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Actinic prurigo on the lip: Two cases report

Miranda AMO *et al*. Two cases of actinic prurigo

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**Abstract**

Actinic prurigo is a photodermatosis that can affect skin, conjunctiva and lips. It is caused by an abnormal reaction to sunlight and is more common in high-altitude living people, mainly in indigenous descendants. Its diagnosis can be challenging, mainly when lip lesions appear as the only manifestation, which is not a common clinical presentation. The aim of this paper is to report two cases of actinic prurigo with only lip lesions. The patients were Afro-American and were unaware if they had Indian ancestry. Clinical exam, photographs, videoroscopy examination and biopsy were performed, and the diagnosis of actinic prurigo was established. Topical corticosteroid and lip balm with ultraviolet protection were prescribed with excellent results. The relevance of these cases is to show that, although some patients may not present the classical clinical presentation of actinic prurigo, the association of clinical and histological exams is determinant for the correct diagnostic and successful treatment.

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**Key words**: Actinic prurigo; Follicular cheilitis; Photodermatosis; High-altitude; Lip diseases

**Core tip**: Diagnosis of actinic prurigo can be challenging sometimes because the absence of classic clinical manifestations. Actinic prurigo is found in a high-altitude living people, mainly in indigenous descendants. Usually its onset is in the childhood and rarely presents only on the lips. Our paper shows two rare cases in Brazil, Rio de Janeiro city, which is located at sea level. The patients were unaware if they had Indian ancestry. Moreover, actinic prurigo began to appear at the adulthood and lip lesions were the only manifestation. The association of clinical and histological exams was determinant for the correct diagnostic and successful treatment.

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**INTRODUCTION**

Actinic Prurigo (AP) is a type of photodermatosis, which is a rare familial inflammatory disease that primarily affects areas of skin exposed to the sun and also affects the lips and ocular conjunctiva (pseudopterygium formation)[1]. Pseudopterygium does not appear as a unique lesion in patients with AP, it is always preceded by skin and lip lesions, suggesting that this expression tends to appear later in the disease course. For this reason, the diagnosis of AP in its early stages is important to prevent later complications[2]. AP of the lip, also known as follicular cheilitis, is mainly found on the vermillion of lower lip. Lip lesions may appear early in the development of this disease and, consequently, its observation and accurate diagnosis can alert physicians or dentists about the possible development of other more severe lesions on the skin or conjunctiva[2]. AP occurs mainly in residents of high altitudes and affects particularly ethnic groups in North and South Americas, which express major histocompatibility complex class I and II (HLA I and II), suggesting a genetic predisposition[3]. The aim of this paper is to present two cases of AP of the lips without the classical features found in this disease (young age of onset, familial history, high-altitude living area people, and association with skin lesions).

**CASE REPORT**

***Case one***

A 63-year-old Afro-American woman presented to our Oral Diagnostic clinic complaining of lower lip lesions with 10 mo of evolution, which worsened in the last 6 mo. She was referred by other two reference centers that had failed to establish the diagnosis. During physical exam, the lower lip presented edema, as well as multiple ulcers covered with yellowish crusts on semimucosa (Figure 1A). Slightest touch or mouth opening resulted in abundant bleeding, which, according to the patient was commonly observed. No alteration was observed during intraoral examination. The lesions were documented by clinical and videoroscopy images (Figure 1B) and were scraped for cytopathologic evaluation, which revealed moderate inflammation. Lip balm with ultraviolet (UV) protection was prescribed.

On the second visit, a debridement of the lesion was performed, as well as a biopsy (the selected area was chosen by clinical and videoroscopy exam) (Figure 1C). The clinical diagnostic hypotheses were erythema multiforme and contact cheilitis. Microscopically (Figure 1E-H), the surface epithelium showed ortokeratosis, with some areas of parakeratoris, atrophy and areas of acanthosis, as well as basal layer degeneration and lymphocytic exocytosis. There was also ulceration. The connective tissue exhibited pigmentary incontinence close to the overlying epithelium, dilated blood vessels, edema and intense and diffuse lymphocytic inflammatory infiltrate, with some plasma cells, extending deeply into the fatty tissue. Some secondary lymphoid follicles were also present. Several mast cells were present predominantly in the deeper area of the connective tissue, mainly in the perivascular and perineural areas. It was also observed nonspecific chronic sialadentitis with ductal ectasia. There was no solar elastosis. The diagnosis of follicular cheilitis was established.

After establishing the diagnosis, an association of triamcinolone acetonide cream, neomycin sulfate, gramicidin and nystatin cream was prescribed three times a day. The patient was instructed to use gauze compresses with cold physiological saline and to continue using lip balm with UV protection. The patient was also referred to the dermatology and ophthalmology service for evaluation of signs and symptoms of AP. No ocular neither skin lesions were observed.

Complete remission of the lip ulcers and crusts was observed after one month of treatment (Figure 1D). The patient was followed-up monthly for three months without evidence of recurrence. Two months after the establishment of the diagnosis and during the follow-up, the patient reported she had found out being Brazilian indigenous descended. After the third consecutive monthly follow-up, the patient has been followed-up every 4 mo and until now (after 2 years of the first visit), the lips present no lesions (Figure 1D). The patient did not develop any skin or ophthalmic lesion.

***Case two***

A 58-years-old Afro-American woman, presented to our Oral Diagnostic clinic complaining of a painful lesion on the lower lip with four years of evolution. The physical examination showed the presence of yellowish crust of 1.3 cm × 0.8 cm, on the left side, which stood out easily during the examination, revealing an ulcerated area. The lips were swollen and dry (Figure 2A). The lesions were documented by clinical and videoroscopy images (Figure 2B) and were scraped for cytopathologic evaluation, which revealed moderate inflammation. No alteration was observed in intraoral examination. Lip balm with UV protection was prescribed. On the second visit, a biopsy was performed (the selected area was chosen by clinical and videoroscopy exam). The diagnostic hypotheses were erythema multiforme and acute actinic cheilitis. Microscopically (Figure 2C and D), the lesion was covered by stratified ortokeratinized squamous epithelium showing atrophy, ulceration, spongiosis and hydropic degeneration of the basal layer. The underlying connective tissue presented pigmentary incontinence close to the overlying epithelium, dilated blood vessels with areas of intense inflammatory infiltrate, mainly composed of lymphoplasmacytic cells, with formation of well-formed secondary lymphoid follicles. Mast cells were also observed between the lymphocytes and plasma cells. The inflammatory infiltration extended deeply into the fatty tissue. There was no solar elastosis. The diagnosis follicular cheilitis was established.

The patient was followed-up one more time (one month after the first visit) and presented the remission of the ulceration on the left side, presenting only a small ulcer on the right side of the lip (Figure 2B). She was referred for dermatological and ophthalmological evaluation and oriented to return to our clinic one month later. Nevertheless, the patient did not return.

A search in the medical literature was performed by two authors separately, using Pubmed, Lilacs, Scielo and Cochrane databases, without year and language restriction, with the terms: (1) prurigo AND actinic; and (2) follicular AND cheilitis. The last search was performed in November 2013. A paper considered eligible for inclusion in review had to include a case report or a study with at least one case under the name “actinic prurigo” or “follicular cheilitis”, and also presents lip lesions as the only manifestation (Table 1). Only two papers attended the criteria: Vega-Memije *et al*[2] and Mounsdon *et al*[4]. In the study of Vega-Memije *et al*[2], 116 patients presented actinic prurigo cheilitis; of these, 74 (63.8%) were female, ages ranged from 9 to 82 years (mean, 27.8 years). Ninety-nine percent of the patients lived in areas more than 1000m above the sea level and only one case came from a geographic area located below this altitude. AP cheilitis was the only manifestation of the disease in 32 (27.6%) patients. Mounsdon *et al*[4] presented two cases of North American Indians, one man and one woman, showing only lip lesions, but there is no reference about the place where they lived. In addition, in Scholar Google, a thesis showing a study with 43 patients with actinic prurigo of the lips was found[5]. Although this study had been done in Brazil, it was a retrospective analysis of patients resident in Mexico, where this disease is very common. In 17 (39.54%) cases, the lesion was located only on the lips. To make comparative analyses with the cases presented in our paper, 16 patients of this study were included; one was excluded because the age was not informed. The ages ranged from 11 to 63 (mean 26 years). The information about where the patients lived was not informed (Table 2).

**DISCUSSION**

Photodermatosis form an important group of skin diseases, which can be disabling to the patient, and represents a challenge in diagnosis and treatment[6]. Although dark skin has melanin in larger quantities comparing to white skin, which gives greater protection against the sun's rays, photodermatosis are common in dark-skinned people[7]. AP is an example of photodermatosis that affects mostly mestizos of the Americas, the result of miscegenation between Europeans and Indians, which prevails in Mexico, Guatemala, Honduras, Colombia, Ecuador, Peru, Bolivia, and Argentina, and in some indigenous communities in North America and Canada[8–10]. It usually begins in childhood, around 4-5 years old[5], although it can manifest at any age, affecting more women than men (2:1), and in some cases with familial history[11].

The severity of the disease is altitude dependent, presumably because of the sustained intensity of the sun exposure. It is believed that this is the reason the AP is found most in regions with altitude above 1000 meters[3]. These data make our cases interesting, since the patients lived in Brazil, in cities at sea level, and did not report during anamnesis being indigenous descendants, nor had a positive familial history, and showed the first signs and symptoms in adulthood.

AP lesions can be found mostly in sun-exposed areas[3,12,13]. Lips and conjunctiva can be also affected[3,12]. Nevertheless, in Asians, conjunctivitis or cheilitis seem not to be common[14]. The patients presented in this paper showed lip lesions as the only manifestation of AP. Although there are few reports and studies in the literature about actinic prurigo with only lip lesions, it may occur in up 40% of the cases[5]. Cases of actinic prurigo with lip lesions as the only manifestation is more difficult to establish the accurate diagnosis, which could alert the clinicians about the possibility of the development of other more severe lesions, such as on the skin or conjunctiva. Therefore, it is important to refer the patients to ophthalmological and dermatological evaluation.

Lip lesions of AP are characterized by swelling, peeling, cracking, crusting, itching, exudation, and secondary ulceration[3,12]. Cheilitis intensity is variable. In acute phase, yellow crusts adhered to the surface are observed, whereas in the chronic phase, the lesions are covered with dry scales, and generally the course is prolonged, with relapses of worsening by the constant sun exposure[2,8,5].

In the evaluation of patients, we used the videoroscopy that enabled better visualization of the lesions present on the lip. As both patients presented extensive lesions, the choice of the biopsy area was difficult and the videoroscopy was used to help to choose of the better biopsy area. The lesions were similar with those described in the literature as of AP of the lip.

Clinical differential diagnoses include actinic cheilitis, frictional contact cheilitis and granulomatous cheilitis[5]. In the present cases, we also considered the possibility of acute actinic cheilitis, which was later discarded by the evolution time and also because the patients did not report intense sunlight exposure. The other clinical diagnoses were erythema multiforme, which was discarded by the course of the lesions, and contact cheilitis, but we were unable to identify any substance, which could cause the lip lesions, especially for so long time. Although several clinical factors associated with follicular cheilitis were missing in the present cases, the clinical exam associated with histopathological diagnosis was determinant in establishing the final diagnostic.

Studies in the literature define the histopathological pattern of AP on the lip as presenting acanthosis, spongiosis and basal layer hydropic degeneration[2]. Areas of ulceration may be seen. In the connective tissue there is edema, dilated and congested vessels, with dense predominantly lymphocytic inflammatory infiltrate, which may contain lymphoid follicles and eosinophils[2,4,12]. Furthermore, some studies report that it is still possible to find discrete exocytosis in the basal epithelium and pigmentary incontinence in the sub epithelial connective tissue[2]. The presence of lymphoid follicles has been considered by some authors as a pathognomonic feature of AP and this is the reason term follicular cheilitis is used[12].Mas cells and macrophages may be found among the inflammatory infiltrate[5]. The histopathological findings of our cases are consistent with the description in the literature. The identification of lymphoid follicles in both cases was important to establish the diagnosis.

No solar elastosis is found in AP lesions, which facilitates the differential diagnosis with actinic cheilitis[2,4,5,12]. It is necessary to differentiate AP from polymorphic light eruption, which is clinically similar, but microscopically never shows lymphocytic infiltrate with lymphoid follicles[12].

Regarding the treatment of AP, as a general measure, it is recommended to reduce sun exposure, use hats, appropriate clothing, and sunscreen. However, these measures are not sufficient to treat AP. There is evidence that the AP is an autoimmune disease and therefore immunosuppressive drugs present good results[3]. Treatment of AP varies according to the severity and extension of the lesions, and includes topical and systemic corticosteroids to reduce the inflammation and itching of active lesions, antibiotics for secondary infections, antihistamines, antimalarials and thalidomide, which have shown to be the most effective drug for the treatment[12,15–18].

AP prognosis is not good, despite several treatment options, the lesions may have a chronic course and be difficult to control if patients live in sunny areas, work exposed to the sun or live in high altitudes[19]. The patient of case 1 responded well to the treatment with topical corticosteroid and prevention measures; she had no lesions until the last follow-up (14 mo after the diagnosis). The patient of case 2 was treated only with prevention measures (including the use of lip balm with UV protection). In the follow-up, one month after the establishment of the diagnosis, the lesions disappeared, but she did not come back for the other follow-up appointment.

AP is well known disease, occurring mainly in mestizos, living in high altitudes with onset during childhood. The cases presented were a challenge to diagnose because the clinical characteristics of were different from the classical manifestations of AP: the lesions had only begun in adulthood, the patients lived at sea level and did not report, at least during the interview, being indigenous descents, neither reported having familial history of the alterations. In these particular cases, without lesions in the skin, the establishment of the diagnosis of the AP in early stages is important, because it can alert the clinician about the possible development of other more severe lesions, and, thus, referring the patients to an ophthalmologic and dermatologic evaluation is mandatory.

**COMMENTS**

***Case characteristics***

This paper is to report two cases of actinic prurigo in which the lower lips were the only sites of involvement.

***Clinical diagnosis***

The relevance of these cases is that, although some important aspects run away from the classical features of actinic prurigo, the clinical and histological exams associated, can be determinant for a correct diagnostic and a successful treatment.

***Imaging diagnosis***

Clinical exam, photographs, videoroscopy examination and biopsy were performed, and the diagnosis of actinic prurigo was established.

***Peer review***

It si an interesting case, it is well written.

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**P-Reviewers:** Chong WS, Torres-álvarez MB, Ozyigit MT **S-Editor:** Wen LL  **L-Editor:**  **E-Editor:**

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**Figure 1 Case 1**. A: Clinical aspect at the first appointment, showing lower lip edema, ulcers and crusts; B: Videoroscopy image showing in detail the presence of ulcer and crust; C: Clinical aspect at the second appointment showing the area of biopsy; D: Clinical aspect one month after treatment, showing remission of the lip edema, ulcers and crusts; E: Histological aspects. Epithelial atrophy, and intense and diffuse lymphoplasmacytic inflammatory infiltrate extending deeply into the fatty tissue (× 10, HE); F: Epithelium showing spongiosis, hydropic degeneration of the basal layer cells and lymphocytic exocytosis. In the connective tissue, lymphocytic inflammatory infiltrate and pigmentary incontinence (arrows) (× 40, HE). G: Secondary lymphoid follicle (× 40, HE); H: Mast cells mainly in the deeper area of the connective tissue (× 20, Giemsa).

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**Figure 2 Case 2.** A: Clinical aspect at the first appointment, showing lower lip edema, dryness and ulcer on the left side of the semimucosa; B: Clinical aspect at the second appointment, showing remission of the ulceration on the left side, presenting only a small ulcer on the right side of the semimucosa; C: Histological aspects. Lower power view showing epithelial atrophy and ulceration. In the connective tissue, there is an intense and diffuse inflammatory infiltrate extending deeply into the fatty tissue, with some lymphoid follicles (HE); D: Secondary lymphoid follicle (HE).

**Table 1 Results of the literature search for “actinic prurigo” or “follicular cheilitis” of the lip**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Actinic prurigo | Follicular cheilitis | Eligible paper1 |
| Pubmed | 143 | 9 | 2 |
| Lilacs | 25 | 0 | 0 |
| Scielo | 3 | 0 | 0 |
| Cochrane | 7 | 1 | 0 |

1A paper considered eligible for inclusion in review had to include a case report or a study with at least one case under the name “actinic prurigo” or “follicular cheilitis”, and also presents lip lesions as the only manifestation.

**Table 2 Data from patients with actinic prurigo, with only lip lesions**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Vega-Memije *et al*[2] | Rizo *et al*[5] | Mounsdon *et al*[4] | Miranda *et al*[1] |
| Age | 9-82 (mean 27.8 yr) | 11-63 (mean 26 yr) | 61 and 69 yr old | 58 and 63 yr old |
| Country | Mexico | Mexico | United States (North American Indians) | Brazil |
| High altitude | 99% more than 1000 m | Uninformed | Uninformed | Sea level |