

# Secondary Syphilis: An Atypical Presentation Complicated by a False Negative Rapid Plasma Reagin Test

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## PRACTICE POINTS

- Fluorescent treponemal antibody absorption testing more accurately detects syphilis than rapid plasma reagin (RPR).
- Rapid plasma reagin testing is more useful in monitoring serum response once treatment has been initiated.
- If only RPR is being performed at your institution, ensure the laboratory is performing serial dilutions to negate the prozone phenomenon.

To the Editor:

According to the Centers for Disease Control and Prevention, the number of syphilis cases in the United States decreased 95% from 1945 to 2000.<sup>1</sup> Since 2000, the number of cases of syphilis in the United States has increased from 2.1 cases per 100,000 to 8.7 cases per 100,000.<sup>1</sup> We report the case of an atypical presentation of secondary syphilis with a false negative rapid plasma reagin (RPR) test, which resulted in delayed diagnosis and treatment. The goal of this report is to raise awareness of the increasing prevalence of syphilis in the United States, draw attention to atypical presentations of syphilis, and inform physicians of some of the pitfalls in current syphilis screening and testing modalities.

A 37-year-old man presented with cutaneous ulcers on the forehead, thighs, and forearms of 3 months' duration. The lesions started as a scarlet fever–like rash consisting of diffuse boils that would burst and become ulcerated. He reported arthralgias and drenching night sweats and had unintentionally lost 20 pounds over the last 3 months. He also had pharyngitis 8 months prior to presentation and sinusitis 4 months prior to presentation. These symptoms were present during his initial

evaluation. One month prior to the current presentation, a nurse practitioner from an outside clinic had prescribed sulfamethoxazole/trimethoprim and ordered an RPR test, which was nonreactive. The lesions did not resolve, and the patient was referred to our dermatology department.

On physical examination, multiple 1- to 3-cm erythematous, well-defined papules were noted on the thighs and forearms. Some of the papules were covered with crusts, some were ulcerated with yellow discharge, and all were nontender. The differential diagnoses included dermatomyositis, polyarteritis nodosa, deep fungal infection, mycobacterial infection, leishmaniasis, and cutaneous anthrax. Secondary syphilis was a possible differential but was discounted due to the nonreactive RPR 1 month prior to presentation.

Punch biopsies were collected from lesions on the forehead, forearms, and thighs and sent to multiple institutions for pathology evaluation, which revealed dermal and pannicular necrosis and acute suppurative and granulomatous inflammation focally involving vessels (Figure 1). The biopsies were negative for acid-fast and fungal organisms, *Mycobacterium tuberculosis*, *Leishmania*, and anthrax. A work-up for Wegener granulomatosis was recommended by the pathology department.

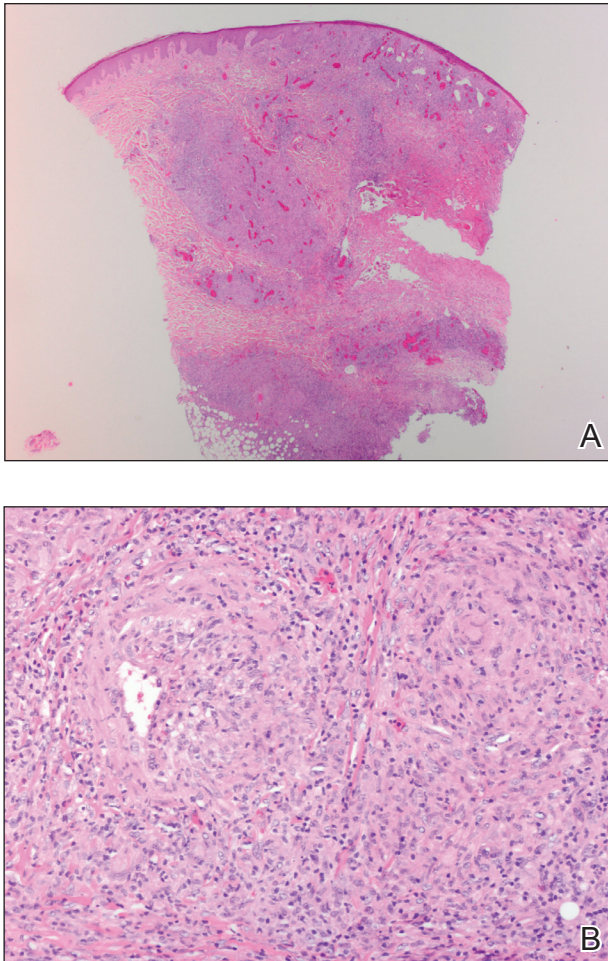
Three days later, the patient was admitted to the hospital for syncope. The hospitalist noted the cutaneous lesions and reordered the RPR test, which was now reactive. The ulcers had worsened since the original presentation (Figure 2). A fluorescent treponemal antibody absorption (FTA-ABS) test confirmed the reactive RPR, and a diagnosis of secondary syphilis was made. He was allergic to penicillin G, so the patient was prescribed doxycycline 100 mg twice daily for 28 days. His cutaneous ulcers have since healed with no recurrence of symptoms.

Secondary syphilis often is preceded by a prodrome of fever, malaise, sore throat, adenopathy, unintentional

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**FIGURE 1.** Punch biopsy of a left thigh lesion showed superficial ulceration with transdermal acute and chronic inflammation with focal necrosis (A)(H&E, original magnification  $\times 20$ ) and deep subcutaneous acute and chronic inflammation with multiple granulomas in a patient with secondary syphilis (B)(H&E, original magnification  $\times 100$ ).

weight loss, myalgias, and headaches. It usually presents as a nonpruritic papulosquamous eruption with painless mucosal ulcers but rarely presents as cutaneous ulcers.<sup>2-4</sup> Cutaneous ulcers are typical of lues maligna, which usually occurs in immunosuppressed patients.<sup>5,6</sup> Our patient was human immunodeficiency virus–negative and was not otherwise immunocompromised.

Rapid plasma reagin is a common screening test for syphilis. In this case, it was initially negative, which may be attributed to the prozone phenomenon, a false negative result due to a high antibody titer that prevents the flocculation reaction from occurring. The prozone phenomenon can occur with a titer as low as 1:8.<sup>7</sup> A 50% dilution of the negative sample should overcome the prozone phenomenon and yield a positive result<sup>7</sup>; unfortunately, this is not standard practice in all hospital laboratories.



**FIGURE 2.** Cutaneous ulcers on the right (A) and left (B) forearms and the medial aspect of the left thigh (C) in a patient with secondary syphilis had worsened since original presentation 3 days prior.

The standard method of diagnosing syphilis in the United States is to screen with nontreponemal tests (eg, RPR) followed by treponemal tests (eg, FTA-ABS) to confirm a positive screen. According to the United States Preventive Services Task Force, the sensitivity of the RPR test is approximately 78% to 86%, while FTA-ABS has a sensitivity of 84% for detecting primary syphilis and 100% for secondary and tertiary syphilis.<sup>8</sup> Seña et al<sup>4</sup> suggest that FTA-ABS should be used as the screening test for

syphilis. Fluorescent treponemal antibody absorption testing more accurately detects syphilis, while RPR testing is more useful in monitoring serum response once treatment has been initiated.

In conclusion, our patient could have benefited from earlier diagnosis and treatment if a treponemal test had been performed earlier or if the initial nonreactive RPR test was diluted and retested.

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#### REFERENCES

1. Syphilis—CDC fact sheet. Centers for Disease Control and Prevention website. <http://www.cdc.gov/std/syphilis/stdfact-syphilis.htm>. Updated June 13, 2017. Accessed May 18, 2018.
2. Sary A, Sary G. Sexually transmitted infections. In: Bologna JL, Jorizzo JL, Schaffer JV, eds. *Dermatology*. 3rd ed. China: Elsevier Saunders; 2012:1368-1426.
3. Habif TP. Sexually transmitted bacterial infections. *Clinical Dermatology: A Color Guide to Diagnosis and Therapy*. 6th ed. China: Elsevier; 2016:377-417.
4. Seña AC, White BL, Sparling PF. Novel *Treponema pallidum* serologic tests: a paradigm shift in syphilis screening for the 21st century. *Clin Infect Dis*. 2010;51:700-708.
5. Bayramgürler D, Bilen N, Yıldız K, et al. Lues maligna in a chronic alcoholic patient. *J Dermatol*. 2005;32:217-219.
6. Bhate C, Tajirian AL, Kapila R, et al. Secondary syphilis resembling erythema multiforme. *Int J Dermatol*. 2010;49:1321-1324.
7. Liu LL, Lin LR, Tong ML, et al. Incidence and risk factors for the prozone phenomenon in serologic testing for syphilis in a large cohort. *Clin Infect Dis*. 2014;59:384-389.
8. Archived final recommendation statement. syphilis infection: screening. US Preventive Services Task Force website. <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/syphilis-infection-screening>. Published December 30, 2013. Accessed May 22, 2018.