When Persistent Ulcerative Cheilitis is the only Manifestation: A Case Report and Literature Review

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Abstract

This paper reports a rare case of persistent ulcerative cheilitis, for several months, with no response to placebo. The patient was scheduled for incisional biopsy and treated via intralesional steroid injection with a substantial improvement in four days. The histological picture suggested an autoimmune disease for clinical correlation and immunofluorescence testing. The direct and indirect immunofluorescence tests were negative. Given the clinical improvement and scarcity of any concomitant signs and symptoms, the diagnosis was based on the prompt response to the steroid injection, with no evidence of recurrence in sixteen months, as idiopathic isolated ulcerative cheilitis. This paper contrasts the reported case against similar cases in the medical literature.

Keywords: Ulcerative cheilitis; Isolated cheilitis; Lip crusting; Systematic oral manifestations; Autoimmunity; Erythema multiforme

1. Introduction

Ulcerative cheilitis (UCH) is either a manifestation of an underlying systemic disease or a local response to a known irritant. Since no detailed information is available on UCH as a sole manifestation, a valiant effort must be devoted to investigate any liable complications, subclinical or indolent systemic disease. Follicular cheilitis, infectious cheilitis, actinic cheilitis, photosensitivity dermatoses, cheilitis glandularis, factitious cheilitis, isolated lichen planus of the lip and neoplasias may reveal a similar clinical picture. (Aydin et al., 2008; Itin et al., 1995). Accordingly, the underlying cause of UCH may be hereditary, bacterial, fungal, psychological, immunological or neoplastic (Regezi et al. 2007). Therefore, it is mandatory to adopted careful diagnostic procedures before recruiting a certain treatment modality.

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2. Case Presentation

A 63-years-old male presented to our department of oral and maxillofacial surgery and diagnosis, with a chief complaint of persistent ulcerative cheilitis. The intraoral and extraoral examination revealed no other association. The patient reported receiving a diaspora of treatments for several months with no significant improvements (figure 1). No pruriginous skin lesions, neither facially nor cutaneously in sun-exposed areas, were observed. The long list of drugs included topical and systemic anti-fungal, antibiotics, antimicrobial gels and non-steroidal anti-inflammatory drugs. The patient has never been abroad. He has been living in Shubra al-Kheima: a Cairene town with no high altitudes but one of the most industrially polluted towns worldwide. Neither mestizos nor pardos live at Shubra al-Kheima.

Fig. 1. (a) Clinical picture showing lower lip ulceration and crusting. (b) The same case in 10 days after receiving corticosteroid treatment.

The patient was assured and educated about the necessity of having an incisional biopsy before describing any treatment. He was referred to a dermatologist and an ophthalmologist to rule out any cutaneous or ocular involvements. According to the dermatologist, the patient had no sexual practice over the past few years. There were no genital discharges or ulcerations. No salient ophthalmological findings were observed.

Serologically, the patient was investigated for differential “Complete Blood Count” (CBC), erythrocyte sedimentation rate (ESR), ANA, Immunoglobulin M (IgM) and IgG. The physicians’ feedback was negative for any conspicuous findings. CBC showed mild lymphocytosis. ANA was negative. Both ESR and IgM were slightly elevated while IgG was normal.

As scheduled, the patient was biopsied and injected intralesionally via corticosteroid at the same setting.
The biopsy was sent for microscopic and immunological (direct immunofluorescence) examinations. Our recommendation to use an additional histochemical staining, Periodic Acid-Schiff (PAS) to detect, if present, any fungal hyphae, was endorsed.

Histological findings revealed an ulcerative epithelium with focally degenerated basal cell layer. The connective tissue stroma showed a massive confluence of inflammatory infiltrates whose subpopulations were mainly lymphocytes, macrophages, and eosinophils. No secondary germinal centers were seen. Neither dysplasia nor atypia was observed (fig 2 &3).

![Fig. 2. A photomicrograph showing a massive confluence of inflammatory infiltrates, atrophic and ulcerative epithelial remnants, and dilated blood vessels. (Original magnification 10x)](image-url)
Fig. 3. A photomicrograph showing the subpopulation of inflammatory infiltrates; mainly lymphocytes, macrophages, and eosinophils.

PAS stain for fungal hyphae was negative. The picture was suggestive of an autoimmune disease for immunofluorescence testing and clinical correlation. Direct immunofluorescence (DIF) was negative for intercellular autoantibodies (Desmolgin 3, IgG, and IgA).

The patient, in his follow up visit, showed a favorable response to the intralesional steroid. Thence, a daily hydrocorticosteroid dosage of 30 mg (oral tablets: Hostacortin-H®) was prescribed. Before removing the stitches, an excellent result was obtained and the corticosteroid dose was diminished gradually (fig 1b). No recurrence of UCH was evident in sixteen months. No other concomitant signs or symptoms were observed.

3. Discussion

Persistent ulcerative cheilitis rarely represents itself as an isolated finding. It is, however, a manifestation of a systemic disease (Miranda et al., 2014). Although a rare isolated case of UCH was
reported as an erosive lichen planus, the incidence of similar occurrence is extremely rare (Itin et al., 1995).

Fundamental to diagnosing the underlying medical condition, if any, is running screening and specific tests. Diagnosis may be reached by treatment and exclusion in such rare cases. Differential CBC, ESR and C-reactive proteins are mandatory to direct the diagnostian to suspect a certain etiological factor. Monocytosis with relative neutropenia is usually suggestive of a viral infection. However, the increase of monocytes, eosinophils or lymphocytes is usually unremarkable and most hematologists consider it within normal conditions. Accordingly, patients must be educated about the diagnostic challenge of their cases. (Neville et al., 2009).

As diagramed in figure 4, etiologic factors of UCH may be genetic, which is commonly seen in actinic prurigo and epidermolysis bullosa. Both manifest themselves as running familial diseases in specific races and population (Mounsdon et al., 1988; Miranda et al., 2014). Other factors include infection; viral, bacterial, or (deep) fungal. Such contagion could be observed in sexually active individuals whose sexual preferences are not straight (STD). (Neville et al., 2009; Regezi et al., 2007).

Most commonly, UCH is observed in immunobullous diseases. This is usually accompanied by other signs and symptoms including cutaneous and ocular manifestations (Abbas et al., 2014). Serologically speaking, The ANA test is not always positive in autoimmune diseases. Despite ANA is a sensitive marker for such category, its specificity is, however, low. Neoplastic conditions can be easily diagnosed through the histological examinations (Neville et al., 2009). Some lesser contributing factors include trauma, psychological involvement and drug-induced manifestations.

To elucidate, factitious cheilitis, or actinic prurigo, is observed in psychologically distressed persons (Aydin et al., 2008). Follicular cheilitis (FCH) is an uncommon idiopathic photodermatosis, presents a distinct clinical picture and can be severely debilitating. (Ross et al. 2008) Similar to the clinical picture of the UCH, lip lesions in FCH are characterized by swelling, peeling, cracking, crusting, itching, exudation, and secondary ulceration. Such cheilitis intensity is variable. In the acute phase, yellow crusts adhered to the surface are observed, whereas in the chronic phase, the lesions are covered with dry scales, and the course is generally prolonged, with relapses worsened by constant sun exposure. (Mounsdon et al., 1988; Miranda et al., 2014) FCH occurs mainly and affects exclusively specific ethnic groups, particularly in North and South America, who express major histocompatibility complex class I and II (HLA I and II), suggesting a genetic predisposition (Hojyo-Tomoka et al. 2003). Other studies consider FCH one of the photodermatoses varieties. Photodermatoses are skin diseases, which can be disabling to the patient, and target, sometimes, people with darker complexion (Yazdani et al. 2003). However, it seem that increasing pigmentation correlates with a lower incidence of photodermatoses (overall prevalence skin type I 32%, II 26%, III 14%, IV 9%) (Bock et al. 2005).

Histologically, the overlying epithelium of FCH shows orthokeratosis, with some areas of parakeratosis, atrophy and areas of acanthosis, spongiosis as well as basal layer hydropic degeneration and lymphocytic exocytosis. Ulceration was also present. The connective tissue exhibits pigmentary incontinence close to the overlying epithelium, dilated blood vessels, edema and intense and diffuse lymphocytic inflammatory infiltrate, with some plasma cells, extending
deep into the fatty tissue. Some secondary lymphoid follicles and eosinophils are also present (Valbuena et al., 2014; Miranda et al., 2014). Such histological picture may be relevant to idiopathic and immune-based UCH.

Conversely, patients who receive regular drugs are more prone to develop similar drug-induced picture of UCH. There are a very long list of predisposing pharmaceuticals including some analgesics (aspirin, codeine, oxicams, propionic acid derivatives), antibiotics (erythromycin, penicillin, streptomycin, sulfonamides, tetracycline), anticonvulsants (barbiturates, phenytoin), antifungals (ketoconazole, indomethacin, antimalarial, cardiovascular, methyldopa, oxprenolol, psychotherapeutical (meprobamate, chlorpromazine), or others (retinoids, cimetidine, gold compounds, local anesthetics). Other rare cases are environmentally induced secondary to solar
over-exposure, this condition is called actinic cheilitis whose malignant potential warrants careful assessment. To keep it simple and straight, table 1 is designed to characterize features of the above mentioned diseases (Neville et al., 2009; Regezi et al., 2007).

Table 1 Distinguishing various conditions with potential to produce persistent UCH.

<table>
<thead>
<tr>
<th>Pathosis</th>
<th>Epidemiology</th>
<th>Cytological/ immunological signature</th>
<th>Histological feature(s)</th>
<th>Other evidences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinic prurigo</td>
<td>Any, mestizos</td>
<td>Pigmentation</td>
<td>Lymphoid follicles</td>
<td>Conjunctivitis, (pseudo)pterygia</td>
</tr>
<tr>
<td>Actinic Ulcerative Cheilitis</td>
<td>50-70, males</td>
<td>Pigmentation</td>
<td>Solar elastosis</td>
<td>Environmental or Occupational hazards</td>
</tr>
<tr>
<td>Drug-induced Ulcerative Cheilitis</td>
<td>Infancy</td>
<td>NA</td>
<td>NA</td>
<td>Debilitation, Blisters</td>
</tr>
<tr>
<td>Epidermolysis bullosa</td>
<td>Infancy</td>
<td>NA</td>
<td>NA</td>
<td>Chronic Systemic disease</td>
</tr>
<tr>
<td>Erythema Multiforme</td>
<td>Young adults, males</td>
<td>parabasal apoptotic keratinocytes</td>
<td>Loss of basal cell layer</td>
<td>Skin, iris</td>
</tr>
<tr>
<td>Factitious Ulcerative Cheilitis</td>
<td>Any, female</td>
<td>NA</td>
<td>NA</td>
<td>Psychological trauma</td>
</tr>
<tr>
<td>Granulomatous Cheilitis</td>
<td>20-50</td>
<td>Schaumann/ asteroid bodies (sarcoidosis)</td>
<td>(Noncaseating) Granulomas</td>
<td>Lethargy, Pulmonary infection</td>
</tr>
<tr>
<td>Histoplasmosis/ Blastomycosis/ Coccidioidomycosis</td>
<td>Any</td>
<td>Yeast in macrophages/ Fungal hyphae (PAS)/ buds</td>
<td>Granulomas/ purulence</td>
<td>Pulmonary infection</td>
</tr>
<tr>
<td>Immunological Ulcerative Cheilitis</td>
<td>40-60</td>
<td>NA</td>
<td>basilar epithelial edema</td>
<td>Positive ANA</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>40-60, females</td>
<td>Civatte bodies</td>
<td>Apoptotic basal cell</td>
<td>Wickham’s striae, Pruritic papules</td>
</tr>
<tr>
<td>Linear IgA disease</td>
<td>Children</td>
<td>DIF: deposits of IgA at the ECTI</td>
<td>NA</td>
<td>Urticarial skin lesions</td>
</tr>
<tr>
<td>Manifestation of STD</td>
<td>Sexually Active individuals</td>
<td>koilocytic cell</td>
<td>Variable</td>
<td>Fellatio or cunnilingus.</td>
</tr>
<tr>
<td>Neoplastic Ulcerative Cheilitis</td>
<td>40-70</td>
<td>Atypia</td>
<td>Dysplastic and neoplastic changes</td>
<td>VUL, Ocular affection</td>
</tr>
<tr>
<td>Pemphigoid Reaction</td>
<td>70-80, equal</td>
<td>NA</td>
<td>subepithelial clefting</td>
<td>VUL, Skin lesions, Nikolsky’s sign</td>
</tr>
<tr>
<td>Pemphigus vulgaris</td>
<td>40-60 y</td>
<td>Tzanck cell/</td>
<td>Intraepithelial clefting</td>
<td>Pulmonary/miliary affection</td>
</tr>
<tr>
<td>Tuberculous Ulcerative Cheilitis</td>
<td>Any</td>
<td>epithelioid cells</td>
<td>Red rods/ Ziehl-Neelsen stain</td>
<td></td>
</tr>
<tr>
<td>Viral Ulcerative Cheilitis</td>
<td>Children to adults</td>
<td>koilocytic cell</td>
<td>NA</td>
<td>Lymphadenopathy</td>
</tr>
</tbody>
</table>

ANA: Anti-nuclear antibody; ECTI: epithelium-connective tissue interface; NA: Not applicable; VUL: vesiculoulcerative lesions. (Compiled from Neville et al., 2009; Regezi et al., 2007)
To our best knowledge, the striking predilection of encountering the lower lip has not been discussed. Given the sparse sources and few reports of UCH, regardless of its cause, speculations should be only suggestive. The arterial flow rate of the blood supply of the upper and lower lips, from superior and inferior labial arteries, is comparable. The higher incidence of encountering actinic changes in the lower lip may be attributed to its broader eversion. Accordingly, a larger surface area is exposed to solar effects.

Treatment depends radically on the etiological cause. Immunosuppressives (corticosteroids, azathioprine, cyclophosphamide, intravenous immunoglobulin or plasmapheresis) treat immunological conditions. (Regezi et al. 2007). Treating actinic cheilitis is recently done by photodynamic therapy or imiquimod 5% and a retractor on the lip. Infection-borne cheilitis is treated by antibiotics, antiviral, and antifungal drugs in bacterial, viral and deep fungal infections respectively. In this study, a small dose of corticosteroid was injected intralesionally and prescribed as oral tablets (30 mg hydrocortisone daily) with excellent prognosis in a matter of days.

4. Conclusion

Persistent ulcerative cheilitis must be assessed carefully because it is usually a manifestation of a systemic disease. In rare cases, it might be the only symptom with idiopathic causes: an isolated case. Such query cases, like this reported one, should be treated and followed up meticulously for some longer time.

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