Case Report

A Case Report of Treatment Idiopathic Membranous Nephropathy with Progressed Renal Insufficiency

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Abstract

Immunosuppressive therapy were commonly used in idiopathic membranous nephropathy patients with nephrotic presentation, however, treatment was poorly tolerated in some patients, especially patients with renal insufficiency. We report the case of a 58 year-old male who resisted to initial immunosuppressive therapy and presented with persistent high-grade proteinuria, severe low serum albumin concentrations and progressive renal failure. The patient achieved partial remission and improved renal function by a regimen of MMF concomitant corticosteroid and traditional Chinese medicine (TCM) herbal medicine ultimately.

ABBREVIATIONS

NS: Nephrotic Syndrome; IMN: Idiopathic Membranous Nephropathy; Scr: Serum Creatinine; ALB: Serum Albumin; PLA2R: Phospholipase A2 Receptor; ANA: Antinuclear Antibody; ANCA: Anti Neutrophil Cytoplasmic Antibody; GBM: Glomerular Basement Membrane; MMF: Mycophenolate Mofetil; PR: Partial Remission; TCM: Traditional Chinese Medicine

INTRODUCTION

About 60% Idiopathic Membranous nephropathy (IMN) patients with nephrotic presentation were possibly treated with immunosuppressive strategies. Corticosteroids and alkylating agents regimen or Calcineurin inhibitors regimen were the most commonly used therapies, however, the treatment was resistant or poorly tolerated in many patients; especially patients with established renal insufficiency [1,2]. How to treat these patients remains challenging, here we describe such a case for discussion.

CASE PRESENTATION

A 58 year-old male was admitted with a more than 3-year history of edema and progressed declining kidney function in recent 9-month. The patient was diagnosed primary nephrotic syndrome (NS) with high-grade proteinuria (6~10g/24hour) but rather normal kidney function [serum creatinine (Scr) 90umol/L] more than 3 years ago. Kidney biopsy did not performed when diagnosed because of acute pulmonary embolism and oral warfarin was used. He was treated with a therapy of maximal dose prednisone 50mg/d and then tapered slowly, Ciclosporin A 75mg twice a day for 6 months. Owing to NS not remission, he alternated to cyclophosphamide 50mg/d with 0.5mg/Kg/d prednisone for another 3 months, which did not make any improvement either. After only symptomatic treatment for 3 months, he was treated with Ciclosporin A 75mg twice a day again with methyl prednisolone 8mg/d for 6 months and then stopped because of no efficiency. In the next 15 months, he took Valsartan, Simvastatin, diuretics and other symptomatic treatment, the Scr gradually increased from 141 to 420 umol/L during recent 9 months. He felt weakness and nausea, phlegmy coughing and shortness of breath, his blood pressure was uncontrolled when three kinds of anti-hypertensive agents were combined used. He also had history of chronic bronchitis for 10-years.

Examination revealed malnutrition and severe edema below the waist. His blood pressure was 164/102mmHg, pulse 86bmp, with inspiratory moist rales in the bilateral lung fields and no other abnormal findings.

On admission, Scr was 433umol/L, blood urea nitrogen was 9.2mmol/L, serum albumin (ALB) was 18.9g/L, serum sodium was 143mEq/L, potassium was 3.9mEq/L, chloride was 116mEq/L, bicarbonate was 15.7mmol/L, cholesterol was 7.56 mmol/L, triglyceride was 1.36 mmol/L. Urinalysis with 4+ protein, 10 red blood cell/high-power field without white blood cells and casts, total urine protein was 6.2g/24hour. Hemoglobin was 130 g/L, and complements were within normal range. Serum anti-PLA2R was positive. Serologies for hepatitis A, B, C, D, E and Human immunodeficiency virus were negative. ANCA, ANA and ds-DNA titers, cryoglobulin, rheumatoid factor and
anti-phospholipid antibodies were negative. The patient had tumor biomarkers test of alpha fetoprotein, carcinoembryonic antigen, prostate-specific antigen, squamous cell carcinoma antigen, neuron-specific enolase, cancer antigen 242 and cancer antigen19-9, and all of the results were within normal range. Immunofixation electrophoresis of blood and urine showed polyclonal immunoglobulin. The chest x-ray showed pulmonary emphysema and pleural effusion. Kidneys were normal size by ultrasound with apparently increased parenchymal echogenicity.

A renal biopsy was performed after the patient’s general status was improved by symptomatic treatment. Immunofluorescence showed granular capillary loop 3+ ~ 4+ intensity for IgG and 3+ for C3, mild intensity for IgA, IgM and C1q were segmental and granular mesangial deposited. The kidney biopsy specimen of light microscopy showed 40 glomeruli, 3 globally sclerosed, other glomeruli showed diffused thickening glomerular basement membrane (GBM) with subepithelial spikes formation and double track appearance, mild mesangial cellularity and matrix increased. Interstitial edema and multi-patchy of inflammatory cell infiltrate composed of lymphomonocyte cells and some eosinophils were identified, with tubular atrophy and loss of brush border and diffused arteriolosclerosis (Figure 1A,B).

Electron microscopy image identified extensive thickened GBM with segmental moth-eaten lesion, extensive epithelial foot process effacement, electron dense deposited subepithelial and within the GBM. Interstitial lymphomonocyte infiltrated and collagen fiber hyperplasia (Figure 2).

The patient was treated with a therapy of prednisone 50mg/d combined with three kinds of anti-hypertensive agents including Calcium channel blocker, α and β blocker, compound recipe of traditional Chinese herbal medicine according to syndrome, and some supporting treatment for 10 weeks. Valsartan was stopped since admission. Scr gradually decreased from Maximum 445umol/L to 290umol/L and stable, ALB increased to 24.6g/L, but total urine protein kept high-grade, 5~8g/24h. Then the patient was tried to treat with mycophenolatemofetil (MMF) initiate 0.5g twice a day and increased to 0.75 g twice a day with tapering prednisone and the integrated treatments above mentioned for 13 month. At 16 months after diagnosed, the patient’s Scr was 233umol/L, ALB was 39.7g/L, he remained proteinuric (3.0g/24h) but no longer had NS and enjoyed his daily life without too much symptoms.

DISCUSSION

IMN is increasing and accounting for 9.89-13.3% of all glomerular nephritis cases in mainland China [3,4], so our patient accepted treatment regimens as IMN until kidney biopsy proved the diagnose. Unfortunately, he was resistant to both CNI-based therapy and cyclophosphamide/steroid-based therapy, moreover, renal function deteriorated. The apparently increased Scr should ascribe to severe tubule-interstitial injury according to the pathologic features, so corticosteroid was given and renal function did improved to some extent, but remission NS remained even tough, as chronic but progressed renal insufficiency proved by clinical features. It has been demonstrated that 30% of the IMN patients progressed to end-stage renal disease (ESRD) or succumbed within 5-10 years despite immunosuppressive therapy [5-7]. Latest studies revealed that persistent high-level proteinuria, age ≥ 60, low serum albumin concentrations and severe tubule-interstitial injury are independent risk factors [8], which almost all manifested in our patient. KIDGO guideline for Idiopathic membranous nephropathy recommended not using immunosuppressive therapy in patients with a Scr persistently 3.5 mg/dl (309umol/L) [9], these patients were considered more likely to concomitant severe adverse events with immunosuppressive therapy and also very unlikely to respond to the treatment [10].

As MMF has proven to be of some benefit in selected
patients with IMN resistant to traditional therapeutic regimens [11], we tried it prudently with adjusted dosage and carefully monitoring. Ultimately, the patient achieved partial remission (PR) and stable renal function by this therapy, and by now it was regarded that PR also seems reasonably likely to predict clinical benefit in MN [12]. In addition to immunosuppressive therapy, contribution of herbal medicine of traditional Chinese medicine (TCM) deserved special mention. To our observation, patients concomitant treated with TCM while immunosuppressive therapy has superiority in increasing albumin and kidney function improvement, less digestive system symptoms and infection. Chen et al demonstrated that a formulation composed of *Astragalus membranaceus*, *Angelica sinensis*, *Salvia miltiorrhiza* and so on, which was similar to the prescription used in our patient, to be an alternative therapy for adults with IMN and nephrotic by a randomized controlled trial [13].

In conclusion, MMF concomitant steroid may be a useful and less costly therapy in patients of IMN with renal insufficiency or resistance to initial therapy, and TCM herbal medicine may do some benefits in these patients either.

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**REFERENCES**