Progress in the Mechanism of IgA Nephropathy Renal Injury

Si-Qi ZHANG¹,a, Rui-Si XU²,b, Jian YIN³,c⁺

¹Nephrology, China-Japan Union Hospital of Jilin University, 126 Xiantai Street, Changchun, Jilin Province, China.
²Endoscopy Center, China-Japan Union Hospital of Jilin University, 126 Xiantai Street, Changchun, Jilin Province, China.
³Vascular Surgery, China-Japan Union Hospital of Jilin University, 126 Xiantai Street, Changchun, Jilin Province, China.

asiqi@jlu.edu.cn , bxrs-email@163.com , c16407026@qq.com

*Corresponding author

Keywords: IgA nephropathy, Mesangial cells, Sertoli cell.

Abstract. IgA nephropathy is the most common primary glomerular disease in the world, accounting for about 25% ~50% of primary glomerular diseases [1]. Clinical IgA nephropathy occurs in young and middle-aged adults, and about 30-40% of patients enter the end-stage renal failure (ESRD) in 10-20 years[2], which brings a heavy burden to the country and society. IgA nephropathy pathogenesis is not clear at present, has long been a mesangial cells is considered to be major cell types of the disease, IgA nephropathy and recent study found that IgA nephropathy mesangial cells and sertoli cell and the interaction between the tubular epithelial cells, the common cause of kidney damage of IgA nephropathy [3-5]. 2009 international IgA nephropathy group proposed IgA nephropathy Oxford disease classification, it included four indicators of clinical outcomes with independent predictive value, namely, mesangial matrix (M), segmental sclerosis (S), endothelial cell hyperplasia (E) and tubular atrophy and interstitial fibrosis (T) [6]. Has rainbow multicenter IgA nephropathy as verification of Oxford's pathological classification in China, M, S, T three pathological indexes closely related to long-term renal outcomes for patients with IgAN, but E no obvious correlation with long-term prognosis. Therefore, mesangial cells, foot cells and tubule epithelial cells play an important role in the development of IgA nephropathy. In this paper, combined with domestic and foreign literature on mesangial cells, sertoli cell and tubular epithelial cells of IgA nephropathy renal injury mechanism, to clarify to the pathogenesis of IgA nephropathy [7], and clinical diagnosis and treatment to provide new inspiration point and basis.

IgA Nephropathy Membrane Reproductive Mechanism

IgA nephropathy is a primary glomerular disease characterized by IgA - based immune complex deposition in the mesangial area, accompanied by different levels of glomerular mesangial proliferation and extracellular matrix accumulation. Abnormal glycosylation IgAI is considered to be the main factor of IgA nephropathy development, the study found that patients with IgA nephropathy abnormal serum glycosylation IgAI levels, and mesangial area sedimentary IgAI exist glycosylation in [8, 9]. From IgA nephropathy patients serum separation contain glycosylation defect IgAI the high molecular weight of immune complex can stimulate the proliferation of mesangial cells and the formation of extracellular matrix, and with low
sugar levels IgAl content of high stimulation effect, the more obvious; But only with a small low sugar levels of IgAl polymer molecular weight or remove IgAl immune complex stimulated mesangial cells will not appear the proliferation of mesangial cells, suggesting that contain glycosylation defect IgAl the high molecular weight of immune complex is the key factor of mesangial cell proliferation, and antigen (low sugar base IgAl) and antibody (low sugar base IgAl specific IgG or IgA1) is very important to the formation of immune complex [10].

Contains IgAl glycosylation defects of high molecular weight immune complex and mesangial cell receptors by IgAl, in turn, stimulates the proliferation of mesangial cells and extracellular matrix formation, and increase of cytokines and extracellular matrix protein gene transfer record [11]. Known IgAl receptors have ASGP - r, pIgR, Fc - α R (CD89), Fc - α/mu receptor and transferrin receptor (CD71 surface), and only the transferrin receptor on mesangial cells with high molecular immune complex knot prescriptions containing IgAl, however whether transferrin receptor direct work, whether there are other in mesangial cells IgAl receptor is unclear [12]. Mesangial cells of the immune complex compound after stimulation of cell proliferation and extracellular matrix overproduction and cells for the child, the release of inflammatory chemokines, the release of cytokines, inflammatory factors and further affect the foot cells, tubular cells and the expression of related factors, mediated foot cells, renal tubular damage.

**Mechanism of IgA Nephrotic Foot Cell Injury**

Focal segmental sclerosis (FSGS) is the most common pathological type of IgA nephropathy and is associated with poor prognosis [13]. Human foot cells can hardly with IgA nephropathy patients of low sugar levels polymer IgAl, in vitro studies show that IgA nephropathy patients polymers IgAl stimulation of mesangial cell activation, and have no direct effect on foot cell. Now think that mesangial cells and foot between the "crosstalk" is the key to cause IgA nephropathy podocyte damage.

Another study by Wang found that the multiple IgAl stimulating foot cells could directly lead to death.Dendrin is a kind of podocyte, which is normally located at the foot of the fascicle of the foot, and in a variety of damage models, Dendrin is displaced to the cell nucleus. In IgA nephrotic acute kidney injury, the dendrin positive cell nucleus was significantly increased, and compared with the small lesions, the staining of the urinary foot cells dendrin and apoptotic marker annexin V was significantly increased in patients with IgA nephropathy. TGF- beta secreted by membrane cells plays an important role in the apoptosis of apoptosis in IgA nephropathy.

TNF-α, a source of mesangial cells, also plays a crucial role in the "crosstalk" between mesenchymal cells and podocytes. Previous studies found that patients with IgA nephropathy polymers IgAl mesangial altogether after cell culture supernatant treatment feet can cause the production of TNF -α was time and dose dependent increase, and healthy controls IgAl mesangial co-culture supernatant will not appear this kind of effect after.

In comparison with IgA nephropathy source polymers IgAl and tubule cells, foot cells, endothelial cells and other cells in the kidney type culture supernatant after treatment podocytes Does not appear the podocyte differentiation effect. Therefore, TNF- -α plays an important role in the damage of IgA nephrotic foot cells.

Angiotensin II mediated IgA nephropathy is another important because tired of sertoli cell damage. Wang found that the source of IgA nephropathy patients polymers IgAl angiotensin n
can promote mesangial cells, and co-culture supernatant can be mediated in podocyte nephrin expression, and this effect can be enalaprilat or valsartan some reversal. At the same time, captopril and losartan significantly inhibited the synthesis of TGF-beta cells in mesangial cells.

**IgA Renal Tubular Interstitial Injury Mechanism**

Previous studies have focused on glomerular lesions, and few studies have been done on renal tubular interstitial damage. In recent years, numerous studies have shown that renal tubular interstitial damage is also an important risk factor for the poor prognosis of IgA nephropathy.

So what is the mechanism of IgA nephrotic interstitial injury?

First, the infiltration of individual nuclear cells and their mediated inflammatory responses play an important role in IgA nephropathy and small tubular interstitial lesions.

At present, the communication between glomeruli and renal tubules has become a research hotspot in the mechanism of IgA nephropathy. Chan, such as the blood of the the study found that source of IgA nephropathy with IgA can with tubular epithelial cells to a combination of IgA receptor connection, but its bond strength is only 1/10 and mesangial, and IgA combined with tubular epithelial cells after does not lead to TNF-α, MIF and ICAM-1, the release of cytokines, further verify the kidney sedimentary IgA doesn't directly result in tubular damage of injury. Next, with IgA nephropathy sources of serum IgA mesangial cell culture, in co-culture supernatant after stimulation of renal tubular epithelial cells, the results found that hyperplasia of renal tubular epithelial cells in the enhancement, the TNF-α, MIF and ICAM-1 content increased, prompt communication between mesangial cells and renal tubular is the key to the tubular damage.

Angiotensin II in glomerular hemodynamics adjustment and played an important role in immune injury, the study found that renal tubular epithelial cells can express angiotensin II receptor 1 (ATR1) and the receptor 2 (ATR2). Renin angiotensin system plays an important role in IgA nephropathy in the glomerulus-tubule communication and tubule interstitial injury. The study reported that angiotensin n and aldosterone were used to regulate the apoptosis of tubule epithelial cells through regulating oxidative damage.

**Summary**

The interaction between mesangial cells which is the key to the progression of IgA nephropathy. The mesangial cells are the source of renal injury TNF-α, angiotensin I, inflammatory factors and related these cytokines can be applied to the foot cells and tubular epithelial cell mediated the damage. The foot cell is the key to the glomerular filtration barrier. In normal circumstances, the large molecular material in the glomerulus can not pass through the membrane to stimulate the damage of the tubule. IgA nephropathy in mesangial cells release caused by child first on foot cell filtration barrier damage, and a large number of cells for children through the filtration membrane in tubular epithelial cell mediated the damage. The cytokines released by mesangial epithelial cells of the foot cells and the epithelial cells of the epithelial cells themselves also produce positive feedback that leads to a vicious cycle of injury and aggravates the progression of the disease. Currently, there are no specific measures for the diagnosis and treatment of IgA nephropathy. It is believed that the diagnosis and treatment of
IgA nephropathy will be more simple and effective with the continuous clarification of the mechanism of IgA nephropathy.

References


