CLINICAL VIGNETTE

Two Cases of Syphilis

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Case #1

A 72-year-old male presented for a regular follow up visit. He suffers from paroxysmal supraventricular tachycardia, hypertension, dyslipidemia, and uncomplicated, non-insulin dependent type 2 diabetes mellitus. He complained of a brownish penile discharge that first appeared a few weeks prior. He noted the discharge after riding his bicycle. He reported that his last sexual partner was several months prior. He denied dysuria, hematuria, inflamed lymph nodes, fevers, or chills. Upon screening for sexually transmitted diseases, he was positive for RPR and the confirmatory TP-PA. The RPR titer was 1:2. The remainder of his STD panel including HIV, gonorrhea, and chlamydia, were negative. There were no previous RPR tests within the electronic health record but labs from a men's health study he has been enrolled in showed positive RPR tests dating back several years. He did not recall being notified of the results or undergoing treatment. Of note, he did recall testing positive for syphilis more than 10 years prior and completing a course of treatment. The diagnosis was most consistent with late latent stage syphilis. The intermittent penile discharge resolved spontaneously prior to treatment. He was treated with 2.4 million units of benzathine penicillin G intramuscularly for three consecutive weeks. Repeat serologic testing will be performed starting three months after the course of therapy.

Case #2

A 46-year-old male with hypertension, prediabetes, and recurrent oral herpes simplex presented for evaluation of a rash. He first noticed the rash on the palms of hands and soles of his feet a few weeks prior. It began as small, non-pruritic red bumps that slowly widened, coalesced, and desquamated. He denied any oral or anogenital ulcerations. Review of systems was positive for a mild sore throat of a few days' duration and negative for fevers or lymphadenopathy. Sexual history revealed a marriage to a male partner with an open sexual relationship with male partners only, the last of which took place two months prior and was unprotected. Of note, three months prior, he was started on Truvada for HIV pre-exposure prophylaxis (PrEP). Review of the Truvada prescribing information, indicates a roughly 10% incidence of rash. Labs returned with an RPR titer of 1:128 and a positive confirmatory TP-PA. He was diagnosed with secondary syphilis and treated with a single intramuscular injection of benzathine penicillin G. He will return for repeat blood work in 3-6 months to confirm eradication by a decreasing RPR titer.

Discussion

The existence of the syphilis has been known for centuries with reports of the disease dating back to the time of Christopher Columbus.[1] It was not until the development of penicillin that it could be successfully treated. Syphilis is caused by the spirochete organism *Treponema pallidum*, which resembles a corkscrew. It uses endoflagella for motility, and the primary and secondary modes of transmission are through sexual contact and transfer across the placenta respectively.[1] The transmissibility has been estimated from 18-80% with the chancre being the most contagious manifestation.[1] The pathogenesis for all stages of disease is thought to be from small and large vessel vasculitis producing necrosis and ulceration.[2]

Syphilis infection is characterized by stages. Primary syphilis is generally a non-painful ulceration that occurs at the initial site of infection. It is thought that microabrasions in the skin from sexual activity allow for penetration of the spirochete. The chancres can occur on the genitals, anus, and oral mucosa within days to weeks of infection and often go unnoticed by the patient increasing the risk of future transmission.[3] Secondary syphilis generally presents six to eight weeks after an untreated primary infection and manifests as a rash involving the face, trunk, palms, and soles of the feet. Additionally, patients can exhibit constitutional symptoms of fever, pharyngeal swelling, lymphadenitis, or in extreme cases, meningitis, ocular inflammation, and cranial nerve palsies. If the disease remains untreated, it will enter the latent stage in which the treponemes can be found in tissue and blood but do not produce symptoms. It is thought that the organism evades detection and immune response by antigenic variation of surface proteins.[3] The final stage of syphilis, tertiary, is characterized by neurologic, cardiovascular, and gummatous involvement and generally occurs years to decades after the initial infection. Late stage disease includes aortitis with aneurysmal dilatation and regurgitation, tabes dorsalis with pains, weakness, sensory deficits predominantly affecting the lower extremities, and paresis with progressive dementia and psychosis.

Syphilis testing and treatment have been the same for decades. It is recommended that all higher risk patients be screened annually regardless of symptoms, and all patients with any concerning findings or complaints be tested. The standard testing protocol is a nontreponemal test (RPR, VDRL) followed by a confirmatory treponemal test (FTA-ABS, TP-PA, TP-EIA). Nontreponemal tests have a relatively high rate of false positives and false negatives making them insufficient for diagnosis alone.[4] Treatment depends on the stage of the disease. Primary and secondary syphilis are treated with a single

intramuscular injection of 2.5 million units of benzathine penicillin G. This formulation of penicillin will stay therapeutic for up to three weeks but notably does not cross the blood brain barrier. Latent syphilis requires longer duration of treatment consisting of three doses of 2.5 million units of benzathine penicillin G at weekly intervals. CNS involvement requires aqueous penicillin G given intravenously to adequately penetrate the blood brain barrier. Penicillin allergic patients can be treated with doxycycline, tetracycline, ceftriaxone, azithromycin, or penicillin desensitization depending on the stage.

Is syphilis on the rise? A press release from the Centers for Disease Control and Prevention issued in November of 2015 indicated that sexually transmitted diseases have been on the rise for the last decade; primary syphilis is up more than 10%.[5] Certain populations are at higher risk including men who have sex with men, African American men and women, and HIV-positive individuals. The trend has brought attention and concern. The USPSTF made recommendations in a June 2016 issue of *JAMA* outlining the need for effective screening and that the benefits outweigh any potential harms. Hicks et al[6] mention possible explanations for the increase in infections: public health funding for prevention programs has declined and safer sexual practices including condom use among MSM have waned as treatment for HIV has improved, and the use of PrEP has risen. The good news is that a meaningful impact can be made with more outreach, better screening, and timely treatment.

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