Dear Editors and Reviewers,

Thank you very much for taking the time to evaluate our manuscript (ID: 74468). We have resubmitted a revised manuscript entitled " Transition from Minimal Change Disease to Focal and Segmental Glomerulosclerosis related to occupational exposure: A case report ", and have resolved all issues point-by-point according to the reviewer's suggestions. Detailed responses are highlighted in red as follows:

Response to reviewers' comments

Reviewer #1:
Specific Comments to Authors: In this manuscript, the authors report a case of focal and segmental glomerulosclerosis (FSGS) related to occupational exposure that had transitioned from minimal change disease (MCD). This case report is clinically useful. However, the following points need to be addressed. Major comments:

1. The authors conclude that this case is a transition from MCD to FSGS. Do the authors consider the possibility that this case is a coincidence for MCD and FSGS? Because MCD had already gone into complete remission 20 years ago.

Response: Thank you for your constructive comments, which will help us to improve the quality of the article. We have supplemented and revised the third paragraph of the discussion section of the manuscript according to your suggestions **(Line 238-252/Page 10-11)**:

"It is no coincidence that pathological changes occurred before and after the repeated kidney biopsy. FSGS is not a diagnosis of a specific disease, but a progressive glomerular pathological change caused by podocyte depletion. Most glomerular diseases eventually result in loss of renal function due to FSGS, and FSGS lesions can be described as an outcome of persistent damage in certain glomerular diseases or as a common endpoint event in some glomerular diseases[11]. MCD and FSGS are both podocyte diseases, and when FSGS is excluded from being missed or misdiagnosed as MCD, their sequential occurrence often suggests that FSGS is the progression of MCD[6]. The patient did not have regular follow-up visits when his NS was in remission, which was also a limitation of this case. Since recurrence of MCD is based on proteinuria, this patient most likely had an undetected recurrence of MCD. We hypothesized that the neglected recurrent MCD lead to persistent podocyte damage that ultimately caused FSGS, and heavy metal exposure is involved in exacerbating this process."

2. The authors suspect that the exposure of cadmium and lead caused FSGS. However, cadmium and lead blood levels were not that high compared to normal

ranges. Do the authors think that these levels of cadmium and lead can induce FSGS?

Response: Thank you for your constructive comments. The levels of cadmium and lead of this patient were not that high compared to the normal range, but long-term exposure to low doses of the metal can also cause kidney damage, even at relatively low levels (Lead < 5μg/dL; Cadmium < 0.6μg/L). And the combination of the two can cause more profound nephrotoxicity.

We have supplemented the references and revised the manuscript **(Line 268-274/Page 11)** according to your suggestions.

Reviewer #2:

Specific Comments to Authors:

1. - Please, in the figures, add a symbol that indicates histological lesions and include into the text:

- vacuolar degeneration glomerular and renal tubular.

- Fusion of glomeruli and epithelial cells.

- Patchy atrophy, lymphocyte infiltration, fibrosis, and thickening of -arterioles.

- Microvillous transformation of podocytes.

Response: Thank you for your professional comments. In consideration of your thoughtful suggestions, we have added symbols **(arrows of different colors)** to indicate histological lesions in the figures and texts. We have provided the original figure documents in a PowerPoint, to ensure that all figures or arrows can be reprocessed by the editor.

2.- In table 1, include:

- ratio proteinuria/creatinine or albumin/creatinine, this parameter is most trustworthy than 24hrUP.

- Percentage of dysmorphic and normorphic erythrocytes.

- Results of total cholesterol and triglyceride (serum) are part of NS presentation.

- Eliminate PRO and BLD because these are redundant with proteinuria and RBC cells.

Response: Thanks again for your professional comments. We have revised Table 1 according to your suggestions. We added the percentage of dysmorphic erythrocytes, total cholesterol and triglyceride, eliminating PRO and BLD. Since the ratio proteinuria/creatinine was not routinely examined, we added this parameter while retaining the data of 24 hrUP.

3.- Discussion section:

Since the authors suggest that NS was developed because of heavy metal exposure, they do not show data correlated with their statement. Please discuss its accumulation in the tissue, exists multiple works about this topic.

Response: Thank you for your constructive comments. In the third paragraph of the "Discussion", we have added a section describing the correlation between NS and heavy metal exposure **(Line 259-274/Page 11)**, and supplemented references **[13-19]** for these contents. We hope the revisions of the manuscript will address your concerns sufficiently. The contents are as follows:

" Nephrotoxicity induced by excess exposure to certain metals is well known, and lithium has been shown to cause MCD and FSGS[13]. Although there is not enough literature to confirm that lead and cadmium can cause FSGS, it has been proven that both of them induce podocytotoxicity and can even induce podocyte apoptosis[14,15]. Kidney exposure to cadmium and lead mainly causes proximal renal tubule dysfunction, acute exposure can lead to Fanconi syndrome, and long-term exposure leads to a persistent decline in kidney function[16,17]. This may explain the positive urine sugar content of the patient, and it may also be the reason for the occurrence of NS and ESKD in this patient. The levels of cadmium and lead in the blood of this patient were not that high compared to the normal range, but chronic, long-term exposure to low doses of the metal can cause kidney damage. Both lead and cadmium can increase the risk of chronic kidney disease, even at low levels (Blood lead < 5 μg/dL; Blood cadmium < 0.6 μg/L)[18,19]. The kidney damage caused by lead and cadmium is long-term and chronic, and combination of the two has a more profound nephrotoxicity. "

Thank you again for your professional review work on our manuscript.

Best regards,

Wen-jing Zhao