Membranous Glomerulonephritis as an Uncommon Presentation of Secondary Syphilis: A Reminder on Therapeutic Decision-Making in Clinical Practice

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Abstract
Membranous glomerulonephritis is one of the common causes of nephrotic syndrome in the adult population. It is idiopathic in the majority of patients, but the secondary forms can be seen in the setting of autoimmune disease, cancer, infection, and following exposure to certain medications. However, subclinical syphilis-related membranous nephropathy remains a particularly rare clinicopathologic entity in modern times. In this article, we chronicle an interesting case of latent syphilis masquerading as membranous glomerulonephritis, which resolved with benzathine penicillin without requiring immunosuppressive treatment. We further supplement this paper with a concise review of the relevant literature that delineates the utility of appropriate antibiotic therapy in the management of luetic membranous nephropathy. Clinicians should remain cognizant of secondary syphilis while evaluating patients for possible glomerulonephritis or those presenting with proteinuria. Additionally, patients with hepatitis B, hepatitis C, and human immunodeficiency virus infections are not infrequently coinfected with Treponema pallidum. Therefore, a high index of suspicion for systemic manifestations of syphilis such as nephrotic syndrome is warranted in the setting of a coinfection. Prompt diagnosis and treatment of syphilis may result in resolution of proteinuria, without the need for standard immunosuppressive therapy commonly used in clinical practice.

Keywords
membranous glomerulonephritis, secondary syphilis, nephrotic syndrome, proteinuria, unique presentation, therapeutic decision-making, antibiotic treatment

Introduction
While the systemic manifestations of a syphilis infection are increasingly reported, cases detailing luetic membranous glomerulonephritis remain relatively uncommon.1,2 Syphilis-associated membranous nephropathy presents as a nephrotic syndrome with varying degrees of proteinuria.3 It is currently understood that the antibody response mounted against Treponema pallidum results in the deposition of immunoglobulin G (IgG) in the renal mesangium, which in turn heralds the onset of nephropathy.3 Even though merely a handful of cases of luetic membranous glomerulonephritis are documented in the past 2 decades, this association can have a multitude of clinical implications.4 For instance, syphilis is seldom seen today in the United States, with most of the cases detected primarily in human immunodeficiency virus (HIV)-positive individuals.5 As hepatitis B, hepatitis C, and HIV infections can also orchestrate membranous nephropathy, this great “imitator” might therefore evade detection.6,7 Consequently, the membranous nephropathy may wrongly be attributed to hepatitis or HIV itself in patients who are simultaneously positive for these viral infections and syphilis. Therefore, a high index of clinical suspicion is warranted for precise etiology establishment, especially in patients with a coinfection.

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Received July 22, 2020. Revised September 1, 2020. Accepted September 19, 2020.

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In luetic nephropathy, massive proteinuria is often observed, and treatment with an appropriate antibiotic is required. However, in clinical practice, specific immunosuppressive regimens are commonly commenced to thwart the pathogenesis underlying the membranous nephropathy. Clinicians should consider the possibility of deterioration with corticosteroid treatment in cases with subclinical syphilis-related nephrotic syndrome. Thus, self-confined membranous nephropathy secondary to syphilis warrants due attention from nephrologists and venereal experts as the treatment approach is different in such cases. This leads us to the general consensus that for the prompt management and resolution of the luetic nephropathy precipitating proteinuria, a timely diagnosis and appropriate intervention is imperative. We herein describe the case of an HIV-positive patient who presented with subclinical syphilis and concomitant early-stage membranous glomerulonephritis. The nephropathy was self-contained, and resolved with syphilis treatment, without any conventional immunosuppressive therapy. Furthermore, we review the medical literature regarding this association, focusing on the therapeutic decision-making in these patients. It is pertinent to highlight this particular duo because it may represent a diagnostic and therapeutic dilemma and more such cases can be encountered due to the reemergence of syphilis worldwide.

Case Presentation
This study involves a 21-year-old African-American male who was admitted to our medical center with the complaints of epigastric pain, nausea, vomiting, and diarrhea for 1 week. His medical history was significant for HIV, which was treated with highly active antiretroviral therapy. Review of systems was unremarkable for abnormalities. Sexual history was positive for a single male partner of less than a year. There was no history of previous renal disease, weight loss, arthralgia, dysuria, gross hematuria, or fever. He denied prior gastrointestinal disorders, upper respiratory tract infections, systemic allergies, and malignancies. He was a non-smoker, nonalcoholic, and drug-free. His family history was negative for cancer and renal disorders. At presentation, the patient was afebrile and normotensive. Physical examination revealed a maculopapular rash on the trunk. A few small axillary and inguinal lymph nodes were palpable, with epigastric and perianal tenderness. In addition, 1+ edema was noted in his legs.

Investigations
Laboratory evaluation showed serum creatinine 7.4 mg/dL (baseline = 1.1 mg/dL) and blood urea nitrogen 53 mg/dL (7-20 mg/dL). Serum concentrations of electrolytes, transaminases, alkaline phosphatase, bilirubin, amylase, and lipase were normal. Total serum protein was initially 8.0 g/L (6.8-8.3 g/dL), with a serum albumin level of 2.4 g/dL (3.4-5.4 g/dL). Urinalysis showed trace ketones, 4+ proteins, 2+ blood, whereas it was negative for nitrite and bacteria. Urine microscopy and culture were unremarkable. Urine protein/creatinine ratio was 7.3 g/gCre (<0.2 g/gCre). Infectious profile was positive for HIV with a viral load of 1917 copies/mL and CD4 count at 306 cells/mm³ (500-1500 cells/mm³). His rapid plasma reagin test was strongly positive. Serological test results for hepatitis C virus and hepatitis B virus turned out negative.

Immunologic testing including, antibodies to phospholipase A receptors (anti-PLA2R), cytoplasmic-antineutrophil cytoplasm antibodies (c-ANCA), perinuclear-ANCA (p-ANCA), myeloperoxidase-ANCA (MPO-ANCA), and antiprotease 3-ANCA (PR3-ANCA) were negative. Furthermore, rheumatoid factor, anti-glomerular basement membrane, anti–Sjögren’s-syndrome–related antigen A, anti-apoptosis signal-regulating kinase 1, anti–double stranded DNA, anti-smooth muscle, anti-streptolysin O titer, and anti-ribonucleoprotein particles antibodies were negative. Complement levels, thyroid function tests, lipid and coagulation profiles, and serum and urine protein electrophoresis were all within normal limits. Renal ultrasound showed no evidence of hydronephrosis, stones, or obstruction. Computed tomography scan of the abdomen without contrast revealed diffuse lymphadenopathy, fat stranding, edema in the perirectal area, generalized anasarca, and a small amount of ascites.

Renal Biopsy
Subsequently, an uneventful percutaneous renal biopsy was performed. The glomeruli had segmental, vague glomerular capillary wall “spikes” on the periodic acid–Schiff stain. The interstitium had a patchy plasmacytic infiltrate. Direct immunofluorescence with routine panel of antibodies (albumin, IgG, IgA, IgM, C1q, C3, fibrinogen, and kappa and lambda light chains) showed granular capillary staining with IgG, C3, and kappa and lambda light chains. On electron microscopy, numerous small subepithelial electron-dense immune-complex deposits were noted.

Diagnosis
The glomerular findings were consistent with an early-stage membranous glomerulonephritis. The interstitial plasmacytic infiltrate was not typical of an idiopathic membranous nephropathy. Given the HIV-positive status of the patient, HIV-associated nephropathy was initially considered plausible. However, a spirochete (treponemal) immunohistochemical stain was strongly positive for focal spirochete aggregates, within the areas of plasma cell-rich interstitial infiltrates, supporting the diagnosis of secondary membranous nephropathy following subclinical syphilis.
Treatment and Clinical Outcome

The patient was immediately informed about his disease and was educated about the clinical importance of contact tracing. Prompt testing and treatment of his current and previous partners were recommended. He was then initiated on 3 weekly doses of intramuscular benzathine penicillin G 2.4 million units. His clinical symptoms resolved with conservative management and he was discharged home in a stable condition. At the 1-week follow-up, a significant improvement was evident in renal function with no treatment-related complications. At the outpatient clinic follow-up 4 weeks later, serum creatinine had returned to 1 mg/dL and the proteinuria had completely resolved as evidenced by a urine protein/creatinine ratio of 0.03 g/gCre. The patient demonstrated sustained recovery at the follow-up visit after 4 months (Figure 1).

Discussion

Membranous glomerulonephritis is an immune-mediated nephrotic syndrome that has the potential to progress to chronic kidney disease. It can either be primary or secondary as determined by the particular etiology and underlying pathogenesis. It is believed that 75% of the cases of membranous nephropathy are idiopathic. In primary disease, M-type PLA2R, which are routinely found on podocytes, are implicated. Notably, the etiology underlying secondary membranous glomerulonephritis is observed to be more diverse. Autoimmune diseases (systemic lupus erythematosus, rheumatoid arthritis, etc), infections (hepatitis B and C, and HIV), various cancers (lung cancer, prostate cancer, and hematological malignancies), and certain medications can be the underlying etiologies of secondary membranous nephropathy. Syphilis has traditionally been termed the great mimicker owing to the potential of this disease to elicit a plethora of diverse systemic ramifications. Of these systemic manifestations, luetic membranous nephropathy remains one of the less often encountered pathologies. In the United States, it is reported that the prevalence of primary and secondary syphilis hovers around 9.5 per 100 000 populations. Despite its resurgence in the Western world, syphilis is not routinely included in the differential diagnosis of membranous nephropathy.

We conducted a review of the English-language literature regarding secondary syphilis-related membranous nephropathy. The data on patient demographics, clinical characteristics, serum creatinine and proteinuria parameters, biopsy status, syphilis testing, and management were collected and summarized (Table 1). The mean age of patients was 22.16 years (range = 18-66 years). A clear gender predominance was noted, with 16 male and 2 female patients. Although a fixed geographical distribution is often difficult to ascertain, most patients were African American or Caucasians. Subclinical syphilis-related membranous nephropathy may present with a variety of symptoms, including facial and peripheral edema, maculopapular rash, lymphadenopathy, night sweating, unexplained weight gain, and/or gastrointestinal abnormalities. Due to vague clinical symptomatology, the luetic nephropathy can possibly be incorrectly regarded as renal manifestation of other systemic diseases. Notably,
Table 1. General Characteristics of Cases of Membranous Glomerulonephritis Secondary to Subclinical Syphilis.

| Authors/year | Country       | Age (years)/gender | Clinical presentation                                                                 | Comorbid conditions                          | Proteinuria (g/24 hours) | Serum creatinine (mg/dL) | Associated findings                                                                 | Biopsy-proven MGN | Syphilis diagnosis | Treatment                                                                 | Clinical outcome |
|--------------|---------------|--------------------|---------------------------------------------------------------------------------------|----------------------------------------------|-------------------------|--------------------------|-----------------------------------------------------------------------------------|--------------------|-------------------|---------------------------------------------------------------------------|------------------|
| Tang et al19989 | USA           | 54/male            | Postprandial vomiting and vague upper abdominal discomfort                              | DM, syphilitic hepatitis, gallstones         | 10                      | Not reported             | Jaundice, maculopapular rash, lymphadenopathy, marked pitting edema up to the knees, abnormal LFTs | Yes                | VDRL titer > 1: 2048, TPHA titer > 1: 2040, FTA-ABS IgG and IgM +          | Procaine penicillin IM 600 000 IU daily for 14 days | Recovered         |
| Hunte et al1993 | USA           | 21/male            | Facial and peripheral edema, weight gain (15 lbs), skin rash, polyuria, polydipsia, myalgia, headaches, and sore throat | DM, HTN                                      | > 3                     | 1.2                      | 3+/4+ pretibial, pedal and hand pitting edema, glycosuria without acetonuria, and nonpruritic eruption over the forearms, trunk, and feet | Yes                | RPR markedly elevated 1:1024, FTA-ABS 4+                                | Benzathine penicillin 2.4 million U IM weekly for 3 weeks | Recovered         |
| Soehardy et al2006 | Malaysia      | 31/male            | Facial puffiness and bilateral leg swelling                                           | Unprotected sex                              | 9.7                     | 0.85                     | Sacral edema, reduced urine output, and frothy urine                               | Yes                | VDRL 1:32, syphilis IgG and IgM +                                      | Benzathine penicillin 2.4 million U IM weekly for 3 weeks | Recovered         |
| Gooskens et al2008 | The Netherlands | 58/male            | Intermittent bloody stools, abdominal pain, and chronic diarrhea                      | Unprotected sex, Chlamydia trachomatis urethritis, and syphilitic GI symptoms               | 3.78                    | <1.2                     | Discrete skin rash on proximal upper extremities                                    | Yes                | VDRL titer 1:64, TPHA+, and Treponema pallidum immunoblot +              | Benzathine penicillin G 2.4 million U IM weekly for 3 weeks  | Recovered         |
| Satoskar et al2010 | USA           | 18/female          | Nausea and vomiting                                                                    | Gynecological bleeding and infantile thoracic neuroblastoma                               | > 3                     | 0.9                      | Facial (3+) and symmetrical lower-extremity (1+) edema, no rash                    | Yes                | RPR +, FTA-, and ABS+                                               | Corticosteroid, mycophenolate mofetil, high-dose, IM penicillin in 3 weekly injections | Recovered         |
| Havill et al2011 | USA           | 20/male            | Pain in the right flank                                                                | HIV infection                                | 4.8                     | 5.2                      | A diffuse maculopapular rash involving trunk, extremities, palms and soles, and hepatosplenomegaly | Yes                | RPR titer 1:128, Treponema pallidum IgM and IgG +                       | Benzathine penicillin 2.4 million U IM                      | Recovered         |
| Authors/year       | Country       | Age (years)/gender | Clinical presentation                                                                 | Comorbid conditions                           | Proteinuria (g/24 hours) | Serum creatinine (mg/dL) | Associated findings                                                                 | Biopsy-proven MGN | Syphilis diagnosis |Treatment                      | Clinical outcome |
|-------------------|---------------|--------------------|---------------------------------------------------------------------------------------|-----------------------------------------------|--------------------------|-------------------------|--------------------------------------------------------------------------------------|------------------|-------------------|---------------------------------|------------------|
| Handoko et al16/2011 | The Netherlands | Late 30s/male     | Malaise, myalgia, headache, sore throat, lymphadenopathy, and night sweating           | Prior anabolic steroid use as fitness regimen | 16.8                     | 1.3                     | Weight gain (10 lbs in 1 week), pedal edema, swollen eyelids, non-itching, and painless “rash” on his glans penis | Yes              | VDRL titer of 1:64, Treponema pallidum CLIA and IgG blot+ | Benzathine penicillin 2.4 million U IM | Recovered         |
| Canney et al20/2011 | Australia     | 41/male            | Drenching night sweats, widespread nonpruritic rash, and facial edema                   | Syphilitic hepatitis and unprotected sex      | 21.96                    | 1.4                     | Pitting lower limb and sacral edema, frothy urine, hepatomegaly, and elevated LFTs    | Yes              | RPR 1:128           | Intravenous benzylpenicillin (1.8 g every 4 hours) | Recovered         |
| Mora Mora et al25/2011 | Spain        | 27/male            | Edema of the lower limbs and genitals, and decreased diuresis                          | Cryptorchidism, adenoidectomy, and amygdalactomy| 13.4                     | 1.73                    | Slight pharyngodynia, right groin induration, penile ulcer, and maculopapular lesions on trunk and extremities | Yes              | RPR 1:32, FTA-ABS+ | Benzathine penicillin G 2.4 million U IM | Recovered         |
| Hannawi et al29/2012 | USA          | 24/male            | Progressive bilateral lower extremity edema                                            | Tonsillectomy                                 | 0.76                     | 1.1                     | Weight gain (8 lbs), dyspnea, painless chancre on genitals, and small hyperpigmented leg macules | Yes              | RPR 1:512, TP-PA+  | Benzathine penicillin G 2.4 million U IM 3 weekly injections | Recovered         |
| Ishiwatari et al21/2012 | Japan        | 66/male            | Peripheral edema and increasing general fatigue                                       | Syphilitic hepatitis                          | 19 g                      | 2.15                    | Penile swelling and induration, sore throat, general fatigue, and a nonpruritic eruption on the arms and back | Yes              | RPR 1:128, TPPHA 1:41.2 | Amoxicillin for 14 days | Recovered         |
| Cheng et al27/2015 | Taiwan        | 23/male            | Pitting leg edema and glans penis ulcer                                               | Drug abuse, unprotected sex, and HIV infection | 13.8                     | 0.81                    | Skin rash on extremities                                                              | Yes              | RPR: 4144 RU, TPPHA: 2310 TU | Intravenous benzathine penicillin | Recovered         |
| Noutong et al27/2016 | USA           | 51/male            | Lower back pain                                                                        | HTN and seizure disorder                      | 4.9                      | 6.09                    | Red lesions on the mucous membrane of soft palate and maculopapular rashes on the palms and the soles | Yes              | RPR 1:512, FTA-ABS+ | Penicillin G 2.4 million U IM | Recovered         |
| Authors/year | Country | Age (years)/gender | Clinical presentation | Comorbid conditions | Proteinuria (g/24 hours) | Serum creatinine (mg/dL) | Associated findings | Biopsy-proven MGN | Syphilis diagnosis | Treatment | Clinical outcome |
|--------------|---------|--------------------|----------------------|--------------------|------------------------|------------------------|------------------------|------------------|------------------|------------|-----------------|
| Makker et al.22/2016 | USA | 51/male | Abdominal pain and bright red blood per rectum | DM, osteoarthritis, drug abuse, diastolic dysfunction, and luetic hepatitis | 5.9 | 0.7 | Nonbilious vomiting, copper-colored papules and macules on the body, and mild bilateral pitting pedal edema | Yes | RPR titer 1:1024 | Benzathine penicillin G 2.4 million U IM | Recovered |
| Fernandes et al.26/2017 | Portugal | 29/female | Small erythematous papules on the trunk and upper limbs, lower limb edema, and inguinal adenopathy | Not reported | 5.3 | Not reported | Hypoaalbuminemia (1.1 g/dL), HCL (total cholesterol 363 mg/dL, LDL 252 mg/dL, triglycerides 305 mg/dL) | Yes | VDRL titer was 1/64; TPHA titer was 1/2560 | Penicillin 2.4 million U IM | Recovered |
| Zhang et al.23/2018 | USA | 37/male | Rectal pain, nausea, vomiting, dark urine, and nonbloody diarrhea | HIV infection, depression, and syphilitic hepatitis | 8.2 | 1.4 | Rectal ulcer, bilateral inguinal lymphadenopathy, and abnormal LFTs | Yes | RPR titer 1:16, FTA-ABS+ | Benzathine penicillin 2400000 IU once per week for 3 weeks | Recovered |
| Sciaudone et al.39/2019 | USA | 21/male | Myalgias, fever, nausea, and nonbilious vomiting | HIV infection and unprotected sex | >3 | 7.1 | Dull, crampy abdominal pain, and dark urine | Yes | RPR titer 1:256, treponemal antigen+ | Benzathine penicillin G 2.4 million U IM | Recovered |
| Sciaudone et al.39/2019 | USA | 35/male | Abdominal pain, nausea, periodic emesis, and right upper quadrant and right flank pain | HIV infection | >3 | 3.2 | Diffuse papular, nonpruritic, nonmender rash, and mildly elevated LFTs | Yes | RPR titer 1:128, treponemal antigen+ | Benzathine penicillin G 2.4 million U IM | Recovered |
| The present report | USA | 21/male | Epigastric pain, nausea, vomiting, and diarrhea | HIV infection | 7.3 | 7.4 | Maculopapular rash on trunk, a few small palpable axillary and inguinal lymph nodes, and 1+ edema in legs | Yes | Strongly positive RPR | IM penicillin G benzathine 2.4 million U in 3 doses over 3 weeks | Recovered |

Abbreviations: MGN, membranous glomerulonephritis; DM, diabetes mellitus; LFTs, liver function tests; VDRL test, venereal disease research laboratory test; TPHA, Treponema pallidum particle agglutination assay; FTA-ABS, fluorescent treponemal antibody-absorption test; Ig, immunoglobulin; IM, intramuscular; HTN, hypertension; RPR, rapid plasma reagin; GI, gastrointestinal; CLIA, chemiluminescence immunoassay; HIV, human immunodeficiency virus; TP-PA, Treponema pallidum particle agglutination; HCL, hypercholesterolemia; LDL, low-density lipoprotein.
patients with syphilitic nephropathy may also concurrently develop acute hepatitis. Given the possibility of deranged hepatic function, liver function testing is important. Furthermore, a detailed clinical history, especially information regarding safer sex practices, is pertinent in these patients. Laboratory evaluation shows significant proteinuria as well as elevations in serum creatinine levels in most cases. However, a few patients may also have baseline serum creatinine levels with no proteinuria at the initial presentation. Additionally, other abnormalities such as hypalbuminemia or abnormal lipid profile should also be considered. In patients with secondary membranous glomerulonephritis, screening and confirmatory serological workup for syphilis should be mandated. An apt and prompt discernment of the etiology underlying proteinuria is therefore pivotal in governing the treatment regimens.

In terms of biopsy findings, membranous nephropathy is often characterized by diffuse capillary and basement membrane thickening. Immunofluorescence often divulges a granular appearance due to immune-complex deposits. On electron microscopy, a “spike and dome” appearance, which represents subepithelial immune-complex deposition, can be appreciated. In patients with syphilis infection, anti-treponemal IgG antibodies are produced and subsequently deposit in the subepithelial layer of the glomerular basement membrane. In syphilis-induced nephropathy, C3 complement levels also rise in conjunction with IgG and IgM antibodies. Therefore, luetic membranous nephropathy ensues in the aftermath of immune-mediated podocyte injury. Thus, the treatment should mainly be tailored toward treating syphilis as it is the potent trigger leading to immune response, culminating in membranous nephropathy in such patients.

A majority of case reports suggest that the membranous glomerulonephritis associated with syphilis infection is readily reversible with penicillin therapy alone, thereby potentially avoiding the need for immunosuppressive agents or even renal replacement therapy. Penicillin G remains the antibiotic of choice in treating a syphilis infection owing to remarkable susceptibility of Treponema pallidum to this drug. The mode of administration often varies in accordance with the disease stage. However, for primary, secondary, and tertiary syphilis, intramuscular injection containing benzathine penicillin G (2.4 million units) remains the ideal therapeutic choice in most cases. While data to support the use of alternatives to penicillin remains limited, options for non-pregnant patients who are allergic to penicillin may include doxycycline, tetracycline, and for neurosyphilis, ceftriaxone. With regard to the stages of syphilis, a detailed venereal history remains pivotal, which may indicate the timeline of infection, providing invaluable cues to the disease progress. In its tertiary stage, for instance, syphilis may manifest debilitating neurological and cardiological repercussions, and prompt treatment aimed particularly toward the disease process is exceedingly imperative. Additionally, the Jarisch-Herxheimer reaction, which ensues in the aftermath of penicillin administration and subsequently results in constitutional symptoms amid a treponemal infection, should also be considered. For individual patient symptoms, conservative management may be considered. In addition, diuretics such as frusemide are employed to improve edema, and an angiotensin-II receptor blocker can also be administered for its anti-proteinuric effect.

Due to the presence of a multitude of variables that may confound patient presentation, commencement of inappropriate initial treatment in the context of luetic membranous nephropathy is possible. For instance, steroids are conventionally employed for the treatment of membranous glomerulonephritis. However, if steroids are instituted for treating patients afflicted with membranous glomerulonephritis secondary to syphilis, adverse outcomes may ensue that may advance the stage of syphilis. By suppressing the immune system, steroids can interfere with the natural process of infection-containment, thereby delaying recovery from luetic nephropathy. Thus, it is better to screen for syphilis before initiation of immunosuppressive treatment even among patients with primary membranous glomerulopathy. The underlying etiology in turn governs the eventual management. A meticulous workup should be duly conducted to deduce the definitive underlying cause in order to institute appropriate medical treatment.

This article highlights several important clinical implications of luetic nephropathy. It illustrates that the immunosuppressing markers, including anti-treponemal IgG, should be carefully evaluated in patients presenting with nephrotic-range proteinuria. Along the same chain of thought, a self-resolving nephritis also does not preclude the diagnosis of a luetic membranous nephropathy. Furthermore, this article points to the riveting possibility of a syphilis infection in patients concomitantly afflicted with a hepatitis B virus, hepatitis C virus, or HIV coinfection. Since HIV and hepatitis may also cause membranous glomerulonephritis, luetic nephropathy might incorrectly be attributed to the presence of these infectious diseases, obscuring the true diagnosis and rendering prompt treatment dilatory. In addition, syphilis is a reemerging disease; global statistics show about 10,000 new cases every year. Therefore, a syphilis-induced, self-resolving membranous nephropathy should be borne in mind in order to appropriately decide treatment and to yield fecund clinical outcomes.

Learning Points

- This study highlights membranous glomerulonephritis in conjunction with secondary syphilis and it serves the purpose of community awareness regarding this potential association as initial presentation may cause much confusion and concern in such cases.
- Clinicians should remain vigilant for syphilis as a possible, albeit rare, cause of proteinuria or nephrotic
syndrome. An exhaustive search should be carried out to identify this secondary cause of membranous glomerulonephritis. Detailed history taking focusing on sexual history, careful review of clinical features, and morphological and immunostaining biopsy findings are imperative.

- In such patients, mandatory serological testing for syphilis should be conducted regardless of the clinical course and histopathologic pattern.
- With regard to therapeutic approaches, an updated knowledge of this uncommon presentation of syphilis is of paramount importance as membranous glomerulonephritis may show clinical remission with the treatment of underlying syphilis alone, without the need for immunosuppressive therapy.
- Immunosuppressive drugs such as corticosteroids may show a propensity to complicate an otherwise self-limited luetic membranous nephropathy. Therefore, therapeutic decision-making should be carefully deliberated upon in these patients.

Authors’ Note
This article was presented as an abstract at the American Society of Nephrology—Kidney Week, October 31 to November 5, 2017, in New Orleans, LA, USA.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval
Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent
Informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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