Author’s response to reviews

Title: Valvular involvement in ANCA-associated systemic vasculitis: a case report and literature review

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Author’s response to reviews: see over
Dear Editors,

Thank you for your interest in our manuscript "Valvular involvement in ANCA-associated systemic vasculitis: a case report and literature review".

We have reviewed with care the reviewer’s reports. You will find below our point by point answers to their pertinent comments.

Again, thank you for your consideration of our work!

Sincerely,

Thomas Hanslik

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Reviewer: Minghui Zhao

The authors reported a case of valvular involvement in ANCA-associated systemic vasculitis with literature review. It is well-written and informative, but need a minor revision.

1. The authors claimed that cardiac valvular involvement is rare in ANCA-associated vasculitis. The other explanation is that the cardiac valvular involvement might be overlooked by both patients and physicians due to absent or subclinical clinical manifestations.

Thank you for this remark. It is true that cardiac involvement, and valvular involvement in particular, are probably underdiagnosed. We modified our conclusion: “although it might be underdiagnosed due to the lack of patent clinical signs and the absence of systematic screening, valvular involvement in ANCA-associated systemic vasculitides is rarely reported”. We also modified the first sentence of the abstract: “…cardiac valvular involvement is rarely diagnosed and its management is not established”.

2. I agree that the reported case is, most probably, Wegener’s granulomatosis. However, he had MPO-ANCA, while in the literature review, nearly all the cases were PR3-ANCA positive. The patient in this case report is from Bangladesh in origin, actually, some reports suggested that Asian patients with ANCA-associated vasculitis predominantly had MPO-ANCA, even for patients with Wegener’s granulomatosis (Chen M, et al. Kidney Int 2005;68:2225-2229). I would like the authors discuss this issue.

Thank you for this interesting comment! We have added the following sentences at the beginning of the discussion: “Although Pr3-ANCA, found in 70 to 90% of patients with Wegener’s granulomatosis, is often considered to be a seromarker of this disease, MPO-ANCA has been reported to be predominant in Asian patients. This could explain the positive p-ANCA and negative c-ANCA in this patient who is from Bangladesh.”

Reviewer: Jose Gomez

Lacoste and colleagues reported an interesting and unusual case of valvular involvement related to AAV. Additionally, a comprehensive review of similar previous reported cases is done.

1. Two case reports (see below) with valve involvement and WG had been recently published. You should include them in the results, discussion and tables.
Thank you for pointing out these two recently published papers. We have added them to the literature review: in the text and in the tables. Attaran’s article is number 3 and Koyalakonda’s is number 13 in the edited references.

2. Did you check for antiphospholipid (lupus anticoagulant and/or anticardiolipin) antibodies in the present case ?. It is well known the association of aPL and valvular disease. Additionally, some cohorts of patients with primary systemic vasculitis had found relation with aPL and thrombotic manifestations (Rees JD, Lança S, Marques PV, Gómez-Puerta JA, Moco R, Oliveri C, Khamashta MA, Hughes GR, D’Cruz DP Ann Rheum Dis 2006;65:109-111)

Thank you for this important remark. We have indeed ruled out antiphospholipid syndrome in our patient. We thus added in the case report that the antiphospholid antibodies were negative.

3. In order understand the complexity and severity of the case it will be useful a diagram (schema) with the sequence of appearing each feature and symptoms and the outcome. In that sense, a severity score index (i.e. BVAS) before and after the treatment must be included

Thank you for this comment. We propose to answer this request with a table rather than a diagram because most of the clinical signs appeared shortly before or during hospitalization which might overload the diagram and make it difficult to read. If the reviewer or the editor would prefer, we can of course draw a diagram instead. Inclosed in the table, you will find a BVAS of when the patient was hospitalized and two years later.

**Table 1** Symptoms, severity score index and main lab and imagery results of the patient described in the case report.

<table>
<thead>
<tr>
<th>Date</th>
<th>Symptoms and findings</th>
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| November 2006 | - Persisting facial pain, right chronic headaches resisting usual pain killers  
- Cerebral CT-scan : pansinusitis |
| March 2007 | - Same symptoms + right hypoacusia and tinnitus  
- Cerebral CT-scan : pansinusitis predominating on the right side with right mastoiditis and otitis media  
- Cerebral MRI : pachymeningitis of the cerebellopontine angle |
| June 2007 | - Violent headaches and vomiting : severe intracranial hypertension  
- Significant weight loss (- 10 kg)  
- Right otitis media  
- Paralysis of the left vocal cord (dysphonia), abolition of the gag reflex, and palatal paralysis  
- Cerebral MRI : unchanged  
- Spinal tap : Aseptic meningitis  
- Discovery of the aortic regurgitation  
- Abdominal CT-scan : focal aortic and mesenteric |
<table>
<thead>
<tr>
<th>June 2009</th>
<th>BVAS = 2</th>
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<tbody>
<tr>
<td>BVAS : Birmingham Vasculitis Activity Score</td>
<td></td>
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</tbody>
</table>

- Elevated C-reactive protein and leukocyte count
- Polyclonal hypergammaglobulinemia
- pANCA+ ; anti-MPO + ; anti Pr3 –
- BVAS = 23