staining for IgG, C3, and kappa light chain (Figure 3). Despite the stitium. Immunofluorescence revealed tubular basement membrane. It accounts for autoantibodies against an antigen of type IV collagen expressed anti-GBM antibody titer. While the pulmonary haemorrhage the most probable diagnosis given the clinical presentation and high haemorrhage, eponymously referred to as Goodpasture syndrome. The progression of symptoms was unusually rapid in this case in comparison to the previously reported cases of anti-GBM disease following alemtuzumab therapy and to the known evolution of Goodpasture’s syndrome. In a retrospective analysis of 28 patients with Goodpasture’s syndrome, only 4% of the patients had developed acute onset of symptoms in the week preceding admission, whereas in up to 39% the symptoms had evolved over a month. Oligoanuria, creatinine >500 μmol/L and immediate dialysis requirement at diagnosis, as in the present case, are strong predictors of long-term dialysis dependence. Recovery is generally variable in anti-GBM disease. Although few cases have been reported, permanent kidney injury has occurred in alemtuzumab treated MS patients who develop this complication with three of the five previously reported cases having evolved to chronic dialysis or transplant.

Secondary autoimmune events occurrence is delayed following alemtuzumab therapy. The most frequent autoimmune adverse event is thyroid disease, affecting 42% of the MS patients treated with alemtuzumab in the phase 3 studies through year 6. Thyroid events peak in year 3, with the most frequent being hyperthyroidism, including Grave’s disease. Immune thrombocytopenia is the second most frequent autoimmune adverse event, with an incidence of 2.3% in the alemtuzumab clinical development program. It also has a delayed occurrence with a mean timing of onset from the last alemtuzumab course of 17 months. Anti-GBM disease was diagnosed between 10 and 39 months after the last course of alemtuzumab in the previously reported MS cases, consistent with the timing of onset in this case. The mechanisms underlying the development alemtuzumab-induced autoimmunity are not well understood. Both B-cells and T-cells are involved in the pathophysiology of anti-GBM disease or Goodpasture’s syndrome, and T and B cell reconstitutions after depletion by alemtuzumab have been postulated to drive secondary autoimmunity. B-cells repopulate rapidly relative to T-cells and thus do so in the absence of regulation from T-cells, which could lead to the development of antibody-mediated autoimmune conditions such as Goodpasture’s syndrome. MS and other autoimmune disorders can co-occur, and at least one case of anti-GBM disease has been described in an untreated MS patient. Some MS patients could have enhanced genetic susceptibility to anti-GBM disease, as the HLA-DRB1*1501 allele has been associated with both conditions. In addition, this patient had a first-degree relative with myasthenia gravis with antibodies to Muscle-Specific Kinase (MuSK) and he was an active smoker. A family history of autoimmune disease and current or past smoker status has both been identified as risk factors for secondary immunity in alemtuzumab treated MS patients, with odds ratio of 7.31 and 3.05, respectively. Smoking also increases the likelihood of pulmonary involvement in Goodpasture’s syndrome and might have prompted the occurrence of lung haemorrhage in this case.

In summary, this case reflects the potential for extremely rapid progression and unfavourable outcome of Goodpasture’s syndrome developing after treatment with alemtuzumab in MS. It highlights the importance of periodic monitoring of creatinine and urinalysis following treatment, especially in light of the non-specific clinical
presentation which may delay the treatment to preserve renal function. Baseline testing of anti-GBM levels is of unclear predictive value as these autoantibodies may exist in asymptomatic carriers. However, a high index of suspicion should be maintained for every alemtuzumab treated MS patient, and creatinine and urinalysis disturbances should be monitored closely with early referral to nephrology and anti-GBM testing. Caution should be exercised when prescribing alemtuzumab to active smokers and patients with a family history of autoimmune disorders who may be at increased risk of secondary autoimmunity.

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STATEMENT OF AUTHORSHIP

Each author has been involved in the case management, preparation, and revision of the manuscript.

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### REFERENCES


### Table 1: Summary of previously reported cases of anti-glomerular basement membrane disease following alemtuzumab therapy in multiple sclerosis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, years</th>
<th>Gender</th>
<th>Timing of occurrence (after last course)</th>
<th>Rapidity of onset</th>
<th>Smoker status</th>
<th>Lung involvement</th>
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<tbody>
<tr>
<td>1,2,4</td>
<td>40</td>
<td>Female</td>
<td>10 months</td>
<td>Antibodies not detected</td>
<td>Unknown</td>
<td>No lung involvement reported</td>
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<tr>
<td>2,4</td>
<td>35</td>
<td>Female</td>
<td>24 months</td>
<td>Creatinine increased over ≥1 month</td>
<td>Male</td>
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<tr>
<td>3</td>
<td>35</td>
<td>Female</td>
<td>39 months</td>
<td>Not rapid, deteriorated due to non-compliance</td>
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<td></td>
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<tr>
<td>4</td>
<td>24</td>
<td>Female</td>
<td>48 months</td>
<td>Asymptomatic</td>
<td></td>
<td></td>
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<tr>
<td>5</td>
<td>Unknown</td>
<td>Unknown</td>
<td>3 months</td>
<td>Very rapid (Figure 1)</td>
<td></td>
<td></td>
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</tbody>
</table>

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# Table 1: Summary of previously reported cases of anti-glomerular basement membrane disease following alemtuzumab therapy in multiple sclerosis

<table>
<thead>
<tr>
<th>Case 1,4</th>
<th>Case 2,4</th>
<th>Case 3,4</th>
<th>Case 4</th>
<th>Case 5</th>
<th>Actual case</th>
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<tbody>
<tr>
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<td>40</td>
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<td>35</td>
<td>24</td>
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<tr>
<td>Smoker status</td>
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<td>Male</td>
<td>Male</td>
<td>Male</td>
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</tr>
<tr>
<td>Lung involvement</td>
<td>No lung involvement reported</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>