Lecture Code : GL01-S3
Session Name : Glomerulonephritis
Session Topic : Glomerular and Tubulointerstitial Disorders
Date & Time, Place : June 20 (Fri) / 10:40-12:20 / Room 1 (GBR 101)

Classification and Management of MGRS

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Monoclonal immunoglobulins are a well-established cause of kidney injury. Recent advances have solidified the idea that kidney injury is not related to the tumor or tumor burden in majority of cases but rather to the innate toxicity of the monoclonal immunoglobulin. The clinical term monoclonal gammopathy of renal significance (MGRS) designates B-cell and plasma cell clones that do not meet the criteria of malignancy or requirement of immediate treatment but result in kidney injury. The kidney diseases associated with MGRS are best classified based on the immunofluorescent (IF) and electron microscopy (EM) characteristics. The first major category must have a positive staining for immunoglobulin or immunoglobulin components on IF and organized structures on EM. There are subgroups in this category. The first subgroup consists of kidney diseases with fibrillar substructures which is represented by immunoglobulin light chain amyloidosis. The second subgroup is characterized by kidney diseases with microtubular substructures represented by immunotactoid glomerulopathy and monoclonal cryoglobulinemic glomerulonephritis which comprises of all type I and some type II cryoglobulinemias. The third subgroup comprises of kidney diseases with crystalline deposits. Light chain proximal tubulopathy, crystal storing histiocytosis, (cryo)crystalglobulinemic glomerulonephritis and the recently added light chain crystalline glomerulopathy belong to this group. The next major category consists of diseases with positive immunoglobulin on IF but no organized substructure on EM. This group is represented by monoclonal immunoglobulin deposition disease and proliferative glomerulonephritis with monoclonal immunoglobulin deposits. Finally, the third major category is represented by those with negative immunoglobulin staining on IF and no organized structure on EM. If there is dominant staining for C3 on IF, then these are monoclonal immunoglobulin related C3 glomerulopathy which consists of C3 glomerulonephritis and dense deposit disease. If there are no deposits on IF, then this is monoclonal immunoglobulin related thrombotic microangiopathy (TMA). The principal treatment strategy for MGRS related kidney diseases is clone directed therapy. Plasma cell clones which

make up majority of the clones should be treated with a daratumumab based regimen either monotherapy or in combination with other anti-plasma cell agents. While B-cell clones expressing CD20 should be targeted with an anti-CD20 antibody such as rituximab. Adjuvant therapy with complement inhibitors may be helpful especially in MGRS related TMA. The kidney diseases associated with MGRS represent a group of kidney diseases with a specific pathogenesis and special treatment to preserve the kidney function.

Keywords: monoclonal gammopathy, glomerulonephritis, amyloidosis, clone direct therapy, daratumumab