Clinico-Pathologic Conference: Case 5

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Received: 25 October 2009 / Accepted: 2 November 2009 / Published online: 22 November 2009
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Clinical Presentation

A 40-year old female patient presented to the Oral Medicine Clinic complaining of discomfort and pain in the oral mucosa. Clinical examination demonstrated lesions on her left buccal mucosa and vestibule (Fig. 1a), maxillary and mandibular gingiva (Fig. 1b, c) and inside both her ears (Fig. 2a, b). A positive Nikolsky sign was elicited from the maxillary aspect of the gingiva while an intact vesicle was noted in the lingual aspect of the mandibular gingiva (Fig. 1d). She reported that the lesions had been present for 2 years with varying intensity in size and discomfort. She has not been free of lesions in her mouth for the duration of the last 2 years and mostly experiences dysphagia. She is aware of no other lesions on her skin except for the “itching blister” in her left ear (Fig. 2b). Dermatologic examination disclosed no other lesions on the skin of her body. Her medical history is unremarkable. Blood and urine analyses were all within normal limits. Serologic tests for total IgG, ANA, anti-Sm, SSA, SSB and rheumatoid factor were negative. A biopsy was performed on the buccal aspect of her left maxillary gingiva.

Differential Diagnosis

The patient presents with lesions on the skin as well as on the oral mucosa which could be interpreted as a related condition or could represent two different processes. It would be therefore necessary to provide a differential diagnosis of the intraoral lesions and a differential diagnosis of the skin lesions and a combined differential diagnosis.

The intraoral lesions can be described as well circumscribed white plaques located in the upper and lower areas of the attached gingiva as well as the buccal mucosa; the latter is characterized by not only the white border but also a distinct erythematous center. These lesions have been present for 2 years with intermittent discomfort and pain.

The differential diagnosis of these intraoral lesions includes lichen planus (LP) [1], which may have this clinical presentation, characterized by the presence of white keratotic plaques with white Wickham striae associated with an erythematous component. In our case, however, there is no bilateral evidence of white lesions on the buccal mucosa and the patient does not appear to have characteristic skin lesions; those on the ears do not represent purple, pruritic papules nor is their location consistent with the usual distribution of LP skin lesions (usually on back of hands and ankles).

Lichenoid mucositis related to contact allergy or drug reaction would be also a consideration. Substances such as cinnamon, mouth washes and amalgam are known to elicit this type of reaction [1].

Discoid lupus erythematosus (DLE) would also be a consideration and the oral lesions fit the characteristic clinical presentation for this disease. Furthermore, the lesions on the ears may represent a component of DLE as well.

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Fig. 1 **a** Red and white lesions on the buccal mucosa and vestibule of the patient. **b, c** Desquamative gingivitis. **d** Intact vesicle on the lingual aspect of mandibular gingival

Fig. 2 **a, b** Intact bullae in the ears with *white* hyperkeratotic border on the *left* ear

The cutaneous ear lesions are characterized by a well circumscribed intact bulla, surrounded by a white keratotic scale. The differential diagnosis of bullous lesions on the skin, taking into consideration the age of this patient and the focal presentation, includes linear IgA disease; this is an idiopathic condition in most instances or it may follow an episode of infection or may be caused by a drug allergic reaction. Vancomycin is the most frequently associated drug, although, cyclosporin, penicillin and phenytoin, among others, have also been implicated. Linear IgA disease has also been infrequently associated with lymphoma, ulcerative colitis and solid tumors.

DLE would be an entity with skin manifestations compatible with those of the patient under discussion. The head and neck areas involved by DLE include the scalp, the bridge of the nose, the ears and the malar areas. Skin lesions of DLE enlarge slowly and develop areas of scarring and hypopigmentation. Patients with DLE limited to the head and neck area usually lack serologic abnormalities [2].

In conclusion, taking into consideration the clinical history and presentation of the lesions, the most likely diagnosis for this case would be DLE. Systemic lupus erythematosus has been ruled out by the negative results of the laboratory tests (serologic test panel for total IgG, ANA, anti-sm, SSA, SSB, Rheumatoid factor were performed).

DLE is an autoimmune disease involving both the cell-mediated and humoral components of the immune system. It is commonly seen in middle aged women. The lesions on the skin appear on the scalp and the face and oral lesions may be present in about 25% of patients. It is not usual for the oral lesions to be the only clinical manifestation of DLE. The typical clinical presentation includes painless erythematous lesions with a white border with striae irradiating from it (as it is seen on this patient's buccal mucosa). The locations most commonly affected include the gingiva, the vermillion border of the lip and the buccal mucosa. The serology tests show no detectable antibodies for cases of DLE, which is in agreement with this patient's negative serology laboratory result [3, 4].

Diagnosis and Discussion

The biopsy from the gingiva demonstrated the histologic findings shown in Fig. 3a–d. The epithelium demonstrates saw-tooth rete ridges, hyperkeratosis, acanthosis and hydropic degeneration of the basal cell layer (Fig. 3a, b). There is separation of the epithelium from the connective tissue and resulting vesicle formation (Fig. 3c). Apoptotic keratinocytes are noted in roof of the vesicle. The underlying connective tissue exhibits chronic inflammation composed of lymphocytes, histiocytes and plasma cells. In areas, a perivascular cuff of plasma cells and lymphocytes can be demonstrated (Fig. 3d).

Fig. 3 **a** $\times 10$ Magnification: lichenoid mucositis. **b** $\times 20$ Magnification: hydropic degeneration of the basal cell layer. **c** $\times 10$ Magnification: separation of epithelium from connective tissue, vesicle formation. **d** $\times 20$ Magnification: perivascular cuff of lymphocytes and plasma cells

Based on the histopathology, a diagnosis of erosive lichenoid mucositis was rendered [5, 6]. Taken together, the clinical and the histopathology findings of the oral cavity, the clinical appearance of the skin lesions and the absence of positive serologic markers led us to the diagnosis of *DLE* [6–8].

The patient was put on a regimen of oral prednisolone starting with 30 mg/day for a week, following with a taper of 10 mg per week. Complete resolution of the oral lesions was observed in 3 weeks while the skin lesions improved greatly but did not disappear. Prednisolone was discontinued. For the skin lesions, the patient was placed on a regimen of plaquenil 200 mg/d day and topical mometasone furoate (Elocon[®]) cream 0.1% [2, 7]. A baseline ophthalmologic evaluation was also obtained and was found to be within normal limits.

DLE is a subset of lupus erythematosus (LE), a complex disease of unknown etiology and autoimmune pathogenesis. DLE is subdivided in localized and generalized variants, a fact of some prognostic significance: about 1% of the patients with localized DLE develop SLE, while 5% of those with the generalized variant progress into SLE [6, 9].

DLE typically affects women twice more often than men and demonstrates a peak prevalence in patients in their late thirties [9, 10]. It occurs more commonly in patients that are in the third to fifth decade. The lesions often present on sun-exposed areas of the skin and patients experience

photosensitivity. Exacerbation after sun exposure is noted and patients are advised to avoid the sun and use sunscreen [11].

The histopathology of DLE is often indistinguishable from that of lichen planus or other subtypes of LE, such as subacute lupus erythematosus (SCLE). A few subtle differences include the fact that the connective tissue lymphocytic infiltrate tends to be more sparse in LE than it is in LP [5], while perivascular infiltrates composed of plasma cells are more often noted in LE than in LP [6]. Direct immunofluorescence may be of some help, but it is not pathognomonic. The lupus band test, a test where the presence of immunoglobulin and complement is evaluated by immunofluorescence or immunoperoxidase means, is positive in all subsets of LE at varying frequency, but may also be positive in other types of unrelated conditions such as lichen planus and, in the skin, rosacea, solar keratosis, dermatomyositis and other conditions [6].

The significance of DLE manifestations in the oral mucosa is uncertain. Although some consider it a sign favoring progression to systemic LE, this association has not been proven [8, 9]. An interesting feature of our case is the presence of vesiculo-bullous lesions both on the skin and in the oral mucosa. The bullous variant of LE is considered to be a variant of systemic LE and is usually associated with positive serologic findings [12]. So far, our patient has not demonstrated any positivity in

serologic tests, despite regular screening. Thus, the diagnosis remains that of DLE. This diversity in clinical manifestations is characteristic of the overlap often observed among different subtypes of lupus erythematosus [11].

As a result, the diagnosis of DLE remains one that is made by piecing together evidence from careful clinical, histologic and serologic evaluation. The variety of clinical manifestations and the changing, dynamic nature of the disease process require vigilance and flexibility in both diagnostic and therapeutic approach.

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