Melanoacanthoma, Plasma Cell Cheilitis and Langerhans Cell Hyperplasia on the Lower Lip: An Unusual Association and Immunohistochemical Analysis

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Abstract

Oral melanoacanthoma is an uncommon reactive lesion, characterized by basal and prickle cell keratinocyte proliferation surrounded by pigment-laden dendritic melanocytes. Plasma cell cheilitis (PCC) is an inflammatory disorder of unknown aetiology, microscopically presenting a dense plasma cell infiltrate. Most PCC cases affect the lower lip. Langerhans cell hyperplasia (LCHyp), a non-neoplastic counterpart of the LC proliferations, has been reported in association with chronic inflammatory skin diseases. Here, we present an unusual association of melanoacanthoma, PCC and LCHyp on the lower lip in a 59-old-year male, expanding the clinicopathological spectrum of these uncommon lesions. The dendritic melanocytes were highlighted by Fontana–Masson stain and HMB-45, whereas S100, CD1a and CD207 evidenced numerous LCs. MUM1/IRF4, EMA, and CD138 highlighted sheets of polyclonal plasma cells, with an IgG4+/IgG+ ratio of 24%. FTA-ABS test for syphilis was negative.

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Introduction

Cutaneous melanoacanthoma is a benign mixed skin tumour composed of basal and prickle cell keratinocyte proliferation surrounded by pigment-laden dendritic melanocytes, considered to be a heavily pigmented variant of seborrheic keratosis.[1] Oral melanoacanthoma (OM) is a rare lesion, preferentially affecting young adult black women. The most common sites of involvement are the buccal mucosa, lips, palate, and gingiva.[2] The lesions can be asymptomatic or associated with pain, burning, or itching. In addition, its preference to affect sites exposed to trauma, resolution after biopsy, as well as association with a mild chronic inflammatory infiltrate, favour a reactive lesion.[2]

Plasma cell cheilitis (PCC) is an unusual benign plasma cell proliferative disease, frequently affecting the lower lip of adult/elderly men.[3,4] Approximately 43 PCC cases have been reported to date.[4] It is characterized by erosive, ulcerative, fissured, bleeding, crusting, and erythematous plaques or patches. Histopathologically, PCC shows a proliferation of reactive plasma cells distributed as a dense band-like subepithelial infiltrate.[3] In addition, hyperkeratosis, spongiosis, and vacuolar or liquefactive degeneration at the epithelial-connective

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tissue junction, can be observed.[3,4] Local therapy, with intralesional steroid injection and topical tacrolimus, seems to be beneficial.[3,4]

Langerhans cell hyperplasia (LCHyp), a non-neoplastic counterpart of the LC proliferations, has been reported in chronic inflammatory cutaneous conditions, such as psoriasis, atopic dermatitis, and even scabies, as well as in mycosis fungoides and lymphomatoid papulosis.[5] Noteworthy, LCHyp should be distinguished from Langerhans cell histiocytosis (LCH), an inflammatory myeloid neoplasia commonly affecting children.[6] Interestingly, there are no studies reporting an association of LCHyp with melanoacanthoma and/or PCC. Here, we present an unusual association of melanoacanthoma, PCC and LCHyp on the lower lip, expanding the clinicopathological spectrum of these uncommon lesions.

Case History

An Afro-Brazilian descendent male patient, 59-year-old, sought care for evaluation of a pigmented lesion associated with a burning sensation on the lower lip 2 years ago. The patient reported smoking habit for several years. Medical history was non-contributory. On physical examination, the presence of blackish-coloured diffuse spots, associated with a focal erosive lesion, located on the mucosal surface and vermillion of the lower lip, were visualized [Figure 1a] Microscopy revealed a surface epithelium with long interconnecting rete pegs, showing acanthosis and spongiosis, associated with an intense lymphoplasmacytic infiltrate in the connective tissue, sparing infiltration into the adjacent adipose tissue. At higher magnification, numerous-pigmented dendritic melanocytes, mainly in the prickle layer, as well as intraepithelial and subepithelial eosinophils, were observed [Figure 1b–f]. The dendritic melanocytes were highlighted by Fontana–Masson stain [Figure 1g] and HMB-45 antibody [Figure 1h]. In addition, by immunohistochemistry, S100, CD1a, and CD207 evidenced numerous LCs. CD3+ T cells were predominant rather than CD20+ B cells, while MUM1/IRF4, EMA, and CD138 highlighted numerous plasma cells with similar expression of both kappa and lambda light chains (supporting a polyclonal nature), and an IgG4+/IgG+ ratio of 24%. The Ki-67 labelling index was 5%, whereas Cyclin D1 highlighted few cells in the basal layer of the surface squamous epithelium [Figure 2]. FTA–ABS test for syphilis was requested, and the result was negative. Thus, the diagnosis of concomitant melanoacanthoma, PCC and LCHyp on the lower lip was established. After 2 years of follow-up, there was partial regression of the blackened spots, and the burning sensation completely ceased.

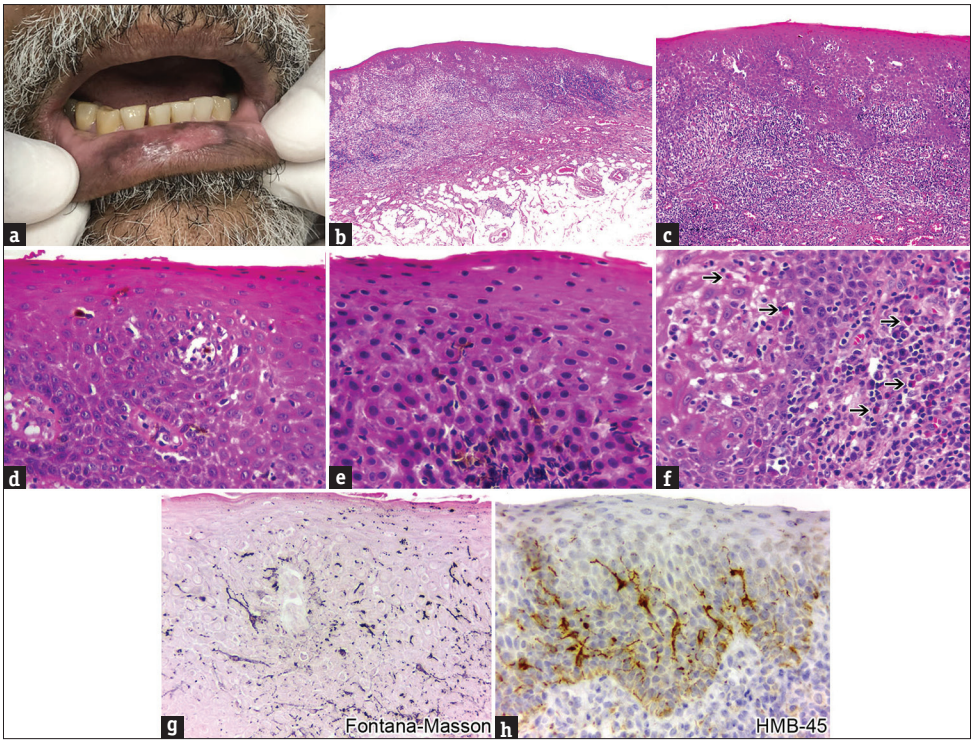

Figure 1: Clinical presentation showing blackish-coloured diffuse spots, associated with a focal erosive lesion, on the mucosal surface and vermillion of the lower lip (a). Histopathological analysis showing surface epithelium with long interconnecting rete pegs, with acanthosis and spongiosis, associated with an intense lymphoplasmacytic infiltrate (b and c). At higher magnification, numerous pigmented dendritic melanocytes in the prickle cell layer (d and e), as well as intraepithelial and subepithelial eosinophils (arrows) (f). (Haematoxylin and eosin-stained [H&E] sections, B, x40; C, x100; D–F, x400). The dendritic melanocytes were highlighted by Fontana–Masson stain and HMB-45 antibody (G, x400; H, x400)

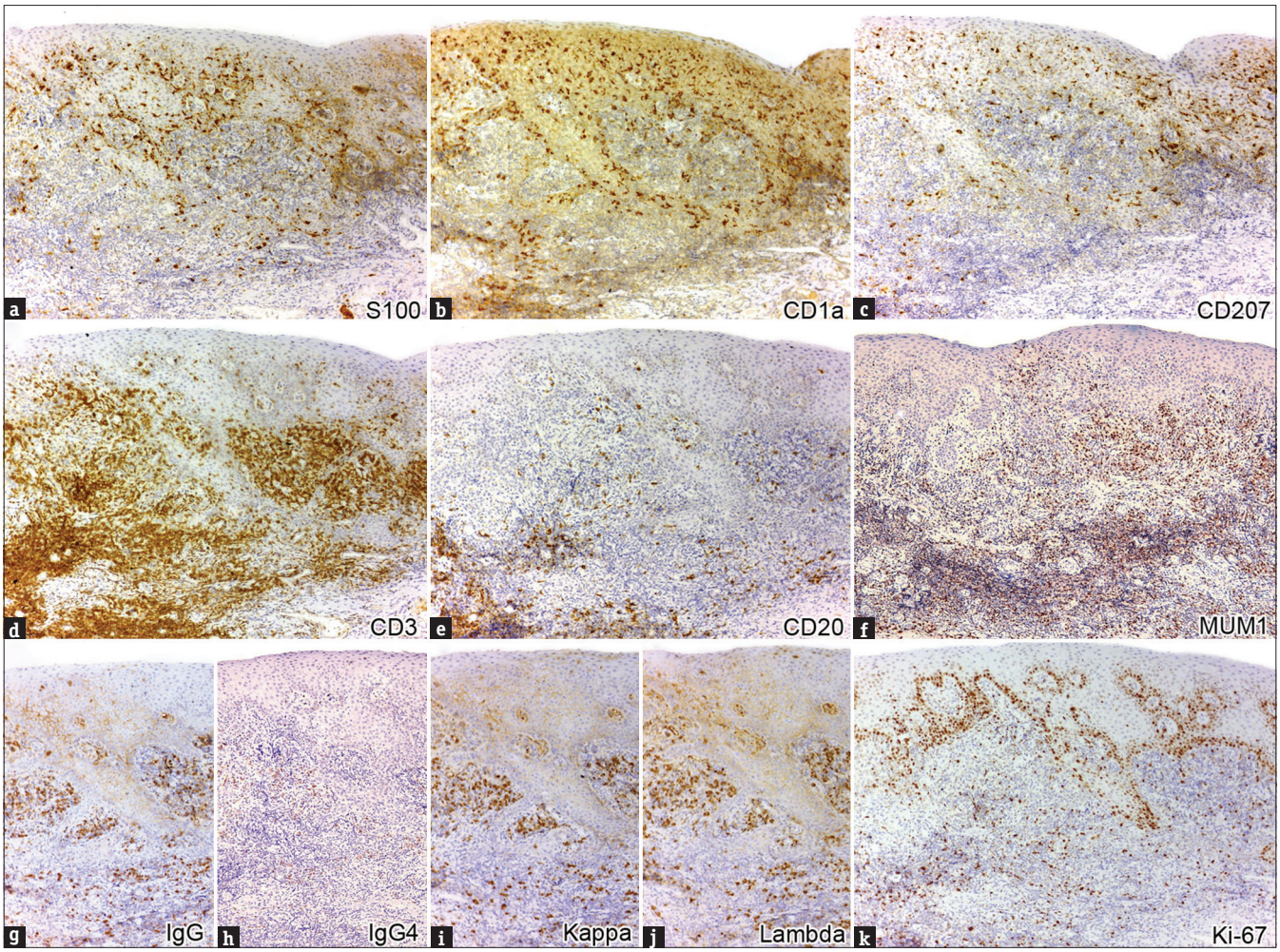

Figure 2: Immunohistochemical analysis for S100, CD1a and CD207 evidenced numerous Langerhans cells (a–c). CD3+ T cells were predominant rather than CD20+ B cells (d, e), while MUM1/IRF4 (f) highlighted numerous plasma cells, showing an IgG4+/IgG + ratio of 24% (g, h). Positivity for both kappa and lambda light chains (i, j), in similar proportion, supported a reactive nature of plasma cells. The Ki-67 labelling index was 5% (k) (All figures, x100)

Discussion

Melanoacanthoma represents 0.9% of oral melanocytic lesions, which may present as a solitary lesion and less frequently as multiple lesions.[2] After careful analysis, about 80 OM cases have been reported to date, with most cases affecting black adults (mean age 35 years, ranging from 5 to 77 years) and female predilection (ratio 2:1). Unusual microscopic findings are rarely described in OM. In fact, we have reported one OM case showing association with pseudomelanocytic nests.[7] The current case was an Afro-Brazilian descendent male patient, in whom the possibility of smoker's melanosis, post-inflammatory pigmentation or melanoma, were initially considered in the clinical differential diagnosis. Although most OM cases are asymptomatic, some are associated with pain, burning, and pruritus,[2] such as observed in the current case. In addition, while some OM cases resolve after biopsy, in the present case there was only partial resolution, probably due in part to its unusual association with PCC and LCHyp, favouring the presence of dendritic melanocytes by immunoinflammatory mechanisms.

By microscopy, the connective tissue stroma shows mild chronic inflammatory cell infiltrate in most OM cases. Differently, in the current case, we have also observed typical microscopic findings of PCC. To our knowledge, concomitant melanoacanthoma and PCC has not been reported to date. PCC is a relatively rare inflammatory disorder of the lips, wherein its pathogenesis remains elusive. One theory speculates that inflammatory cells, such as T cells and macrophages, affect the proliferation and differentiation of B cells, while another theory holds that PCC might be a response to exogenous factors such as trauma and solar damage.[3,4] PCC is histologically characterized by dense infiltration of polyclonal plasma cells in subepithelial location.[4] To date, about 43 PCC cases have been reported, with most cases affecting elderly (mean age of 61 years, ranging from 39 to 86 years) and male predilection (ratio 2:1).[4] All but one case involved the lower lip, with only one case

affecting both lips.[8] In the present case, there was no need for local corticosteroid therapy, so each case must be managed appropriately. Relevantly, the IgG4 profile in PCC cases is sparsely reported.[9] The IgG4-related disease (IgG4-RD) is a fibroinflammatory condition of the skin, mucous membranes, and other organs, microscopically characterized by dense lymphoplasmacytic infiltrate, storiform fibrosis, obliterative phlebitis, ratio of IgG4+/IgG+ cells >40% in tissues, and serum IgG4 concentration ≥135 mg/dL. Some studies show that IgG4+ plasma cells can be observed in specific and non-specific plasma cell-rich chronic inflammatory lesions.[10] Thus, a strict clinicopathological correlation is necessary to establish the IgG4-RD diagnosis. Moreover, PCC should be differentiated from syphilis. In fact, oral lesions of syphilis not uncommonly affect the lips. By microscopy, epithelial hyperplasia and inflammatory cell infiltration, especially plasma cells in subepithelial location and perivascular and perineural distribution pattern, are typical. Serological examination (FTA–ABS) is essential for conclusive diagnosis.[11] Accordingly, FTA–ABS test in the current case was negative.

Interestingly, LCHyp has been mainly reported in the skin, lung, and lymph nodes, usually in association with psoriasis, atopic dermatitis, scabies, as well as in mycosis fungoides, lymphomatoid papulosis, and dermatopathic lymphadenopathy.[5] Noteworthy, LCHyp should be distinguished from LCH, an inflammatory myeloid neoplasia commonly affecting children.[6] In the current case, numerous LCs with dendritic morphology in predominant intraepithelial location was evident, which is different from LCH findings. In fact, LCH presents histiocytes with angulated, grooved "coffeebean" nuclei and abundant eosinophilic cytoplasm surrounded by lymphocytes, eosinophils, macrophages and multinucleated giant cells.[6] It is known that, unlike LCH, reactive LCs are Cyclin D1 negative.[6] In the current case, Cyclin D1 was negative, a finding that aids the diagnosis. Moreover, in LCH cases frequent mutations include $BRAF^{V600E}$ (about 65% of cases) and MAP2K1 (about 20% of cases), which are not detected in LCHy.[6] In summary, association with an underlying disease, dendritic morphology, negativity for Cyclin D1, and absence of $BRAF^{V600E}$ mutation, support a LCHy diagnosis.

Home messages

1. OM rarely shows association with PCC and LCHy; however, it must be recognized to establish the correct diagnosis.
2. PCC shows an infiltration of polyclonal plasma cells (unlike plasmacytoma) and microscopically mimics the morphological pattern described in syphilis (here, serological examination is essential in distinguishing).
3. LCHy usually shows association with an underlying disease, not uncommonly exhibits dendritic morphology, cyclin D1 expression is negative, as well as absence of $BRAF^{V600E}$ mutation, which allow it to be differentiated from LCH.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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