Acute Nephrotic Syndrome and Otosyphilis

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ABSTRACT

Syphilis, also known as the "the great masquerader," is a re-emerging infectious disease in the Western world, and may present with various signs and symptoms, making it difficult to distinguish from other diseases. Nephrotic syndrome due to syphilis has been rarely reported in modern times. Here, we describe a young male with acute hearing loss and peripheral edema, found to have acute nephrotic syndrome in the setting of otosyphilis. Given increasing incidence of syphilis, physicians must remain alert to syphilis as a possible cause of nephrotic syndrome.

KEYWORDS: syphilis, neurosyphilis, nephrotic syndrome, otosyphilis, membranous glomerulonephritis

INTRODUCTION

Nephrotic syndrome is characterized by overt proteinuria, hypoalbuminemia, peripheral edema, and hyperlipidemia. Often, the etiology is primary or idiopathic. Rarely, a secondary underlying cause such as syphilis can be identified, which simplifies management. We describe a young immunocompetent male who presented with acute hearing loss and peripheral edema, diagnosed to have acute nephrotic syndrome due to otosyphilis.

CASE PRESENTATION

A 30-year-old male presented to the hospital with acute hearing loss in his left ear beginning 4 weeks prior to presentation. He also endorsed having fevers, chills, leg swelling and worsening malaise over the past few weeks. He was empirically treated by his primary care provider with valcyclovir and steroids without regaining hearing. On the day of admission, he could not begin his usual workout routine at the gym due to shortness of breath and left anterior chest pain and presented to the emergency department for further evaluation.

The patient appeared well upon arrival. Additional history revealed intermittent vertigo, report of an oral ulcer that had resolved by admission, as well as a skin rash. He reported having had his COVID-19 vaccine. The patient reported having sex with one male partner and until several months ago had used emtricitabine/tenofovir for HIV prevention. He denied chronic NSAIDs use, use of herbal medications or any other medications, and reported drinking beer and using marijuana occasionally. He had no recent sick contacts, insect bites or contact with children.

On admission, the patient's vital signs were normal. Physical exam was remarkable for macular skin lesions on the palms and soles, with moderate desquamation on palms. He also had generalized anasarca. Concern for syphilis was raised and labs were positive for RPR 1:128, and a positive Treponema Antibody. Liver panel revealed transaminitis with elevated AST 50 IU/L, ALT 103IU/L. Lipid panel showed LDL of 201 (70-129 mg/dl). HIV, Lyme antibodies, hepatitis panel and respiratory pathogen panel were negative. Urine studies showed 4.8g proteinuria in 24h and microalbumin 2.9g in 24h. Lumbar puncture was performed to rule out neurosyphilis. CSF showed 13 nucleated cells, 47% lymphocytes and 47% protein. Renal biopsy was deferred. Given suspicion for neuro/otosyphilis, he was started on continuous infusion of penicillin G for 2 weeks with clinical improvement. For nephrotic syndrome, he was started on aspirin 325mg daily, lisinopril 20mg daily, and furosemide. Dietary modification was recommended for hyperlipidemia. He was discharged with infectious disease and nephrology follow-up.

DISCUSSION

The association between syphilis and nephrotic syndrome has been previously recognized. In a series of over 1,000 patients with syphilis, Herman and Marr in 1935 described 7.1% patients with proteinuria and 0.28% patients with nephrotic syndrome.[1] During the antibiotic era, there have only been a handful of cases, proving this to be an increasingly rare occurrence.[2-9] To our knowledge, this is the first reported case of acute nephrotic syndrome associated with otosyphilis.

Syphilis is caused by infection with Treponema pallidum. It is a common sexually transmitted disease, with rising prevalence in the last few years. If left untreated, the disease may progress through four stages of infection (primary, secondary, latent, tertiary). *T. pallidum* may affect the eighth cranial nerve within or outside the CSF space, the temporal bone, or the cochleovestibular apparatus. Serological tests for syphilis (treponemal and non-treponemal) remain the

mainstay of diagnosis. Otosyphilis is diagnosed and treated similarly to neurosyphilis. To diagnose neurosyphilis, the patient must have CNS signs or symptoms, serologic evidence for infection, plus one of the following: positive CSF-VDRL, increased CSF protein (>40 mg/dl), increased CSF WBC count (>5 mononuclear cells/uL). Parenteral penicillin is the treatment of choice for all stages of syphilis. Adjunctive steroids are sometimes recommended if hearing loss does not improve after antibiotics.[10,11] For patients who have history of anaphylaxis with use of penicillin, doxycycline can be used if they opt against undergoing desensitization.

In adults younger than 60 years, membranous glomerulonephritis (MGN) is the most common cause of nephrotic syndrome. MGN is characterized by immune complex formation beneath podocytes on the subepithelial surface of the glomerular basement membrane, resulting in podocyte detachment and increased glomerular permeability. MGN can be idiopathic or due to infection, malignancy, autoimmune causes, medications, or other etiologies.[12] Most cases are idiopathic, and these tend to be associated with phospholipase A2 receptor antibodies, the levels of which are used to predict disease course and guide therapeutic management. The exact mechanism for syphilis to trigger immune complex formation and MGN is unknown. Gamble and Reardan demonstrated the presence of anti-treponemal antibody within the immune complex deposits in the glomerulus.[13] In another report, treponemal antigen was demonstrated in the glomeruli of two patients with nephrotic syndrome using immunofluorescence studies.[14]

Treatment is often supportive, and includes salt and water restriction, ACE-inhibitors, loop diuretics, and statins. Steroids or immunosuppressants are the mainstay therapy when etiology is idiopathic or primary. Most patients with nephrotic syndrome and syphilis show recovery and resolution of illness within months after treatment.[15] Although proof is not possible in our case, clinical improvement following treatment with penicillin is consistent with a causal relationship.

Otosyphilis is a less recognized complication of syphilis that can lead to irreversible hearing loss. Physicians must remain vigilant about the possibility of syphilis as a cause of the nephrotic syndrome. Early diagnosis can be helpful in avoiding inappropriate testing and use of immunosuppressants. Furthermore, this will be helpful in preventing relapse of the disease and irreversible hearing loss.

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