Dear Editors,

We thank you for reviewing our manuscript and have made corresponding changes according to both the guides for revision and the comments of the editor and reviewers. Please see below for a point-by-point detail regarding these changes.

Also, we would like to make subtle changes to the current title. We hope that you will consider the following proposed title: “Clinical and pathological features of concurrent polyomavirus nephropathy and rejection-associated endarteritis in renal allografts”.

Again, thank you for consideration of our manuscript and the current revisions.

Kind regards,
Shane Meehan

1. Editorial comments & accompanying guides for revision

- A conflict-of-interest statement, biostatistics statement, data sharing statement, informed consent statement, and institutional review board statement have all been added to the manuscript.

- The abstract has been reformatted.

- An audio core tip has been prepared and submitted.

- A Crosscheck has been performed and submitted.

- A Google Scholar search has been run and submitted.

2. Reviewer #00227610

The manuscript by McGregor et al. studies the concurrency between polyomavirus nephropathy and endarteritis in 94 kidney transplant patients. They found 7 patients (all male) that developed both PVN and endarteritis. In four of them endarteritis arose after reduction of immunosuppression, and three of them lost their grafts. Patients that got PVN and endarteritis after lowered immunosuppression had high serum creatinine levels and Banff interstitial inflammation and tubulitis scores. Minor comments:

1. The International Committee on Taxonomy of Viruses recommends using the abbreviations BKPyV and JCPyV for BKV and JCV, respectively [Johne R et al., Arch Virol 2011,156:1627-1634].

   The abbreviations have been changed according to the reviewer’s suggestion.

2. How many of the 94 kidney transplant patients that developed PVN were male? Because all the patients that developed PVN and endarteritis were male, it may seem that gender may play a role, unless the male sex was overrepresented in their 94 renal transplant patients.

Among the 94 kidney transplant patients with PVN, 51 were male and 23 were female, which is a ratio of 2.2. Within the same time frame, there were 111 biopsies with intimal arteritis (77 male and 34 female, ratio 2.3). It therefore does appear that the gender is disproportionately male in our study.

3. Maybe the abbreviations ATG (page 9, 7th line from the bottom), IVIG (first line on page 10), and DSA (line 5, page 11) should be explained the first time they are used.

   ATG and IVIG have now been defined accordingly. DSA was previously defined on page 10 under the "Patient demographics" section.

4. The labels A and B in Figure 1 are lacking.

   The labels have been added.

5. Legend of Figure 1 should be improved.

   More description of the pathologic features has been added.

3. Reviewer #00521885

1. The authors describe a series of cases with PVN and arteritis and state that the 7.4% incidence is higher than expected. To put this finding in perspective, the incidence of arteritis in the rejection biopsies over the 11 year study period should be presented.

   We identified 384 transplant biopsies with rejection over the 11-year study period, 111 of which demonstrated intimal arteritis (29%). Therefore, evidence of PVN was identified in 6.3% of transplant biopsies with intimal arteritis. This additional information has been added to the manuscript text in Results, paragraph 1.

2. The manuscript is poorly written with contradictions between the text and figures. For example, page 9, para 2 states that 3 patients had reduction of immunosuppression PRIOR to biopsy. These patients cannot be identified in Table 2, while Table 1 says there are 4 such patients.

   There were 4 patients that had reduction in immunosuppression prior to the index biopsy. Three of these had reduction due to PVN, whereas one patient had reduction due to pulmonary tuberculosis (see continuation of "Immunosuppressive therapy" on page 10). We have clarified this in the manuscript text. These patients can be identified in Table 2 in the columns addressing change of immunosuppression after diagnosis of PVN by the "C" superscript, which designates that the change occurred prior to the index biopsy. We have highlighted this designation by using an asterisk instead of a letter.

3. Figure 2 shows only 3 points at the 12-month point.

There are only 3 points at 12 months because one patient had a nephrectomy at 144 days, as indicated by the single asterisk and defined in the legend.

4. Patients with simultaneous PVN and arteritis are claimed to do better, but the simultaneous detection may not be the critical determinant. It may just be the reduction of immunosuppression for a longer period or to a greater degree. Data is not presented in sufficient detail to allow judgment as to whether or not this is so.

   We have not tried to claim that simultaneous detection of PVN and arteritis is a critical determinant of the outcome of these lesions. To put this in perspective, we strongly suspect that known prolonged prior reduction of IS, for treatment of infections, predisposed 4 of these patients to development of AR and subsequent graft loss. However, the 3 patients with simultaneous rejection associated endarteritis and PVN had no known or clinically measured reduction of their IS. We cannot determine if there was subclinical noncompliance in the 3 patients with simultaneous lesions. We have tried to make this clear in the text and tables.

5. Changes (dose and duration) before and after diagnosis should have been presented in the same table to prevent confusion.

   Given the degree of heterogeneity within the population regarding therapy, we are of the opinion that adding additional detail will only add confusion.

6. Previously published literature should be more carefully for prior cases with arteritis and PVN and the clinical course described.

   We have performed careful and thorough literature searches to identify prior reports of the coincidence of these lesions. While there are reviews suggesting that there are many reports of the concurrence of these lesions, this is a misconception, and we have included all the available literature on this topic.

4. Reviewer #00504146

Some minor wordings are suggested:

1. Title: Change "7" to "kidney transplant."

   The title has been changed accordingly.

2. In abstract, change the wordings of the conclusion - as mentioned in the paper, only the case report was found in literature, so there is no comparison between the number (7.4%) in this paper and the number(?) in literature. Authors should draw a new conclusion based on the new finding.

   We have changed the wording to reflect the rarity of prior descriptions of the concurrence of these lesions.