**Objective.** To describe refractory BS in a GPA patient.

**Case.** In 2008, a 30-year-old man consulting for dyspnea, wheezing, hemoptysis, nasal congestion and epistaxis was diagnosed as having GPA with anti-neutrophil cytoplasm antibodies to proteinase 3, BS, and ear, nose & throat, pulmonary (nodules, alveolar hemorrhage) and renal involvements. Corticosteroids (CS) were combined with IV cyclophosphamide (CYC), IV immunoglobulins (IVig), mycophenolate mofetil and, finally, azathioprine (AZA). His refractory GPA led to rituximab (RTX) induction therapy (375 mg/m²/week for 4 weeks) in September 2009. He was admitted 2 months later with acute respiratory distress syndrome due to multiple, bilateral BS. Therapeutic bronchoscopy with balloon dilation was successful, and methotrexate (MTX) was added to RTX and AZA. Readmitted for relapsed BS, he received oral CYC induction therapy that achieved remission but BS persisted as sequelae. Maintenance therapy combined AZA and MTX. Follow-up was marked by recurrent, severe, *Pseudomonas aeruginosa* bronchial pneumonia. In December 2011, despite maintenance therapy (AZA, MTX & CS), he was admitted for a new and severe BS relapse. MTX was stopped; infliximab (5 mg/kg) was started, combined with AZA and CS; this regimen stabilized GPA for 10 months. In October 2012, BS relapsed again, requiring silicone prosthesis insertion. Cytomegalovirus viremia and recurrent, bacterial bronchial pneumonia led to replacing infliximab by IVig.

**Conclusions.** This case illustrates the difficulty of managing GPA-associated BS. Tracheal and endobronchial stenoses must be sought in every GPA patient with a pulmonary abnormality. General and local treatments must be given early because systemic and local management is difficult and ineffective after the inflammatory stage.

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### A22

**Rituximab therapy for granulomatous polyangiitis (Wegener’s granulomatosis) with refractory granulomatous manifestations**

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**Introduction.** Granulomatous polyangiitis (GPA) is a potentially fatal granulomatous disease. Cyclophosphamide (CYC) and corticosteroids (CS) remain the preferred treatment for severe GPA, but the in cases with persistent or refractory disease activity treatment remains unclear. Rituximab (RTX) has been reported useful in some cases but data are controversial.

**Patients.** Data from five patients with GPA and refractory granulomatous manifestations who received RTX were reviewed. All patients were PR3-ANCA positive at time of RTX, and in all cases disease activity persisted despite standard treatment with different immunosuppressant drugs (IS) and glucocorticoids. Patients had granulomatous manifestations like retro-orbital granuloma (n = 1), lung nodules (n = 1), necrotizing scleritis (n = 1), and subglottic stenosis (n = 2). Clinical characteristics of the patients are summarized in Table I. RTX was given intravenously in 2 weekly doses of 1 gm, in combination with other IS. Clinical activity was assessed using BVAS, ANCA serology, and imaging tests.

**Results.** RTX was well tolerated. Following RTX, circulating B lymphocytes became undetectable by month 3, and ANCA titers became negative in four patients. Complete clinical remission was achieved in four cases. One patient died due to a bacterial pneumonia and septic shock. GS were tapered off by 6 to 12 months after RTX infusion. IS therapy was withdrawn in two patients. Two patients experienced a clinical flare after B lymphocyte reconstitution and were successfully retreated with RTX.

**Discussion.** There have been few reports of the use of RTX in GPA-patients with refractory granulomatous manifestations. A beneficial response to RTX was seen in four out of five patients with complete remission and PR3-ANCA negativization. RTX was well tolerated, although one patient died due to a severe infection.

**Conclusion.** Our results show that RTX therapy can be useful for remission induction in patients with GPA and refractory granulomatous manifestations.

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### Table I

**Clinical characteristics of the patients.**

<table>
<thead>
<tr>
<th>Patient/ Age/sex</th>
<th>Time since diagnosis (mo)</th>
<th>n° prior relapses</th>
<th>Previous involved organs</th>
<th>IS previously used</th>
<th>Falling therapy at time of RTX</th>
<th>Active organ involvement at time of RTX</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/ 48 M</td>
<td>144</td>
<td>5</td>
<td>ENT, trachea, lungs, joints</td>
<td>CS, AZA, MMF, CF</td>
<td>cf, CS</td>
<td>Trachea (SGS), Kidney, Joints</td>
<td>Dead due to pneumonia and septic shock</td>
</tr>
<tr>
<td>2/ 38 F</td>
<td>140</td>
<td>7</td>
<td>ENT, trachea, lungs, pericardium, gastrointestinal system</td>
<td>CS, MTX, CF, AZA, MMF</td>
<td>CF, CS</td>
<td>Trachea (SGS), peripheral nerve</td>
<td>Complete remission. Anca negativization</td>
</tr>
<tr>
<td>3/ 40 M</td>
<td>120</td>
<td>5</td>
<td>ENT, lungs, aortic valve, episcleritis, joints</td>
<td>CS, MTX, CF, AZA, MMF</td>
<td>MMF, CS</td>
<td>Diffuse bilateral necrotizing scleritis</td>
<td>Complete remission. ANCA negativization</td>
</tr>
<tr>
<td>4/ 48 M</td>
<td>164</td>
<td>5</td>
<td>ENT, lungs, retroperitoneal pseudo tumor</td>
<td>CS, CF, AZA, MMF</td>
<td>CS, CF</td>
<td>Retro-orbital granuloma, ENT</td>
<td>Complete remission. ANCA negativization</td>
</tr>
<tr>
<td>5/ 73 F</td>
<td>1</td>
<td>1</td>
<td>ENT, lungs</td>
<td>CS, CF</td>
<td>CS, CF</td>
<td>Diffuse cavitated lung nodules, pachymeningitis</td>
<td>Complete remission. ANCA negativization</td>
</tr>
</tbody>
</table>

### A23

**Upper airway gene expression profiling in granulomatosis with polyangiitis**

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**Introduction.** Nasal disease occurs in the majority of patients with granulomatous polyangiitis (Wegener’s, GPA). We performed whole-genome gene expression profiling of upper airway disease in GPA using a minimally-invasive sampling technique to understand the biology of nasal disease activity in GPA.

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