Atypical presentation of syphilis: rapidly progressive glomerulonephritis

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Abstract

Introduction: Rapidly progressive glomerulonephritis is a very rare and atypical form of renal syphilis. Case presentation: 50 year old lady presented facial swelling, hematuria, and elevated creatinine. Both RPR and TPHA was reactive. Treatment with weekly benzathine penicillin resulted in dramatic response. Conclusion: consider syphilis as reversible cause of RPGN.

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Abstract

Introduction: syphilis is a sexually transmitted disease caused by spirochete Treponema pallidum that causes a wide variety of symptoms and signs. With a recent worldwide resurgence of syphilis, it's imperative to recognize various presentation of this great imitator. Renal syphilis is rare and most commonly present as nephrotic range proteinuria associated with pathological features of a membranous glomerulonephritis. Rapidly progressive glomerulonephritis is a very rare and atypical form of renal syphilis.

Case presentation: A 50-year-old Ethiopian woman presented with periorbital swelling, hematuria, proteinuria, and rapidly progressive renal failure. Rapid plasma reagin and confirmatory Treponema pallidum hemaglutination agglutination (TPHA) was reactive. Treatment with a weekly Benzathine penicillin for 3 weeks resulted in rapid return of renal function to baseline.

Conclusion: with increasing rate of new syphilis, clinicians should be mindful of the various renal manifestation of syphilis. This case highlights the significance of considering syphilis as a reversible cause in any patient presenting with a clinical feature suggestive of RPGN.

Keywords: Syphilis, Rapidly progressive glomerulonephritis, Hematuria, Ethiopia, Case report

Background

Syphilis is a multisystemic infectious disease with various presentation hence the designation "great imitator". Even though renal involvement is rare, there is increasing reports of various renal lesions due to recent global resurgence of syphilis. Kidney involvement can be seen during the primary, latent, and tertiary stages of syphilis [1]. Various types of glomerulonephritis have been described. Nephrotic range proteinuria due to membranous nephropathy is the most common form. On the other hand, rapidly progressive glomerulonephritis pattern is an atypical and very rare presentation of syphilis, with only three case reports [2-4]. We report a case of immunocompetent patient presenting with hematuria, proteinuria and rapidly deteriorating renal function suggestive of RPGN.

Case presentation

A 50-year-old Ethiopian woman presented with a 2-week history of facial swelling, and reddish discoloration of urine. She was in her usual state of health until 2-week before admission, when she developed a non-projectile vomiting of ingested matter and facial swelling that progressed to involve both legs. She also complained of reddish discoloration of urine, decreased urine volume, dull aching left flank pain with no radiation, anorexia, and fatigue. She also provided history of shortness of breath on exertion and intermittent dry cough. Otherwise she denied any hemoptysis, nasal discharge, epistaxis, skin rash, joint pain, atopy, asthma, fever, night sweat and other systemic symptom. She didn't have preceding diarrhea, gastrointestinal bleeding, sore throat, orthopnea, PND, visual disturbance, headache, neck pain, neck stiffness, and change in mentation. Her past medical history was non-revealing. Similarly, her sexually history was also unremarkable. She have never been diagnosed or treated for syphilis. She is not on any medication; she did not smoke tobacco, use illicit drugs, or drink alcohol. Her family history was unremarkable.

On examination, her blood pressure was 190/100 mmHg, the pulse rate 77 beats per minute, respiratory rate 20 breaths per minute, the temperature 36.8 degree Celsius, and the oxygen saturation 98% while breathing ambient air. There was peri-orbital swelling and grade one symmetric bilateral pitting edema of legs. Cardiac examination revealed grade 2 diastolic murmur heard at aortic area, but JVP was not raised and there was no pericardial rub. There was no sinus tenderness, nasal mucosal ulceration and septal deviation, skin rash, lymphadenopathy, genital ulcer, joint swelling and tenderness. Chest and neurologic examination was non-revealing.

Laboratory workup disclosed Serum creatinine of 9.28 mg/dl, blood urea nitrogen 145 mg/dl, and hemoglobin 10.3 mg/dl with MCV of 79.8 fl (Table 1). Urinalysis was positive for +2 albumin and +3 blood. On urine microscopy, there was 10-15 RBC/HPF and 0-4 WBC/HPF. Rapid plasma reagin was and confirmatory Treponema pallidum hemaglutination agglutination (TPHA) reactive. But other serologic tests like ANA, ANCA, ant-GBM and complement level were not done because of financial reason and unavailability of laboratory setting in the region. Abdominopelvic ultrasound showed normal sized kidneys with increased parenchymal echogenicity and mild ascites. Chest radiography revealed minimal bilateral pleural effusion and increased cardiothoracic ratio. Trans-thoracic echocardiography showed thickening of aortic valve with mild aortic regurgitation but no signs of vegetation and intracardiac abscess. Renal biopsy wasn't done due to lack of service in our institution.

Table 1. Laboratory data on admission

variables
White cell count (per µl) Differential cell count (per µl) Neutrophils Lymphocytes Hemoglobin (mg/dl) Hematocrit (%) MC
Creatinine (mg/dl) Blood urea nitrogen (mg/dl) Sodium (mmol/l) Potassium (mmol/l) Chloride (mmol/l) AST (IU/l) ALT
Urinalysis Specific gravity PH Albumin Blood WBC RBC Cast 24 hour urine protein UPCR/UACR
Serology Hepatitis B Hepatitis C HIV RPR TPHA Anti-ASO antibody ANA ANCA Anti-GBM antibody Complement (C3

With a working diagnosis of syphilis-related rapidly glomerulonephritis, patient was admitted and started on intramuscular benzathine penicillin G 2.4 million IU weekly for 3 doses, intravenous furosemide 40 mg twice daily, amlodipine 10 mg once daily by mouth, intravenous metoclopromide 10 mg thrice daily, intravenous

omeprazole 20 mg once daily, and no salt added diet. She was also challenged with 500 milliliters of normal saline for possible superimposed pre-renal component due to vomiting. She did not receive steroid or any other form of immunosuppressive therapy. Two days after first dose of benzathine penicillin G, the serum creatinine declined rapidly from 9.28 to 7mg/dl. After the third dose it became 0.98 mg/dl and had been stable since (Table 2). Currently she feels well, non-edematous, normotensive and normal and stable renal function.

Table 2. Timeline of the patient's serial laboratory investigation

Variables	Admission (Day 0)	29/3/21	31/3/21	5/4/21 (2 day post treatment)	23/5/21 (2wk post treatment)	22/6/21 (6wk post treatment)	22/7/21 (10wk post treatment)
Creatinine (mg/dl)	9.28	9.7	9.03	7	1.2	0.98	0.7
Urinalysis Albumin Blood RBC cast	+2 +3 10-15/HPF				+2 +3 many	+2 +2 many	+1 +1 0-2

Discussion and Conclusions

Syphilis is a sexually transmitted infection caused by spirochaeteTreponema pallidum. It presents with a wide range of symptoms and sign depending on the stage of the disease. Kidney involvement is rare but a well described manifestation of syphilis with the prevalence ranging from 0.3% to 10% of patients diagnosed with secondary syphilis [5]. It can cause glomerulopathies, tubular pathology and vasculitic lesions in the kidney. The most common glomerular lesion is membranous nephropathy presenting as acute onset nephrotic syndrome [6]. Other syphilis associated glomerular diseases are MCD, FSGS, MPGN, and RPGN.

Rapidly progressive glomerulonephritis (RPGN) is an atypical and very rare presentation of syphilis. Patients present with hematuria, proteinuria, and rapidly increasing serum creatinine over a short period of time. This may or may not be accompanied by other features suggestive of secondary syphilis [2, 4]. The pathogenesis consists of immune complex-mediated glomerular injury as evidenced by the presence of treponemal antigens and antibody to *Treponemal pallidum* on pathologic examination of renal tissue [7]. Syphilis related glomerulonephritis is diagnosed based on positive serology, histologic evidence of GN with rapid and sustained resolution after treatment with penicillin or the presence of anti-treponemal antibodies or treponemal antigens in the glomerular deposits [8].

Treatment of syphilis-related RPGN includes parenteral penicillin for underlying syphilitic infection [9-10]. There are prior reports describing complete and rapid resolution of renal lesion and normalization of kidney function with penicillin alone [2, 11]. The role of immunosuppressive therapy is unknown, given the paucity of evidence whether it's beneficial for induction in the acute treatment phase.

Our patient presented with typical clinical feature compatible with RPGN pattern, active urine sediment with rapidly deteriorating renal function. Positive confirmatory treponemal test along with rapid and sustained improvement in renal function after a course of penicillin supports the diagnosis of syphilis related RPGN.

There were several limitations in management of this case, namely lack of renal biopsy to confirm RPGN and lack of serologic tests to rule out other causes of RPGN.

RPGN is a very rare and atypical presentation of syphilis. However, with a global re-emergence of syphilis it's essential to recognize this atypical renal manifestation of syphilis. This case highlights the significance of considering syphilis as a reversible cause in any patient presenting with a clinical picture suggestive of RPGN.

Abbreviation

RPGN: Rapidly progressive glomerulonephritis; anti-GBM: Anti-glomerular basement membrane; ANA: Anti-nuclear antibodies; RF: Rheumatoid factor; HIV: Human immunodeficiency virus; RPR: Rapid plasma reagin test; VDRL: Venereal Disease Research Laboratory; GN: glomerulonephritis, MCD: minimal change disease; FSGS: focal segmental glomerulosclerosis; MPGN: membranoproliferative glomerulonephritis.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report. A copy of written consent is available for review by an editor in chief of this journal.

Ethical approval and consent to participate

Not applicable.

Competing interest

The authors declare no competing interest.

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Availability of data and material

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Authors' contribution

SA and TA contributed in acquisition of history, laboratory investigation, and interpretation of case and the patient data. SA carried out literature review and was a major contributor to the writing of manuscript. All authors have read and approved the final manuscript.

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