

A case report and a review of the literature of the most common extragenital localization of primary syphilis

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ABSTRACT

Syphilis is a chronic bacterial infection caused by *Treponema pallidum* and is schematically divided into 4 stages. Its primary form usually appears as an indolent ulcer called chancre, which spontaneously heals in 2-8 weeks. The most commonly affected site is the anogenital region, but extragenital lesions are also seen, especially in the oral cavity. In this study, we aimed to investigate this specific localization of the primary form. We present the case of a 62-year-old male with an unusual presentation of primary syphilis on the upper lip along with a review of the literature on primary syphilis of the oral cavity, reporting 32 patients. Oral primary syphilis may have unusual clinical features and may present as painful, multiple, or non-ulcerative lesions. This condition leads to a difficult differential diagnosis with many other infectious, neoplastic, and inflammatory conditions; owing to its transient nature and low symptomatology, it may also go unnoticed and reoccur in more advanced and dangerous stages. In conclusion, a primary treponemal infection must always be considered in the differential diagnosis of oral lesions of undetermined etiology, and proper investigation (with treponemal/non-treponemal tests and eventually a biopsy) should always be performed.

Keywords: Oral lesions, primary syphilis, chancre, differential diagnosis, early diagnosis

Introduction

Syphilis is a chronic bacterial infection caused by the spirochete *Treponema pallidum* (1). There is no consensus about its origins, and it is debated whether it was imported from the new world or if its spread in Europe at the end of the 15th century was due to an increase in the virulence of a pre-existing treponemal disease (2).

With the exception of maternofetal transmission, which is accountable for a significant percentage of infections in low- and middle-income countries but is rare in high-income countries, syphilis spreads almost exclusively through direct contact with treponemal lesions.¹ Consequently, the most common primary sites of syphilitic lesions are the genitals, with extragenital chancres representing 5% to 14% of cases (3). Potentially affecting any site of the body, syphilis has a high probability of transmission through oral sex or even kissing, and oral mucosa is the site of primary infection in 40-75% of extragenital chancres (4). Widely used serological tests such as the

Venereal Disease Research Laboratory (VDRL), the *Treponema Pallidum* Hemoagglutination Assay (TPHA), and the Fluorescent *Treponemal* Antibody Absorption (FTA-ABS) are valid instruments for the diagnosis of syphilis in the oral cavity as for any other site, whereas direct observation of treponemas with dark-field microscopy (DFM) is affected by the colonization by saprophytic spirochetes in the mouth (1). A specific antibiotic course is highly effective for its treatment (1); unfortunately, its presentation may consistently vary, especially in the presence of human immunodeficiency virus (HIV) coinfection, and the early manifestations spontaneously regress, leading to consistent underdiagnosis of the disease (1).

Here, we present the case of a 62-year-old man with an upper lip lesion ultimately recognized as a chancre of primary syphilis and describe the main clinical, serological, and radiological findings of a unique presentation that might complicate the differential diagnostic process. In addition, the literature was reviewed in search of cases of primary syphilis of the oral mucosa to highlight its variable clinical features.

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This study was designed in adherence with the Declaration of Helsinki.

Case Presentation

A 62-year-old man, returning from a business and leisure trip to Brazil, was admitted to the outpatient dentistry clinic of the San Raffaele University Hospital (Milan, Italy) because of a herpetic-like lesion of the vestibular mucosa of the left upper lip. The injury did not involve the vermilion and appeared as an erythematous, depressed area with whitish patches (Figure 1a). The lesion had been asymptomatic for the first 3 weeks, after which the patient reported the onset of moderate local discomfort. He denied the presence of any other symptom, and regional lymphadenopathy, skin rashes, alopecia, and any other signs of the disease were excluded at physical examination. The specialist initially prescribed topical applications of 1% chlorhexidine gel, and after 14 days, the lesion had extended toward the labial fornix, thus becoming pink and thin, suggesting a forthcoming healing (Figure 1b). When asked about risk behaviors, the patient admitted to having unprotected orogenital sex with a woman during his stay in Brazil.

On the basis of clinical history and physical examination, the specialist raised the suspicion of a syphilitic infection. VDRL, TPHA, and FTA-ABS were all positive. A biopsy of the lesion was not performed because, as suggested by many authors, a DFM on an oral biopsy could have determined a false positive owing to the presence of saprophytic spirochetes (1, 4, 5). Tests for other sexually transmitted diseases (STDs) were negative.

Because of the evolution and clinical features of the disease (especially the single localization of the lesion and absence of other symptoms), diagnosis of primary syphilis was preferred over the diagnosis of the secondary form. As a consequence, the patient underwent antibiotic therapy with intramuscular penicillin G 2,400,000 IU once a week for two weeks, with the first signs of healing seen a few days after the first injection (Figure 1c). No Jarisch-Herxheimer reaction was observed, and at the 6-month follow-up, the patient had a complete clinical and serological recovery.

Results

Considering the literature available from 1970 to 2020, 32 cases of oral cavity primary syphilis were reported, mainly as case reports, as shown in Table 1, (3, 6-24).

In almost all the patients, primary syphilis appeared as an ulcerative lesion, consistent with the typical description of chancre from other sites, although the syphilis of the patient re-

ferred to in the paper by Huang et al. (23). had evolved from papular and nodular lesions. The most affected sites were the lips and tongue, followed by buccal mucosa, gums, and palate. In 4 patients (7, 9, 10, 13), more than 1 ulcer was observed. In 5 patients, the chancres were unusually painful (7, 10, 13, 15, 19) and in 3 patients (10, 13, 23), non-ulcerative lesions were also present, a case that was similar to our patient's. In 10 patients (6, 8-11, 14, 20), lymphadenitis or constitutional symptoms were reported, although in the paper by Kutsuna et al. (20), it may have been because of the overlapping of primary and secondary stages. Among the 15 patients in whom HIV status was specified, only 2 were positive (8, 10). Five patients had been treated with local antiseptic or topical steroids owing to the suspicion of the presence of other diseases (mainly aphthous stomatitis) (15, 19, 20, 23, 24) and in 5 patients, the lesions were biopsied (3, 8, 9, 13, 16).

Discussion

Syphilis is a chronic treponemal infection that can potentially affect any organ or apparatus (1, 4). Although it is easy to cure, its variable, multifaceted oral presentation compels to investigate many possible differential diagnoses, and diagnostic delay is therefore frequently observed with potentially fatal consequences (1, 10, 25).

Epidemiology

Paradoxically, syphilis is a victim of the high effectiveness of its therapy: in the popular imagination, it is an infection belonging to the past or limited to extreme fringes of society (1). However, more than 5 million patients are diagnosed with syphilis every year, especially, but not exclusively, in low- and middle-income countries where syphilis is endemic, and mother-to-fetus infection represents a significant fraction of such patients (1). Curiously, in high-income countries, the epidemiology of syphilis had displayed a reduction in incidence starting in the first half of the 20th century but had a pattern of periodic resurgences in the last decades (1, 4). The reduced use of barrier protection, sexual promiscuity, and insufficient knowledge about the disease are key factors for its spread (1, 4). In particular, the predominance of the oral cavity between the extragenital sites can be, at least in part, attributed to the incorrect but widespread belief that oral sex is risk-free. Many patients, in fact, declare they have safe penetrative intercourse but unprotected oral sex (8, 14, 15, 17).

Clinical Features and Differential Diagnosis

Schematically, the course of the non-antenatal infection has been divided into 4 distinct periods (primary, secondary, latent, and tertiary syphilis); however, clinical experience suggests that they frequently overlap (1, 4, 14, 26). The primary stage typically presents as a macule that may evolve into a painless, non-purulent ulcer with a clean base and hardened, indurated margins (1, 4, 26). Such lesions, known as chancre, are caused by proliferation of treponemas at the site of first contact, spontaneously regressing in 2-8 weeks, and these lesions may be associated with regional lymphadenopathy (4, 14, 26). The secondary stage appears after 2-12 weeks of the first contact, and as it is the product of hematogenous dissemination, it may arise with constitutional symptoms, mucocutaneous lesions, or localizations in virtually any organ (1, 4). Unfortunately, the

Main Points:

- Oral primary syphilis usually appears as an ulcer commonly called chancre; it may have unusual presentations, which may complicate the differential diagnosis.
- A proper investigation for oral primary syphilis includes anamnesic collection, clinical examination, blood tests, and/or biopsies.
- Early diagnosis is crucial to avoid progression to more advanced and dangerous stages.

Table 1. Cases of primary oral syphilis

First author	Sex	Lesion and Site	HIV status	Other symptoms/ notes
Fiumara (1973) ⁶	M	Hard palate ulcer	Unsp	Lymphadenitis/ concurrent gonococcal infection
Alam (2000) ⁷	M	Deep painful ulcer with erythematous non-rolled border on upper labial mucosa + superficial ulcers on the mouth floor	-	None
	M	Palate ulcer	Unsp	None
Scott (2005) ⁸	M	Upper labial mucosa ulcer	+	Lymphadenitis
	M	Commissure ulcer	-	Lymphadenitis, mild fever
	F	Commissure ulcer	-	None
Veraldi (2008) ⁹	M	Ulcers on lower lip mucosa, vestibular fornix, buccal mucosa	Unsp	Lymphadenitis
Shumway (2009) ¹⁰	M	Fissures, a white plaque and multiple deep ulcers on tongue + superficial, painful, exudative ulcers on inferior gums	+	Lymphadenitis
Ramoni (2009) ¹¹	M	Vestibular fornix/commissure ulcer	Unsp	Lymphadenitis
	M	Tongue ulcer	Unsp	Lymphadenitis
	M	Tongue ulcer	-	Lymphadenitis
Staines (2011) ¹²	M	Tongue ulcer	-	None
Friuli (2013) ¹³	F	Painful erythema on the cheeks and mandibular vestibules + painless tongue ulcer + painful gingivitis	-	None
Leuci (2013) ¹⁴	M	Hard/soft palate ulcer	-	None
	M	Buccal mucosa ulcer	-	Suppurative lymphadenitis
Hertel (2014) ¹⁵	M	Painful commissure ulcer	Unsp	None
Vera- Kellet (2014) ¹⁶	F	Upper lip mucosa ulcer	Unsp	None
Watts (2016) ¹⁷	M	Lower lip mucosa ulcer	-	Genital lesion
Fregnani (2017) ¹⁸	M	Tongue ulcer	-	None
Sugaya (2018) ¹⁹	M	Painful upper gingival mucosa ulcer	Unsp	None
Kutsuna (2018) ²⁰	F	Lower lip ulcer	Unsp	Face rash, fever/ Overlapping primary and secondary stage
Matias (2019) ²¹	5 oral primary cases in a cohort of 85 patients with oral manifestations at any stage. Impossible to extract the specific features of the primary stage group.			
Schuch (2019) ²²	M	Lip ulcer	Unsp	Not available
	M	Lip ulcer	Unsp	Not available
	M	Buccal mucosa ulcer	Unsp	Not available
Huang (2020) ²³	F	Upper lip papular and nodular lesions evolving in exudative ulcer	-	None
Calvo (2020) ³	M	Lower lip mucosa ulcer	-	None
Porterfield (2020) ²⁴	M	Lower lip crusted plaque	-	None

Unsp:unspecified, +:positive, -:negative

primary and secondary stages (comprehensively named early syphilis) present with a spectrum of unspecific manifestations and regress spontaneously; as a consequence, syphilis may evolve into its feared tertiary phase, which is characterized by granulomatous lesions called gummas, which may affect the skin, the central nervous and cardiovascular system, spleen, and many others (4).

The primary lesion appears at the site of the first contact, and, as syphilis is a STD, in the majority of patients it involves the anogenital region (86-95%) (1, 3). Thus, syphilis differs from other STDs as it can be transmitted through direct contact between the infected region and an area of abrasion, and it has been reported on fingers, hands, arms, eyelids, and even the nose as a consequence of both non-penetrative sexual inter-



Figure 1. a-c. The lesion (a) at the time of first evaluation, (b) after 14 days of local therapy with chlorhexidine, and (c) a few days after the first penicillin administration.

course and non-sexual (including healthcare-related) contacts with lesions (27, 28). The frequency of infection due to oral sex, however, accounts for the oral cavity being the most frequent extragenital site (40-75%), (4). Within this location, the upper lip is the most common site among men and the lower lip and tongue among women, probably reflecting the anatomy involved in fellatio and cunnilingus, followed by the palate and buccal mucosa (3, 26).

Despite the usually standardized aspect of chancre, some authors have described atypical variants, occurring particularly in extragenital sites: non-ulcerative/apthoid in nature, non-circular or papular in form, multiple in number, occurring with satellite lesions, or presenting as painful and pruritic ulcers. This evidence is confirmed for the oral cavity as shown in this review: the most common presentation was a painless single ulcer with indurated margins, frequently associated with neck lymphadenitis, but unusual cases have also been observed as painful, multiple, and non-ulcerated forms were reported (7, 9, 10, 13, 15, 19, 23).

Moreover, when an unusual presentation of oral primary syphilis is suspected, an additional confounding factor of frequent coinfections with other STDs and especially HIV must be kept in mind (1, 4, 26). Although HIV and syphilis have common patterns of contagion, they mutually reinforce the probability of infection (29). A paper on 31 coinfecting Nigerian patients by Nnoruka et al. (29) reported that in the event of HIV coinfection, the chancres at any site may be multiple, wider, and more painful and ragged; the constitutional symptoms may be more severe; the progression through the different stages of the disease and spreading of infection may be faster; the skin involvement may be more extensive and more prone to ulceronecrotic lesions. Unfortunately, in the studies included in this review, HIV status was specified in only half of the patients. It does not appear to be a coincidence, however, that 1 of the most unusual manifestations (reported by Shumway et al. (10)) occurred in a patient with HIV.

Given its variable presentation, including traumatic injuries; oral malignancies; pemphigus; HIV-related ulcers; and localization of other infectious diseases such as tuberculosis, mycosis, and cytomegalovirus, differential diagnosis of oral primary syphilis is incredibly wide (7, 8, 14, 30-34). Accordingly, the title of the "great imitator" is well-deserved, to such an extent that Ramoni et al. (11) suggested that any indurated asymptomatic oral lesion should be suspected as being primary syphilis.

Diagnostic Tools

The diagnostic tools for oral syphilis are mostly the same as those for other localizations; treponemal and non-treponemal tests are complementary and common instruments but are affected by reduced sensitivity in the primary phase compared with the sensitivity in the secondary phase (35).

Indeed, when primary oral syphilis is suspected through negative serologic tests, further investigations should be performed. Growing *T. pallidum* in a culture is difficult, and direct detection is therefore necessary; a biopsy of an oral lesion with standard staining thus cannot detect the pathogen. However, DFM and the expertise to use it are not easily accessible in all settings, and many authors suggest that DFM should not be used for samples from the oral cavity as it may lead to false-positive results owing to the presence of saprophytic spirochetes (1, 4, 5). Fluorescence microscopy and nucleic acid amplification are scarcely widespread but more reliable; recent studies have also reported moderate to good sensitivity of nested polymerase chain reaction on swabs and blood samples for early syphilis, identifying, in some cases, seronegative patients (1, 5, 35).

On the basis of the aforementioned information, diagnostic work-up for primary syphilis should be tailored on the center's availability of tests. Considering the effortless accessibility of the oral mucosa, a biopsy should be performed when the clinical and anamnestic data are consistent with oral primary syphilis and the serologic tests are negative. Even a standard stain biopsy may suggest the correct diagnosis if it shows an inflammatory infiltrate composed mostly of lymphocytes and plasma cells with a predilection for perivascular areas (3, 27); an obliterative endarteritis may be seen in all stages of the disease (4). In addition, a biopsy may add crucial information for differential diagnosis.

Eventually, the limited reliability of early tests, together with the transient nature and low annoyance of syphilis, justify why only a limited percentage of oral cases are diagnosed in the primary stage 1. Subsequently, all healthcare professionals involved should be aware of a resurgence of syphilitic oral infection, and in the event of unspecific oral lesions, syphilis must be ruled out with more than 1 test. When test results are negative but there is high-risk behavior or a temporal evolution consistent with treponemal infection, we suggest biopsy of the oral cavity.

Shortcomings and Possible Biases

Considering the shortcomings of this review, we must include the report bias—although rare, primary syphilis of the oral cav-

ity presenting with a classical chancre may be underreported, privileging uncommon manifestations. This may explain the limited number of cases found while reviewing, although the oral cavity is described as the most commonly affected extragenital site. An interesting fact that we observed was the increasing frequency of reports in the past years; 21 of the 32 patients identified in this review were diagnosed after 2010. This may be related to both an epidemiologic resurgence of oral syphilis and increased awareness of the infection.

We must also admit that in some patients, a diagnosis of primary over secondary syphilis was made as it was considered more fitting on the basis of clinical history; the lack of a laboratory test specifically distinguishing the 2 stages and the presence of overlapping forms may thus fade such distinction.

Conclusion

The oral cavity is a rare localization of primary syphilis; however, its incidence may be underestimated owing to its low annoyance and tendency to self-heal. The disease should always be considered as a possible differential diagnosis for oral lesions, especially in the event of ulcerated and painless lesions. A careful anamnestic interview, together with proper tests, is required. Specific sex education is needed to inform the general population, especially the groups who are most at risk, of the hazards of unprotected oral sex, which is often wrongly considered to be safe.

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References

- Hook EW. Syphilis. *Lancet* (London, England) 2017; 389: 1550-7. [\[Crossref\]](#)
- Tampa M, Sarbu I, Matei C, et al. Brief history of syphilis. *J Med Life* 2014; 7: 4-10.
- Calvo DF, Cassarino D, Fernandez-Flores A. Syphilitic Chancre of the Lip. *Am J Dermatopathol* 2020; 42: e143-e146. [\[Crossref\]](#)
- Ficarra G, Carlos R. Syphilis: the renaissance of an old disease with oral implications. *Head Neck Pathol* 2009; 3: 195-206. [\[Crossref\]](#)
- Grange PA, Gressier L, Dion PL, et al. Evaluation of a PCR test for detection of *treponema pallidum* in swabs and blood. *J Clin Microbiol* 2012; 50: 546-52. [\[Crossref\]](#)
- Fiumara NJ, Berg M. Primary syphilis in the oral cavity. *Sex Transm Infect* 1974; 50: 463-4. [\[Crossref\]](#)
- Alam F, Argiriadou AS, Hodgson TA, et al. Primary syphilis remains a cause of oral ulceration. *Br Dent J* 2000; 189: 352-4. [\[Crossref\]](#)
- Scott CM, Flint SR. Oral syphilis-re-emergence of an old disease with oral manifestations. *Int J Oral Maxillofac Surg* 2005; 34: 58-63. [\[Crossref\]](#)
- Veraldi S, Lunardon L, Persico MC, et al. Multiple aphthoid syphilitic chancres of the oral cavity. *Int J STD AIDS* 2008; 19: 486-7. [\[Crossref\]](#)
- Shumway BS, Islam NM, Kapoor R, et al. Clinico-Pathologic conference: Case 3. *Head Neck Pathol* 2009; 3: 286-9. [\[Crossref\]](#)
- Ramoni S, Cusini M, Gaiani F, et al. Syphilitic chancres of the mouth: three cases. *Acta Derm Venereol* 2009; 89: 648-9. [\[Crossref\]](#)
- Staines K, Sloan P. Images in clinical medicine. Syphilitic chancre of the tongue. *N Engl J Med* 2011; 365: e11. [\[Crossref\]](#)
- Friuli S, Crippa R. Misunderstood oral early syphilis: a meaningful case report. *Ann Stomatol (Roma)* 2013; 4: 17.
- Leuci S, Martina S, Adamo D, et al. Oral Syphilis: a retrospective analysis of 12 cases and a review of the literature. *Oral Dis* 2013; 19: 738-46. [\[Crossref\]](#)
- Hertel M, Matter D, Schmidt-Westhausen AM, et al. Oral syphilis: a series of 5 cases. *J Oral Maxillofac Surg* 2014; 72: 338-45. [\[Crossref\]](#)
- Vera-Kellet C, Harz-Fresno I, Manriquez J. Labial ulcer: oral manifestation of syphilis. *Braz J Infect Dis* 2014; 18: 570-1. [\[Crossref\]](#)
- Watts PJ, Greenberg HL, Khachemoune A. Unusual primary syphilis: Presentation of a likely case with a review of the stages of acquired syphilis, its differential diagnoses, management, and current recommendations. *Int J Dermatol* 2016; 55: 714-28. [\[Crossref\]](#)
- Fregnani ER, Pérez-de-Oliveira ME, Parahyba CJ, et al. Primary syphilis: an uncommon manifestation in the oral cavity. *J Formos Med Assoc* 2017; 116: 326-7. [\[Crossref\]](#)
- Sugaya N, Braz-Silva PH, Bergamini ML, et al. Primary syphilis occurring as an extensive ulceration on the palatal gingival mucosa diagnosed by immunohistochemical staining. *J Eur Acad Dermatol Venereol* 2018; 32: e461-e462. [\[Crossref\]](#)
- Kutsuna S, Fujiya Y. Primary and secondary syphilis as chancre of the mouth with rash. *Intern Med* 2018; 57: 155. [\[Crossref\]](#)
- Matias MDP, Jesus AO de, Resende RG, et al. Diagnosing acquired syphilis through oral lesions: the 12 year experience of an Oral Medicine Center. *Braz J Otorhinolaryngol* 2020; 86: 358-63. [\[Crossref\]](#)
- Schuch LF, da Silva KD, de Arruda JAA, et al. Forty cases of acquired oral syphilis and a review of the literature. *Int J Oral Maxillofac Surg* 2019; 48: 635-43. [\[Crossref\]](#)
- Huang S, Lu R, Yang J-Y, et al. A nonspecific ulcer on upper lip presented as the first and sole sign of syphilis. *J Infect Chemother* 2020; 26: 1309-12. [\[Crossref\]](#)
- Porterfield C, Brodell D, Dolohanty L, et al. Primary Syphilis Presenting As a Chronic Lip Ulcer. *Cureus*; 12. Epub ahead of print] 24 February 2020. [\[Crossref\]](#)
- Klausner JD. The great imitator revealed: syphilis. *Top Antivir Med* 2019; 27: 71-4.
- Leão JC, Gueiros LA, Porter SR. Oral manifestations of syphilis. *Clinics* 2006; 61: 161-6. [\[Crossref\]](#)
- Epstein E. Extragenital syphilis in physicians. *Calif Med* 1952; 77: 149-50.
- Trimarchi M, Bellini C, Toma S, et al. Back-and-forth endoscopic septoplasty: analysis of the technique and outcomes. *Int Forum Allergy Rhinol* 2012; 2: 40-4. [\[Crossref\]](#)
- Nnoruka EN, Ezeoke ACJ. Evaluation of syphilis in patients with HIV infection in Nigeria. *Trop Med Int Health* 2005; 10: 58-64. [\[Crossref\]](#)
- Biafara M, Bertazzoni G, Trimarchi M. Maxillary sinusitis caused by dental implants extending into the maxillary sinus and the nasal cavities. *J Prosthodont* 2014; 23: 227-31. [\[Crossref\]](#)
- Lanzillotta M, Campochiaro C, Trimarchi M, et al. Deconstructing IgG4-related disease involvement of midline structures: Comparison to common mimickers. *Mod Rheumatol* 2017; 27: 638-45. [\[Crossref\]](#)
- Trimarchi M, Bondi S, Della Torre E, et al. Palate perforation differentiates cocaine-induced midline destructive lesions from granulomatosis with polyangiitis. *Acta Otorhinolaryngol Ital* 2017; 37: 281-5. [\[Crossref\]](#)
- Morassi ML, Trimarchi M, Nicolai P, et al. Cocaina, ANCA e granulomatosi di Wegener. *Pathologica* 2001; 93: 581-3.
- Alfano M, Grivel J-C, Ghezzi S, et al. Pertussis toxin B-oligomer dissociates T cell activation and HIV replication in CD4 T cells released from infected lymphoid tissue. *AIDS* 2005; 19: 1007-14. [\[Crossref\]](#)
- Wang C, Cheng Y, Liu B, et al. Sensitive detection of *Treponema pallidum* DNA from the whole blood of patients with syphilis by the nested PCR assay. *Emerg Microbes Infect* 2018; 7: 1-7. [\[Crossref\]](#)