Reviewer’s report

Title: Cilostazol-induced acute tubulointerstitial nephritis accompanied by IgA nephropathy: a case report

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Reviewer: Thomas Robert

Reviewer’s report:

The author describes a case of acute kidney injury with suspected acute tubulo-interstitial nephritis secondary to cilostazol. Moreover, they discover in the same time IgA nephropathy.

General comments:

I’m not convinced about the diagnostic of ATIN with sur-imposed IgA nephropathy. The author does not discuss the possibility that IgA nephropathy with rapidly progressive nephritis might be the diagnostic.

Major Comments:

1. The author doesn't explain all the history of the case: where the patient was admitted and for what reason? This is important in the description of the case.

2. Authors must specify the chronology of events including the number of days between the introduction of cilostazol and the discovery of acute kidney injury.

3. Does the patient have medical history of allergy? The author should specify this detail.

4. Gallium 67 scanning is useful to distinguish ATIN from acute tubular necrosis. The signification of the Ga67 scintigraphy if the patient has glomerulopathy is difficult to interpret. So, the authors must interpret cautiously the result.

5. About the biopsy:
   a. The author should to precise the stains (hematoxylin and eosin for figure 3a? PAS for figure 3b?) and the magnification (x400?)
b. Description of the light microscopy is a major point of the case. The authors should describe in more detail the injury and some points need to be clarify and discuss:

i. For the tubule-interstitial compartment:

1. They describe diffuse monocyte infiltration. The author should increase magnification of the picture 3a to see morphology of interstitial infiltrate and tubular cell. The hallmark of ATIN is the infiltration of inflammatory cell with T lymphocyte, B lymphocyte and sometimes plasma cell. They have to demonstrate presence of lymphocyte. By the way, IgA nephropathy can be accompanied by nonspecific mononuclear cell inflammatory infiltrate.

2. We can also see on figure 3a sparse acute tubular necrosis.

3. It seems also to have hematic cylinder, it will be suitable to perform trichom stain. If it's the case, it would be a reason to have elevation of creatinine. Furthermore, Uromodulin seems to be present in the Bowman's space and in some tubule, suggesting obstructive cause. It will be suitable to perform Horseradish peroxidase staining.

ii. Is there any granuloma?

iii. I'm not totally agree with the description of the glomeruli. The authors stated that IgA nephropathy was not active. However, we can see mesangial and endocapillary proliferation, and increase in mesangial matrix with maybe capsular adhesion. The authors report also cellular crescent, and mild interstitial fibrosis and tubular atrophy. So, the patient has 3 different type of inflammatory lesion which signify an active IgA nephropathy. If we use the oxford classification, the score is: M1E1S1T1C1. In this case, IgA nephropathy is active and steroid treatment might be beneficial.

6. The authors use specifically B2M to support ATIN diagnostic. Why? B2M is not specific of ATIN and the urinary measurement is cumbersome: it's unstable in urine at room temperature and it requires alkalinization of the urine prior the collection. I think it would be more appropriate to have a follow-up of the proteinuria in figure 1.

7. Concerning the treatment, it's not usual to use such high dose of steroid. Why don't use steroid at 1 mg/kg/d for the beginning for 2 or 3 weeks follow by gradually tapering over 3 or 4 weeks as reported in literature?

Minor comments:
1. Acute interstitial nephritis is not appropriate in this case. It would be preferable to use Acute tubule-interstitial nephritis (ATIN) because interstitial nephritis is accompanied by tubular damage.

2. It is perhaps best to use the term "acute kidney injury" (AKI) instead of "acute renal dysfunction".

3. Author should specify if the patient had others medications.

4. The author should develop physical examination in the manuscript and specify absence of some physical sign such as flank pain reflecting edema-induced distention of the renal capsule, arthralgia, hypertension.

5. The authors should specify that obstruction of urinary tract was absent on renal ultrasound. They also should precise the kidney's size on ultrasonography (increased?)

6. The authors should precise micro or macroscopic hematuria. Did they research acanthocyte? The urinary culture is steril?

7. It is important to precise if there is any change in the normal function of the tubule: bicarbonaturia, glucosuria, aminoaciduria, 2-microglobulinuria, phosphaturia, and uricosuria; nephrogenic diabetes insipidus, polyuria, and nocturia.

8. It is, perhaps, of interest to have a word about Gell and Coombs classification for allergic reactions.

9. It will be of interest to precise the serum level of IgE.

10. Authors have to specify the method of lymphocyte stimulation test

Reference:

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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