Autopsy Case Reports

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Plasma cell cheilitis: the diagnosis of a disorder mimicking lip cancer

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ABSTRACT

Plasma cell cheilitis (PCC) is an inflammatory disorder of unknown etiology that affects the lip. It is characterized histologically by a dense infiltrate of plasma cells with a variety of clinical features. The response to different therapeutic modalities is controversial, especially regarding the effectiveness of corticosteroids. We present a case of a 56-year-old Caucasian man with a painful ulcerated and crusted area in the lower lip, resembling a squamous cell carcinoma or actinic cheilitis. Topical corticosteroid was used for one week, which resulted in partial regression and motivated a biopsy. The histological examination provided the diagnosis of PCC. The patient has been disease-free for six months. We also provide a discussion on the criteria of differential diagnosis and management of this rare condition.

Keywords
Cheilitis; Lip; Lip diseases; Plasma cell.

INTRODUCTION

Plasma cell cheilitis (PCC) is a rare site-specific type of plasma cell mucositis reported in older adults, with higher prevalence in men.[1,2] The lesion is presented as circumscribed erosive or erythematous plaques or patches on the labial mucosa, predominantly on the lower lip.[1,3,4] Histopathologically, PCC consists of a proliferation of mature plasma cells distributed as a dense band-like subepithelial infiltrate.[2,5,6] Additionally, the epithelium may present dyskeratosis, intercellular edema, erosion or ulceration, hyperkeratosis, and vacuolar degeneration in the conjunctival-epithelial junction.[2,7] When these clinical and microscopic findings are located intraorally, they are called plasma cell mucositis.[8-11] Different therapeutic approaches have been performed, but the outcomes remain paradoxical.[5] We present a case of PCC clinically similar to lip squamous cell carcinoma or actinic cheilitis, but responsive to topical corticosteroid.

CASE REPORT

A 56-year-old Caucasian male farmer sought the Oral Diagnosis Clinic complaining of a pricking pain in the lower lip where he had an unhealed wound for about six years. His medical history included hypertension and diabetes and there was no history of drinking or smoking. However, the patient reported being exposed daily to the sun without UV protection.

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The examination showed a 3-cm ulcerated and crusted area on the lower lip (Figures 1A and 1B). There were no clinical changes in the intraoral examination. The clinical findings and the patient's occupation led to the diagnosis of lip squamous cell carcinoma or actinic cheilitis.

An incisional biopsy could not be performed at the first appointment due to the patient's high blood pressure (200/120 mmHg). The topical use of 0.1% triamcinolone acetonide cream was prescribed until the next appointment. After seven days, the patient returned to the clinic with significant clinical improvement. The incisional biopsy was performed under local anesthesia and the tissue specimen was sent to histopathological analysis. The tissue sections showed parakeratotic stratum corneum with ulcerated areas, showing in the lamina propria a dense sheet-like infiltrate predominantly of mature plasma cells, some

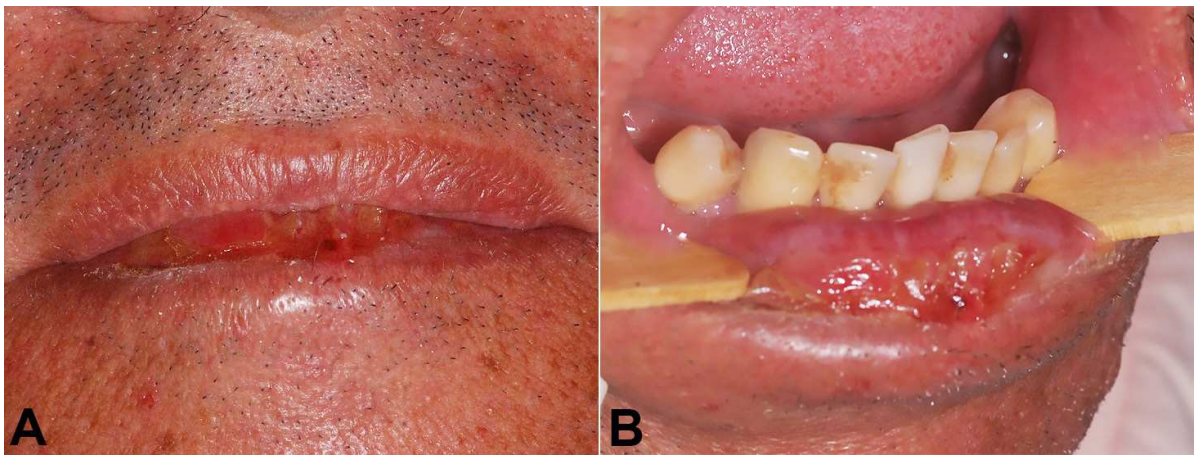

Figure 1. Clinical aspect of lips. **A –** Absence of upper lip changes; **B** – Well-marked ulcerated and crusted area on the lower lip.

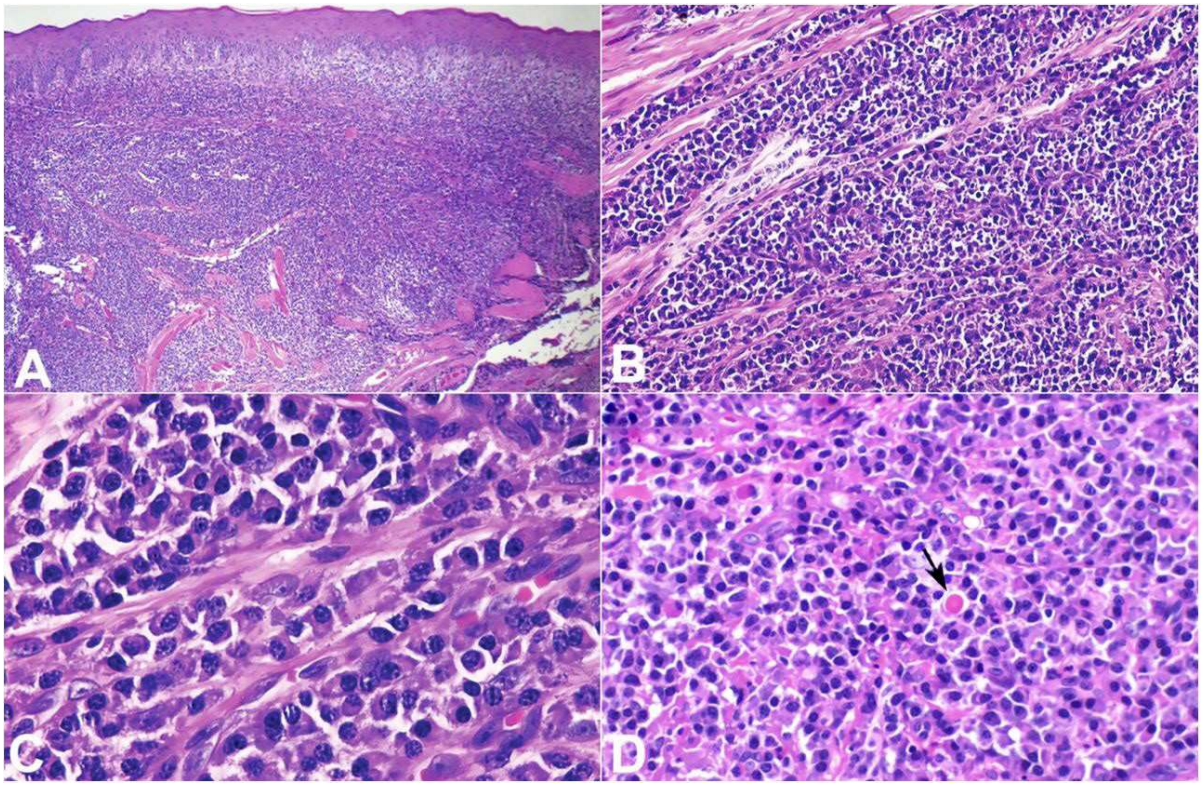

Figure 2. Photomicrograph of the biopsy specimen. **A –** Hyperplastic and parakeratinized stratified squamous epithelium with dense infiltrate of plasma cells in the lamina propria (Hematoxylin-eosin, 20X); **B** – Presence of a band-like infiltrate of plasma cells. (Hematoxylin-eosin, 100X); **C –** Monomorphic mature plasma cells. (Hematoxylin-eosin, 400X); **D –** Presence of Russel body (arrow) (Hematoxylin-eosin, 200X).

lymphocytes, few eosinophils, and sparse Russell bodies (Figures 2A-D). The plasma cells infiltrated the entire connective tissue up to the minor salivary glands. It is worth noting the absence of cellular atypia, pleomorphic figures, and mitotic activity. Immunohistochemistry to kappa and lambda immunoglobulin light chains showed polyclonal plasma cells, with a predominance of lambda (Figures 3A and 3B).

Considering the clinical and histopathological findings and a negative serological test for syphilis, PCC was diagnosed. The topical corticosteroid was suspended after 10 days of use. Lip balm cream and sunscreen were prescribed and the lesion completely regressed 35 days after the biopsy (Figure 4).

There was no recurrence after six months of follow-up and the administration of lip balm and sunscreen was maintained.

DISCUSSION

Plasma cell cheilitis (PCC) is a type of mucositis enriched with plasma cells. Plasma cell mucositis was first described in 1952 by Zoon[12] and it has been identified in distinct anatomical areas and in other mucosae such as glans and vulva.[8] Plasmacytosis circumorificialis and plasmacytosis mucosae are other terms used in the literature.[13] Although PCC is mentioned in the literature as a rare disorder, the data on its incidence is scarce.

The PCC affects more commonly the lower lip of men, with the peak of incidence in the elderly.[1,2] The clinical features are characterized by erosive, ulcerative, fissured, bleeding, crusting, and erythematous plaques or patches on the labial mucosa,[4,5,14] usually accompanied by the symptom of

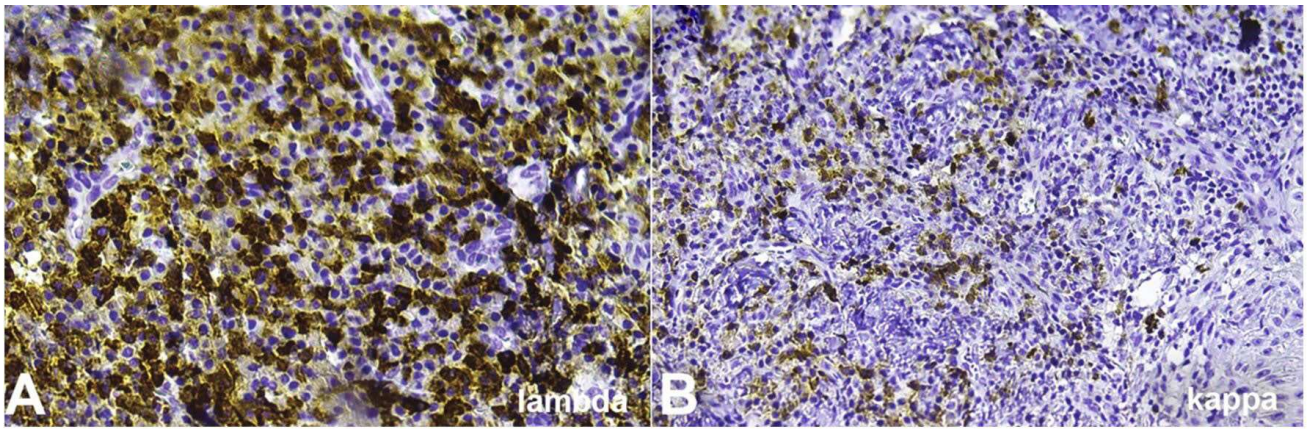

Figure 3. Photomicrograph of the biopsy specimen. Plasma cells showing positivity for both lambda (**A**) and kappa (**B**) (Immunohistochemistry, 200X).

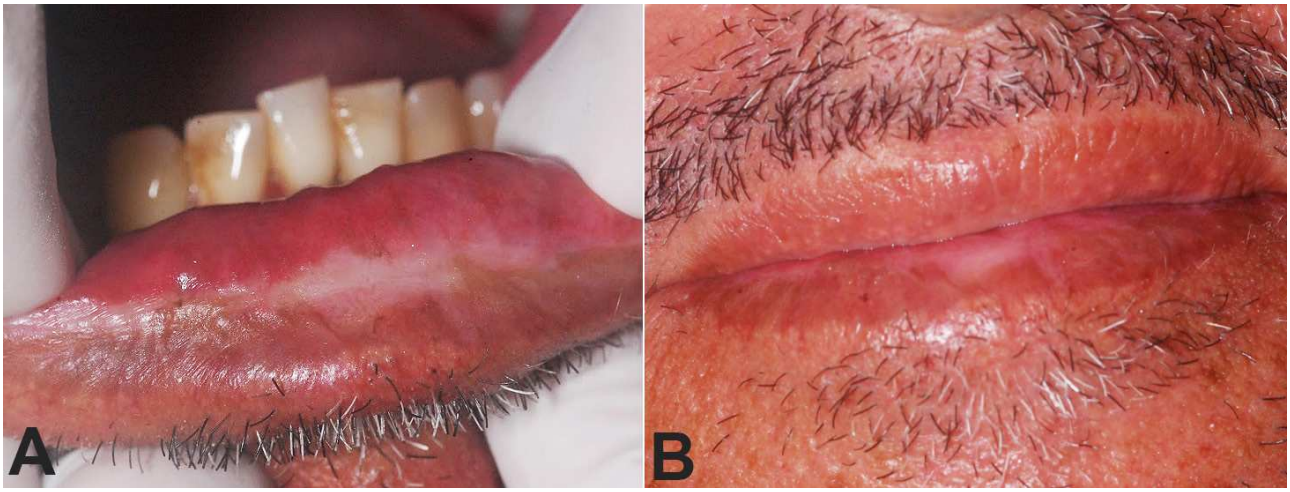

Figure 4. Clinical aspect of lower lip during follow-up. **A, B –** Complete regression of ulcerated and bleeding area 35 days after the biopsy.

pricking.[2] The clinical evaluation of PCC frequently leads to an initial misdiagnosis, which requires biopsy and additional investigations.[11] The clinical differential diagnoses are actinic cheilitis, allergic contact cheilitis, exfoliative cheilitis, granulomatous cheilitis, lichen planus, and lip squamous cell carcinoma.[5] Considering that PCC is rarely considered a differential diagnosis in the clinical routine, our provisional clinical diagnosis (actinic cheilitis or lip squamous cell carcinoma) was based on the most frequent ones for the clinical features of the patient. The histological diagnosis is based on the identification of a sheet-like infiltration of monomorphic mature plasma cells without anaplasia or prominent nucleoli, and Russel bodies are found occasionally.[2,5,6] The clinicopathologic features of the current case were consistent with PCC.

The etiology of PCC remains unknown. One theory speculates that inflammatory cells such as T cells and macrophages affect the growth and differentiation of B cells.[4,5,15,16] Another theory holds that PCC might be a response to exogenous factors such as trauma and solar damage.[2,6] We assume that solar damage might have triggered PCC, considering our patient is a farmer who is constantly exposed to the sun without UV protection. In addition, neoplastic plasma cell disorders are composed mainly of monoclonal cells, whereas inflammatory ones consist of polyclonal cells.[17] Therefore, considering that oral plasma cell mucositis is composed of polyclonal plasma cells,[12] PCC might be considered a benign inflammatory condition. A predominance of kappa immunoglobulin light chain was mentioned in nine out of 13 cases evaluated previously,[2] which contrasts with the higher levels of lambda positivity of cells in the present case.

Considering the histological character of PCC diagnosis,[14] the microscopic differential diagnosis may include a variety of lesions such as allergic contact cheilitis, secondary syphilis (mucous patches - erosions or ulcers with an erythematous margin), actinic cheilitis, squamous cell carcinoma, cheilitis granulomatosa, and plasmacytoma.[7,8,18] These lesions may be excluded depending on the histomorphology. Allergic contact cheilitis shows inflammatory infiltrates mainly consisting of lymphocytes, Langerhans cells, macrophages, and eosinophils rather than plasma cells.[19] Our case showed a consistent infiltrate of mature plasma cells and the patient did not report allergies or sensitivities to a specific substance. The histopathological features of syphilis are inflammatory infiltrates containing plasma cells, lymphocytes, and macrophages, usually with a perivascular distribution.[20] The present case was not marked by a perivascular location of plasma cells and a serological screening ruled out syphilis. Actinic cheilitis is represented by hyperkeratosis with epithelial hyperplasia or atrophy, acanthosis, solar elastosis, chronic inflammatory infiltrate, vasodilatation, and it may present dysplasia,[21-23] which were not detected in our case. Lip squamous cell carcinoma shows variable degrees of squamous differentiation featured by the invasion of the underlying stroma,[24] which was not observed in our findings. Cheilitis granulomatosa shows noncaseating granulomatous inflammation,[25] which was not found in the present case. Plasmacytoma is a rare malignant neoplasm that usually affects the mandible when occurring in the oral cavity,[26] and it is characterized by the proliferation of atypical monoclonal plasma cells.[20] Our biopsy specimen did not show cellular atypia, pleomorphic figures, and mitotic activity, and the cells were polyclonal, thus ruling out the diagnosis of plasmacytoma.

Different therapeutic approaches to PCC have been proposed, such as surgical excision, radiation therapy, electrocauterization, cryotherapy, topical application of fusidic acid, systemic and topical corticosteroids, administration of systemic griseofulvin, and immunomodulatory agents.[1,5,8,18,27-32] Nevertheless, the outcome with topical corticosteroid therapy varies from poor[15] to successful[1]. Such sliding response to topical corticosteroid may be explained by epithelial width, as distinct results of topical corticosteroid treatment between atrophic, mild acanthotic, and marked acanthotic variants have been reported.[8,33] Our patient presented clinical improvement with topical steroid treatment. Thus, we assume that the presence of ulcerative lesions increased the effectiveness of topical corticosteroid treatment.

In addition, it is worth emphasizing that disorders featured by plasma cell mucositis, considered as benign entities, have a favorable prognosis.[11] The absence of recurrence in the present case contributes to this concept. Moreover, to the best of our knowledge, PCC has a benign clinical behavior, as the development of malignant neoplasia from PCC has not been reported yet.

In summary, PCC is an uncommon disorder in the clinical routine, which may present some similar

clinical and histopathological findings with different conditions. Biopsy is required to confirm the diagnosis. Clinicians and pathologists should consider PCC when evaluating lesions on the lip, and corticosteroid treatment should be considered when detecting such condition.

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