

Specific Clinical Findings of Secondary Syphilis In The Oral Mucosa: A Series of Six Case Reports

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Case Study

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ABSTRACT

Syphilis (SyS) is a systemic infectious disease caused by the anaerobic spirochetes *Treponema pallidum*. This condition is further divided into primary, secondary latent and tertiary stages. Oral manifestations are most common in secondary stage and frequently are the only clinical sign of the disease. These lesions are characterized by having high rates of infection and peculiar clinical characteristics. Therefore, the purpose of this article is to highlight the common and not-so-common clinical appearances of secondary SyS in adults. Tongue, lips, jugal mucosa and palate lesions were selected to illustrate the similarity of oral SyS with other diseases. The diagnosis was performed by clinical and serological correlation. Furthermore, it was emphasized the importance of the knowledge of different forms of oral SyS lesions by clinicians in order to provide early diagnosis and faster treatment for infected patients.

INTRODUCTION

SyS is an infectious systemic disease of compulsory notification, caused by the microorganism *Treponema pallidum*. This disease remains prevalent nowadays, affecting millions of individuals worldwide ^[1]. Primary, secondary and tertiary stages are related to the time of infection and to the host response ^[2]. Different ways of transmission are related: congenital vertically transmitted via the placenta and acquired SyS ^[3]. The acquired form of SyS is a sexually transmitted disease and is the most prevalent way of transmission. The primary stage may have subclinical manifestations without showing any symptom for years, although some patients could present a hard painless lesion (chancre) in this stage ^[3]. Secondary manifestations of syphilis may begin 3–5 months after infection, and in a third of patients with secondary disease, a residual chancre will be present ^[2]. The secondary stage is characterized by the involvement of the skin, oral mucosa and internal organs corresponding to the distribution of *Treponema pallidum* for all the body. Involvement of hands and feet regions is typical ^[4]. The third stage of SyS includes the most serious complications involving vascular and central nervous systems. In the mouth, lesions of tertiary SyS may appear as syphilitic leukoplakia and could have a malignant potential ^[3].

The primary and secondary oral SyS lesions are highly infectious ^[2]. Frequently, oral SyS lesions are the only clinical sign of the disease. However, since these lesions may mimic many other oral abnormalities, the diagnosis can be difficult and clinicians must be aware of the diversity of manifestations. In this way, we aimed to report a series of six clinical cases of secondary SyS oral lesions, once a detailed knowledge of oral manifestations of the disease is crucial for correct diagnosis and early treatment of patients.

CASE PRESENTATION

In this article a series of six clinical cases are reported. These patients presented oral lesions of secondary SyS as a first

sign of the infection with *Treponema pallidum*. Diagnosis was performed after clinical-serological correlation. All the patients were attended at the Clinic of Oral Medicine of the Odilon Behrens Hospital (Belo Horizonte, Brazil). The serologic analysis was performed for all patients using two types of tests for SyS: Nontreponemal (*Venereal Disease Research Laboratory*, VDRL) and treponemal (fluorescent treponemal antibody absorption, FTA-ABS) tests. The use of one type of test alone is not sufficient for diagnosis. Nontreponemal test antibody titers were correlated with the disease activity and results were reported quantitatively. VDRL tests were always positive in a dilution >1:32. The positive treponemal test (FTA-ABS) usually remains for a lifetime and antibody titers correlate poorly with disease activity, therefore it was not used to assess response to treatment. All patients were treated under a protocol which consisted of intramuscular injection of Benzathine penicillin G, 7.2 million units, administering three doses of 2.4 million each, for 3 weeks. Patients were followed for 24 months until the complete remission of oral lesions and nonreactive response of nontreponemal serologic tests. Additionally, patients' partners also were referred to receive the same treatment protocol.

Patient 1 - Buccal Mucosa Lesions

A 20 year old caucasian woman with good general health was referred to our unit with symptomatic oral ulcers. Physical examination revealed mucous patches located in the right buccal mucosa with slightly rounded shape and irregular surface covered with a grayish white membrane and surrounded by a hyperemic halo (**Figure 1**). A clinical characteristic sign of secondary SyS was observed in the lesion. This sign is called serpiginous form and it is also known as ulcer on "snail trail". VDRL and FTA-abs tests confirmed clinical hypothesis of SyS and HIV serology was negative. After the conclusion of the diagnosis, treatment was carried out for secondary SyS as established.



Figure 1. Clinical presentation of secondary syphilis in buccal mucosa. Patient 1.

Patient 2 – Tongue Lesions

A 56-year-old caucasian man was referred to our unit with a history of a several week symptomatic lesion of the tongue and complaining of a persistent sore throat. In the clinical examination, it possible to observe the presence of two lesions in the tongue, presenting similar aspects as reddish pink patches covered with oval fibrinopurulent membrane. Diffuse erythematous spots were noticed in both lesions. Lingual papillae had disappeared and the tongue surface was atrophic (**Figure 2**). VDRL and FTA-abs tests were positive and HIV serology was negative. Then the diagnosis was confirmed and the treatment for secondary SyS was performed as previous reported.



Figure 2. Clinical presentation of secondary syphilis in tongue. Patient 2.

After three months follow up, patient presented a new VDRL reagent. Even though no clinical manifestation of SyS was observed, we considered that a new syphilitic infection might be occurring, since patient's partner presented positive serological tests and did not performed the protocol treatment as recommended. In this moment, both received Benzathine Penicillin G treatment protocol and presented negative serological tests with no clinical evidence of the disease in the following controls.

Patient 3 – Soft Palate Lesions

A 25 year old caucasian woman reported that she had been previously examined by several medical specialties, however, professionals could not perform a definitive diagnosis to the existing oral lesion. The patient did not describe any risk factor for sexually transmitted diseases in the anamnesis. Our group observed a greyish white plaque with the format of a half moon in the soft palate, during clinical oral examination of the patient. The borders of the lesion were lightly erythematous. It was possible to observe another oral lesion covered with plaque presenting the same clinical aspect in the retro molar trigone region (**Figure 3**). Clinical characteristic was compatible with secondary SyS oral manifestation. In this way, VDRL and FTA-abs tests were carried out and in fact, the result was positive. HIV serology was negative. After proper diagnosis, the patient was subjected to antibiotic therapy.



Figure 3. Clinical presentation of secondary syphilis in soft palate. Patient 3.

Patient 4 – Upper Lip Lesions

A 20 year old black woman was referred to our unit with painless ulcer more evident in the oral mucosa of the lips. The lesions were ulcerated with whitish plaques on its edges and also had a characteristic appearance of oral secondary SyS. Therefore, it was requested a VDRL and FTA-abs test, that confirmed the clinical diagnosis. HIV serology was negative. Then, treatment was conducted as previously described (**Figure 4**).



Figure 4. Clinical presentation of secondary syphilis in oral mucosa of upper lip. Patient 4.

Patients 5 and 6 – Commissure Mucosa and Lower Lip Lesions

In these last two cases, patients were referred to our unit with a history of multiple lesions in the mouth that have emerged for over a year. Patients were black men, aged 24 and 27 years, respectively. These patients had pathognomonic signs of oral secondary infection by *Treponema pallidum*. The oral mucous patches possessed the following characteristics: multiplicity, rapidity of onset, oval shape, covering membrane of glistening grayish white character and an indefinite inflammatory areola surrounding the lesions (**Figures 5 and 6**). The oral lesions were combined with a generalized eruption on the skin and palm-plantar hyperkeratosis in Patient 6. Patients were tested to VDRL and FTA-abs with positive results. HIV serology was negative, for both. Treatment was performed as described. It is noteworthy that all patients had complete remission of lesions after appropriate therapy.

DISCUSSION

SyS continues to be a global health concern with 12 million infections each year worldwide [5]. The increased incidence over the last decade requires a renewed awareness of this infection and its heterogeneous manifestations. Infected patients often report a great variety of symptoms such as malaise, sore throat, headache, weight loss, low-grade fever, lymph node enlargement, pruritus, muscle aches and dermatological manifestations. Even though oral lesions have clinical patterns, it could manifest in

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several forms, as localized or lush, symptomatic or asymptomatic lesions. Clinical manifestations in the oral cavity may not be concomitant with the cutaneous manifestations [3]. The described cases in this article presented a classic clinical feature that allowed proper diagnosis of secondary SyS with oral manifestation. Because of the heterogeneity of the oral clinical aspects, the differential diagnosis includes a huge group of diseases, including traumatic or cancerous ulcers, autoimmune (pemphigus/pemphigoid) or immune-related lesions (lichen planus, erythema multiform, pyostomatitis vegetans), traumatic lesions (frictional keratosis) or hyperplastic/dysplastic plaques (leukoplakia) and other infectious diseases such as tuberculosis, fungal infections, herpes lesions and hairy leukoplakia [5]. Oral lesions arise in at least 30% of patients with secondary syphilis [6]. The six cases presented confirm that oral manifestations of syphilis are multiple and highly variable, and often detected in secondary stage. The evaluation of the morphology of the oral lesions in our six cases revealed that most of the lesions were presented as ulcers and all cases were diagnosed as secondary stage of SyS. In agreement with the literature, secondary syphilis is detected as ulcer in about 50% of cases.



Figure 5. Clinical presentation of secondary syphilis in commissure mucosa. Patient 5.



Figure 6. Clinical presentation of secondary syphilis in oral mucosa of lower lip. Patient 6.

The diagnosis of SyS requires gathering ample information of the patient's sexual history, physical examination and interpretation of serological and microbiological exams. It is important to emphasize that sexual partners should perform serologic tests for SyS as well [3], also because SyS is constantly associated with other sexually transmitted diseases. Risk groups behaviors include multiple sexual partners and unsafe sexual practices, which may have contributed to the increase of oral lesions [2]. In the present report, only one case exhibited risk behavior and presented a recurrence of SyS after three months follow up. Therefore, the patient was retreated under standard treatment and his sexual partner initiated the antibiotic therapy protocol. Other individuals had diagnostic hypotheses performed from the clinical observation of oral lesions.

The most used approach for the diagnosis of SyS is the nontreponemal and treponemal serologic tests. These tests are considered the standard methods of detection for all stages of SyS. Nevertheless, histopathological analysis can also be useful to determine the correct diagnosis, even though it is rarely used because of its limitations in identifying the pathogen during the inflammatory response at second stage of SyS. The typical non-treponemal test is the VDRL, which is the most appropriate method for follow-up during and after treatment. Treponemal tests are used to verify reactivity in nontreponemal testing. As a screening procedure, the *Treponema pallidum* particle agglutination (TPPA) test is also used. Particles sensitized by *Treponema pallidum* antigens cause a positive agglutination reaction if specific immunoglobulins are present in the patient's serum. Because of the possibility of false-positive results, FTA-Abs (Fluorescent treponemal antibody absorption) test should be used in cases when TPPA results are positive. In the current study, it was demonstrated that all patients were submitted to the nontreponemal and treponemal tests in order to confirm the diagnosis.

Therapeutic approach depends on the disease stage. If therapy is successful, serologic follow-up will show a decrease of the VDRL index. The most widely used antibiotic in the treatment of SyS is penicillin G Benzathine. Although penicillin is still highly

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effective, resistance to second-line antibiotics, especially azithromycin, has been reported [4]. If the disease is left untreated, up to 90% of patients with primary SyS will develop the secondary stage. Untreated individuals might have a proliferation of the microorganism through the lymphatic system presenting several manifestations on the body, including: pharyngitis, tonsillitis, laryngitis, cervical lymphadenopathy, hoarseness, palmar and plantar lesions [7]. All of our six patients presented complete remission of SyS oral manifestations after the first or second treatment dose of Benzathine Penicillin G. Serological exams were performed every three months after initial approach.

CONCLUSION

A careful observation of key clinical characteristics combined with secondary SyS serology, allows proper diagnosis by clinicians. It is relevant to notice that SyS oral lesions may be first seen by dentists since these manifestations can be the only clinical finding of SyS. Therefore, dentists must be prepared to identify these lesions in order to perform an early diagnosis since it can provide better and faster treatment for infected patients.

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