To the Editors:

A case of self-limiting Coomb’s negative haemolytic anaemia following dengue shock syndrome

In addition to dengue haemorrhagic fever and dengue shock syndrome, involvement of other organ systems has been reported in dengue fever. Hepatic dysfunction and neurological manifestations are common [1,2]. We report a patient who developed a self-limiting Coomb’s negative haemolytic anaemia following dengue shock syndrome.

A 27-year old woman who was clinically diagnosed to have dengue fever developed shock (dengue shock syndrome) 12 h after admission to hospital. She was transferred to the intensive care unit and resuscitated. On the sixth day after admission dengue lgM antibodies became positive. She recovered and her haemoglobin was 12 g/dL and platelet count was 140 x 10^9/L on the seventh day. During the next 2 days she became increasingly pale without evidence of haemorrhage and developed icterus. The haemoglobin had dropped to 6 g/dL. The following investigations were done: platelet count 205 x 10^9/L, blood picture normochromic normocytic red cells with marked red cell agglutination, reticulocyte count 8.2%, white cell count 6.4 x 10^9/L, total bilirubin 168.9μmol/L (indirect fraction 100 μmol/L), ESR 98 mm in the first hour, direct and indirect Coomb’s tests repeatedly negative. Her prothrombin time/INR, partial thromboplastin time, C-reactive protein and D-dimer levels were normal. Liver enzymes were mildly elevated (SGPT=56 U/L and SGOT=94 U/L). *Mycoplasma pneumoniae*, Epstein-Barr IgM and IgG antibodies, antinuclear factor and anti-dsDNA antibodies were negative. Chest x-ray, abdominal ultrasound scan, blood urea, serum electrolytes and serum creatinine were also normal.

She recovered spontaneously and her haemoglobin was 10.2 g/dL when she was discharged from the hospital 6 days after haemolysis was first detected. Two weeks after admission dengue antibodies showed an IgG titre of more than 2560, confirming recent secondary dengue infection. At follow up she was asymptomatic and had normal haematological and biochemical parameters.

This patient had a self-limiting haemolytic anaemia 6 days after dengue shock syndrome. An extensive literature survey did not reveal previous reports of such an association. We have excluded, as far as possible, other likely causes of haemolysis. The mechanism of the haemolytic anaemia is not clear. Cold-type autoimmune haemolytic anaemia is a recognised complication of certain infections, characterised by destruction of antibody-coated red blood cells. The mechanism that initiates production of autoantibodies remains unclear. Regulatory cytokines are thought to play an important role, and activation of immunoregulatory T lymphocyte subsets has been observed in dengue infection [3]. In our patient, an immune mechanism was considered because of delay between the infection and onset of haemolysis. Furthermore, her blood film was suggestive of a cold-type autoimmune haemolysis. However, the Coomb’s test was repeatedly negative. Coomb’s negative autoimmune haemolytic anaemia is known to occur when haemolysis is caused solely by lgA antibodies [4]. We checked only IgM and IgG antibodies and had no facilities to test for lgA antibodies.

References


To the Editors:

Safety and efficacy of subcutaneous adrenaline as a treatment for anaphylactic reactions to polyvalent antivenom

Antivenom serum (AVS) is widely accepted as an effective form of treatment in snake envenoming [1]. However, anaphylactic and pyrogenic reactions are common for both polyvalent and monovalent AVS [1-4]. Many premedications including antihistamines and hydrocortisone have been used to minimise such reactions without much benefit [2,3]. Premedication with low dose adrenaline subcutaneously (sc) has shown a significant reduction of the acute adverse reactions to AVS [4]. A major concern with the use of adrenaline pre-treatment is the risk of intracerebral haemorrhage and the potential danger in children, pregnancy and in heart disease [5,6]. Published data on the safety of adrenaline in the treatment of established AVS reactions are sparse. Accordingly, we planned this study to assess the safety and efficacy of adrenaline as the sole treatment of moderate to severe AVS reactions. The sc route was used because it was considered safer than the intramuscular (im) route.

This study was conducted at the General Hospital, Anuradhapura, in the North Central Province of Sri Lanka from April to May 2002. The subjects were 36 patients who had developed reactions to the polyvalent antivenom (lyophilised enzyme refined, manufactured in India, Batch no: AVS30-2001).

The reactions were categorized as mild, moderate and severe based on the criteria of a former study [3]. Twenty-one patients with moderate to severe reactions qualified to receive adrenaline. The AVS reaction profile, the blood pressure and the pulse rate in particular, was recorded just before the treatment and observed for 2 h initially and 4 hourly for 48 h. These reactions were treated initially by discontinuing the AVS infusion temporarily and administering 0.5mL (1:1000) of adrenaline subcutaneously. Data such as age and sex, previous history of eczema, catarrh, urticaria, allergy, nature of the snake bite and other medical conditions were also recorded.

Ethical approval was obtained from the Research and Ethical Committee of the Faculty of Medicine, University of Peradeniya.

Mean values of the pre-treatment and post-treatment blood pressure, pulse rate and time of blood pressure rise were calculated. The mean difference between pre- and post-treatment systolic BP, diastolic BP, and pulse rate were compared by using paired t-test. Data analysis was done by using the Windows-based SPSS statistical package, standard version 10.0.1.

The severity of the AVS reactions were: mild 15(28.8%), moderate 19(36.5%) and severe 2(3.9%). The 21 cases (17 males) with moderate to severe reactions who qualified to receive adrenaline had a mean age of 34.2 years (range 18–55). The mean blood pressure values and mean pulse rates of pre-treatment and post-treatment were tabulated (Table 1). The differences between the pre- and post-systolic BP, diastolic BP and pulse rate were statistically significant with p values < 0.001 (Table 2).

### Table 1. Blood pressure response with adrenaline (n=21 patients)

<table>
<thead>
<tr>
<th></th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-SBP (mmHg)</td>
<td>0</td>
<td>130</td>
<td>80</td>
<td>27.9</td>
<td>6.0</td>
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<tr>
<td>Pre-DBP (mmHg)</td>
<td>0</td>
<td>90</td>
<td>46.6</td>
<td>26.7</td>
<td>5.8</td>
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<tr>
<td>Post-SBP (mmHg)</td>
<td>90</td>
<td>150</td>
<td>114.7</td>
<td>13.6</td>
<td>3.0</td>
</tr>
<tr>
<td>Post-DBP (mmHg)</td>
<td>50</td>
<td>90</td>
<td>73.9</td>
<td>9.2</td>
<td>2</td>
</tr>
<tr>
<td>Pre-Pulse (/min)</td>
<td>72</td>
<td>140</td>
<td>107</td>
<td>16.9</td>
<td>3.7</td>
</tr>
<tr>
<td>Post-Pulse (/min)</td>
<td>60</td>
<td>120</td>
<td>85.8</td>
<td>17.3</td>
<td>3.8</td>
</tr>
</tbody>
</table>

SBP-systolic blood pressure, DBP-diastolic blood pressure, Pulse-radial pulse rate.