Challenges in Diagnostic and Management of Nephritic Syndrome in Diabetic Nephropathy Patient: a Case Report

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ARTICLE INFO

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[https://doi.org/10.21776/
ub.crjim.2021.002.01.7](https://doi.org/10.21776/ub.crjim.2021.002.01.7)

Received on Dec 24, 2020;
Revised on Jan 25, 2021;
Accepted on Feb , 2021

ABSTRACT

The clinical presentation of patients with acute glomerulonephritis (GN) varies widely, from asymptomatic to clinical presentations of acute kidney injury (AKI), edema, and hypertension. Diagnosis of GN in patients with diabetic nephropathy (DN) is a challenge due to pre-existing edema, hypertension, and decreased renal function. Likewise in terms of management of steroid immunosuppressants related to blood sugar regulation. It has been reported that 35-year-old male patients with diabetes mellitus (DM) with DN whose kidney function deteriorated rapidly. The patient complained of cola-red urine and decreased urine volume the day before admission. Physical examination showed blood pressure of 160/95 mmHg, bilateral leg edema, active chronic ulcer in the left lower leg, hemoglobin level was 8.7 g / dl, leukocytes 17.400 / ul, serum urea level 96 mg / dl, serum creatinine level 7.01 mg / dl, ASTO titer + 800 IU / ml, macroscopic hematuria, and albuminuria +4 on urinalysis. Ultrasonography revealed enlarged kidney size and signs of acute renal inflammation. Based on these data the patient was diagnosed clinically as rapidly progressive GN due to post-infectious GN. The patient received 3 days of pulse methyl prednisolone therapy continued orally, blood sugar regulation with insulin, RAS blockers, intravenous antibiotics and ulcer debridement. After 1 week of therapy, clinical and laboratory improvements were found and at the next follow-up renal function returned to baseline about 2 weeks later.

Keywords: nephritic syndrome, diabetic nephropathy, diabetes mellitus, skin ulcer

INTRODUCTION

The kidney is an organ that is often the target of a pathogenic immune response, both to local autoantigens and by local manifestations of a systemic autoimmunity. Based on clinical, immunological and

experimental data, it supports the hypothesis that the majority of glomerulonephritis (GN) in humans is the result of immunological mechanisms. The pathogenetic mechanisms of GN are numerous and complex, involving both humoral and cell-mediated immune responses.

The nature of the immune response that causes GN is strongly influenced by its immunogenic phenotype.^[1] The most common mechanism of GN is the deposition of immune deposits (antigen-antibody complexes), on the glomerular basement membrane (GBM), the sub-endothelium and on the sub-epithelium which is often associated with clinical manifestations. Immune complex deposition is followed by an inflammatory response with activation of the complement factor cascade and infiltration of hematopoietic cells (such as neutrophils and macrophages), as well as glomerular cell proliferation. Furthermore, these effector cells induce thrombosis, necrosis and crescent formation which can lead to renal insufficiency and rapidly progressive nephritis.^[2]

The most common causes of nephritic syndrome are post infectious GN, IgA nephropathy and lupus nephritis. Acute PSGN is an immune complex-mediated GN associated with streptococcal infection of the skin or throat. In contrast to pediatric patients, the source of infection in adults is more heterogeneous, which can come from infections of the skin, upper respiratory tract, lungs, oral mucosa, and urinary tract. Currently, the incidence rate has decreased, especially in developed countries. Most cases affect adults, especially those who are elderly or people with impaired immune systems.^[3,4] Clinical features vary widely from asymptomatic microscopic hematuria to severe acute nephritic syndrome.^[3] The diagnosis of PSGN is generally based on clinical and laboratory information, whereas a kidney biopsy is generally rarely required. Treatment of PSGN focuses on managing hypertension and edema. Antibiotic penicillin to eradicate the nephritogenic strain

of streptococci when the infection is active, whereas steroid therapy is generally only given to patients with progressive renal failure or the presence of crescents on the renal biopsy.^[5] PSGN has an excellent prognosis especially in children with complete recovery usually occurring within 6 to 8 weeks. In adults, around 50% of the patients continue to have reduced renal function, hypertension, or persistent proteinuria.^[6,7] The following reports a case with problems in diagnosis and management in a patient with underlying DN who experienced rapid decline in renal function and hematuria.

CASE REPORT

A 35-year-old man came to the emergency room with complaints that his urine was red like cola (Figure 1) and his urine production had decreased since 1 day before going to the hospital. He is a DM patient for 12 years and is regularly taking oral anti-diabetes drugs. The patient was known to have hypertension since 2 years ago and was receiving 300 mg of irbesartan and 10 mg of amlodipine. The patient complained of swelling of both legs and ulcers on the left lower leg since 3 months ago. Physical examination revealed obesity, blood pressure 160/95 mmHg, pulse 105 beats / minute, respiratory rate 18 times / minute, temperature 36.7 C. There was bilateral leg edema, open necrotic, peeling, and wound on the lower left leg (Figure 2). Since the onset of edema, patient mobilization has become more limited.

Laboratory tests showed leukocytosis (17.400 / μ L), hemoglobin level 8.7 g / dl, serum urea level was 96 mg / dl, serum creatinine level was 7.01 mg / dl, level of HbA1c was 9.7% and ASTO titer was + (800) IU / ml. The urine was cola red and on urinalysis protein 4+. Ultrasonography revealed a relatively enlarged kidney size and signs of inflammation consistent with the acute condition (Figure 3). Based on clinical and laboratory data the

patient was diagnosed as acute post-streptococcal glomerulonephritis, diabetic nephropathy, type II diabetes mellitus, and chronic ulcer in cruris. The patient received intravenous antibiotic therapy, Irbesartan 300 mg, amlodipine 10 mg, pulse steroid using methylprednisolone 750 mg for 3 days and continued orally and planned for hemodialysis. During methyl prednisolone therapy, the blood sugar level was 380 mg / dL, so that the oral antidiabetic was replaced by insulin. After 1 week of therapy, there was clinical and laboratory improvement and at the next follow-up renal function returned to baseline about 2 weeks later.

Figure 1. Clinical picture of the patient's urine that looks like cola.

Figure 2. Clinical picture of the patient's skin ulcer that appears to be still active.

Figure 3. Renal sonography showing enlarged kidneys with normal cortex density and clear cortical medullary boundaries. The length of the right kidney was 14.23 cm and the left was 13.18 cm.

DISCUSSION

Diagnosis of rapidly deteriorating renal function in patients with DN background is a challenge. Many factors or conditions can be the cause, including DM-related conditions and the metabolic syndrome itself as well as DN conditions, as a secondary nephrotic syndrome. This patient was obese, had prominent bilateral edema, impaired mobility, hypoalbumin, poor blood sugar control (HbA1C 9.7%) and had chronic ulcers in the lower limbs which appeared to be still active. Based on the

patient's clinical condition, several possible diagnoses can be made, including acute GN, papillary necrosis, or renal vein thrombosis.

Patients with nephrotic syndrome, low levels of albumin in the blood, a high level of cholesterol in the blood and swelling, triggering a hypercoagulable state and increasing chances of clot formation. Almost two-thirds of patients have bilateral renal vein involvement. Thrombosis may extend from the vena cava into the peripheral venules or may originate in the peripheral veins and propagate to the main renal vein. The severe passive congestion that develops causes the kidney to swell and become engorged, leading to degeneration of nephrons and causing symptoms of flank pain, hematuria and decreased urine output.^[8]

Renal papillary necrosis involves a severe destructive process, possibly as a result of ischemia of the medulla and papilla. The papilla

is very sensitive to these ischemic changes because even in normal settings it is exposed to a relatively hypoxic environment. Clinically, papillary necrosis often manifests as low back pain, hematuria, and fever. Urinalysis shows red and white blood cells, bacteria, and papillary fragments. These papillary fragments can cause ureteral obstruction which requires immediate intervention.^[9]

The differential diagnosis of GN is very broad and complex. Based on the clinical presentation the above patient is presenting with a nephritic syndrome with rapid progression (rapidly progressive GN). GN that is rapidly progressive can occur in the conditions of PSGN, IgAN, HSP, LN and MPGN.^[10] Based on existing data with additional ASTO examination with high titers, the patient above was diagnosed as RPGN due to PSGN with the existing source of infection being cellulitis in the lower left leg, poor control type 2 diabetes mellitus and DN.

Raised on anti-streptolysin O (ASO) titer is only found in 80% of patients who did not receive antibiotics during the phase of streptococcal infection. ASO titers increase when there is infection by Group A beta hemolytic streptococci, Group C or Group G streptococci. The antibody response to streptococcal extracellular products is a useful marker of recent infection. If the test result is positive, it confirms a recent invasive streptococcal infection. The antibody response usually detected during the 2nd or 3rd weeks of an acute episode and peaks at 4th to 5th weeks. ASO titer tend to increase in 1st week after infection, peak at weeks 3 to 5, and begin to decrease after 8 weeks; and a stronger response is due to pharyngeal infections vs skin

infections. However, a high ASO titer is not definitively diagnose poststreptococcal complications.^[11]

Management recommended for patients with acute post-streptococcal nephritic syndrome is symptomatic based on the severity of the disease. The main goals are controlling hypertension and edema. During the acute phase, the patient's diet was 35 cal / kg / day, the protein diet reduced from 0.5 to 0.7 grams / kg / day, unsaturated fat, and low salt, namely 2 grams of sodium per day. Electrolyte intake must also be limited, sodium 20 mEq per day, potassium less than 70–90 mEq per day and calcium 600–1000 mg per day. Strict fluid restriction by limiting the intake of 1 liter of fluids per day, to treat hypertension. The therapy for hypertension is diuretics, if remains unresolved, the 2nd line is calcium channel blockers, ACE inhibitors or intravenous nitroprusside for malignant hypertension. In severe cases with hyperkalemia and severe uremic syndrome is indicated for hemodialysis.^[5]

Intravenous steroid is indicated for the glomerulonephritis with a lesion more than 30% of the total glomerulus. Methylprednisolone 500 mg intravenously per day in 4 divided doses for 3–5 days. Methylprednisolone pulse is globally tolerable in diabetic patients.^[12] However, some references stated that the usage was not indicated for long-term. Serial insulin and continuous glucose measurements should be performed to elucidate the side effect of steroid. The patient was given Methylprednisolone 500 mg intravenously per day for 3 days. Patient had a clinically significant improvement as well as kidney

function after the treatment. During the administration of pulse steroids, the patient's blood sugar increases. The patient was treated initially with oral diabetes drug, then changed to basal bolus insulin when the patient is started on pulse steroids. In theory, it should be considered to change the dosage of basal insulin and increase short/fast acting insulin by 10-20% daily until the glycemic target is reached.

CONCLUSION

A case has been reported in a 35-year-old male patient with a nephritic syndrome with clinical manifestation of rapidly progressive GN due to streptococcal infection. Diagnosis and management are constrained by the condition of patients with underlying diabetic nephropathy and poor glucose control. The patient received pulse steroid therapy, blood glucose control with insulin, systemic antibiotics and debridement of the ulcer. Renal function improved to baseline values around 14 days of therapy.

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