Author’s response to reviews

Title: Immune thrombocytopenic purpura presenting in a patient after renal transplant for diabetic nephropathy.

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Author’s response to reviews:

We appreciate the input by respected reviewers and believe that the feedback will result in improvement of the manuscript. We have updated the paper in response to the insightful reviewer comments and changes in manuscript have been highlighted. Please also find the point to point response to reviewer’s comments below.

Ryszard Grenda (Reviewer 1):

We appreciate the write up, inputs and comments by the reviewer.

We have updated the discussion in manuscript with the proposed potential utility of positive platelet antibody testing from reference labs in refractory cases.

Response to the comment:
Evidence based American society of hematology guidelines (ASH 2011), British society of hematology guidelines (BCSH-2003), Immune thrombocytopenia articles on Medscape and uptodate: all echo the following points completely in agreement. (1-3)

- More than two decades have passed since the availability of assays of platelet specific antibodies. Yet, based on sensitivity, specificity and the lack of correlation of platelet associated IgG with clinical outcomes, they are still not recommended for either the diagnosis or management of ITP.

- ITP still remains a clinical diagnosis and treatment decisions are till now based on bleeding episodes and unsafe platelet counts rather than on laboratory markers. Furthermore, no laboratory marker as yet, is able to consistently predict the future natural history in the individual patients (1,3).

ASH guidelines are the evidence based, comprehensive and widely cited documents for ITP diagnosis and management and have been cited in the manuscript.

British society of hematology guidelines (BCSH-2003) also find the routine use of membrane glycoprotein antibodies unjustifiable. They are, however, the only set of guidelines that, do speculate their role in setting of thrombocytopenia with accompanying marrow failure or refractory cases and have been referenced in the manuscript.(2)

Apart from the clinical side, the literature from immune-hematology and laboratory medicine also acknowledges that the utility of platelet autoantibody testing in the routine management of patients with immune thrombocytopenia (ITP) remains uncertain.(4). There are concerns regarding sensitivity and specificity of different techniques and a recent international workshop concluded that there needs to be improvements in sensitivity and specificity of assays used for platelet autoantibody detection. (5) Furthermore, compared to commercially available tests, multiple tests and techniques are required to ensure a proper workup. Testing
is complex and best performed and interpreted by an experienced platelet immunology reference laboratory.(5,6)

- Both of the previous papers on post Renal transplant ITP have not used these platelet glycoprotein antibodies assays in diagnosing or treating their respective cases.

- Neylon AJ et al, in one of the largest prospective study of moderately thrombocytopenic ITP patients, did not consider or discuss glycoprotein antibodies in either the diagnosis of any patient or on follow up management of even treatment refractory patients (7)

- The clinical scenario, work up and management in our case is in line with established and agreed upon principles of diagnosis and management for ITP. The presence or absence of platelet glycoprotein antibodies would not have altered the diagnosis and therapeutic interventions in our case. The steroid responsive nature of the disease also re-enforced the diagnosis and patient remained in remission.8

References:


Roman Reindl-Schwaighofer (Reviewer 3)

We are grateful for the input and appreciate the time and effort for the review. Thank you for helping us in improving the manuscript. In light of the review, the changes have been highlighted and incorporated in the draft.

Response to comments:

The case is of a post renal transplant middle aged, completely asymptomatic gentleman with isolated thrombocytopenia as the only clinical or laboratory abnormality. Hence the focus is on the platelet count for one whole year of follow-up. His Blood pressure, Urine output, Hemoglobin level, repeated peripheral films (no clumps, no fragmentation), LFT’s and creatinine (Cr) remained stable and normal throughout this entire time; ruling out Thrombotic microangiopathies.
1. TLC count, Hemoglobin, and creatinine at the time of presentation have been incorporated in the manuscript. They remained stable throughout the course; this fact has now been added more clearly to the manuscript and highlighted.

2. LDH and graft function remained normal throughout the entire period of follow up. There was no evidence of hemolysis, as mentioned in the manuscript. (hemoglobin remained stable throughout and coombs test was negative. In addition, repeated peripheral smears, LDH and Bilirubin consistently remained normal and stable)

3. Please and kindly note that the course of the thrombocytopenia is already shown for an entire year, from November 2015 to November 2016 (and not for just one month). The figure also shows dose titration of steroids and curve depicts the response. Hemoglobin, RFT’s and LFT’s remained normal during this whole time, and this detail is now being mentioned with the diagram. The picture is formatted in the same manner as in previous two post renal transplant cases.

4. We were following the patient very closely as a post transplant patient. In a given clinical scenario, where there were either flu like symptoms, or even a slight fluctuation in hemoglobin, or skin involvement, or refractoriness of the disease; further testing for B19 or varicella zoster would have been considered. Our patient had no such clinical features and remained stable for a prolonged follow up time without refractory thrombocytopenia. It has however been incorporated in discussion.

Serum Haptoglobins were normal. Since its mentioned that hemoglobin remained stable throughout, coombs was negative and repeated peripheral smears, LDH and Bilirubin consistently remained normal and stable, Haptoglobins are hence not mentioned in the manuscript separately.
Thrombocyte count confirmation from citrated sample is added in the manuscript. It was mentioned in the manuscript that thrombocytopenia was reconfirmed – and was also mentioned that peripheral smear had no clumps,