A Rare Case of Orofacial Granulomatosis

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ABSTRACT

Introduction: Orofacial Granulomatosis(OFG) is a rarely occurring disease with greater propensity for females which presents with swelling of the maxillofacial and oral tissue worsening overtime. It is often considered as part of a spectrum of diseases including the more severe process, Cheilitis Granulomatosa (CG) which may be a sign of Melkersson-Rosenthal Syndrome (MRS) which includes facial paralysis along with CG and lingual fissures.

Case Report: A 49y/o female presented with possible chronic angioedema. She has experienced chronic lower lip swelling over the past 9-10 with episodes lasting 1-2 days. Recurrence, chronicity and severity of swelling have increased in the past 2 years. Physical exam showed enlarged lower labia as well as some minor facial swelling and several small fissures on the tongue.

Results: Biopsy showed mild lymphocytic and histiocytic infiltrate of the lip with no signs of amyloid on congo red stain. Diagnosis of Orofacial Granulomatosis (OFG) was made. Patient was started on Dapsone 50mg QD.

Conclusion: OFG is a rare disorder but must be evaluated for in a patient with this presentation do to its association with more severe debilitating disease.

INTRODUCTION

Orofacial granulomatosis is a term for a disease first coined in 1985 which normally presents with recurrent soft tissue enlargement around the maxillary facial and oral region (Johani, Moles, Hodgson, Porter, & Fedele, 2009). This may eventually lead to persistent enlargement of the lips which does not resolve (Grave, McCullough, & Wiesenfeld, 2009). Furthermore lip ulceration and gingival swelling may take place (Grave, McCullough, & Wiesenfeld, 2009). A study of 49 individuals found the mean age of diagnosis in females to be 43.6 years in contrast males presented significantly earlier at 23.3 years (Johani, Moles, Hodgson, Porter, & Fedele, 2009). Another study of 119 Researchers in Ireland found a 1:1 male to female ratio (McCartan, Healy, McCreary, Flint, Rogers, & Toner, 2011). This same study noted average years before definitive diagnosis was made of OFG after initial presentation of symptoms was 44 months (Johani, Moles, Hodgson, Porter, & Fedele, 2009). Delay in diagnosis is caused by the complexity and lack of knowledge of the disease .

As the name implies there are often noncaseating granulomas present on biopsy however this is not always a finding and therefore not mandatory for diagnosis (Johani, Moles, Hodgson, Porter, & Fedele, 2009).. In this case of localized granulomatous inflammation of the lips the manifestation is known as, Granulomatous cheilitis and/or Miescher Cheilitis (Johani, Moles, Hodgson, Porter, & Fedele, 2009). The finding that is necessary to diagnose OFG on histopathology is lymphatic dilation, with slight fibrosis (Johani, Moles, Hodgson, Porter, & Fedele, 2009). Langerhan giant cells and lymphocytes are common as well on biopsy (Johani, Moles, Hodgson, Porter, & Fedele, 2009). Labial swelling was the first presenting feature in 75.5% of patients. Another 73.5% presented with other intraoral mucosal features. (Johani, Moles, Hodgson, Porter, & Fedele, 2009). Cobelstoning of the oral mucosa was seen in 63% of patients (McCartan, Healy, McCreary, Flint, Rogers, & Toner, 2011).

The disease is considered by many to be a symptom of larger diseases processes with Crohns disease, Sarcoidosis and Delayed hypersensitivity all being implicated as underlying causes however at this point there is no definitive connection and the diagnosis is made by exclusion of these as much as with biopsy. (Grave, McCullough, & Wiesenfeld, 2009). OFG has been reported to be a primary presenting symptom in some patients with Crohns disease (Bogenrieder, Rogler, Vogt, Landthaler, & W, 2003). Amalgam and Cobolt have both been implicated as possible dental agents which when removed may reduce OFG symptoms however evidence at this point is tentative. Infective pathology has also been implicated with TB as the most implicated pathogen do to its nature to form granulomas (Grave, McCullough, & Wiesenfeld, 2009). There have however been contradictory reports on the matter and the studies conducted thus far lack large sample populations which would be definitive (Grave, McCullough, & Wiesenfeld, 2009). Allergic angioedema may be suspected in patients presenting with recurrent lip swelling and is an important rule out do to possible progression to anaphylactic reactions.

The triad of facial paralysis, tongue fissuring or scrotal tongue and labial/facial swelling are known as Melkersson-Rosenthal Syndrome (MRS) which was first described in 1928 many years before OFG was was first identified as its own process. This syndrome can cause significant paralysis of the face and therefore should be evaluated by a neurologist if suspected. The first manifesting sign of this syndrome is usually the labial swelling which may make it appear as isolated OFG (Grave, McCullough, & Wiesenfeld, 2009).

Many different treatments for OFG have been described. Treatment however are not 100% effective and have been seen to be less effective with more delay in diagnosis (Grave, McCullough, & Wiesenfeld, 2009). The facial features also may cause severe problems which often are more than cosmetic with obstruction of speech and ability to eat being concerning findings (Grave, McCullough, & Wiesenfeld, 2009). These may require surgical treatment which is preferred for the most severe of cases. Corticosteroids are the most effective therapy for recurrent episodes however do to the dangers of prolonged steroid use many other medications have been studied as possible cures (Grave, McCullough, & Wiesenfeld, 2009). For mild cases topical steroids may be used. In more severe cases Triamcinolone injection was effective however has proven to be difficult do to painful nature of injections (Grave, McCullough, & Wiesenfeld, 2009). Surgical treatment was only undertaken in severe cases and only after the disease progression was controlled by steroids. Do to the possible association with mycobacterium Dapsone and other anti-mycobacterium drugs have also been trialed in several studies for treatment with little evidence to support effectiveness at this point (Johani, Moles, Hodgson, Porter, & Fedele, 2009). Clofazimine and low dose thalidomide have also been researched as possible controlling agents with some reports of success (Johani, Moles, Hodgson, Porter, & Fedele, 2009). Although there is no definitive treatment at this point, with trial of drugs 50% of patients will find complete resolution in 3 years and 25% in the first year of initiating therapy (Johani, Moles, Hodgson, Porter, & Fedele, 2009).

CASE REPORT

Our patient is a 49y/o African American female with history of hypertension, DMII, glaucoma and asthma presented with paraoral and inner oral swelling over the past 10 years with recent worsening over the past 2-3 years. The patient smokes half a pack of cigarettes daily. The swelling initially began with recurrent episodes which would last 1-2 days and then resolve spontaneously. However over time the disease has evolved to the point of where her lip is always swollen causing cosmetic problems as well as discomfort. At this time she denied any difficulty swallowing or swelling of her tongue. The patient had previously tried controlling the swelling with heat, cold and moisterizer at home.

The patient had also had coughing and increased swelling 2 years ago. She was evaluated and diagnosed with ACE-I induced angioedema. At this point she stopped taking her lisinopril which she started in 2007 after a left thalamic stroke. This however did not cause swelling to resolve. The patient also claims to have been on steroids in the past but never at the same time as when she had swelling occurring. Recent colonoscopy showed several polyps w/ and diverticuli but no mention of Crohns disease. Sleep study was done earlier this month which showed moderate obstructive sleep apnea.

Physical exam showed enlarged lower labia with questionable maxillary facial swelling. The patients tongue had possible early developing fissure. No oral ulcers were identified. . The patient was started on prednisone with a taper. On follow up she did feel there was decrease of swelling during her course however that since discontinuing steroids the swelling had returned.

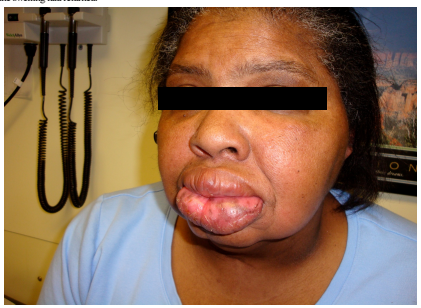

Figure 1: Significant chronic lip swelling in our patient

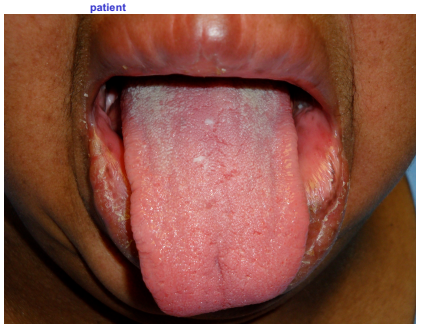

Figure 2: Possible early fissuring of tongue

RESULTS SUMMARY

- C1 esterase inhibitor and C4 were in normal limits to rule out possible hereditary angioedema.
- Patient had an instance of elevated Anti-SM antibodies in 2006 with no other markers of autoimmune disease identified.
- Recent colonoscopy ruled out Crohns disease.
- Biopsy was performed and showed dilation of blood vessels as well as lymphatics with focal histiocytic and mild lymphocytic infiltrate which is consistent with OFG.
- No granulomas were Identified.
- Congo Red stain for amyloid of the biopsy showed no signs of localized amyloidosis.
- Diagnosis of Orofacial Granulomatosis was made. The patient was advised to follow up with her neurologist with diagnosis in order to monitor possible evolution to MRS do to questionable tongue fissuring.
- The patient was started on Dapsone 50mg Daily and advised to have weekly labs drawn for first month
- Patient is to follow up in one month for re-evaluation.

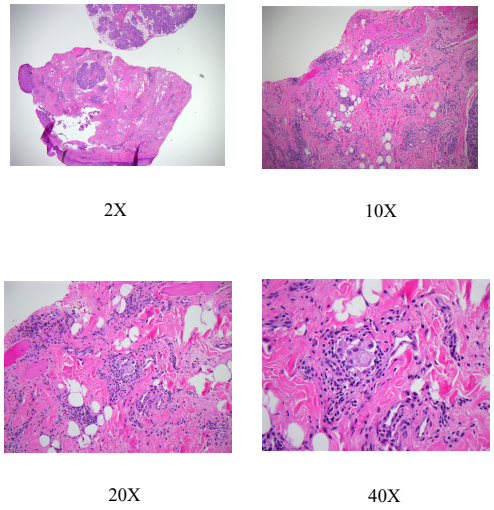

Figure 3: Biopsy of lip showing dilation of blood vessels as well as lymphatics with focal histiocytic and mild lymphocytic infiltrate which is consistent with OFG.

DISCUSSION

OFG is a rare but serious condition and must be a differential diagnosis in all patients presenting with chronic labial swelling. Do to the rarity of the condition as well as the sparse data available it may be overlooked by many physicians (Johani, Moles, Hodgson, Porter, & Fedele, 2009). In our patient the definitive diagnosis took 10 years and in many a delay such as this may lead to debilitating problems with airway, eating or communication. Delaying diagnosis in a patient mean delayed initiation of treatment and with this there has been reports of poorer quality outcomes (Grave, McCullough, & Wiesenfeld, 2009).

Crohns disease is another important consideration in all patients presenting with chronic labial swelling. Crohns disease should be in particular evaluated for in those with ulceration, and buccal-sulcal involvement as these are the most common distinguishing oral features (Campbell, et al., 2011). In general younger age is more common in OFG then Crohns (Campbell, et al., 2011). Sarcoides, another disorder which may appear with non-casseating granulomas, may also produce orofacial features similar to OFG. Signs of Lung and lymph node involvement should cause one to be suspicious of this systemic process (Grave, McCullough, & Wiesenfeld, 2009). Finally it is important to remember the triad of fissured tongue, facial swelling and facial paralysis in order to prevent neurologic symptom progression of MRS

CONCLUSION

Many treatments have been successful in causing remission of OFG and therefore even with the sparse availability of research there is a bright prognosis for most patients. This case should be used to illustrate the importance of properly evaluating the cause of chronic lip swelling. Because the swelling itself is often irreversible and the quicker it is diagnosed the sooner we may act to prevent consequences. Identifying systemic diseases through this relatively harmless presentation may both help reduce cosmetic symptoms as well as protect the patient from more debilitating symptoms down the road.

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ACKNOWLEDGEMENTS:

I would like to sincerely thank Dr. Robert Hostoffer, Dr. Haig Tcheurekdjian, Dr. David Swender And Dr. Leah Chernin for encouraging and helping guide this presentation as well as harboring me at their practice for a month.