

Reviewer #1:

Specific Comments to Authors: Dear author, I would like to thank for your effort and bringing up this interesting finding to the scientific community. I have gone through the manuscript and suggest some minor corrections. The errors and comments are marked in the text.

Respond: Thank you for your suggestions. We have revised.

Reviewer #2:

Specific Comments to Authors: The Authors reported a case of a 7-year-old boy with steroid-resistant nephrotic syndrome (SRNS). After kidney biopsy, idiopathic membranous nephropathy (IMN) was diagnosed. The article is interesting and deserves attention. IMN is rare in children. There are not recommendations on IMN therapy in children. However, the paper needs revision. 1. Data concerning the presented case are scarce. The Authors should add information about the patient's weight and height in both hospitals. What were the total daily doses of prednisone and methylprednisolone (as pulses) in the first hospital? The sentence " (...) pulse therapy (8 mg/kg each time, two times every two weeks)" isn't precise. Did the patient have leukocyturia and hematuria at admission to the first hospital? What about edema? Were they stable during the time of observation? Additional laboratory data: What tests were performed to exclude secondary MN? Were autoantibodies to the M-type phospholipase A2 receptor (PLA2R) in the patient's serum determined? At admission and during follow-up? On what did the authors base their decision to treat with Tacrolimus and its dose? Was the patient treated with Tacrolimus only or also with steroids? 2. The Authors stated: "As a rare cause of nephrotic syndrome (NS) in children, idiopathic membranous nephropathy (IMN) may progress to chronic kidney disease (CKD) and even end-stage renal disease." Please add some references. Was kidney function normal and stable in the presented case? 3. The Authors didn't present other described cases of children with IMN. Only one article was mentioned (ref. no 11). 4. In discussion, possible therapeutic strategies in children with IMN should be discussed. 5. The conclusions didn't appropriately summarize the data

that the study provided. The diagnosis of MN was made on the basis of a renal biopsy. That fact was not underlined in conclusions. On the other hand, “the possibility of progressing to CKD” is mentioned. It didn’t correspond to the case. 6. Table 3 needs modification. Primary nephrotic syndrome can be steroid-resistant also. It is not the same as MCD. 7. References are given improperly. For example, ref. [1]: Luisa, Albina etc. are first names. The same concerns ref. [3]

1. Data concerning the presented case are scarce.

1.1 The Authors should add information about the patient's weight and height in both hospitals.

Respond: The patient's weight and height in local hospital were 20Kg and 115.3cm.

The patient's weight and height in our hospital were 26Kg and 115.9cm.

1.2 What were the total daily doses of prednisone and methylprednisolone (as pulses) in the first hospital?

Respond: The total daily doses of prednisone and methylprednisolone (as pulses) in the first hospital were 40mg and 400mg respectively.

1.3 The sentence” (...) pulse therapy (8 mg/kg each time, two times every two weeks)” isn’t precise.

Respond: We have revised in the manuscript. Cyclophosphamide (CTX) pulse therapy refers to 8 mg/kg • d each time used for continuous two days every two weeks.

1.4 Did the patient have leukocyturia and hematuria at admission to the first hospital? What about edema? Were they stable during the time of observation?

Respond: The patient had leukocyturia, hematuria and facial edema at admission to the first hospital. They were not stable during the time of observation. After methylprednisolone pulse followed by oral prednisone and cyclophosphamide pulse therapy, proteinuria, hematuria, leukocyturia, and facial edema had remission, but there was no obvious incentive to aggravate again. We changed the therapeutic strategy which were tacrolimus combined with prednisone. The proteinuria, hematuria, leukocyturia and facial edema gradually improved.

1.5 Additional laboratory data: What tests were performed to exclude secondary MN? Were autoantibodies to the M-type phospholipase A2 receptor (PLA2R) in the

patient's serum determined?

Respond: To exclude secondary MN, we performed anti streptolysin O(ASO), autoantibody, anti neutrophil coated antibody(ANCA), complement, hepatitis virus, syphilis, AIDS, tuberculosis, urine culture, sputum culture, chest CT plain scan and urinary ultrasound. We did not perform autoantibodies to the M-type phospholipase A<sub>2</sub> receptor (PLA<sub>2</sub>R) in the patient's serum, but in renal tissues at admission.

1.6 At admission and during follow-up?

Respond: The first admission time was 6 months after onset. The follow-up time was 15 months.

1.7 On what did the authors base their decision to treat with Tacrolimus and its dose? Was the patient treated with Tacrolimus only or also with steroids?

Respond: Tacrolimus is the first choice of treatment for SRNS in children. The dose of tacrolimus referred to the literatures with respect to the treatment of MN. The patient treated with Tacrolimus and steroids.

2. The Authors stated: "As a rare cause of nephrotic syndrome (NS) in children, idiopathic membranous nephropathy (IMN) may progress to chronic kidney disease (CKD) and even end-stage renal disease." Please add some references. Was kidney function normal and stable in the presented case?

Respond: We had added some references. Kidney function remained normal in the presented case during follow-up.

3. The Authors didn't present other described cases of children with IMN. Only one article was mentioned (ref. no 11).

Respond: Thank you for your suggestions. We had added some references.

4. In discussion, possible therapeutic strategies in children with IMN should be discussed.

Respond: We had documented in second paragraph in the part of discussion.

5. The conclusions didn't appropriately summarize the data that the study provided. The diagnosis of MN was made on the basis of a renal biopsy. That fact was not underlined in conclusions. On the other hand, "the possibility of progressing to CKD" is mentioned. It didn't correspond to the case.

Respond: We have revised the part of conclusion. Additionally, CKD referred to renal impairment (pathological, blood, urine, and imaging abnormalities)  $\geq 3$  months. Therefore, the patient with normal level of SCr can be diagnosed CKD I stage.

6. Table 3 needs modification. Primary nephrotic syndrome can be steroid-resistant also. It is not the same as MCD.

Respond: Thank you for your suggestions. We have revised.

7. References are given improperly. For example, ref. [1]: Luisa, Albina etc. are first names. The same concerns ref. [3]

Respond: Thank you for your suggestions. We have revised.

Reviewer #3:

Specific Comments to Authors: - the child described was treated with cyclophosphamide (CTX) pulse therapy after diagnosis of corticoreistant nephrotic syndrome, but CTX is a drug used mainly in steroid dependent nephrotic syndrome. could you explain the raisons of the utilize of thi drug? -a complement study was not indicated in the initial assessment of the child with steroid resistant nephrotic syndrome.

1. The child described was treated with cyclophosphamide (CTX) pulse therapy after diagnosis of corticoreistant nephrotic syndrome, but CTX is a drug used mainly in steroid dependent nephrotic syndrome. could you explain the raisons of the utilize of thi drug?

Respond: CTX was used for this patient in other hospital, so we don't know the reasons. However, 2019 Kidney Disease Improving Global Outcomes (KDIGO) pointed out that alkylating agents remain the only agents proven effective in preventing ESKD or death. There were some other practice guidelines also mentioned the efficacy of CTX.

2. A complement study was not indicated in the initial assessment of the child with steroid resistant nephrotic syndrome.

Respond: Before the diagnosis of SRNS, methylprednisolone pulse therapy

(20mg/Kg.d for 3 days) followed by oral prednisone (2 mg/kg • d for two weeks) was used to confirm the diagnosis.

Reviewer #4:

Specific Comments to Authors: The occurrence of Idiopathic MN is indeed rare. Reporting this case could be of interest. However, i think the authors should detail their medical checkup regarding idiopathic MN (serologies, CT-scan results, etc), and maybe provide histological images to illustrate their case. The long-term follow-up of this child could also be precised.

1. However, I think the authors should detail their medical checkup regarding idiopathic MN (serologies, CT-scan results, etc), and maybe provide histological images to illustrate their case.

Respond: The laboratory tests of the patient revealed heavy proteinuria, hypoproteinemia, hyperlipidemia, leukocyturia, hematuria and pathological casts. Blood count, complement, renal function and CT scan were normal. Urinary ultrasound was the echo of bilateral renal parenchyma was slightly enhanced. These results were shown in tables, and histological images were presented in Figure 1.

2. The long-term follow-up of this child could also be precised.

Respond: Thank you for your suggestions. We have revised.