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Case Report

Persistent lip enlargement: An unusual presentation of lupus erythematosus☆

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ABSTRACT

Macrocheilia is a challenging problem with a variety of underlying causes that are both local and systemic, and granulomatous causes underlie the majority of cases. In this study, we report on a 31-year old man who presented with a chronic lower lip enlargement and a nodular submental erythematous lesion. He was otherwise clinically healthy. Laboratory test results were within the normal limit except for a positive anti-double stranded DNA test result. A diagnosis of cutaneous lupus erythematosus was made on the basis of histopathology and direct immunofluorescence. The lesions resolved dramatically after treatment with hydroxychloroquine. Lupus erythematosus should be considered when examining patients who present with chronic lip swelling.

Background

A 31-year-old man presented with a 1-year history of recurrent lower lip swelling, which eventually became persistent. At the time of his physical examination, the lower lip was diffusely swollen and firm to palpation with no tenderness (Fig. 1). In addition, an erythematous nodular firm lesion of 5 cm by 5 cm with sparse hair was noted in his submental region (Fig. 2). The latter appeared simultaneously with his lip swelling. The patient's other systems were otherwise clinically healthy.

A histopathologic examination of a biopsy specimen from the lower lip showed a lichenoid reaction, telangiectasia, and edema in the papillary dermis, as well as severe chronic lymphoplasmacytic inflammation that permeated the deep dermis and striated muscles. Only a few loose granulomata were observed (Fig. 3). A subtle lichenoid reaction, dense mononuclear cell infiltration of the dermis, vasculopathy, partial destruction of skin appendages, and considerable mucinous changes were observed in the biopsy specimen of the submandibular lesion. A positive test result for lupus band (immunoglobulin G, complement C3, and immunoglobulin M) was also found during direct immunofluorescence testing.

Chest radiography, routine blood tests, and angiotensin-converting enzyme serum levels were within normal limits. A skin smear tested negative for Leishman body. Ziehl-Neelsen, Gram, and periodic acid Schiff stainings, as well as a culture and polymerase chain reaction for Mycobacterium tuberculosis yielded negative test results.

Antinuclear antibody titer was 1:6 (negative) and anti-double stranded DNA titer was 1:120 (positive >1:30). Serum C3 and C4 levels were 118 mg/dl (80-190 mg/dl) and 40 mg/dl (10-40 mg/dl), respectively. A diagnosis of chronic cutaneous lupus erythematosus (LE) was made and treatment with hydroxychloroquine was initiated at a daily dose of 400 mg. At the time of the first post-treatment visit after 2 to 3 weeks, the patient's lip swelling and submental lesion had improved significantly (Fig. 4). He continued treatment with hydroxychloroquine for approximately 6 months along with the use of sun protection cream. At the time of the last follow-up visit, 2 years after the first examination, the patient was still in complete remission with no scarring.

Discussion

Chronic lip enlargement or macrocheilia is a challenging problem because it not only impairs the normal daily function of the lips but can also lead to major disfigurement (Park et al., 2008). Both local and systemic conditions can contribute to macrocheilia and chronic macrocheilia may even herald a systemic disease (Williams and Greenberg, 1991).

☆ Conflict of interest: None.

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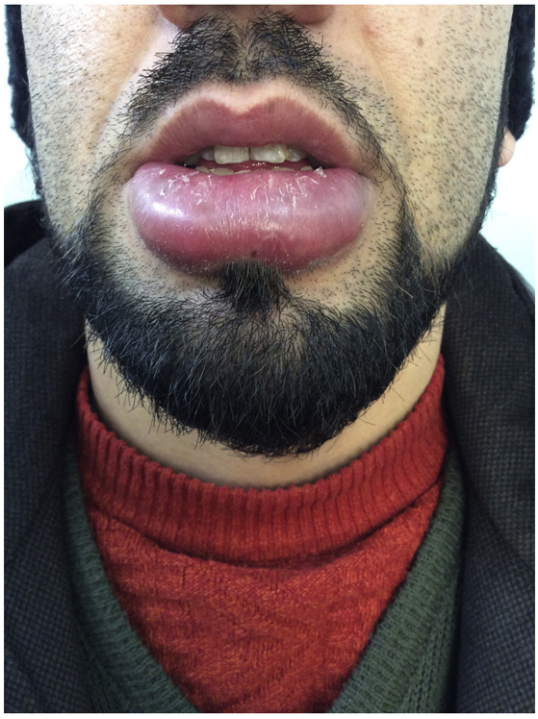

Fig. 1. Lupus erythematosus: Chronic lip swelling.

Causes of constant lip enlargement are protean and may include cheilitis granulomatosa and Melkerson-Rosenthal syndrome, Crohn's disease, infections (deep fungal infection, leishmaniasis, leprosy, syphilis, tuberculosis, and erysipeloid), sarcoidosis, glandular cheilitis, neoplasms (non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, acute myeloblastic leukemia, chronic lymphocytic leukemia, hairy cell leukemia, and natural killer/T-cell lymphoma), fibroadenoma, oro-facial granulomatosis, silica granuloma, amyloidosis, port-wine stain, lymphangiectasia, cyclosporine usage, and Ascher's syndrome (Criton et al., 1995; Handa et al., 2003; Khadir et al., 2013; Schulman and Chu, 2014; van der Waal et al., 2001). Only when these specific entities are ruled out, chronic idiopathic macrocheilia, a rare nonspecific clinical entity whereby only minor salivary gland hyperplasia without ductal ectasia is seen, should be considered (Park et al., 2008).

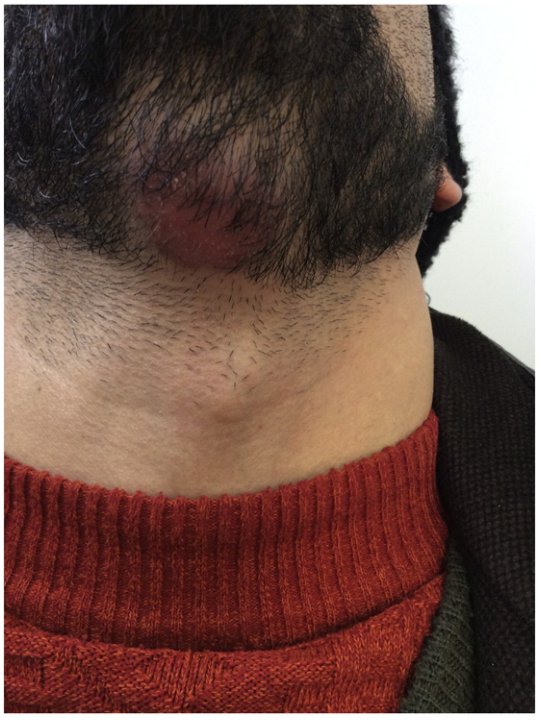

Fig. 2. Lupus erythematosus: Nodular lesion under the chin.

Despite this causal diversity, epidemiological studies on macrocheilia are limited in the literature. Handa et al. (2003) recently reported on a clinicopathologic analysis of 28 patients with chronic macrocheilia and the most prevalent cause was cheilitis granulomatosa (13 patients). In addition, six patients suffered from tuberculosis of the lip and three patients had macrocheilia due to leprosy. Nonspecific cheilitis was observed in two patients. Multiple endocrine neoplasia type IIb (two patients), non-Hodgkin's lymphoma and Ascher's syndrome (one patient each) were other underlying causes that were identified (Handa et al., 2003).

In another study, Khadir et al. (2013) reviewed 19 patients with granulomatous macrocheilitis. Eleven patients had Melkersson-Rosenthal syndrome and 6 patients had an underlying cause of Miescher's granuloma. Sarcoidosis and Crohn's disease were seen each in one patient (Khadir et al., 2013). Ratzinger et al. (2007) evaluated 14 patients with cheilitis granulomatosa and found an interesting association with close to 30% of patients diagnosed with Crohn's disease.

Depending on the different etiologies, various treatments are available for this disfiguring condition, including oral or intralesional corticosteroids, antimalarial medications, antibiotic medications, clofazimine, thalidomide, sulfasalazine, erythromycin, azathioprine, cyclosporine, and TNF-α inhibitors (infliximab) (Williams and Greenberg, 1991). Reduction cheiloplasty is typically suggested for stabilized diseases (Oliver and Scott, 2002; Williams and Greenberg, 1991).

The first clinical impression for the 31-year-old patient in our case was granulomatous cheilitis and lymphoproliferative disorders. However, repeated biopsy specimen, direct immunofluorescence, and immunohistochemistry test results were in favor of a diagnosis of LE. Histopathologically, granulomatous cheilitis, the most common cause of lip enlargement, is characterized by small, noncaseating histiocytic granulomas that are often seen with multinucleated giant cells. Biopsy specimens that are obtained during the early stages of the disease may reveal only edema and perivascular aggregations of lymphocytes (Allen et al., 1990; Worsaae et al., 1982). Surrounding perivascular and interstitial infiltrates of lymphocytes, plasma cells, and histiocytes are also seen (Allen et al., 1990; Worsaae et al., 1982). In this case, there was heavy inflammation that extended deeply up to the striated muscles, vascular damage, and epidermal involvement as subtle lichenoid reaction in addition to positive lupus band test results, which were all highly characteristic for LE. A positive anti-double stranded DNA test result despite a negative antinuclear antibody test result was unusual but did not rule out the diagnosis. Clinical and paraclinical findings did not satisfy the criteria for systemic LE according to the Systemic Lupus International Collaborating Clinics classification criteria (Petri et al., 2012) despite the high anti-double stranded DNA titer.

The skin, lips, and oral mucosa are common sites of LE involvement. Although the diagnosis of labial LE is frequently not difficult, exclusive involvement of the lips could be a clinical challenge. Nico et al. (2014) reviewed different aspects of lip involvement in LE in a comprehensive article and concluded that the extension of LE lesions from the vermilion to the skin is a distinctive feature that is frequently seen in labial LE. Severe scarring may also be problematic with this disease (Nico et al., 2014; Nico and Lourenço, 2013). Multiple blisters

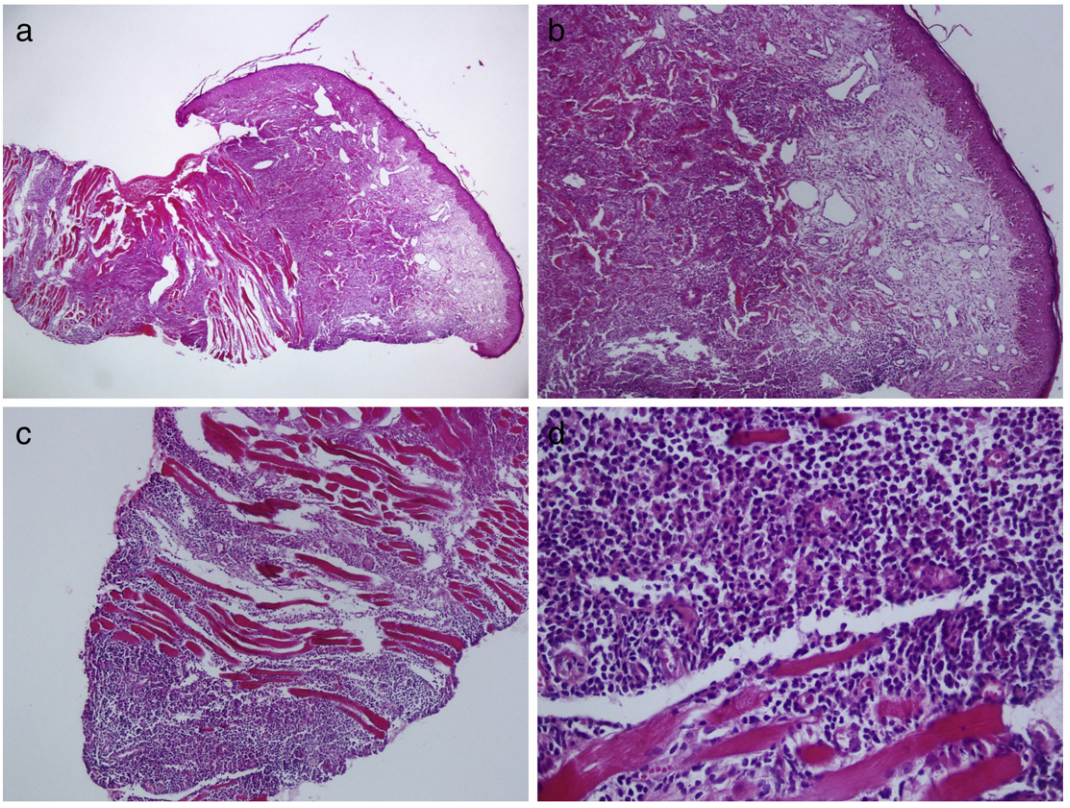

Fig. 3. Lupus erythematosus: Lip biopsy that showed nodular dermal infiltration, subtle lichenoid change, and lymphocytic vasculopathy up to striated muscle [H&E, (a) ×30; (b) ×100; (c) ×100; (d) ×400].

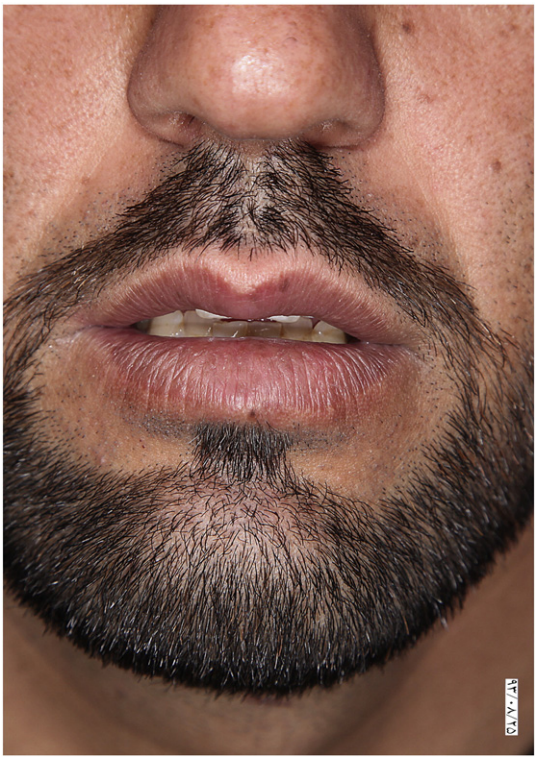

Fig. 4. Lupus erythematous: Dramatic improvement of lip swelling after a few weeks of treatment with hydroxychloroquine.

along the vermilion were also considered a symptom of bullous LE (Nico et al., 2014; Nico and Lourenço, 2012).

We found only one published case of labial LE that presented as macrocheilia (Mael-ainin and Senouci, 2013) and involved a 30-year old female patient with chronic LE. Seven years after the initial examination, the patient developed a painful upper cheilitis with a gradual enlargement of the lip. The biopsy specimen and antinuclear antibody test results were in favor of her underlying disease. The test results for other diseases were unremarkable. The patient was in complete remission within 6 months of initiating treatment with 4 mg/kg/day of chloroquine and had no recurrence after one year (Mael-ainin and Senouci, 2013).

In our patient, the histology of the lips and the submandibular lesional biopsy specimen, lupus band on direct immunofluorescence, and positive anti-double stranded DNA test results along with the exclusion of other more common possible causes retained LE as the etiology of this case of macrocheilia. The dramatic improvement with the introduction of hydroxychloroquine as treatment was also interesting. In conclusion, LE should be kept in mind as a rare atypical presentation of LE.

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