Author's response to reviews

Title: A de novo monoclonal immunoglobulin deposition disease in a kidney transplant recipient: a case report

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Author's response to reviews: see over
I) Answer to Reviewer 1

Reviewer's report
Title:
De novo monoclonal immunoglobulin deposition disease in a kidney transplant recipient
Version:
1
Date:
7 December 2013
Reviewer:
Paul Cockwell

Which of the following following best describes what type of case report this is?:
Unexpected or unusual presentations of a disease

Has the case been reported coherently?:
No

Is the case report authentic?:
Yes

Is the case report ethical?:
Yes

Is there any missing information that you think must be added before publication?:
Yes

Is this case worth reporting?:
Yes

Is the case report persuasive?:
No

Does the case report have explanatory value?:
No

Does the case report have diagnostic value?:
No

Will the case report make a difference to clinical practice?:
No

Is the anonymity of the patient protected?:
Yes

Comments to authors:
This is an interesting case – however it needs to be far more accurately reported to be suitable for publication.

1. Why is this a diagnosis of myeloma?? Clonal light chain production can be associated with clonal proliferation of any cell of B-cell lineage. Precision in the haematological diagnosis is required. What does the marrow show on biopsy (are you confusing myelogram and bone marrow biopsy? they are completely different tests). Please identify the % of clonal plasma cells in the bone marrow aspirate or biopsy. If there was a plasma cell infiltrate then there should have been further studies to demonstrate that this was clonal. Please report the marrow clonal studies.

   We can assert that it was a true myeloma. Indeed, as written in the first version of the article, we performed a myelogram (no confusion about this exam, there was no bone marrow biopsy performed). It showed 16% of tumoral plasmocytes (high nucleus-cytoplasm ratio, mature chromatin, nuclear inclusions). However, no further studies were performed to demonstrate that it was clonal…

2. In February 2007 did the patient have tests for an immunoglobulin light chain clone – either by serum or urine tests. A normal serum protein electrophoresis does not exclude a monoclonal gammopathy. The sensitivity of the test is for 0.5 g of a heavy chain (intact Ig) M protein. You have not excluded recurrent disease in this patient – this needs to be made clear in the case report.

   We have precised this point in the revised version of the article. Indeed, we excluded a monoclonal gammapathy in February 2007 by a normal serum protein electrophoresis (no hypogammaglobulinemia) and a negative Bence Jones proteinuria. Moreover, as precised in the discussion of the revised article, we have other arguments for the de novo character of the plasma cell dyscrasia: two graft biopsies were performed before the diagnosis of myeloma (episodes of borderline acute rejection) and there was no evidence of monoclonal Ig deposits in immunofluorescence.

3. Serum protein electrophoresis does not measure light chain levels in the serum. What test did you use to quantify light chain levels?? Presumably the patient has stored serum from the time of transplantation. You should carry out serum light chain levels on any serum previously available for this patient. Accuracy in reporting and utilising all relevant tests is a requirement for publication.

   We have precised this point in the revised version of the article. When myeloma was diagnosed, we quantified light chains levels with a Freelite® assay from Sonora Quest Laboratories®. We also found out an important Bence-Jones proteinuria. It is true that it was quite difficult to prove the de novo character of the plasma cell dyscrasia. But as we noted in the discussion, the authors of other case reports dealing with a MIDD in renal graft recipients faced the same problems and could not always prove the de novo character of hemopathy. The absence of Bence-Jones proteinuria in 2007 and the absence of monoclonal Ig deposits in the two previous graft biopsies are for us strong arguments to exclude a recurrent gammapathy.

   Unfortunately I asked our laboratory if they had stored serum samples from the time of transplantation but they did not…
4. You must report electron microscopy on the kidney biopsy. For monoclonal gammopathy of renal significance this is required for diagnostic accuracy. We have precised this point in the revised version of the article. When the renal graft function worsened with a nephrotic syndrome, we did not expect to find out a MIDD in the graft biopsy. We expected to find a chronic allograft nephropathy or a new acute rejection episode. Thus, no sample was fixated in glutaraldehyde for electron microscopy. Moreover, the diagnosis of MIDD or Randall disease was evident since there was a monoclonal deposit of kappa light chains in both glomeruli (with a nodular glomerulosclerosis) and tubular basement membranes, which is quite specific for MIDD. Red Congo staining was negative. Thus we could exclude the other forms of renal monoclonal immunoglobulin deposits (AL amyloidosis, GOMMID…).

5. The light chain immunofluorescence needs to be shown against controls
We added in the figures the lambda light chain immunofluorescence control.

Quality of written English:
Needs some language corrections before being Published
We tried to improve the English level and to make a few language corrections.

Declaration of competing interests:
I declare that I have no competing interests
II) Answer to Reviewer 2
Reviewer's report
Title:
De novo monoclonal immunoglobulin deposition disease in a kidney transplant recipient
Version:
1
Date:
23 December 2013
Reviewer:
Nader Nouri-Majalan

Which of the following best describes what type of case report this is?:
Unexpected or unusual presentations of a disease

Has the case been reported coherently?:
Yes

Is the case report authentic?:
Yes

Is the case report ethical?:
Yes

Is there any missing information that you think must be added before publication?:
No

Is this case worth reporting?:
Yes

Is the case report persuasive?:
Yes

Does the case report have explanatory value?:
Yes

Does the case report have diagnostic value?:
No

Will the case report make a difference to clinical practice?:
Yes

Is the anonymity of the patient protected?:
Yes
Comments to authors:

- Conclusion part is not relevant to the case. In this part, the clinical importance of case report is suggested.

As suggested by the reviewers, we changed the discussion and the conclusion of the article. In the discussion, we focused on the problems raised by this disease in a renal graft situation and we compared our case report with other reports of the literature.

In the conclusion, we tried to insist on the clinical importance of our report which illustrates very well all the problems of this clinical situation (unexpected diagnosis in a renal graft recipient, difficulties to prove the de novo character of plasma cell dyscrasia, risk factors of this very special kind of post-transplant lymphoproliferative disorder, difficulties to treat especially because of the lack of guidelines, bad prognosis with serious infectious complications…)

There are some other case reports regarding MIDD in literature. Please refer to some published articles in literature related to your study. For example


As suggested, we included these two references in our report and referred to them in our discussion. We also referred to two other reports of MIDD in renal graft recipients (references 3 and 5)

In discussion, authors should focus on the other reports of de novo MIDD in kidney transplant and compared with present case regarding clinicopathological features and therapy.

As suggested, we changed our discussion and referred to the other reports of de novo MIDD.

Quality of written English:

Needs some language corrections before being published

We tried to improve the English level and to make a few language corrections.