BRIEF ARTICLES

Aseptic Syphilitic Meningitis in an HIV-Negative Patient with Concomitant Primary and Secondary Syphilis

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ABSTRACT

Background: Syphilis is a sexually and vertically transmitted disease caused by the *Treponema pallidum* species. Aseptic syphilitic meningitis (ASM) is a subcategory of neurosyphilis. Neurosyphilis is typically considered a tertiary manifestation of syphilis; however, ASM typically occurs within six months of exposure and may be concurrent with the rash of secondary syphilis.

Case Presentation: A 58-year-old immunocompetent male presented to the dermatology clinic with an erythematous morbilliform rash that involved his trunk and upper extremities. He was prescribed benzonatate 100 mg 3 weeks prior for cough and was diagnosed with a drug-induced morbilliform rash. The patient was seen one month later by urology for a penile ulcer. At his urology appointment, a rapid plasmin reagin test was done and resulted positive with a titer of 1:256. He was referred to dermatology again and was noted to have a diffuse, copper-colored maculopapular rash involving the palms and soles. During this appointment, the patient complained of a 4-week headache and was found to have nuchal rigidity. He was admitted for neurosyphilis work up, including CSF and CSF-VDRL examination. His neurologic symptoms improved with IV Penicillin G. Repeat RPR testing at six months follow up confirmed adequate treatment and his RPR declined from 1:256 to 1:4.

Conclusion: We present a case of ASM in an immunocompetent individual with concomitant primary and secondary syphilis. Dermatologists are trained to recognize the cutaneous manifestations of syphilis, but also should be familiar with the variable presentations of the disease, including the early neurological findings of ASM.

INTRODUCTION

Syphilis is a sexually and vertically transmitted infection caused by *Treponema pallidum* subspecies *pallidum*. The spirochete penetrates the skin via intact mucous membranes or dermal micro-abrasions and causes disseminated infection.[1] Syphilis has a protean presentation and is thus known as the "Great Mimicker."[2] The deceptive nature of the disease can lead to under-recognition of

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serious complications or lead to a failed treatment regimen.

A rare and insidious neurosyphilis sub-type called aseptic syphilitic meningitis (ASM) can present in primary or secondary syphilis, with most recorded cases occurring in secondary syphilis.[1,3] Because neurological symptoms are not typically seen in early syphilis, ASM can go unrecognized. In literature, most reported cases of ASM involve HIV-positive patients; however, the disease can also afflict immunocompetent individuals.[4] We present a case of an HIV-negative patient who presented with the classic cutaneous manifestations of primary and secondary syphilis as well as ASM.

CASE PRESENTATION

A 58-year-old immunocompetent Caucasian male presented to the dermatology clinic with a diffuse, pruritic rash on his face, trunk, and upper extremities for 3-4 weeks. The patient denied pain, recent sexual contacts, or eruption of a similar rash. He had a past medical history of alcoholic cirrhosis and no pertinent family or social history. He had been prescribed benzonatate 100 mg for cough 3 weeks prior. A physical examination demonstrated erythematous papules coalescing into small plaques in a morbilliform array. It was suspected that he had a morbilliform drug eruption secondary to his benzonatate use, and he discontinued the medication. He was prescribed topical corticosteroids to treat the rash. In addition, 0.4 cm punch biopsies of his left and right chest were done. The biopsy results were non-diagnostic and there was no evidence of a drug-induced skin eruption on histology.

The patient returned to the dermatology clinic one month later after he was noted to have an ulcerated plaque on his glans penis at a urology appointment. At his urology visit, a RPR, reactive syphilis IgG/IgM, HIV, and HSV/VZV PCR test were obtained. His HIV test was negative, HSV PCR was negative, and his RPR was positive with a titer of 1:256. His syphilis IgG/IgM were reactive. At his dermatology appointment, the physical examination demonstrated a copper-colored maculopapular rash that involved the palms and soles (Fig 1A, 1B). A skin biopsy of his right ankle, back, and right chest were obtained. A pemphigus panel, anti-nuclear, anti-histone, anti-SSB, and anti-SSA antibody tests were ordered. The pemphigus panel was negative for IgG antibodies to desmoglein-1 or -3; the anti-nuclear, anti-SSB, and anti-SSA antibodies were negative. A Treponema pallidum particle agglutination test (TPPA) was ordered and was reactive. The repeat biopsy demonstrated a lichenoid as well as superficial and deep lymphocytic infiltrate with abundant plasma cells. T. pallidum immunohistochemical staining also revealed abundant dermal spirochetes.

At this visit, the patient complained of a 4-week headache and was noted to have nuchal rigidity on physical examination. The patient was admitted to the hospital directly from the clinic for a neurosyphilis work-up and a lumbar puncture was done. His CSF analysis demonstrated elevated protein levels but no evidence of lymphocytic pleocytosis. The CSF-VDRL was negative; a meningoencephalitis panel was also negative. The patient was treated with IV Penicillin G for ten days (60 doses). The patient had a drastic improvement and his headache and nuchal rigidity resolved within 48 hours of treatment initiation. While the patient's CSF results were non-diagnostic, the clinical response to penicillin and the lack of an alternative explanation led to a diagnosis of aseptic syphilitic meningitis.

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Over the course of six months, the patient's RPR titer decreased from 1:256 to 1:4.

Figure 1. (A) Secondary Syphilis. The patient demonstrated a copper-colored maculopapular rash on his chest.

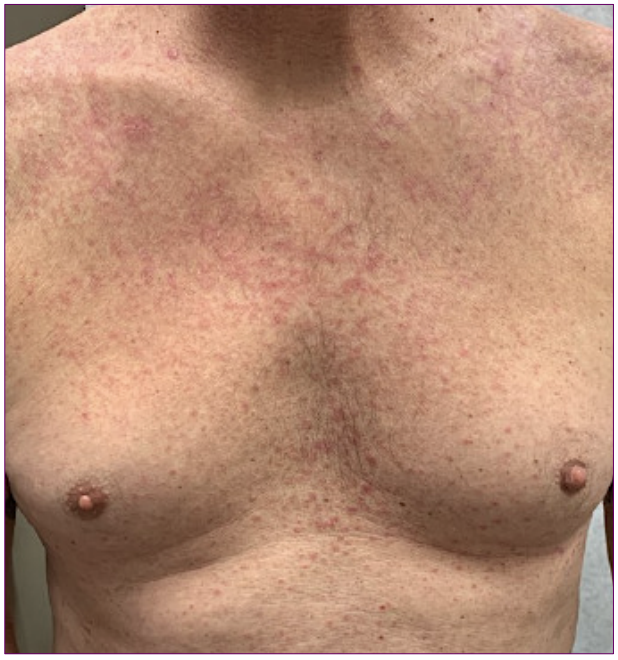
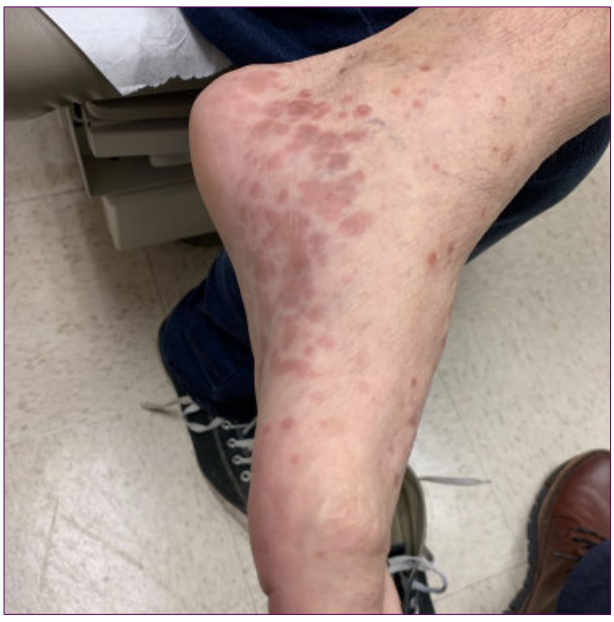


Figure 2. (B) Secondary Syphilis. The patient demonstrated a copper-colored maculopapular rash on his soles.



DISCUSSION

Syphilis presents in four consecutive clinical stages if left untreated: primary, secondary, latent, and tertiary infection. In clinical practice, one-third of patients present with concomitant symptoms and thus complicate the management of the disease.[1]

Tertiary syphilis is often mistakenly synonymous with neurosyphilis – a classic presentation of general paresis, tabes dorsalis, and the Argyll-Robertson pupil. The CDC's updated classifications on syphilis, however, have refrained from describing tertiary syphilis as a stage, but, rather, as a late clinical manifestation of the disease.[5] Therefore, neurosyphilis is not limited to a specific presentation or stage of syphilis. It is a broad term used to encompass a multitude of clinical syndromes.[5] These syndromes include aseptic syphilitic meningitis, meningovascular syphilis, parenchymatous syphilis, and gummatous neurosyphilis.[6] Before the presentation of full-fledged meningitis becomes evident, there is often a subacute syphilitic prodrome that presents with non-specific neurological symptoms, including headache, vision changes, vertigo, and psychological abnormalities.[1] The gold standard tests to diagnose neurosyphilis include a lumbar puncture and CSF examination. A CSF-VDRL or CSF FTA-ABS can also be done to establish the diagnosis of neurosyphilis; however, a non-reactive test should not exclude the diagnosis because the sensitivity and specificity of each test is variable.[3,7]

ASM is a subtype of meningovascular syphilis and occurs around six-months post-chancre. It often presents in concurrence with the generalized rash of secondary syphilis.[1] The meningeal syndrome is termed

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"aseptic" because there is no spirochetal CNS invasion; instead, the pathogenesis of ASM involves diffuse meningeal inflammation via a heightened humoral and cell-mediated immune response toward systemic spirochetes.[8] ASM was rare post-penicillin; however, the HIV epidemic and the co-infection of syphilis in HIV-positive patients has led to a re-emergence of the phenomenon.[9] Most recorded cases of ASM have involved HIV-positive patients and are the result of an inadequate penicillin dose to treat a past syphilis infection.

CONCLUSION

We present a patient with classic symptoms of primary and secondary syphilis, in addition to neurologic findings concerning for neurosyphilis, specifically ASM. ASM is less common in immunocompetent patients and may not always be considered in the differential diagnosis of patients presenting with primary or secondary syphilis. As physicians that are trained to recognize, evaluate, and treat the cutaneous manifestations of this disease, we should be well aware of ASM occurring most often in the secondary stage. We should also know how to screen for ASM by asking pertinent review of systems questions to ensure accurate and timely workup and treatment.

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