Plasma exchange in Goodpasture syndrome associated with Turner’s syndrome: A case report

Jiao LP, Fan JF, Sun Q, *Shen Y

National Key Discipline of Pediatrics (Capital Medical University) Ministry of Education, Beijing Children’s Hospital, Capital Medical University, Beijing, 100045, China

Abstract

Background: Goodpasture syndrome (GPS) has been paid much attention recently for the dangerous illness and high mortality.

Objective: To investigate the efficiency of plasma exchange (PE) to treat Goodpasture syndrome (GPS) in children associated with Turner’s syndrome.

Method: We report a case of a 15 year old female with GPS and Turner’s syndrome. The patient has intermittent fever and cough for 45 days and oliguria for 6 days. Turner’s syndrome was determined through blood karyotype analysis, and GPS was diagnosed because the patient was negative for antinuclear antibodies and antineutrophil cytoplasmic antibodies (ANCA), but positive for anti-glomerular basement membrane (anti-GBM) antibodies (200 RU/ml). PE was carried out in combination with immunosuppression therapy.

Results: The results show PE treatment can efficiently decrease the levels of anti-GBM antibodies. The antibody levels were >200 RU/ml and 184 RU/ml before and after the first PE treatment, respectively. The removal efficiency were 40%, 47%, 42%, 54%, 52% for the fifth, sixth, seventh, eighth and ninth PE procedures, respectively.

Conclusion: The therapy with PE, hemodialysis, pulse methylprednisolone followed by oral prednisone and cyclophosphamide greatly contributed to improvement of this patient’s condition, and resolved the patient’s pulmonary haemorrhage. All these results demonstrate that PE contributed efficiently to the treatment for GPS in children.

Keywords: Goodpasture syndrome (GPS), Turner’s syndrome, plasma exchange (PE).

Introduction

Goodpasture syndrome (GPS) is rare in children. The role of anti-glomerular basement membrane (anti-GBM) antibodies in the pathogenesis of GPS is well-known, and plasma exchange (PE) has been used for antibody removal . We reported the first case of GPS associated with Turner’s syndrome in children. The patient was treated with a combination of PE, steroids and immunosuppression, which has previously been reported to be effective. The levels of anti-GBM antibodies were tested pre- and post-PE, and the efficiency of removal was calculated to evaluate the efficiency of PE therapy for treatment of GPS.

Case report

A 15-year-old female was hospitalized in our hospital with a 45-day history of intermittent fever and cough. She received antibiotics from her local hospital, but symptoms did not improve. Oliguria was developed at 6 days before admission, and was accompanied by two episodes of blood-streaked sputum and pallor. Haemodialysis (HD) was performed 2 days before admission. She did not experience any rash or joint swelling.

Her past medical history includes a diagnosis of Turner’s syndrome diagnosed at the age of 14 years and 1 month by blood karyotype analysis (figure 1). Her height was 132 cm at diagnosis and growth hormone (GH) treatment was commenced, but was discontinued by her parents 8 months later (height 140 cm) due to an upper respiratory tract infection. There was no family history of renal disease.

This patient was admitted in the first affiliated Hospital of Harbin Medical University on May 2th, 2010. On admission she was in no apparent distress, and weight was 35.5 kg. Eyelid oedema was
noted. She had normal breath sounds, and heart and abdominal examinations were normal. Cubitus valgus and lower limb oedema were observed, with a good range of motion of all joints. Breasts and pubic hair were Tanner stage 1. No adenopathy was detected.

Blood sampling before HD revealed blood urea nitrogen (BUN) 36.33 mmol/L, serum creatinine (Cr) 974.6 μmol/L (11.0 mg/dL), normal liver function, haemoglobin (Hb) 85 g/L, white blood cells 11.49 × 10^9/L, platelets 193 × 10^9/L and C-reactive protein 160 mg/L. Urinalysis showed 2+ protein and >50 red blood cells per high-power field. Complement levels (C3, C4) were normal. Antinuclear antibodies and antineutrophil cytoplasmic antibodies (ANCA) were negative. Anti-glomerular basement membrane (anti-GBM) antibody levels were high at >200 RU/ml (enzyme-linked immunosorbent assay, normal value <20 RU/ml). Abdominal ultrasound revealed enlarged kidneys with increased cortical echogenicity. Chest computed tomography scan revealed mild bilateral interstitial and parenchymal infiltrates.

Renal biopsy was performed 11 days after admission. Light microscopy of 12 glomeruli revealed 11 glomeruli with global sclerosis and 1 with segmental sclerosis. Immunofluorescence staining for IgG, IgA, IgM, C3 and C1q was negative. A diagnosis was made of sclerosing glomerulonephritis. Pulmonary haemorrhage was diagnosed on flexible bronchofibroscopy (many red cells and occasional haemosiderin in the irrigating solution, figure 2).

HD was continued after admission. Plasma exchange (PE) was performed when GPS was diagnosed on day 11, using a Gambro plasma filter and a PRISMA machine. Intravenous access was via femoral vein cannulation. Volume exchanged was 40 ml/kg (1,400 ml) with blood flow 150 ml/min. Fresh frozen plasma (1,000 ml) and substitute plasma (400 ml) were used as replacement fluid, and heparin sodium was used as anticoagulant. The duration of each exchange was 2 hours, with nine exchanges completed. Anti-GBM antibody levels were tested pre- and post-PE for each exchange. Antibody levels were >200 RU/ml before and 184 RU/ml after the first PE. After the fourth PE, antibody levels remained <200 RU/ml. Removal efficiency was 40%, 47%, 42%, 54% and 52% for the fifth, sixth, seventh, eighth and ninth PE procedures, respectively (table 1).

After PE, HD and pulse methylprednisolone followed by oral prednisone and cyclophosphamide, the patient’s pulmonary haemorrhage resolved. Renal function did not improve and she continued to require intermittent HD.
Table 1: Determination of anti-GBM antibody pre- and post-PE (RU/ml)

<table>
<thead>
<tr>
<th></th>
<th>First</th>
<th>Second</th>
<th>Third</th>
<th>Fourth</th>
<th>Fifth</th>
<th>Sixth</th>
<th>Seventh</th>
<th>Eighth</th>
<th>Ninth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-PE</td>
<td>&gt;200</td>
<td>&gt;200</td>
<td>185</td>
<td>&gt;200</td>
<td>146</td>
<td>135</td>
<td>113</td>
<td>68</td>
<td>63</td>
</tr>
<tr>
<td>Post-PE</td>
<td>184</td>
<td>139</td>
<td>120</td>
<td>118</td>
<td>88</td>
<td>71</td>
<td>65</td>
<td>31</td>
<td>30</td>
</tr>
<tr>
<td>Removal</td>
<td>------</td>
<td>------</td>
<td>35</td>
<td>-------</td>
<td>40</td>
<td>47</td>
<td>42</td>
<td>54</td>
<td>52</td>
</tr>
</tbody>
</table>

efficiency (%)

Discussion

GPS is characterized by rapidly progressive glomerulonephritis, pulmonary haemorrhage and the presence of anti-GBM antibodies. Anti-GBM disease accounts for approximately 10–20% of patients with rapidly progressive glomerulonephritis. GPS is rare in children, and usually occurs from ages 6-13, although the youngest reported case was 11 months old. One study of GPS in children reported a male to female ratio of 0.43, with positive anti-GBM antibody levels in all patients who were tested. Our patient was a female adolescent, with an anti-GBM antibody level above the upper limit of the test range and negative ANCA. Microscopy 17 days after the onset of oliguria showed global sclerosis in 92% of glomeruli and segmental sclerosis in 8%, indicating rapid progression. She had mild symptoms of haemorhage and thus a flex bronch was performed to confirm the diagnosis.

PE was first used for the removal of immune complexes in GPS in the early 1970s, and is now a grade 1B recommendation. In the current case, serum anti-GBM antibody levels decreased following PE, confirming that PE is an effective therapeutic approach for GPS in children. Efficiency of antibody removal was 35–54%, which is similar to that demonstrated by double-filtration plasmapheresis. PE with immunosuppressive therapy may also be useful in cases of idiopathic rapidly progressive glomerulonephritis in children. Instead of waiting for anti-GBM antibody and renal biopsy results, PE should be undertaken on admission. The current case with severe renal dysfunction requiring HD had a poor prognosis.

Renal transplantation can be performed in children requiring chronic HD after disappearance of the circulating anti-GBM antibodies. There are no data indicating the recurrence rate in children after renal transplantation. Graft loss due to recurrence has been estimated to be approximately 14% in adults, but the recurrence of anti-GBM antibodies has rarely been documented.

In conclusion, GPS is rare in children, and we present the first reported case of GPS associated with Turner’s syndrome. GH therapy can result in a remarkable gain in height. This patient had showed a good response to GH therapy, with a height gain of 8 cm in 8 months. Unfortunately she did not receive further GH after starting HD, as her parents were unable to manage both financially. She had no further height gain after her GPS diagnosis. We have not seen any other reports of GPS associated with Turner syndrome, and the relationship between the two syndromes should be further researched.
Turner's syndrome. Prompt diagnosis and initiation of treatment with PE, steroids and immunosuppression should be undertaken as soon as possible in GPS.

References