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Clinical Challenges Q&A

3. Persistent Lip Swelling

A 12-year-old schoolgirl complained of swollen lips. The complaint was first noticed just after orthodontic treatment in 2007–2008, about one month after she started wearing her wire retainer (July 2008). She began with painless persistent swelling, first of the right upper lip, spreading to the left upper and then also to the lower lip. This persisted, despite her replacing the wire retention with plastic retention, though she still had wire in the lower. She had patch tests for metals which were positive for mercury, chromium and iridium.

She had always suffered from recurrent oral ulcers, as had her mother and brother. She had had no oral lumps or gingival lesions. There were no cutaneous, gastrointestinal, genital, ocular or joint problems and no history of fever. She had no weight loss. In 2007–2008, she was on antibiotics for latent TB as she was in a class taught by a person with open TB. In 2008, she had an ear piercing slightly complicated by inflammation.

The medical history was otherwise clear. There were no

cardiorespiratory or bleeding problems. The patient was on no medication and had no other known allergies.

The social history included no current tobacco use and no alcohol consumption. Her diet was relatively normal but she drank quite a lot of *Coca Cola*. She spends considerable time in Asia with her parents, so was exposed to quite a lot of monosodium glutamate.

Extra-oral examination revealed diffusely swollen upper and lower lips (Figure 1a) and mild angular stomatitis, but no other significant abnormalities and specifically no pyrexia, cervical lymph node enlargement, or cranial nerve, salivary or temporomandibular joint abnormalities.

The dentition was good. There was no clinical evidence of periodontal attachment loss or pocketing, but she did have a full thickness gingival swelling labially in the lower anterior region. She had some cobble-stoning in both buccal mucosae with tags posteriorly, especially on the left (Figures 1b and c).

Q1. What is the likely cause of her diffuse swelling of upper and lower lips?

- (a) Angioedema;
- (b) Contact allergic cheilitis;
- (c) Orofacial granulomatosis;
- (d) Cheilitis glandularis;
- (e) Endocrinopathies.

A1. The answer to what is the likely cause of her diffuse swelling of upper and lower lips?

(c) *Orofacial granulomatosis*. The history and clinical findings are most consistent with a diagnosis of orofacial granulomatosis (OFG),



Figure 1. (a) Diffusely swollen upper and lower lips. (b, c) Cobble-stoning in both buccal mucosae.

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of which the cheilitis is one part, or Crohn's disease. Chronic diffuse swelling of upper and lower lip or both is often accompanied by gingival swelling, mucosal lumps or tags, and ulceration. OFG is characterized histologically by the presence of numerous focal granulomas within the connective tissue. The young age of our patient, and the absence of serious diseases (lungs, gut) largely rule out the possibility of sarcoidosis or Crohn's disease, and TB had already been excluded by her physician. The presence of similar lesions on her gingivae and buccal mucosa (tags) and lack of neuropathies excludes Meischer cheilitis and Melkerson Rosenthal syndrome and leaves OFG or Crohn's disease as the most likely cause.

(b) *Contact allergic cheilitis* can arise from various allergens applied to the lip with lipsticks, and appears as a diffuse, sometimes painful lip swelling associated with desquamation, fissures and crusting. Our patient did have allergies to some metals (mercury, chromium and iridium). Replacement of orthodontic metallic wires, however, did not change the swelling, suggesting that the orthodontic treatment was not solely responsible for the lip swelling. OFG may be caused by an immune response to various allergens in foods/drinks, such as benzoates, cinnamonaldehyde, or monosodium glutamate. Our patient spent considerable time in Asia eating foods rich in monosodium glutamate. Carbonated beverages are sometimes implicated.

(a) *Angioedema* presents with acute diffuse swelling of upper or lower lip and face, usually caused by either an allergic reaction to various foods (nuts, chocolate, strawberry) or drugs (NSAIDs, antibiotics, antihypertensives) – or it can be inherited (lack of C1 esterase inhibitor). The swelling is painless, lasts from a few hours to <3 days, and is accompanied by an itching sensation but not lip crusting. The chronic duration and constant swelling of our patient's lip exclude angioedema.

(d) *Cheilitis glandularis* is characterized by inflammation of minor salivary glands of one or both lips and appears as a diffuse lip swelling, which can become super-infected with various bacteria, and is slightly tender on palpation with crusting and exudates from the salivary glands. Biopsy reveals inflammation of minor salivary glands with acinar atrophy without granuloma formation. In our patient, the lip swelling was diffuse, non-tender and with no exudates seen on lip squeezing.

(e) *Endocrinopathies* may cause lip enlargement. Increased production of growth hormone can cause enlargement of the lips (gigantism). Hypothyroidism can cause a diffuse oedema of the face with swelling of lips and tongue.

Q2. Which investigations are commonly used by the clinician for the correct diagnosis of lip swelling? Specify one or more.

- (a) Biopsy;
- (b) Allergic patch tests;
- (c) Radiographs;
- (d) Culture;
- (e) Blood tests.

A2. The answer to which investigations are commonly used by the clinician to make the correct diagnosis of lip swelling?

(a) *Biopsy* may be useful for giving histological information regarding tissue oedema,

granuloma formation, accumulation of eosinophils and other inflammatory cells, such as polymorphs and lymphocytes into the underlying connective tissue, as seen in OFG or Crohn's disease.

(b) *Allergic patch tests* are used to identify a possible allergen responsible by applying various agents, via special cups, on a patient's skin and looking for a reaction in less than 48 hours.

(c) *Radiography* may be needed to exclude Crohn's disease, TB or sarcoidosis.

(e) *Blood tests* may help, such as looking for anaemia in Crohn's disease, excluding sarcoidosis (serum angiotensin converting enzyme levels are often raised in sarcoidosis); others are more specific for looking at the level of certain hormones in various endocrinopathies, as well as the concentration of C1-esterase inhibitor, and complement detecting hereditary angioedema.