Archives of Immunology and Allergy

ISSN: 2639-1848 | Volume 4, Issue 1, 2021

DOI: https://doi.org/10.22259/2639-1848.0401001

False Positive Syphilis Serology after IVIG Administration

Kaur, Kamalmeet MD, Sohal, Aalam MD, Sandhu, Sunny MD, Kelley, William DO

Department of Internal Medicine UCSF Fresno.

***Corresponding Author:** Sohal Aalam, Department of Internal Medicine UCSF Fresno, USA.*

Abstract

We report a case of a 44 year old female with Systemic Lupus Erythematosus (SLE) who received intravenous immunoglobulin (IVIG) and was subsequently found to have positive Immunoglobulin G (IgG) syphilis serology. The chronology of the positive serologies, with documented testing prior to IVIG administration being negative, suggests that the tests represent a false positive result secondary to the passive transfer of the immunoglobulin component. While the phenomenon of multiple positive serologies in a short time span after IVIG administration has been described, it is rarely recognized, and poses risks to the patient through unnecessary treatment.

Background

Our intention is to highlight the importance of recognizing the chronological pattern of positive serologies after IVIG administration to prevent improper diagnosis, unnecessary treatment, as well as distress to the patient and partner. In brief, IVIG is used widely to treat an array of autoimmune, hematological, and immunodeficient conditions. Given that it is derived from a pool of purified human plasma and consists predominantly of an IgG component, the chances of contracting a blood-borne infection have been known to be extremely low [1]. Though the phenomenon of IVIG causing positive serologies secondary to passive transfer of antibodies has been documented in medical literature, the duration of serologic positivity and physician awareness of this phenomena is poorly studied.

Case Presentation

This is a case of a 44 year old female with a history of systemic lupus erythematosus(SLE), class IV lupus nephritis, treated hepatitis C, and heart failure with reduced ejection fraction who presented with two days of altered mental status and agitation. Upon presentation, she was found to be uremic and anuric and underwent emergent hemodialysis without improvement in mentation. Her hospital course was complicated by persistent encephalopathy, renal failure, along with multi-organ failure and tenuous hemodynamics requiring recurrent ICU admissions.

Investigations

Given persistent encephalopathy and tenuous hemodynamics, an extensive infectious workup was performed including lumbar puncture, thoracentesis, fungal and bacterial blood cultures, respiratory cultures, COVID-19 PCR, tuberculosis quantiferon, coccidioidomycosis, Epstein Barr virus(EBV) DNA PCR, Cytomegalovirus(CMV) Antibody, Varicella Zoster PCR, Hepatitis antigen and antibody, human immunodeficiency virus, and Syphilis IgG, were negative. Autoimmune testing revealed elevated ANA (titer >1:1280, speckled pattern), elevated double-stranded DNA (74 IU/mL), positive anti-Smith antibody (93U/mL), and hypocomplementemia with C3 22.9 mg/dL and undetectable C4. Hematological workup was insignificant. Several CT and MRI studies of the head, neck, chest, abdomen, and pelvis were performed during the hospitalization and were inconclusive. Given concern for an underlying SLE flare, IVIG was initiated, and two days initiation of therapy she subsequently had stroke-like symptoms which prompted further workup. Syphilis IgG returned as reactive. Rapid plasma reagin and fluorescent treponemal antibody absorption were nonreactive, EBV DNA PCR (>750 U/mL), and CMV DNA PCR(11,744 U/mL) with the IgM remaining negative.

Differential Diagnosis

In this 44 year old female, given encephalopathy, lactic acidosis, renal failure, anemia, and thrombocytopenia, the differentials were kept broad and included uremia, steroid induced psychosis, meningitis, encephalitis, SLE flare, cerebrovascular accident, sepsis, TTP, HUS, and HLH.

Treatment

The patient was supported with broad spectrum antibiotics, high dose methylprednisolone, plasmapheresis, and rituximab. Given positive syphilis serology two days after IVIG administration with persistent encephalopathy, treatment was initiated with benzathine penicillin 2.4 million units once weekly for 3 weeks for presumed late latent syphilis.

Outcome And Follow Up

Due to persistence of multi-organ failure 38 days into admission, persistent encephalopathy, and tenuous hemodynamics, requiring multiple ICU admissions, the family decided to transition care to a comfort focused approach and did not want further aggressive measures.The patient subsequently succumbed to hypoxic respiratory failure attributed secondary to multifocal pneumonia.

Discussion

Given documented negative syphilis serologies prior to administration of IVIG, our patient likely acquired syphilis IgG from passive transfer from IVIG infusion. IVIG consists primarily of concentrated IgG, and this can potentially lead to passively acquired antibodies of syphilis IgG. From our literature review, although uncommon, there have been documented cases of passive transfer of antibodies to a variety of diseases, including syphilis [2,3] and hepatitis B [4,5]. The half life of IVIG is approximately 21 days [6], however no data exists regarding the length of time that passively transferred antibodies can remain positive in the recipient, which can pose a challenge to physicians when interpreting serologies after IVIG administration. . We found one other case report in our literature review that described a positive syphilis IgG titer after IVIG infusion, with repeat testing 11 weeks later showing negative titers [7]**.** Unfortunately, in our case the family initiated comfort care measures soon after the serologies resulted, and as a result we were not able to investigate for a subsequent negative IgG.

Given the negative syphilis serology before IVIG treatment, lack of risk factors, clinical symptoms, and negative history of prior syphilis infection, the chronology of syphilis IgG positivity two days after immunotherapy favors the diagnosis of a false positive result due to passive transfer of antibodies. This is further supported by negative confirmatory diagnostic workup with rapid plasma reagin and and treponemal antibody, with specificities of 98% and 97%[8] respectively, along with failure of a clinical response after a three week course of penicillin. Our case highlights that serologies for not only syphilis, but other infections should be interpreted carefully after administration of IVIG as false positives are known to occur and can be difficult to interpret. Physicians should take into account a patient's personal history with risk factors, symptoms, and chronology of the disease process and prior lab results before initiating therapy. If a false positive result is suspected, further confirmatory and more specific testing should be performed to clarify the diagnosis.

Learning Points

1. Do not initiate treatment for patient with positive IgG serologies post IVIG transfusion without clinical history of patient
2. Screening for syphilis should be done with specific tests such as TPPA(Treponema pallidum particle agglutination assay) or FTA-ABS rather than VDRL or RPR, which may have false positive results
3. Document for future providers the administration of IVIG and chronology of serologic tests

References

[1] "Intravenous Immunoglobulin (IVIG)." *Rheumatology.org*, www.rheumatology.org/I-Am-A/Patient-Caregiver/Treatments/Intravenous-Immunoglobulin-IVIG.

[2] Rossi KQ, Nickel JR, Wissel ME, et al. Passively acquired treponemal antibody from intravenous immunoglobulin therapy in a pregnant patient. *Arch Pathol Lab Med*. 2002;126(10):1237-1238. doi:10.1043/0003-9985(2002)126<1237:PATAFI>2.0.CO;2

[3] Hui EP. Immunoglobulin therapy and passive transfer of anti-HBc: too often forgotten. *Lancet Haematol*. 2018;5(10):e437-e438. doi:10.1016/S2352-3026(18)30158-3i

[4] Lu H, Lok AS, Warneke CL, et al. Passive transfer of anti-HBc after intravenous immunoglobulin administration in patients with cancer: a retrospective chart review. *Lancet Haematol*. 2018;5(10):e474-e478. doi:10.1016/S2352-3026(18)30152-2

[5] Lünemann, J. D., Quast, I., & Dalakas, M. C. (2015). *Efficacy of Intravenous Immunoglobulin in Neurological Diseases. Neurotherapeutics, 13(1), 34–46.* doi:10.1007/s13311-015-0391-5

[6] Hanson, Kimberly E, et al. "2031. False-Positive Serologic Results Attributable to IVIG Therapy." *Open Forum Infectious Diseases*, Oxford University Press, 26 Nov. 2018, www.ncbi.nlm.nih.gov/pmc/articles/PMC6253139/#:~:text=Use%20of%20IVIG%20has%20increased,positive%20and%20false%2Dnegative%20results.

[7] Cantor, Amy. "Table 3, Sensitivity and Specificity of Commonly Used Syphilis Tests* - Screening for Syphilis in Nonpregnant Adolescents and Adults - NCBI Bookshelf." *Screening for Syphilis in Nonpregnant Adolescents and Adults: Systematic Review to Update the 2004 U.S. Preventive Services Task Force Recommendation [Internet].*, U.S. National Library of Medicine, www.ncbi.nlm.nih.gov/books/NBK368468/table/ch1.t3/.

[8] .Constable, S. A., Parry, C. M., Enevoldson, T. P.,et al (2006). *Positive serological tests for syphilis and administration of intravenous immunoglobulin. Sexually Transmitted Infections, 83(1), 57–58.* doi:10.1136/sti.2006.020503

Citation: **Kaur, Kamalmeet, Sohal, Aalam, Sandhu, Sunny, Kelley, William.** *False Positive Syphilis Serology after IVIG Administration. Archives of Immunology and Allergy. 2021; 4(1): 1-3. DOI: https://doi.org/10.22259/2639-1848.0401001*