

Nonhealing Ulcer on the Lower Lip

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A 54-year-old HIV-negative man with a history of having sex with men presented to his primary care physician with an ulcer on the lower lip of 3 weeks' duration. The patient reported that the lesion had appeared as a typical cold sore with pain in the area. A 9-day course of oral valacyclovir prescribed by the primary care physician provided no relief or improvement. A 2-mm punch biopsy was performed.

WHAT'S YOUR DIAGNOSIS?

- a. fixed drug eruption
- b. Mpox
- c. pyogenic granuloma
- d. syphilis
- e. valacyclovir-resistant herpes simplex virus

PLEASE TURN TO **PAGE 187** FOR THE DIAGNOSIS

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THE DIAGNOSIS:

Syphilis

The differential diagnosis of oral lesions can be complex; in our patient, we considered conditions such as pyogenic granuloma, herpes simplex virus, and syphilis, despite the presence of pain. Immunohistochemical staining for spirochete antigens was positive, and serologic confirmation through a positive rapid plasma reagin (RPR) test confirmed the diagnosis of primary syphilis. The patient was promptly referred back to the primary care physician for treatment with intramuscular penicillin, leading to resolution of the lesion. At 3 months' follow-up in our clinic, the lesion was fully resolved.

A primary syphilitic chancre is the initial lesion caused by *Treponema pallidum*, typically manifesting as a painless ulcer at the infection site, usually in the genital area; however, chancres also may manifest in other locations (eg, the anus or oral cavity) due to direct contact with infectious lesions on another individual. Our case represents an atypical presentation of an oral syphilitic chancre.

Syphilis is a sexually transmitted infection with various clinical manifestations. It is crucial to consider syphilis in the differential diagnosis of ulcerative lesions even when pain is present, especially in high-risk individuals such as those who engage in unprotected sex.^{1,2} Oral syphilitic chancres have been documented in the medical literature for more than a century, underscoring the importance of maintaining a high index of suspicion for diagnosis and a low threshold for obtaining an RPR test to facilitate early detection and treatment.^{2,3} Notably, the prevalence of syphilis is higher in men who have sex with men, particularly among those who engage in unprotected oral and anal sex. Increased screening and early treatment are essential to control the spread of disease within all populations. Doxycycline postexposure prophylaxis (doxyPEP) is used as a preventive measure for syphilis, chlamydia, and gonorrhea.⁴ This regimen consists of 200 mg of doxycycline taken within 24 hours but no later than 72 hours after unprotected anal, vaginal, or oral sex.

Our case highlights the importance of considering the differential diagnosis of oral ulcers, particularly in high-risk populations such as men who have sex with men. Prompt diagnosis, effective treatment, and preventive strategies such as doxyPEP are essential for controlling syphilis. Comprehensive patient education and regular follow-up appointments are critical components of successful management.

The United States has experienced a considerable rise in primary and congenital syphilis cases, with an 80% increase between 2018 and 2022.⁶ Serologic testing is the primary method for diagnosing, staging, and managing syphilis. Sexually active patients with suspected syphilis or unexplained symptoms should undergo testing. Prompt

diagnosis and treatment can prevent systemic complications, including ocular involvement and permanent blindness.

Syphilis is transmitted through direct contact with a syphilitic ulcer or saliva or blood from an infected individual. Oral syphilitic ulcers can develop on the lips, tongue, oral mucosa, and tonsils. Chancres can range from a few millimeters to several centimeters, with an incubation period of 10 to 90 days (average, 21 days). The chancre lasts 3 to 6 weeks and heals spontaneously. Without treatment, primary syphilis can progress to secondary syphilis, characterized by a papulosquamous eruption and mucosal involvement, and potentially tertiary syphilis, which can affect the central nervous system, heart, bones, and skin.⁷

Immunocompromised patients, especially those diagnosed with HIV, face increased risks including altered clinical presentations (eg, multiple or deep chancres), delayed healing, overlapping stages of disease, and increased severity of organ involvement. All sexually active individuals should be screened for syphilis every 3 to 6 months, particularly those with unexplained oral ulcers.

Serologic testing is fundamental for syphilis diagnosis and management. Nontreponemal tests such as RPR and treponemal tests such as the fluorescent treponemal antibody absorption test provide comprehensive diagnostic information. Early diagnosis and empiric treatment are crucial in suspected cases. Ocular screening is recommended for suspected or confirmed syphilis cases.⁷

Management of syphilis includes treating all sexual partners and providing thorough patient education on the disease. Monitoring for the Jarisch-Herxheimer reaction—an acute febrile reaction following penicillin therapy—is important, especially in pregnant patients.⁵ Serologic evaluation at 6 and 12 months posttreatment is recommended, with more frequent evaluations if follow-up is uncertain, particularly for those with inconsistent access to health care or in whom reinfection is suspected. Guidelines from the Centers for Disease Control and Prevention advocate for intramuscular penicillin G benzathine as the preferred treatment, with specific dosing for adults and children.⁷ Due to the ongoing bicillin shortage, alternatives such as ceftriaxone have temporarily been allowed for use in the United States.⁸

The rising incidence of syphilis in the United States underscores the critical need for enhanced public health initiatives focusing on education, screening, and early intervention. Comprehensive sexual education that includes information about syphilis and other sexually transmitted infections, proper use of prophylactic measures such as condoms, and the benefits of doxyPEP can considerably reduce transmission rates. Health care providers should

CONTINUED ON PAGE 190

PHOTO CHALLENGE DISCUSSION

CONTINUED FROM PAGE 187

routinely discuss these preventive measures with their patients, especially those in high-risk groups.

Our case highlights the importance of considering syphilis in the differential diagnosis of oral ulcers, particularly in high-risk populations. Timely diagnosis, effective treatment, and preventive measures such as doxyPEP are essential for managing and controlling syphilis. The rising incidence of syphilis in the United States warrants increased screening, patient education, and public health interventions to address this notable health challenge. The syphilis crisis calls for coordinated efforts from health care providers, public health officials, and community leaders to curb the spread of this infection and protect public health.

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