Case Reports and Reviews

Case Report

Secondary Syphilis with Ocular Neurosyphilis and a Jarisch–Herxheimer Reaction to Treatment: A Case Report

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Abstract

A 33-year-old man was admitted to the hospital with a two-week history of fever, chills, arthralgias, malaise, anorexia, and a generalized non-pruritic erythematous rash. He also noted several days of blurring of vision in his right eye. Pertinent findings on physical examination included a temperature of 38° C, generalized lymphadenopathy, hepatosplenomegaly, and a maculopapular rash involving his face, trunk, and extremities, including his palms and soles. Ophthalmologic examination of his right eye revealed a posterior placoid chorioretinitis. Laboratory findings were notable for a lymphocytosis with increased Th17 and Th22 cells and markedly elevated liver enzymes. A liver biopsy showed bile canaliculi heavily colonized by spirochetes. Cerebrospinal fluid analysis revealed a mononuclear pleocytosis and a positive FTA-ABS test. Dark-field microscopy of a skin scaping was positive for Treponema pallidum. The patient was diagnosed with secondary syphilis with neurological involvement. He was treated with intravenous penicillin G for 14 days, during which he experienced a transient Jarisch–Herxheimer reaction. The patient was discharged in stable condition with plans for long-term serologic monitoring.

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Case Report

A 33-year-old man was admitted to the hospital with a history of fever, chills, arthralgias, malaise, anorexia, and a generalized nonpruritic maculopapular rash on his chest, abdomen, and palms and soles of 2 weeks duration. He also had "blurry" vision in his right eye of several days duration.

His admission physical examination revealed a temperature of 38.2°C, a blood pressure of 120/75 mm Hg, a regular pulse of 92 beats/minute, and a respiratory rate of 12 breaths/minute. He had a macular papular rash involving his face, trunk and extremities, including his palms and soles (Figure 1). Ophthalmic examination of his right eye revealed an acute posterior placoid chorioretinitis (Figure 2). His cervical, axillary and inguinal nodes were moderately enlarged and non-tender and his abdominal examination revealed hepatosplenomegaly. His joint and neurologic examinations were normal.

The patient's complete blood count showed a lymphocytosis with a relative increase in T helper (Th) type17 and Th22 cells. The CBC was otherwise normal. His liver studies revealed an alanine aminotransferase (ALT) of 359 U/L, an aspartate aminotransferase (AST) of 161 U/L, an alkaline phosphatase (ALP) of 580 U/L, and a gamma-glutamyl transpeptidase (GGT) of 883 U/L. His bilirubin levels were normal. On liver biopsy, the bile canaliculi were ladened with spirochetes. A lumbar puncture revealed a normal opening pressure, a mononuclear pleocytosis (20 monocytes per cumm), a negative Grams stain and a positive FTA-absorbed anti-treponema antibody test (FTAabs). Other laboratory studies, including a chest x-ray and urinalysis were within normal limits.

A dark field microscopic examination of a skin scraping from the sole of his right foot revealed Treponema pallidum, and a diagnosis of secondary syphilis with neurological involvement was made.

The patient was treated with intravenous penicillin G at a dose of 4 million units four times daily for 14 days. One day into treatment, he developed a Jarisch–Herxheimer reaction which resolved in several days without treatment. He was discharged from the hospital three weeks after admission with a planned revisit for monitoring of his FTA-abs 6, 12, 18, and 24 months post-treatment to confirm falling titers.

Discussion

Sometimes referred to as the "Great Imitator," secondary syphilis can involve any organ in the body and should be suspected in any sexually active person with unexplained findings [1]. Clinical manifestations may include mucous membrane erosions, skin rashes, condyloma latum, lymphadenopathy, arthritis, meningitis, encephalitis, stroke, cranial neuropathies,

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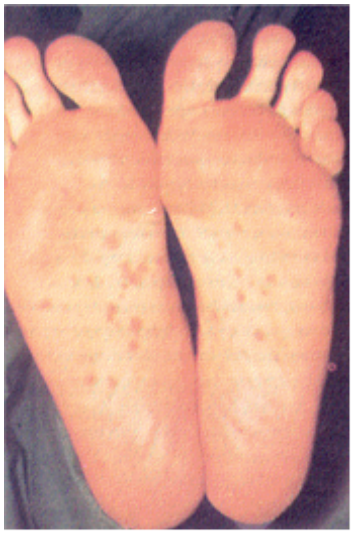

Figure 1. *Secondary syphilis*
The soles of the patient's feet show a characteristic maculopapular rash. This eruption begins as a macular mottling resembling measles, but the rash is more dusky. Typically, the rash is distributed over the chest, abdomen, and, of great diagnostic importance, on the palms and soles.

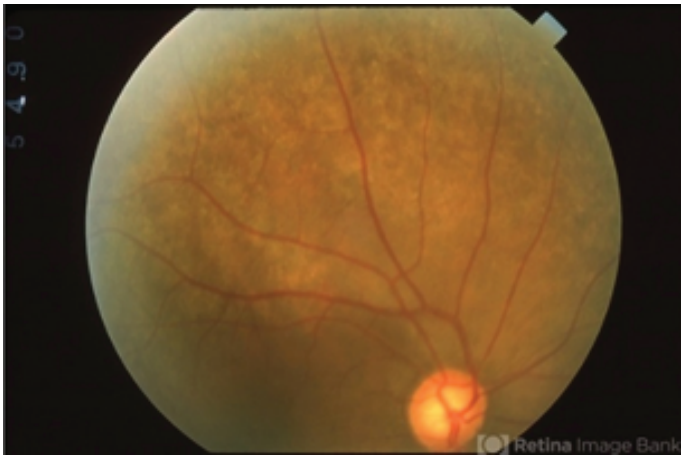

Figure 2. *Syphilitic chorioretinitis*
An AI generated picture of acute syphilitic posterior placoid chorio-retiinitis, a manifestation of neurosyphilis. The patients fundus, which was not photographed, was described by the ophthalmologist as being compatable with this disorder.

anterior uveitis, retinitis, glomerulonephritis, cholangiolytic hepatitis, splenitis, osteitis/periostitis, and alopecia [1-3].

As in the presented case, the diagnosis of secondary syphilis can be confirmed by a dark field examination of skin scrapings, noting that these lesions are highly contagious [4]. In all cases of suspected syphilis, the clinician should obtain a specific treponemal test such as the fluorescent treponemal antibody absorbed (FTA-abs) or the T. pallidum passive particle agglutination assay (TP-PA) [5]. It is important to recognize that the VDRL and the rapid plasma reagin (RPR) test are nonspecific, and do not measure anti-treponemal antibodies [5].

It is of interest that the patient's blood count showed an increase in Th17 and Th22 lymphocytes. Th17 cells are known for their production of interleukin-17, which plays a pivotal role in defending against extracellular pathogens but is also implicated in the pathogenesis of various autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis [6]. Similarly, Th22 cells produce interleukin-22 and have been associated with inflammatory conditions, including autoimmune thyroid disorders and certain skin diseases [6]. Importantly, elevated levels of these phenotypes have previously been reported in patients with secondary syphilis, suggesting their involvement in the disease's immunopathogenesis [7].

All patients with secondary syphilis should have a lumbar puncture with examination of the CSF for white blood cells, glucose, and protein, and for VDRL testing [8]. Keep in mind that HIV+ patients may have impaired antibody responses to T. pallidum [9].

Both primary and secondary syphilis are treated with 2.4 million units of benzathine penicillin G intramuscularly in a single dose [10]. Persons allergic to penicillin can be treated with doxycycline 100 mg twice daily or tetracycline 500 mg four times daily for 14 days [10].

CNS syphilis is treated with 3–4 million units of penicillin G given intravenously every 4 hours for 10–14 days [8,11]. Alternatively, patients can be given 2.4 million units of benzathine penicillin G intramuscularly every day along with probenecid 500 mg four times daily for 10–14 days [8]. An FTA-abs or TP-PA should be done at 6, 12, 18, and 24 months post-treatment to confirm falling titers (anti-treponema titers stay positive for life) [12].

The presented case developed a Jarish-Heimlich reaction (JHR) several hours after the institution of penicillin therapy. JHR is an acute inflammatory response that can occur within 24 hours of initiating antibiotic treatment for certain infections, notably those caused by spirochetes such as syphilis, Lyme disease, leptospirosis, and relapsing fever [13]. This reaction is believed to result from the rapid lysis of bacteria, leading to the release of endotoxin-like substances that trigger a systemic inflammatory response (release of pro-inflammatory cytokines, including tumor necrosis factor-alpha, interleukin-6, and interleukin-8) [14]. Clinical manifestations may include fever and chills, headache, muscle and joint pains, tachycardia, hypotension, tachypnea, flushing, and worsening of existing skin lesions [13,14]. These symptoms and signs are typically self-limiting, resolving within a few hours to 24 hours of onset [14]. Management of JHR is generally supportive, focusing on symptom relief: this may include antipyretics such as acetaminophen or nonsteroidal anti-inflammatory drugs [14].

Understanding JHR is crucial for healthcare providers and patients, as recognizing this reaction can prevent unnecessary discontinuation of effective antibiotic therapy and alleviate patient concerns regarding treatment-related adverse effects [14].

Conclusion

The presented case highlights the diverse manifestations of secondary syphilis, reinforcing its reputation as the "Great Imitator." His diagnosis was confirmed by dark field microscopy of his skin rash, a liver biopsy, an examination of his cerebral spinal fluid, and serologic testing. Initiation of intravenous penicillin G led to clinical improvement, although treatment was complicated by a transient Jarisch–Herxheimer reaction.

This case underscores the importance of maintaining a high index of suspicion for syphilis in patients with multisystem symptoms and signs in order to ensure a timely diagnosis and treatment.

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Conflict of Interest

The author declares no conflict of interest.

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