EMMA COLEMAN, DO

Internal Medicine Residency Program, Cleveland Clinic

ANDRE FIAHLO, MD

GI/Hepatology Fellowship, University of Florida, Jacksonville

ANDREI BRATEANU, MD, FACP

Department of Internal Medicine, Cleveland Clinic

Secondary syphilis



FIGURE 1. Ulcerated plaque on the upper lip.



FIGURE 2. Macular rash with painless scarred lesions.

Untreated primary and secondary syphilis may progress to latent or asymptomatic disease

A 39-YEAR-OLD MAN presented to the emergency department reporting several weeks of generalized weakness, headache, nausea, and migratory arthralgia. The patient had exclusively had sex with men, had participated in condomless anal insertive and receptive intercourse, and had been in a monogamous relationship during the past 6 months.

See related editorial, page 514

Physical examination revealed a painful ulcerated plaque on the upper lip (Figure 1), a macular rash with 3 crater-like scarred painless lesions (considered to be healing chancres) on the glans (Figure 2), a nonpruritic hyperkeratotic maculopapular palmar rash, and bilateral submandibular lymphadenopathy. No alopecia, gummas, neurologic deficits, or ocular or cardiovascular abnormalities were noted.

Results of laboratory testing included a positive reactive syphilis immunoglobulin

doi:10.3949/ccjm.84a.16089

G (IgG) enzyme immunoassay and a positive rapid plasma reagin (RPR) test (titer 1:256). Human immunodeficiency virus (HIV) testing was negative, and serologic testing demonstrated prior immunization to hepatitis B virus. Given the clinical presentation and laboratory findings, secondary syphilis was considered the most probable diagnosis.

The patient was treated with benzathine penicillin G 2.4 million units intramuscularly.

SYPHILIS: A REEMERGING CONDITION

Epidemiology

The rate of reported primary and secondary syphilis cases in the United States has risen since 2001.¹ Most cases occur in men who have sex with men.¹ Additional risk factors include condomless intercourse and drug use.²

Signs and symptoms of the 3 stages

Primary syphilis begins 2 to 3 weeks after inoculation of a mucosal surface.³ This stage is marked by one or more painless chancres and, in some cases, local nontender lymphadenopathy.^{3,4} Secondary syphilis presents 4 to 8 weeks later with systemic symptoms including rash, classically involving the palms or soles, lymphadenopathy, myalgia, fever, and weight loss.^{2,3} Untreated primary and secondary syphilis may progress to latent or asymptomatic disease.⁵

Tertiary syphilis, defined by the US Centers for Disease Control and Prevention (CDC) as gummas or cardiovascular syphilis, occurs 15 to 30 years after an untreated exposure. ^{4,6} Neurosyphilis can present at any stage of the disease. ⁶

Diagnosis

The diagnosis of syphilis involves a nontreponemal test such as RPR or Venereal Disease Research Laboratory (VDRL) to screen for disease, followed by a treponemal antibody test such as fluorescent treponemal antibody-absorption, *Treponema pallidum* particle agglutination assay, or syphilis IgG to confirm the diagnosis. There is no screening test for tertiary disease in patients previously diagnosed with primary or secondary syphilis, but a cerebrospinal fluid (CSF) examination is recommended if neurologic or ocular manifestations are present.

Treatment

Treatment of primary, secondary, and early latent syphilis is a single dose of 2.4 million units of benzathine penicillin G given intramuscu-

REFERENCES

- Centers for Disease Control and Prevention (CDC). 2015 Sexually transmitted disease surveillance. www.cdc.gov/std/stats15/. Accessed May 22, 2017.
- Nyatsanza F, Tipple C. Syphilis: presentations in general medicine. Clin Med (Lond) 2016; 16:184–188.
- French P. Syphilis. BMJ 2007; 334:143–147. Erratum in: BMJ 2007; 335:0.
- Centers for Disease Control and Prevention (CDC). Appendix C1.
 Case definitions for nationally notifiable infectious diseases. www.cdc.gov/std/stats14/appendixc.htm. Accessed May 18, 2017.

larly. The treatment of late latent and tertiary syphilis is less well defined by the current literature but generally includes penicillin. 7

Patients with primary and secondary syphilis undergo serologic and clinical evaluation at 6 and 12 months to be assessed for treatment failure or reinfection.⁶ Patients with latent disease require serologic follow-up at 6, 12, and 24 months.⁶ Additionally, CSF analysis should be done if baseline high titers do not fall within 12 to 24 months of treatment or if symptoms suggest syphilis.⁶ Patients with neurosyphilis often require CSF evaluation every 6 months.⁶ Follow-up for patients with tertiary syphilis is less well defined.

Patients coinfected with HIV have special needs and considerations, as outlined in the CDC's 2015 Sexually Transmitted Diseases Treatment Guidelines.⁶

Sexual contacts of patients with syphilis deserve evaluation. Exposure within 90 days of a patient's diagnosis with primary, secondary, or latent disease requires treatment regardless of the results of serologic testing.⁶ Persons exposed more than 90 days before diagnosis may undergo serologic testing; however, if results are not immediately available or follow-up is unlikely, the individual should be treated for early syphilis.⁶ If serologic testing results are negative, no treatment is required.⁶

- Centers for Disease Control and Prevention (CDC). Syphilis—CDC fact sheet (detailed). www.cdc.gov/std/syphilis/STDFact-Syphilisdetailed.htm. Accessed May 18, 2017.
- Centers for Disease Control and Prevention (CDC). 2015 Sexually transmitted diseases treatment guidelines. Syphilis. www.cdc.gov/ std/tg2015/syphilis.htm. Accessed June 15, 2016.
- Clement ME, Okeke NL, Hicks CB. Treatment of syphilis: a systematic review. JAMA 2014; 312:1905–1917.

ADDRESS: Emma Coleman, DO, Internal Medicine Residency Program, NA10, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; colemae4@ccf.org