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Case Report

Guillain-Barré Syndrome with transient syphilis seropositivity: A case report

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Abstract

While confirmatory syphilis tests are highly specific, conflicting or transient results, as seen in this case, can pose significant diagnostic challenges. This report details the case of a 43-year-old female diagnosed with Guillain-Barré Syndrome (GBS) who subsequently exhibited transient serological reactivity for syphilis following intravenous immunoglobulin (IVIG) therapy. The patient presented with acute progressive weakness consistent with GBS, for which she received a five-day course of IVIG, leading to complete clinical recovery. Post-IVIG, screening revealed a weakly reactive Venereal Disease Research Laboratory (VDRL) test and a positive Treponema pallidum particle agglutination (TPPA) test. Subsequent repeat testing showed a non-reactive VDRL but persistently positive TPPA, followed by complete seroreversion of both tests two months later, confirming the absence of syphilis. This case underscores the crucial need for cautious interpretation of syphilis serology in patients who have recently received IVIG, highlighting the potential for false-positive results due to passive antibody transfer and emphasizing the importance of clinical correlation and serial testing to prevent misdiagnosis and unnecessary treatment.

Keywords: Guillain-Barré Syndrome, syphilis, VDRL, TPPA, IVIG

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Introduction

Guillain-Barré Syndrome (GBS) is an acute, post-infectious, immune-mediated polyneuropathy characterized by rapidly progressive ascending muscle weakness and areflexia. It is the most common cause of acute flaccid paralysis globally. The cornerstone of GBS treatment involves immunomodulatory therapies such as intravenous immunoglobulin (IVIG) or plasma exchange, both of which aim to mitigate the

immune attack on peripheral nerves (1). IVIG, a therapeutic preparation derived from pooled human plasma, contains a broad spectrum of antibodies that can modulate the immune system through various mechanisms, including neutralization of pathogenic autoantibodies, saturation of Fc receptors, and modulation of cytokine production (1).

Syphilis, caused by the spirochete Treponema pallidum, is a sexually transmitted infection with diverse clinical manifestations. Its diagnosis primarily relies on serological tests, which are broadly categorized into non-treponemal tests (e.g., VDRL, Rapid Plasma Reagin [RPR]) and treponemal-specific tests (e.g., TPPA, Fluorescent Treponemal Antibody Absorption [FTA-ABS]). Non-treponemal tests detect antibodies against cardiolipin, a lipid antigen released from damaged host cells and T. pallidum, and are useful for screening and monitoring treatment response due to their quantitative nature. Treponemal tests, on the other hand, detect antibodies specific to T. pallidum antigens and are used for confirmation, typically remaining positive for life even after successful treatment (2).

While these serological assays are highly specific, false-positive results can occur, leading to diagnostic confusion and potential overtreatment. Various conditions, including autoimmune diseases, infections, pregnancy, and vaccinations, have been reported to cause false-positive non-treponemal tests. However, false-positive treponemal tests are less common. This case report describes a unique presentation of transient syphilis seropositivity in a patient with GBS following IVIG administration, underscoring a less commonly recognized cause of diagnostic challenge in syphilis serology.

Case presentation

A previously healthy 43-year-old female presented to the neurology ward with a three-day history of progressive numbness and weakness of bilateral lower limbs. Her symptoms began in the lower limbs, characterized by a tingling sensation and difficulty walking, and gradually ascended to involve her fingertips. She denied any recent febrile illness, gastrointestinal symptoms, or other neurological complaints prior to the onset of her current symptoms. Her medical history was unremarkable, and she reported no known risk factors for sexually transmitted infections.

On admission, clinical examination revealed symmetric, flaccid weakness, predominantly affecting the distal muscles of both upper and lower extremities. Deep tendon reflexes were absent bilaterally in the ankles and knees, and diminished in the biceps and triceps. Sensory examination showed a stocking-glove distribution of paresthesia, with reduced sensation to light touch and pinprick in the distal limbs. Cranial nerves were intact, and there were no signs of autonomic dysfunction.

Given the clinical presentation, Guillain-Barré Syndrome was suspected. A lumbar puncture was performed, and cerebrospinal fluid (CSF) analysis revealed an elevated protein level of 0.8 g/L (normal range: 0.15-0.45 g/L) and a normal cell count (2 lymphocytes/µL). Electromyography (EMG) and nerve conduction studies (NCS) further supported the diagnosis, demonstrating features of acute motor neuropathy with resolving conduction blocks, consistent with the electrophysiological criteria for GBS.

Following the diagnosis, the patient promptly commenced treatment with intravenous immunoglobulin (IVIG) at a dose of 25 grams per day for a total of five consecutive days. The treatment was well-tolerated, and she showed remarkable clinical improvement, with gradual resolution of weakness and paresthesia. By the end of the IVIG course, her motor strength had significantly improved, and she was able to ambulate with minimal assistance. She achieved complete clinical recovery and was discharged home.

Five days following the completion of IVIG therapy, syphilis and HIV serological tests were performed. The Venereal Disease Research Laboratory (VDRL) test showed a weakly reactive result (1:1 dilution), and the Treponema pallidum particle agglutination (TPPA) test was positive. These results raised suspicion of possible syphilis infection. However, the patient remained completely asymptomatic, reported no recent high risk sexual exposures, and denied

any history of syphilis or its treatment. There were no physical signs suggestive of syphilis.

Given the discrepancy between the serological findings and the patient's clinical picture and history, further evaluation was deemed necessary. Ten days after the initial positive syphilis serology (and fifteen days post-IVIG), repeat VDRL and TPPA tests were conducted. At this point, the VDRL test had become non-reactive, while the TPPA test remained persistently positive. The treating clinicians, considering the recent IVIG administration and the patient's lack of risk factors or clinical signs of syphilis, suspected that the serological reactivity might be an IVIG-induced interference rather than a true infection. Consequently, specific anti-syphilis treatment was withheld.

To definitively rule out syphilis, the patient was advised to undergo further follow-up testing. Two months after the initial serological reactivity, repeat VDRL and TPPA tests were performed. This time, both the VDRL and TPPA tests were non-reactive, confirming the complete absence of syphilis infection. The transient nature of the seropositivity, coupled with the patient's clinical course, strongly supported the hypothesis of IVIG-induced false-positive syphilis serology.

Discussion

This case report highlights a critical diagnostic pitfall: the potential for intravenous immunoglobulin (IVIG) therapy to induce false-positive syphilis serological results. GBS is an autoimmune disorder where the immune system attacks the peripheral nerves. IVIG is a standard treatment for GBS, acting by modulating the immune response. It is a pooled product derived from the plasma of thousands of healthy donors, containing a wide array of antibodies (3).

The transient seroreactivity observed in our patient, characterized by an initial weakly reactive VDRL and positive TPPA, followed by seroreversion of both tests, is highly suggestive of passive antibody transfer. IVIG preparations can contain pre-existing antibodies against Treponema pallidum acquired from previously infected donors (2). When administered to a recipient, these antibodies can circulate in the patient's bloodstream, leading to transiently positive treponemal and, less commonly, non-treponemal tests. The VDRL, being a non-treponemal test, detects antibodies against cardiolipin, which can be elevated in various non-syphilitic conditions. However, a positive TPPA, a treponemal-specific test, is usually considered highly indicative of syphilis infection or past exposure. The simultaneous positivity of both tests initially suggested active syphilis.

However, several factors in this case pointed away from a true syphilis infection. Firstly, the patient was completely asymptomatic for syphilis and reported no risk factors for sexually transmitted infections. There were no clinical signs of primary (chancre) or secondary syphilis (rash, lymphadenopathy). Secondly, the rapid seroreversion of the VDRL to non-reactive within ten days, and the subsequent seroreversion of the TPPA to non-reactive within two months, is inconsistent with the typical serological course of untreated syphilis. In true syphilis, treponemal tests like TPPA usually remain positive for life, even after successful treatment, while non-treponemal tests like VDRL become non-reactive or show a significant decline in titer following treatment (2). The transient nature observed here is a hallmark of passively acquired antibodies, which are gradually cleared from the circulation over time.

This phenomenon has been previously documented. Constable et al. (2007) reported cases of positive serological tests for syphilis following IVIG administration, emphasizing the importance of considering this possibility in the context of IVIG therapy (2). The mechanism is attributed to the presence of anti-Treponema pallidum antibodies within the pooled plasma used to manufacture IVIG. These antibodies, though not indicative of active infection in the recipient, can bind to the antigens used in the serological assays, leading to false-positive results.

This case underscores the critical importance of clinical correlation when interpreting syphilis serological results, especially in patients who have recently received blood products or immunomodulatory therapies like IVIG. A positive syphilis serology in the absence of clinical signs, symptoms, or risk factors for

syphilis, particularly after IVIG, should prompt suspicion of a false-positive result. In such scenarios, serial testing is paramount. Monitoring the trend of VDRL titers and the persistence of TPPA positivity over time can help differentiate between true infection and passive antibody transfer. A decline in VDRL titers and eventual seroreversion of treponemal tests strongly supports the latter. Unnecessary antibiotic treatment for syphilis, which carries its own risks and costs, can thus be avoided.

Conclusion

This case report serves as an important reminder for clinicians regarding the potential for false-positive syphilis serological results following intravenous immunoglobulin (IVIG) therapy. The transient nature of VDRL and TPPA reactivity observed in our patient, coupled with the absence of clinical signs or risk factors for syphilis, strongly supports the hypothesis of passive antibody transfer from the IVIG product. Clinicians should exercise caution when interpreting syphilis serological tests in patients who have recently received IVIG, prioritize thorough clinical correlation, and consider repeat testing to confirm or rule out true infection. This approach is essential to prevent misdiagnosis, avoid unnecessary antibiotic administration, and ensure appropriate patient management.

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