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Usefulness of immunohistochemical staining in diagnosing a challenging case of oral primary syphilis

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Abstract

Clinicians involved in the diagnosis of mucocutaneous diseases should be aware that syphilis is still prevalent among humans and its accurate diagnosis may require substantial clinical evaluation. Herein, we report a case of primary syphilis presenting as an isolated ulcer on the upper left labial oral mucosa. The lesion exhibited no specific features and could have been easily mishandled. An important clinical observation was the presence of a satellite-enlarged lymph node in the left submandibular area, which was highly indicative of primary syphilis. Histopathological examination of the specimen obtained by punch biopsy revealed features suggestive of syphilis and immunohistochemical staining with antitreponemal antibody confirmed its diagnosis with the detection of numerous *Treponema pallidum* in the specimen.

Keywords: cervical lymphadenopathy, differential diagnosis, primary syphilis, oral ulceration

Introduction

The oral manifestations of primary syphilis are among the most challenging diagnoses in oral medicine. Apart from being the great imitator of several mucocutaneous diseases, oral primary syphilis may go unnoticed since the lesion is painless and of short duration. Therefore, patients usually fail to report the oral mucosal manifestation of primary syphilis; the lesion heals spontaneously following its

natural course. Additionally, there is no clear characterization of the oral manifestations of primary syphilis. The main characteristic sign of primary syphilis, known as a chancre, is a solitary, painless, ulcer with a slightly raised and indurated border, which arises at the site of the penetration of *Treponema pallidum*, the microorganism causing syphilis. Notably, unilateral, satellite lymphadenopathy is usually present [1-4].

This study reports a case of oral primary syphilis, highlighting the differential clinical diagnosis and effectiveness of immunohistochemical staining using antitreponemal antibody for a conclusive diagnosis of syphilis based on biopsy tissue.

Case Synopsis

A 47-year-old man was referred to our clinic for the evaluation and diagnosis of an ulcer on the upper left lip that had been present for 7 weeks. He reported that the lesion appeared after dental trauma and caused moderate pain. As he did not notice any improvement in the lesion after two weeks, he sought medical help and was given 40mg a day of a systemic corticosteroid taken orally for three weeks, but there was no relief. At our clinic, oral examination revealed an ulcer with irregular margins surrounded by an inflammatory halo and measuring approximately 1.5cm in diameter and 3–4mm in depth (**Figure 1A**). On palpation, the border and underlining tissue were fibrous and slightly indurated. A satellite-enlarged lymph node

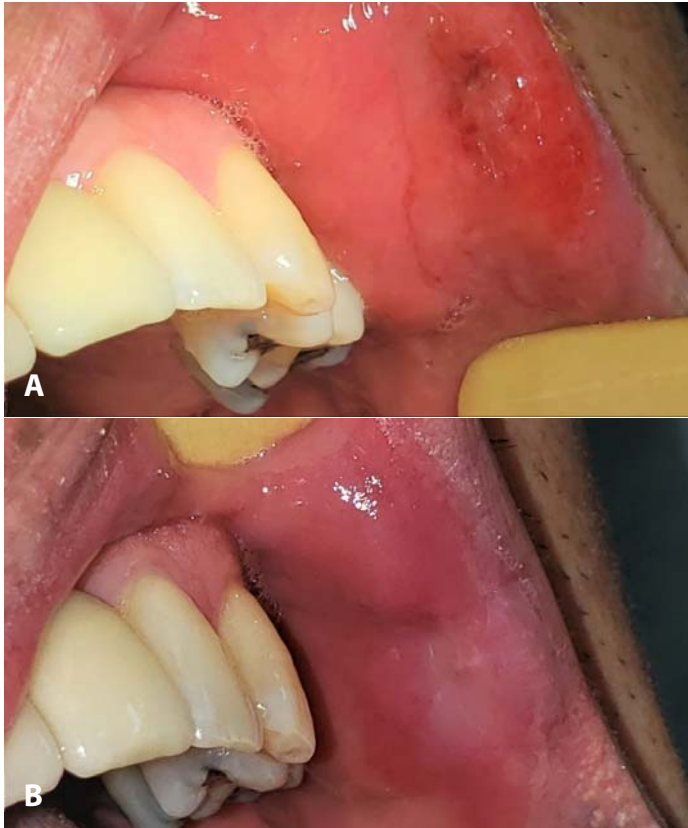


Figure 1. **A)** An irregular ulcerated lesion with a moderate destruction of the connective tissue; **B)** partial healing after one week following therapy with penicillin injection.

measuring 3cm was also noted. Additional examination was carried out on some parts of the skin surface such as the palms, the arms, and the trunk and no lesions were observed. He also denied any lesions on his genital area. Overall, he was a healthy person and neither a smoker nor a habitual consumer of alcohol.

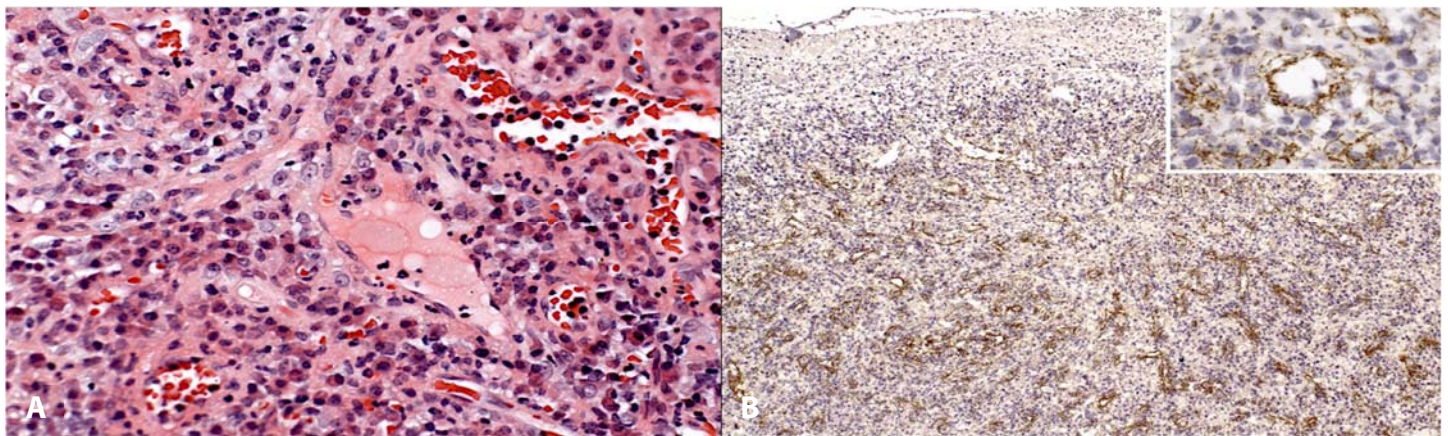


Figure 2. **A)** Plasma cell-rich infiltrate and vascularization. H&E, 400x; **B)** immunohistochemical staining for *Treponema pallidum* revealed numerous spirochetes in the connective tissue, 100x. Inset, high-power magnification (1000x) shows stained spirochetes by anti-*Treponema pallidum* antibody in blood vessel walls and scattered in connective tissue.

The differential diagnosis included primary syphilis, granulomatous ulcer, oral eosinophilic ulcer, and possible malignancy. The signs presented were strongly indicative of primary syphilis, mainly due to the presence of satellite lymphadenopathy, in spite of his persistent denying of any sexual behavior that increased the risk of sexually transmitted diseases. Diagnosis of granulomatous ulcer related to sarcoidosis was also possible in this case, despite its rare oral manifestations. Oral eosinophilic ulcer and possible malignancy, however, seemed less likely because lymphadenopathy with a palpable and enlarged lymph node is not associated with oral eosinophilic ulcer and neither to an early stage of oral carcinoma. Hence, a 5mm-punch biopsy was performed for confirmed diagnosis.

Histological examination revealed a completely ulcerated mucosal fragment lined with a fibrinopurulent membrane. The lamina propria showed dense inflammatory infiltrate that was notably lymphoplasmacytic. The section was richly vascularized and most endothelial cells were swollen. The amount of plasma cells was so substantial that they were not restricted to the perivascular zones (**Figure 2A**). Based on these histopathological findings and a provisional clinical diagnosis of syphilis, an immunohistochemical evaluation using antitreponemal pallidum antibody (Biocare Medical, Pacheco, CA, USA) was performed. A massive number of spirochetes was detected (**Figure 2B**), thus confirming the diagnosis of primary syphilis [5,6].

Furthermore, a laboratory investigation of the nontreponemal test showed a titer of 1:250. The patient was treated in conjunction with his general physician with an intramuscular, single dose of benzathine penicillin G 2.4 million units, which produced a rapid improvement in the lesion after one week (**Figure 1B**). Follow-up was scheduled every three months to check the decline in the titer. His anti-HIV and hepatitis C test results were negative. At his last follow up with his physician, the serological nontreponemal test was decreasing and repeat HIV testing was negative.

Case Discussion

Retrospectively, this case seems to represent a classical manifestation of primary syphilis. However, the diagnosis process involved a thoughtful consideration of the symptomatology and history of the case. First, the lesion was located on the upper labial mucosa of the lip and not exactly on the lip surface, which is the usual location in such cases as previously reported [1-3]. The appearance and duration of the lesion were not explicit enough to lead to a confirmed diagnosis of primary syphilis. Moreover, the patient adamantly denied any sexual behavior that could have exposed him to a sexually transmitted disease.

In this case, the presence of satellite lymphadenopathy played a relevant role in the diagnosis of primary syphilis. A significant enlargement of the cervical lymph nodes is an important sign when assessing an isolated ulcer on the oral mucosa, which may help to rule out other pathological entities and simplify the clinical diagnosis process. Herein, lymphadenopathy was crucial in indicating the possible diagnosis of syphilis and avoiding mismanagement of the case. Notably, the lymph node enlargement was not part of the patient's clinical complaint. It was revealed on

palpation, thus highlighting the importance of a thorough physical examination for oral ulcerated lesions [4-6].

Also of note, the histopathological examination, suggestive of syphilis, was followed by immunohistochemical antitreponemal staining, which effectively showed the presence of spirochetes and provided a conclusive diagnosis of primary syphilis [7,8]. As a reminder, the histological structure of the oral mucosa lacks plasma cells [9,10]. When their numbers are observed in great quantity (as was the case presented here) a laboratory investigation using treponemal test (such as FTA-ABS) or immunohistochemical staining with anti-treponemal antibody or both, should be performed, either to confirm or rule out infection by *Treponema pallidum*, the microorganism that causes syphilis.

Finally, it is known that syphilis has not been eradicated in the human race and it may have only subsided for a while [4,7,8]. It is important for clinicians dealing with cutaneous and/or oral mucosal lesions to consider the diagnosis of syphilis in challenging clinical cases.

Conclusion

In spite of being repetitive in calling attention of health professionals on oral manifestations of sexually transmitted diseases, syphilis is a tricky, prototype of this kind as it can mimic almost any cutaneous and mucosal clinical manifestations. This particular case well illustrates the difficulties in producing a diagnosis of primary syphilis. Fortunately, the case was managed properly, including the diagnosis and treatment.

Potential conflicts of interest

The authors declare no conflicts of interest.

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