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A Brief Analysis of the Prognosis and Treatment of Idiopathic Membranous Nephropathy

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Abstract: ***Membranous nephropathy (MN) refers to a group of diseases characterized by the deposition of immune complexes under the epithelial cells of the glomerular basement membrane (GBM) with diffuse thickening of GBM. The prognosis of IMN is diverse, untreated, about 1/3 of patients can achieve spontaneous remission, but the course of the disease is long, it takes 15~20 months to achieve partial remission, 25~40 months to achieve complete remission, and the recurrence rate after complete remission is as high as 30%, and about 1/3 of patients will progress to end-stage renal disease (ESRD) or die of related complications within 5~15 years, and the remaining one-third of patients present with non-progressive chronic kidney disease. It is of great significance to summarize the clinical features of IMN and identify and actively intervene in the risk factors of IMN prognosis as early as possible to protect renal function. Although the etiology and pathogenesis of this disease are not clearly understood, and there is great controversy in the treatment plan, many literature studies have shown that active treatment can effectively alleviate proteinuria and improve renal survival, thereby greatly prolonging the time to reach ESRD, and greatly reducing the mental and economic pressure of patients and families.***

Keywords: Idiopathic membranous nephropathy, Prognosis, Treatment, Pathologic features**.**

Membranous nephropathy (MN) refers to a group of diseases characterized by the deposition of subepithelial immune complexes in the glomerular basement membrane (GBM) with diffuse thickening of GBM [1], and idiopathic membranous nephropathy (IMN) is one of the common pathological types of nephrotic syndrome in adults [2], IMN is another high-incidence pathological form of kidney disease after IgA nephropathy and an important cause of end-stage renal disease, with about 20% of patients with IMN progressing to end-stage renal disease or dying from related complications within 5 to 15 years [3]. The pathogenesis is still unclear, the prognosis is very different, and the treatment of this disease is also controversial [4]. It is hoped that through the study of its distribution characteristics, we can promote the understanding of the essence of the disease and effectively guide the clinical formulation of personalized treatment plans, which is a subject worthy of in-depth research and has broad prospects, so as to achieve multi-faceted understanding and understanding of the clinical characteristics and prognosis of idiopathic membranous nephropathy (IMN), and achieve early detection, early diagnosis and early treatment.

Modern medicine believes that IMN is a chronic progressive disease with a diverse prognosis, with some patients in spontaneous remission during disease progression, and another 15%~20% of patients will progress to end-stage renal disease within 15 years [5-6]. Although there is a great deal of controversy about the treatment of this disease, studies have shown that [7] active treatment can effectively alleviate proteinuria and improve renal survival, thereby greatly prolonging the time to end-stage renal disease (ESRD) and greatly reducing the mental and financial pressure of patients and families.

The pathological characteristics of membranous nephropathy are mainly the diffuse deposition of immune complexes on the basement membrane of the glomerular capillary fold, resulting in diffuse thickening of the basement membrane and the formation of nail processes. Through complement-mediated podocyte and hiatal membrane injury, glomerular capillary permeability is increased, resulting in increased leakage of plasma substances, and the mesangial area is mostly normal, and crescents are rare. The immunopathology of membranous nephropathy is dominated by IgG and C3 granular deposition along the capillary wall, which may be accompanied by the deposition of other immunoglobulins such as IgA, IgM, and C1q [8-9].

Literature data show that the renal tubules and interstitium are basically normal in the early stage of IMN, and the basement membrane is significantly thickened, the mesangial stroma is increased, the glomerulosclerosis is sclerosis, and non-selective proteinuria and different degrees of renal tubular and interstitial lesions are accompanied by different degrees.

Previous studies at home and abroad have mostly suggested that male sex, advanced age, massive proteinuria, hypertension, and elevated serum creatinine at the onset of the disease are independent risk factors for poor prognosis of IMN [5-7,10]. Persistently large proteinuria is not only associated with serious complications, but is also an independent risk factor for progression to end-stage renal disease from IMN [10]. The pathological mechanism of IMN is causally due to changes in the physiological structure of the glomeruli, which further affects the persistence of proteinuria, resulting in the appearance of low serum albumin, which has been shown to be a prognostic factor for spontaneous complete remission and progression to nephrotic syndrome in patients with nephrotic proteinuria [10]. Hypoalbuminemia causes a significant decrease in intravascular colloid osmotic pressure, and the water in the blood vessels penetrates into the interstitial fluid, causing edema, causing blood vessels to be in a hypercoagulable state, and further causing abnormal protein and lipid metabolism and hyperlipidemia. This consequence leads to the common complications of IMN patients: 1) Infection: due to the loss of protein, antibody synthesis is reduced, and the common sites are respiratory tract, urinary

system, skin and spontaneous peritonitis, and non-nephrotoxic and effective antibiotics should be selected to fight infection; 2) Blood hypercoagulability causes thrombosis and embolism: renal vein thrombosis is the most common; 3) Acute renal failure: manifested as oliguria or anuria, volume expansion or diuretic therapy, the cause is not clear; 4) Disorders of protein and fat metabolism. Approximately 30 percent of patients with IMN progress to end-stage renal disease or die from related complications within five to 10 years [3,7,11], particularly those presenting with nephrotic syndrome, and nearly half of patients presenting with nephrotic syndrome will naturally progress to renal failure [12]. Therefore, for male, elderly, massive proteinuria, hypoproteinemia, hypertension, and patients with decreased renal function, it is necessary to give more active symptomatic supportive treatment, such as protein lowering, blood pressure lowering, infection prevention, anticoagulation and albumin supplementation if necessary, pay close attention to disease progression and complications, and improve patient prognosis.

Therefore, the clinical prognosis of IMN patients is mainly analyzed in combination with the above pathological features and clinical manifestations. Clinical literature data show that the risk factors affecting the prognosis of patients with membranous nephropathy are: first, age, gender, hypertension, male age is greater than 50 years old, the analysis may be due to the fact that elderly patients tend to have high blood pressure, and there are already tissue lesions such as glomerulosclerosis, vascular lesions, renal interstitial fibrosis, and renal tubular atrophy before the onset of the disease, resulting in low serum creatinine clearance rate at the onset of elderly patients; Studies have found that patients with hypertension at the onset often have pathological features such as severe tubulointerstitial lesions and arteriosclerosis during renal biopsy, and due to the high arterial pressure in hypertensive patients, vasoconstriction leads to reduced oxygen delivery, resulting in decreased renal oxygenation and damage to kidney tissue, resulting in poor prognosis of IMN patients. second, persistent proteinuria, 24-hour urine protein<4g for more than 6 months, normal renal function is low-grade risk; 8 g > 24 hours urine protein> 4 g for 6 months and normal renal function are considered moderate risk; 24-hour urine protein >8 g for 6 months or abnormal renal function are considered high risks. Third, serum creatinine, which has been elevated at the time of renal biopsy. Fourth, the pathology of the kidney: stage I and stage I.-II can be relieved, stage II and stage II.-III. are better, stage III, stage III.-IV are poor, diffuse deposition of basement membrane immune complexes (especially the appearance of crescents, renal function can deteriorate rapidly), tubulointerstitial fibrosis, glomerulosclerosis, glomerular vascular lesions, etc.

Treatment is recommended in accordance with the Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines [13]. IMN risk assessment is performed, and treatment options (conservative symptomatic supportive care and corticosteroid plus immunosuppressant therapy) are determined based on the results of the assessment. Risk assessment for renal disease progression: IMN risk assessment is recommended based on the degree of proteinuria and renal function. 24-hour urine protein<4g for more than 6 months, normal renal function is a low-grade risk; 8 g > 24 hours urine protein> 4 g for 6 months and normal renal function are considered moderate risk; 24-hour urine protein >8 g for 6 months or abnormal renal function are considered high risks. Appropriate treatment should be adopted according to the degree of risk: for patients with low risk, conservative treatment is recommended, based on angiotensin-converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor antagonists (ARBs), to control blood pressure, control proteinuria, and protect renal function. Symptomatic supportive treatment such as low-salt and low-fat diet, blood lipid regulation, and anticoagulation is given; For patients with moderate risk, it is recommended to first give the same symptomatic supportive care for low risk, observe for 3 to 6 months, and if nephrotic syndrome persists and worsens, or if there are poor prognostic factors, glucocorticoids combined with immunosuppressant aspiration therapy; For high-risk patients, combination of glucocorticoids and immunosuppressants is recommended. Some intermediate-risk patients can be treated immediately for high-risk patients according to the actual situation. If the clinical effect is still poor, it is recommended to switch to more advanced biologics, such as rituximab, which is a human-mouse monoclonal antibody specific to CD20 on the surface of B lymphocytes, which can bind to the CD20 antigen with high affinity, resulting in the clearance of B lymphocytes, thereby inhibiting the renal immune response; or there should be a combination of multiple drugs in small doses; Or give some traditional Chinese medicine extraction preparations, such as tripterygium wilfordii polyglycosides, animal experiments have proved that tripterygium wilfordii polyglycosides can efficiently and non-selectively inhibit T lymphocytes and B lymphocytes, and have a significant effect on humoral immunosuppression.

Evidence-based studies have shown that the use of corticosteroids alone is not recommended for the treatment of IMN because it has no significant efficacy [14], and in the 2011 Clinical Practice Guidelines of the Global Organization for the Improvement of Prognosis in Kidney Disease (KDIGO), it was clearly stated that "hormone monotherapy is not recommended" for the treatment of IMN [15]. Therefore, most patients need to take immunosuppressants at the same time, and the result is not only an increase in the cost of treatment, but also a sharp increase in the risk of treatment. Therefore, it is very important to identify high-risk IMN patients through clinical and pathological indicators at an early stage to reduce the additional treatment costs and risks of low-risk patients. Studies have shown [7] that early and active treatment can effectively alleviate proteinuria and improve renal survival in high-risk IMN patients. Because of the insidious onset of IMN, which is a common glomerular disorder, approximately 80 percent of adults with IMN are diagnosed with nephrotic syndrome because they do not experience discomfort or some kind of pain in the early stages of IMN [16]. In the clinical training, I learned through the inquiry of the first patient that most of them came to the hospital through the physical examination of the unit, and found abnormal urine test or kidney function, followed by the treatment of edema of the lower limbs or eyelids, then for foamy urine, hematuria, and finally for digestive symptoms such as decreased appetite. Among them, abnormal renal function and digestive symptoms usually indicate that the disease has passed through the early stage, and edema in the

lower limbs also indicates that serum albumin has been severely lost, and urine protein has persisted for a period of time. Therefore, it is recommended that first of all, regular hospital physical examination, followed by foamy urine, edema, hematuria and other symptoms to seek medical attention in time, and finally if diagnosed with glomerular disease, it is recommended to perform renal biopsy in time to determine the pathological type and pathological stage to standardize the treatment, although renal puncture is a kind of harm to the kidney, but the clinical manifestations can not replace pathological diagnosis, renal biopsy is the gold standard for IMN diagnosis. Therefore, patients with IMN should be treated as soon as possible, and renal biopsy and puncture should be performed as soon as possible, and active treatment should be given after the diagnosis is clear, so as to protect renal function, prevent complications, and improve prognosis.

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