

PEER-REVIEW REPORT

Name of journal: World Journal of Nephrology

Manuscript NO: 40003

Title: Case of human immunodeficiency virus infection presenting as a tip variant of focal segmental glomerulosclerosis

Reviewer's code: 00503176

Reviewer's country: Croatia

Science editor: Fang-Fang Ji

Date sent for review: 2018-06-01

Date reviewed: 2018-06-01

Review time: 0 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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SPECIFIC COMMENTS TO AUTHORS

None. This is an interesting and illustrative case, well written and presented.

INITIAL REVIEW OF THE MANUSCRIPT



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PEER-REVIEW REPORT

Name of journal: World Journal of Nephrology

Manuscript NO: 40003

Title: Case of human immunodeficiency virus infection presenting as a tip variant of focal segmental glomerulosclerosis

Reviewer's code: 00503179

Reviewer's country: Denmark

Science editor: Fang-Fang Ji

Date sent for review: 2018-06-01

Date reviewed: 2018-06-01

Review time: 2 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting case presentation of HIVAN with FSGS in the subgroup with tip lesion. The clinical course and laboratory measurements are well written. In addition, the response to steroid therapy is documented. I have one important question, which

must be solved. That is about the diagnostic criteria of the tip lesion. According to the Columbia Classification, the diagnosis can be made, when the lesion is demonstrated in only one glomeruli, but there additive demands as shown in the following: 'David B. Thomas (2009) Focal Segmental Glomerulosclerosis: A Morphologic Diagnosis in Evolution. Archives of Pathology & Laboratory Medicine: February 2009, Vol. 133, No. 2, pp. 217-223. About the tip variant: Tip Variant. The Columbia classification diagnosis of the FSGS tip variant requires the exclusion of FSGS "collapsing variant" and at least one glomerulus with the defining feature of a segmental lesion involving the tip domain of the glomerular capillary tuft (Figure 3). In this scenario the definition of a segmental lesion is defined as foam cells, endocapillary hypercellularity (involving <50% of the tuft), or sclerosis (involving <25% of the tuft). Also, the tip domain is additionally defined as the outer 25% of the glomerulus next to the origin of the proximal tubule. Although the tip domain is typically opposite the vascular pole of an individual glomerulus, the classification additionally demands the identification of the origin of the proximal tubule with the confluent or adherent segmental lesion for the diagnosis FSGS tip variant. A perihilar lesion precludes the diagnosis of FSGS tip variant in the Columbia classification of FSGS. This somewhat awkward definition with curious restrictions in defining the segmental lesion yet exclusion based on the presence of perihilar abnormalities appears to be a nod to the early description of the glomerular tip lesion presented by Howie and Brewer.¹⁵ This early description of the glomerular tip lesion was not restricted to FSGS, but rather a novel report of a curious glomerular abnormality seen independently in patients with proteinuria as well as being found in other heterogeneous renal abnormalities with associated proteinuria, including membranous glomerulopathy and diabetic glomerulosclerosis.' Consequently, I think the authors shall have the possibility to include the problems about diagnostic classification in their manuscript. Extension should be made both in 'results' regarding



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description of the biopsy and in 'discussion' regarding the safety of the diagnosis. Among other things the following need to be dealt with: 'the classification additionally demands the identification of the origin of the proximal tubule with the confluent or adherent segmental lesion for the diagnosis FSGS tip variant'. It goes without saying that if the diagnosis is minimal change disease, the response to steroid is easy to understand.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Nephrology

Manuscript NO: 40003

Title: Case of human immunodeficiency virus infection presenting as a tip variant of focal segmental glomerulosclerosis

Reviewer's code: 00503014

Reviewer's country: Taiwan

Science editor: Fang-Fang Ji

Date sent for review: 2018-06-01

Date reviewed: 2018-06-03

Review time: 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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SPECIFIC COMMENTS TO AUTHORS

Thanks for the opportunity to review your article. In general, it is interesting for readers of the journal. But, there are some quaries to be clarified to improve the quality of draft. 1. In the biopsy, just one glomerulus revealed the picture of collapsing variant



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of FSGS. Minimal change disease could be more suitable for the tissue diagnosis. 2. Following 3 weeks steroid treatment, the patient was remitted. It seems faster than the average treatment course of FSGS. Are there any other trigger factors, such as heart failure or high BMI (the patient's BW reaches 80 more Kg)?

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PEER-REVIEW REPORT

Name of journal: World Journal of Nephrology

Manuscript NO: 40003

Title: Case of human immunodeficiency virus infection presenting as a tip variant of focal segmental glomerulosclerosis

Reviewer's code: 00502999

Reviewer's country: Argentina

Science editor: Fang-Fang Ji

Date sent for review: 2018-06-01

Date reviewed: 2018-06-04

Review time: 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Major concerns: In this case report there is no new information regarding tip lesion approach and therapy. The fact that a patient with HIV and FSGS with the tip variant does not prove that there is a firm association between the virus and its pathogenicity.



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That is the reason why viral particles have not been found in these kind of lesions. Moreover, the retrieval of atazanavir could have also contributed to the improvement of the patient, particularly with respect to CKD, as commented by the authors. Tip lesions are common responders to steroids, therefore I do not find any new information to be offered to the reader. English polishing is mandatory. Minor concerns: The Clinical Case (Case) is too long and laboratory data should have been depicted in a Table.

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PEER-REVIEW REPORT

Name of journal: World Journal of Nephrology

Manuscript NO: 40003

Title: Case of human immunodeficiency virus infection presenting as a tip variant of focal segmental glomerulosclerosis

Reviewer's code: 00503199

Reviewer's country: Greece

Science editor: Fang-Fang Ji

Date sent for review: 2018-06-01

Date reviewed: 2018-06-04

Review time: 3 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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SPECIFIC COMMENTS TO AUTHORS

1. My main comment is that the case the way it is presented may mislead to associations of HIV with FSGS tip variant. The patient in this case was on remission from HIV, with no evidence of recurrence or exacerbation of HIV infection, with no HIV

RNA or other HIV component found in renal biopsy. He was fat, and the most likely is that the presence of tip FSGS in this patient is a coincidence. HIV patients can experience diabetic nephropathy, membranous, minimal change disease etc like all other people. Mentioning that “However, the dysregulation of the immune system due to HIV infection might be associated with the tip variant of FSGS” is not enough to support a relation between HIV and tip variant. Unless you prescribe a specific pathway, you cannot associate tip variant with HIV, especially if you consider that you present only one case. Thus I would like to see major changes focusing on the above and that a coincidence is the more likely cause of the association. In this context I propose some changes (and more are needed): - Abstract and core tip: “We report an HIV infected case presenting as a rare tip variant of FSGS under remission with ART treated with corticosteroid therapy” I would suggest changing to “We report an HIV infected patient under remission with ART, who presented with a rare tip variant of FSGS which resolved with corticosteroid therapy” - Discussion: “We came across an HIV infected patient with a tip variant of FSGS, in whom steroid treatment but not ART corrected the renal dysfunction and nephrotic-ranged proteinuria.” I would suggest changing to “We came across an HIV infected patient on remission with ART, with a tip variant of FSGS, in whom steroid treatment corrected the renal dysfunction and nephrotic-ranged proteinuria.” - “In conclusion, this was a rare case of HIV with tip variant of FSGS” I would suggest changing to “In conclusion, this was a rare case of a patient on remission of HIV who presented with tip variant of FSGS” 2. After incorporating the above changes, then the authors should mention how this case report adds in the existing literature 3. The main conclusion is that HIV patients, especially when on remission, may present with different nephropathies like all other people and not only with HIVAN, thus a careful examination and a renal biopsy are warranted when indicated.



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