Circumorificial plasmacytosis/plasma cell orificial mucositis: a case series and a review of the literature

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Circumorificial plasmacytosis is a rare plasma cell proliferative disorder of the orificial mucous membranes. The etiology is unknown, and there are no reported effective treatments to date. We report three cases of idiopathic circumorificial plasmacytosis with varying clinical presentations and responses to treatment, including a first reported case of resolution with adalimumab therapy. (Oral Surg Oral Med Oral Pathol Oral Radiol 2016;122:e77-e81)

Circumorificial plasmacytosis (CP) is a rare plasma cell proliferative disorder of the orificial mucous membranes with an unknown etiology. Zoon, over half a century ago, first described a plasma cell infiltrate occurring on the glans penis; he termed it "chronic benign balanoposthitis with plasmacytes."[1] There have since been many changes in the nomenclature. Schuermann[2] and Luders[3] used the terms *plasmacytosis circumficialis* and *plasmacytosis mucosae*, depending on the site involved. In 1986, White introduced the term *plasma cell orificial mucositis* (PCOM) to describe plasma cell infiltrates of the mucous membranes of body orifices.[4] Since then, plasma cell orificial mucositis, plasma cell mucositis, and CP have been the most commonly used terms,[5] although there is still no consensus. Cutaneous and systemic variants of plasmacytosis have been reported but appear to be exceedingly rare and unrelated to CP; arising primarily in patients of Japanese descent.[6]

The etiology of CP is unknown, although the majority of reported cases has been associated with a synchronous or metachronous autoimmune or immunologically mediated disease.[5] There are no reported associations with dermatoses or plasma cell or other neoplasms.

Various clinical presentations have been reported, but typically, florid erythematous mucosa with papillomatous, cobblestone, nodular, or granulomatous surface changes are found. The condition can be completely asymptomatic, but more usually, it is painful, leading to difficulties with speaking, eating, and swallowing.

Histologically, the condition has a dense polyclonal submucosal plasma cell infiltrate, similar to extramedullary plasmacytoma and plasma cell gingivitis, and clinical correlation is needed to differentiate these conditions. There is no consensus on management, with most cases being refractory to treatment.

CASE REPORTS

Case 1 is a 68-year-old female, referred in December 2006 by her general dental practitioner for "a mucogingival infection." She was asymptomatic, her only complaint being an ill-fitting upper partial denture. Further questioning revealed a 6-year history of a nonpruritic lower leg rash. Her medical history included hypertension and a hiatus hernia for which she took lercanidipine, ramipril, and lansoprazole. She did not smoke or drink alcohol.

Physical examination revealed an erythematous macular rash on the extensor surface of the lower legs. There was no cervical lymphadenopathy. Intraorally, there was widespread nontender oral ulceration on the right and left maxillary alveolar ridges and hard palate, with marked palatal erythema of the denture-bearing mucosa and buccal mucosa adjacent to the upper denture. Desquamative gingivitis was observed on the maxillary and mandibular labial gingivae, and there were white striae on the right and left posterior buccal mucosae. The preliminary clinical differential diagnosis included a

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lymphoproliferative disorder on a background of lichen planus.

Initial investigations included microbiologic swabs and various blood tests, including complete blood cell count (CBC), hematinics, erythrocyte sedimentation rate, cross-reactive (C-reactive) protein, immunoglobulins, serum electrophoresis, antineutrophil cytoplasmic antibodies, antinuclear antibodies (ANAs), pemphigus vulgaris and bullous pemphigoid antibodies, renal and liver profiles, and a screening for diabetes. An incisional biopsy for histopathology was also carried out. While awaiting the results of investigations, initial treatment included oral fluconazole and chlorhexidine mouthwash, followed 1 week later by amoxicillin and metronidazole for bacterial superinfection. She was referred to a dermatologist for an opinion on the skin rash and patch testing.

Significant findings included lymphopenia of 0.9×10^9/l (1.5-3.5), serum ferritin of 15.1 μg/L (23-393), positive ANA of 1:80, and elevated immunoglobulin E of 277 u/mL (0-100). Swab results showed commensals only. Histology showed a partly ulcerated squamous epithelium with an underlying dense polyclonal plasma cell infiltrate. No interface mucositis was seen. Periodic acid—Schiff stain was negative for *Candida*. The appearance was suggestive of circumorificial plasmacytosis. Full skin examination by the dermatologist revealed cutaneous lichen planus on her back, which was confirmed by biopsy. The leg rash was thought to be fungal. Patch testing was negative to the British Contact Dermatitis Society standard battery. Subsequent biopsies of the striated white patches on the left buccal mucosa and lower anterior attached gingiva were suggestive of lichen planus and lichenoid reaction, respectively. Direct immunofluorescence of both areas was nonspecific. Thus, her final diagnosis was circumorificial plasmacytosis on a background of oral lichen planus.

She was started on bethamethasone 0.1% cream, for use under her partial denture, and betamethasone 0.5 mg tablets, to be dissolved in water and used as mouthwash. These were minimally effective, and as she remained asymptomatic, these medications were discontinued after several months. A benzoate- and cinnamaldehyde-free diet also did not have any effect. The cutaneous lichen planus was asymptomatic and thus did not need treatment. The florid palatal changes gradually resolved without treatment over time; at the most recent review, 7 years after her initial presentation, there was only evidence of inactive lichen planus in the buccal mucosa.

Case 2 was a 61-year-old woman, referred to the emergency department of the Dublin Dental University Hospital by her general dental practitioner, with a 6-month history of a sore mouth, unresponsive to treatment with betamethasone mouthwash. She had no skin, genital, gastrointestinal, or ocular complaints. Her medical history included celiac disease and hyperlipidemia, for which she took rosuvastatin. She did not smoke and drank minimal amounts of alcohol.

Clinical examination revealed diffuse, vegetative ulceration of both buccal mucosae, along with florid strawberry-like gingival erythema and edema (Figures 1 and 2). Initial investigations included multiple blood tests, including CBC; hematinics; C-reactive protein; immunoglobulins; serum electrophoresis; antineutrophil cytoplasmic antibodies; ANAs; pemphigus vulgaris and bullous pemphigoid antibodies; renal, liver, and bone profiles; and Hb_{A1c} (glycosylated hemoglobin). Microbiologic swabs and incisional biopsies for histopathology and direct immunofluorescence were also carried out. The only abnormal blood results were positive antineutrophil cytoplasmic antibodies of 1:80 and weakly positive antimyeloperoxidase antibodies. Initial biopsies showed ulcerated squamous mucosae with a mixed inflammatory infiltrate, focal acantholysis, and subepithelial and intraepithelial microabscesses, suggestive of pyostomatitis vegetans, but, clinically, this was thought to be unlikely. Direct immunofluorescence showed only C3 in a nonspecific pattern. Repeat biopsy showed a dense, polyclonal subepithelial and perivascular plasma cell infiltrate suggestive of circumorificial plasmacytosis. There was no interface mucositis, and periodic acid—Schiff stain was negative.

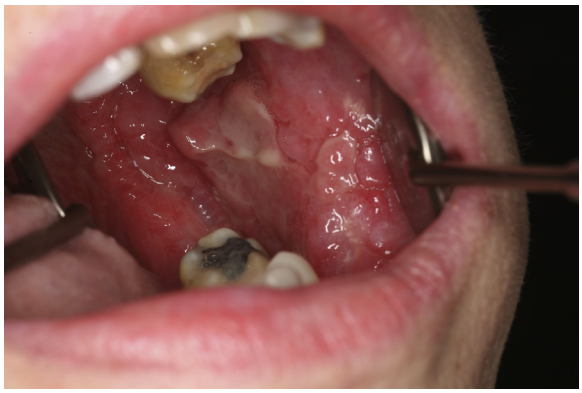

Fig. 1. Left buccal mucosa showing extensive ulceration and sloughing.

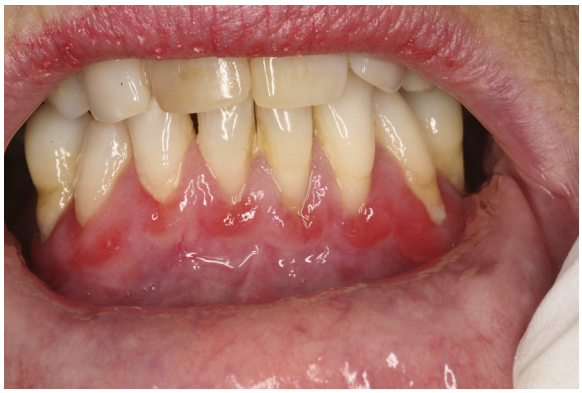

Fig. 2. Lower gingiva with strawberry-like edema and erythema.

As there was no response to topical steroids, prednisolone 20 mg daily was commenced and increased quickly to 40 mg daily, with minimal effect. Azathioprine was added but discontinued because of profound lymphopenia. The patient developed Cushingoid facies and insomnia; therefore,