u>			
Alone	9	9	0
Combined	10	10	0
<u>Debulking</u>			
Alone	9	8	1
Combined	9	9	0
<u>Systemic steroids</u>			
Alone	13	8	5
Combined	5	5	0
<u>Clofazimine</u>			
Alone	3	2	1

Table 1. Treatments for primary periocular orofacial granulomatosis that showed efficacy. Treatments used alone or in combination (combined) with other treatments simultaneously.

Many treatments have been tried for the treatment of primary periocular OFG. Not all are shown in this table.

Intralesional steroids (19/19; 100%), surgical debulking (17/18; 94.4%) and systemic steroids (13/18; 72.2%) showed the best evidence for treatment success. Clofazimine (2/3; 66.6%) showed promise but numbers were limited.

Although these treatments helped, there was relapse in nearly all cases when treatment was stopped completely. Many patients received ongoing intralesional steroids.

### Conclusion

Primary periocular OFG is rare and a cure remains elusive. Surgical debulking with intralesional steroids, and ongoing intralesional steroid injections, may be a good management strategy that limits systemic side effects.