

Short Communication

Idiopathic Membranoproliferative Glomerulonephritis Type 1 Refractory to Immunosuppressive Therapy: An Educational Article and Expert Opinion

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Keywords

- Primary (Idiopathic) membranoproliferative glomerulonephritis
- Dipyridamole
- Aspirin
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Abstract

Background: Membranoproliferative glomerulonephritis which is also known as mesangio-capillary and mesangioproliferative glomerulonephritis has been established as a clinical-histopathological entity as early as the 1960s. As early as 2004, Gareth Jones from the United Kingdom and his research group reported a study which showed that treatment of patients with membranoproliferative glomerulonephritis with oral prednisolone and mycophenolate mofetil may help in preserving renal function in patients.

Patients and methods: The case of a female who developed primary membranoproliferative glomerulonephritis at about the age of 38 years, and experienced deterioration in renal function despite immunosuppressive therapy is described. The relevant medical literature was reviewed with aim of determining the available evidence-based therapeutic options.

Results: Following the birth of her fourth child after a pregnancy complicated by hypertension, a 38-year female was experiencing hypertension and gradual elevation of serum creatinine and blood urea. A histopathologic diagnosis of membranoproliferative glomerulonephritis was made after performing renal biopsy, and immunosuppressive therapy with oral prednisolone and mycophenolate mofetil was started. Early during June, 2023, serum creatine was 4.39 mg/dL and blood urea was 85 mg/dL despite the patient was on low protein diet, and therefore the immunosuppressive treatment was stopped and the patient was referred to us. Urea was lowered to 72 mg within a week by adding acacia gum supplementation. The use of dipyridamole plus aspirin was considered in this case based on the evidence provided by Schmidt (1975) and Donadio et al (1984).

Conclusion: The current evidence-based expert opinion suggests the use of dipyridamole plus aspirin in cases of membranoproliferative glomerulonephritis not responsive to treatment with oral prednisolone and mycophenolate mofetil.

INTRODUCTION

Membranoproliferative glomerulonephritis which is also known as mesangio-capillary and mesangioproliferative glomerulonephritis has been established as a clinical-histopathological entity as early as the 1960s [1].

In 1977, Jones emphasized that there are two main histopathological types of membranoproliferative glomerulonephritis with similar clinical manifestations. Including type 1 which is associated with subendothelial deposits, and type 2 which is associated with intramembranous dense deposits. Jones also emphasized that most cases have no identifiable cause, but its occurrence in associations with infections such as hepatitis should be considered [2].

As early as 2004, Gareth Jones from the United Kingdom and his research group reported a study which showed that treatment of patients with membranoproliferative glomerulonephritis

with oral prednisolone and mycophenolate mofetil may help in preserving renal function in patients [3].

PATIENTS AND METHODS

The case of a female who developed membranoproliferative glomerulonephritis at about the age of 38 years, and experienced deterioration in renal function despite immunosuppressive therapy is described. The relevant medical literature was reviewed with aim of determining the available evidence-based therapeutic options.

RESULTS

Following the birth of her fourth child after a pregnancy complicated by hypertension, a 38-year female was experiencing hypertension and gradual elevation of serum creatinine and blood urea. On the 26th of June, 2022 serum creatinine was 1.9 mg/dL and blood urea was 42 mg/dL. On the fourth of July, 2022,

serum creatinine remained 1.9 mg/dL, but blood urea was 47 mg/dL. Serum potassium was within normal range at 4.3 mEq/L.

Urinalysis detected the presence of hematuria and proteinuria. Renal ultrasound showed normal sized kidneys with normal parenchymal thickness. The right kidney was 10.7x3.5 cm with normal parenchymal thickness (16 mm). The left kidney was 11.5x4.6 cm with normal parenchymal thickness (17 mm). Both kidneys showed increased cortical echogenicity with poor cortico-medullary differentiation.

Antinuclear antibody and anti-double stranded DNA antibodies were negative. C3 and C4 levels were within normal range. Serologic tests for hepatitis B and C viruses were negative,

Late during the year 2022, she was having microscopic hematuria and proteinuria, and renal biopsy performed on the 17th of October, 2022 (38 year) showed a uniform pattern of mesangial hyper cellularity and increased mesangial matrix accentuating the lobules. There was also mesangial interposition with development of double contour basement membrane. Some glomerular adhesions were present to the Bowman's capsule. No globally sclerotic glomeruli were seen. Interstitial fibrosis with tubular atrophy was also present and was involving more than 10% of the cortex. Blood vessels showed no important histological changes.

Immunofluorescence microscopy revealed positive IgG positive and C3 positive glomeruli. Glomeruli were negative for IgA, IgM, and C1q.

Therefore, the histopathological diagnosis was immune complex mediated membranoproliferative glomerulonephritis type 1.

Immunosuppressive therapy with oral prednisolone and mycophenolate mofetil was started.

On October 27, 2022, serum creatinine was 2.3 mg/dL and blood urea was 58 mg/dL. Therefore, dietary protein restriction was started.

Renal ultrasound (April 25, 2023, age 39 years) showed increased cortical echogenicity with loss of cortico-medullary differentiation the sizes of both kidneys were within normal lower size with the right kidney 10.5 cm in length and the left kidney 9.5 cm the length. Abdominal ultrasound showed small polyp.

On the 25th of April, 2023, serum creatinine was 3.41mg/dL, total serum protein was 5 g/dL (Normal: 6-8 g/dL), serum albumin was 3.24g/dL (Normal: 3.5-5.2 g/dL), Antinuclear antibody and anti-double stranded DNA antibodies were negative. C3 was within normal limit at 90 mg/dL (Normal: 90-180 mg/dL), but C4 was elevated at 31 mg/dL (Normal: 20-50mg/dL).

Anti-neutrophil cytoplasmic antibodies (PR3-ANCA) and Peri-nuclear Anti-neutrophil cytoplasmic antibodies (P-ANCA) were both negative.

Early during June, 2023, serum creatine was 4.39 mg/dL and blood urea was 85 mg/dL despite the patient was on low protein diet, and therefore the immunosuppressive treatment was stopped and the patient was referred to us.

On referral, the patient was hypertensive, and her blood pressure was poorly controlled earlier with nifedipine, and remained poorly controlled after replacing nifedipine with valsartan in a relatively large dose of 160 mg twice daily. However, her blood pressure was controlled after stopping valsartan using oral bumetanide 1 mg three times daily plus oral pentoxifylline 400 mg three times daily.

Pentoxifylline was used in this case based on the evidence provided by Al-Mosawi concerning its use in renal diseases and hypertension [4,5].

Urea was lowered to 72 mg within a week by adding acacia gum supplementation based on the evidence provided by Al-Mosawi [6-21].

The use of dipyridamole plus aspirin was considered in this case based on the evidence provided by [22,23].

DISCUSSION

As early as 2004, Gareth Jones from the United Kingdom and his research group reported a study which showed that treatment of patients with membranoproliferative glomerulonephritis with oral prednisolone and mycophenolate mofetil may help in preserving renal function in patients [3].

However, as early as 1975, Schmidt emphasized that many cases of adult chronic glomerulonephritis are poorly responsive to immunosuppressive therapies. However, anticoagulants and platelet aggregation inhibitors can have a role in the treatment of membranoproliferative glomerulonephritis and rapidly progressive glomerulonephritis [22].

Therefore, the use of dipyridamole plus aspirin was considered in this case based on the evidence provided by [22,23].

In [23] reported a placebo-controlled study which included 40 patients with membranoproliferative glomerulonephritis type I treated with dipyridamole, 225 mg daily, and aspirin, 975 mg daily for 12 months. The study showed that fewer patients treated with aspirin and dipyridamole experienced progression to end-stage renal failure. Therefore, Donadio et al suggested that dipyridamole and aspirin can slow the decline of renal function and thus slow the progression to end-stage renal failure [23].

CONCLUSION

The current evidence-based expert opinion suggests the use of dipyridamole plus aspirin in cases of membranoproliferative glomerulonephritis not responsive to treatment with oral prednisolone and mycophenolate mofetil.

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