Anti-MPO ANCA-Associated Diffuse Alveolar Hemorrhage is Associated with Increased Mortality Compared to Anti-PR3 Disease

Grace M. Lee, Yara A. Park, Marshall Mazepa, Jay S. Raval
Introduction

• Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis encompasses a spectrum of immune-mediated disorders

• The most common ANCA target antigens are:¹
  
  • Proteinase 3 (PR3): 70-80% (Wegener's granulomatosis, microscopic polyangiitis)
  
  • Myeloperoxidase (MPO): 10% (microscopic polyangiitis, Churg-Strauss syndrome, other vasculitides)

• Prior studies looking at anti-PR3 and anti-MPO-positive patients, who were not selected for a particular organ manifestation, did not find any difference in survival², ³

1. Drooger, 2009
2. Franssen, 1998
3. Geffriaud-Ricouard 1993
Introduction

• Diffuse alveolar hemorrhage (DAH) is a life-threatening pulmonary manifestation of ANCA-associated vasculitis, and it is the major factor contributing to morbidity and mortality\(^1\)

• ANCA-associated DAH is an ASFA Category I (1C) indication for therapeutic plasma exchange (TPE)\(^2\)

• Despite aggressive intervention, ANCA-associated DAH is associated with a high mortality rate

• Little has been described regarding differences between DAH in the anti-MPO vs. anti-PR3 patient population

1. Franks, 2000
2. ASFA Guidelines 2013
Aims

• To characterize patients with ANCA-associated DAH with respect to anti-MPO and anti-PR3 positivity

• To determine the association between serologic subgroup and clinical outcome in patients with ANCA-associated DAH
Methods

• Apheresis medical records at UNC Hospital were analyzed:
  
  • Between 1/2010-8/2014

  • Keywords: “ANCA”, “Wegener’s granulomatosis”, “polyangiitis”, “diffuse alveolar hemorrhage”, or “pulmonary hemorrhage”

• Only patients with ANCA-associated DAH along with a detectable anti-MPO or anti-PR3 titer were included for analysis

• Number of TPE treatments, serologic testing results, and ANCA-associated in-hospital mortality were recorded

• Continuous variables were compared with Mann-Whitney test, and categorical variables were compared using Fisher’s exact test

  • Statistical significance was defined as $p < 0.05$
Our apheresis protocol

• At our institution, all patients with DAH attributed to vasculitis receive:
  
  • During period of active hemorrhage: daily TPE replacing 1.0 plasma volume with plasma

  • Upon resolution of hemorrhage: every-other-day TPE using 5% albumin/plasma or 5% albumin alone as the replacement fluid
Results

82 patients with ANCA vasculitis

34 patients without DAH

5 patients had negative anti-MPO and anti-PR3 testing or testing was not done

48 patients had DAH

43 had positive serologic testing for anti-MPO or anti-PR3

23 patients were positive for anti-MPO

20 patients were positive for anti-PR3
# Results

<table>
<thead>
<tr>
<th>Gender</th>
<th>Anti-MPO (n = 23)</th>
<th>Anti-PR3 (n = 20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>48%</td>
<td>56%</td>
<td>0.76</td>
</tr>
<tr>
<td>Female</td>
<td>52%</td>
<td>44%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Race</th>
<th>Anti-MPO (n = 23)</th>
<th>Anti-PR3 (n = 20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>72%</td>
<td>89%</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>24%</td>
<td>11%</td>
<td>0.26</td>
</tr>
<tr>
<td>Other</td>
<td>4%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Anti-MPO (n = 23)</th>
<th>Anti-PR3 (n = 20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>62</td>
<td></td>
<td></td>
<td>0.02</td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th></th>
<th>Anti-MPO (n = 23)</th>
<th>Anti-PR3 (n = 20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Titer (U/mL)</strong></td>
<td>84.6</td>
<td>120.7</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Ave. # of TPE procedures</strong></td>
<td>6.1</td>
<td>6.3</td>
<td>0.61</td>
</tr>
<tr>
<td><strong>In-hospital mortality</strong></td>
<td>6 (26%)</td>
<td>0 (0%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Summary of Results

- Patients with ANCA-associated DAH are equally likely to be positive for anti-MPO or anti-PR3
- Both serologic subgroups received an equal number of TPE treatments
- ANCA-MPO-positive patients with DAH have significantly higher in-hospital mortality
Strengths

• Large number of patients given that ANCA-associated DAH is a low incidence disease

• Anti-MPO and anti-PR3 titers were available for all included patients

• All patients were treated at a single institution allowing for a consistent clinical approach
Limitations

• Retrospective study
  • Association, not causality

• Single institution's experience

• Age difference in two cohorts may be a confounding factor
Conclusions

• In patients with ANCA-associated DAH, specific ANCA serology may have prognostic value

• Patients with ANCA-MPO-positive DAH may benefit from closer monitoring of pulmonary status

• These results need to be confirmed in larger, prospective studies with matching of baseline demographics and comorbid conditions
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