**Revisor A**

Commentary 1: ABSTRACT- The sentence “MGRS can cause serious renal and systemic lesions” – is better change to MGRS can cause serious renal lesion (not systemic).

* In the section “Abstract”, 1st paragraph, 2nd phrase was reformulated. Correction: “Nevertheless, MGRS can cause serious renal lesions, leading to high morbidity”.

Commentary 2: ABSTRACT- In C3GN, a monoclonal protein can cause renal damage (…) through continuous activation of the alternative (…)” – the monoclonal protein do not activate the alternative pathway. It acts as an antibody against the inhibitors of the pathway or acting as a C3 nephritic factor. Please review the sentence.

* In the section “Abstract”, 1st paragraph, the 3th phrase was reformulated: “In C3 Glomerulonephritis (C3GN), a monoclonal protein can cause renal damage indirectly. Acting as an autoantibody, the protein cannot be detected in the kidney biopsy, promoting the dysregulation of the alternative pathway of complement.”.

Commentary 3: ABSTRACT- Conclusion – “(…) of the complex interaction between monoclonal complement and renal damage” - what is monoclonal complement? This is a wrong sentence and has to be changed.

* In the section “Abstract”, 3st paragraph, 1st phrase, the error “monoclonal complement” was corrected to monoclonal gammopathy: “With the increasing understanding of the complex interaction between monoclonal gammopathy and renal damage, such as C3GN, it becomes clear that an early recognition is crucial, as Ig-directed therapy might improve outcome.”.

Commentary 4: MANAGEMENT - I would change the subtitle “management” to “diagnostic approach”.

* We thank you for the suggestion and have reformulated as suggested: section “Diagnostic approach”.

Commentary 5 and 6: MANAGEMENT - Starting with the presentation – de novo renal failure / nephritic syndrome that leads to a renal biopsy and explain why is important to do the renal biopsy (for instance the 1st paragraph of the Renal Biopsy section). Then, enter the Renal Biopsy section. Here the authors have to describe what are the predominant glomerular lesions (2nd and remaining paragraphs). After, they have to explain that all C3GN deserves to have two things: complement study and monoclonality exclusion.

* We appreciated the suggestion and we have reformulated the section “diagnostic approach”, including the subsection “presentation” and “renal biopsy”. However, we believe that in the subsection “presentation” a review of the clinical characteristics of C3GN associated with monoclonal gammopathy should be done, allowing the readers to understand the importance of all the subsections of the “diagnostic approach”, which include not only renal biopsy but also the complement study: screening for monoclonal immunoglobulin and clonal identification.

Commentary 8: After this explanation, move to complement evaluation. I think authors should create a picture of classical, lectin and alternative pathways, and explain with more details the alternative pathway.  Just in this way the readers can understand what is written about the “complement evaluation”.

* We thank you for the suggestion and in order to explain the complement cascade, figure 1 “Complement cascade” was added in the subsection “complement evaluation”.

Commentary 7: Move to screening for monoclonal Ig: and please first explain what is a monoclonal protein (…)

* We followed the suggestion, and have reformulated the section “Introduction” in order to explain that a monoclonal protein can correspond either of a intact monoclonal immunoglobulin or immunoglobulin light chains. This explanation can be found as mentioned, in the section “Introduction”, 5th paragraph, 2nd sentence: “The nephrotoxic monoclonal immunoglobulin (Ig) or fragment can affect any structure in renal parenchyma, and the pattern of renal lesion is mostly determined by the intrinsic structural and physicochemical characteristics of the monoclonal protein (intact monoclonal immunoglobulins or immunoglobulin light chains), rather than by the rate of production, and clone features”.

Commentary 7, 8 and 9: MANAGEMENT – 7-Move to screening for monoclonal Ig: and please first explain what is a monoclonal protein and what are the methods to diagnose that (use the part of “clonal identification” already written). 8-After this explanation, move to complement evaluation. (…) 9-Finally, the association between a monoclonal protein and the complement cascade can be resumed (authors called the “screening for monoclonal Ig”)

* We are grateful for your suggestion, and as referred previously, we have reformulated the section “diagnostic approach”, including the subsection “complement evaluation”, “screening for monoclonal immunoglobulin” and “clonal identification” in order to highlight the importance of each step of evaluation. However, since C3GN is characterized by dysregulation of the alternative pathway of the complement system, we consider that the second step after the diagnosis of C3GN by renal biopsy should be the evaluation of complement. On the other hand, we know that 31,2% of patients older than 50 years with C3GN will have a detectable serum monoclonal immunoglobulin, and this monoclonal immunoglobulin can be a trigger to this disease, acting as an autoantibody against alternative pathway regulating proteins. With this in mind, we proposed as the third step the screening for monoclonal immunoglobulin, and finally, and as the fourth step the search for the clone responsible for monoclonal immunoglobulin production “clonal identification”.

Commentary 10: TREATMENT - The sentence “Prophylaxis against reactivation of herpes zoster should not be missed” should be in another place. If authors want to talk about prophylaxis in QT, they should also speak about fungal prophylaxis, pneumocystis and so on.

* As the main point of the “Treatment” section is not the prophylaxis approach, we followed the suggestion and eliminated the sentence at the 2nd paragraph of that section.

**Revisor B**

Commentary 1: As a major observation I think it should be stated, in the "methods" section, the number of searched publications, as well as the exclusion and inclusion criteria for this non-systematic review.

* We appreciated for the suggestion and have reformulated as suggested: “We performed a comprehensive search in databases and scientific journals, such as PubMed, Nature Reviews Nephrology and Kidney International, including the terms ‘C3 Glomerulonephritis’ and ‘Monoclonal gammopathy of renal significance’ until December 2019. A total of 58 articles were initially selected, with subsequent exclusion of 28 (language not in English, and/or inclusion of glomerulonephritis other than C3GN).”.

Commentary 2: Introduction: please add "%" after 5.3 and 7.5 in the phrase "monoclonal Gammopathy of Undetermined Significance (MGUS) is the most common plasma cell disorder. The prevalence in general population is about 0,7% and increases with age, to 3.2%, 5.3 and 7.5 in [SPC1] people older than 50 years, 70 years and 85 years, respectively. It is also estimated to be more prevalent in men (4,0%) than in women (2,7%)."

* In the section “Introduction”, 1st paragraph, 2nd phrase we add “%” as required: “The prevalence in general population is about 0,7% and increases with age, to 3.2%, 5.3% and 7.5% in people older than 50 years, 70 years and 85 years, respectively. It is also estimated to be more prevalent in men (4,0%) than in women (2,7%).”.

Commentary 3: Correct the word "healthy" in the section "Screening for monoclonal immunoglobulin".

* In the section “screening for monoclonal immunoglobulin”, 1st paragraph, 6th phrase, we correct the word “healthy”: “On the other hand, only free lights chains are filtered by healthy glomerulus, and consequently urine protein electrophoresis is the lowest sensitive test.”.

Commentary 4: In the section "treatment" I think the comment referring Thalidomide should be rephrased. "Thalidomide is an immunomodulatory drug with activity against plasma and B cells, but with significant side effects". The authors give their personal opinion and it should be changed for "significant neurotoxicity", as stated in major publications ("Common and rare side-effects of low-dose thalidomide in multiple myeloma: focus on the dose-minimizing peripheral neuropathy", European Journal of Haematology. 72(6):403-409, June 2004.")

* In the section “treatment”, 3th paragraph, 8th phrase, we rephrased the side effects of Thalidomide and add the correspond bibliography: “Thalidomide is an immunomodulatory drug with activity against plasma and B cells, albeit with potential neurotoxicity.”.

Commentary 5: In the same section, the phrase "Autologous stem cell transplant can be beneficial as a complementary therapy,  helping to achieve a deeper and sustained or even a complete hematological response, essential to reduce the risk of recurrence, particularly after renal transplant" should be addressed for plasma cell disorders.

* In the section “treatment”, 3th paragraph, 8th phrase, we correct the sentence about autologous stem cell transplant: “Furthermore, in patients with a plasma cell disorder, autologous stem cell transplant can be beneficial as a complementary therapy, helping to achieve a deeper and sustained or even a complete hematological response, essential to reduce the risk of recurrence, particularly after renal transplant”.

**Revisor C**

Commentary 1: C3GN associated with MGRS is a rare disorder, with a complexity that deserves a separate review of the pathophysiology, differential diagnosis and treatment.

* We agree with your suggestion and will keep it in mind for a future article.

Commentary 2: The title is instructive, all sections are well summarized, however treatment section, in my opinion, should mention its limitations: no disease- specific treatments are available, although Ig-targeted agents may be helpful in some patients.

* We include this limitation at the 2nd paragraph of the section “Treatment”: “Despite the absence of specific guidelines for the treatment of C3GN associated to MGRS, there is some evidence that Ig-target therapy is useful in delaying the progression of renal disease, highlighting the correlation between the reduction of monoclonal Ig and better renal outcome”.

Commentary 3: Also, it should be stressed that some of the potential Ig-targeted agents have a considerable toxicity, precluding their use (when renal survival is to achieve without compromising patient survival).

* We include this limitation at the 2nd paragraph of the section “Treatment” (5th sentence): “The type and nature of monoclonal protein is important for the selection of Ig-targeted agent, but the clinician has also to take in account histological features of C3GN (balance between active and chronic lesions), renal function, and potential toxicity, which can preclude some of them”.