Severe pneumococcal disease and temporary splenic dysfunction

MDE Pelly, Z Huo, DC Henderson, N Soni

Summary
We report a patient presenting with pneumonia in whom temporary splenic dysfunction was diagnosed by counting pitted red blood cells. This under-recognised condition caused a transient immunosuppression which may have had serious implications for our patient's recovery.

Keywords: splenic dysfunction, pneumococcal disease, immunosuppression

We present a case of a common disease that demonstrates a new immunological observation. The case highlights temporary dysplasia (box 1) which we believe is an under-recognised condition which could contribute to morbidity and mortality.

Case report
In March 1994 a previously fit 40-year-old caucasian woman presented to the Accident and Emergency department at the Chelsea and Westminster Hospital with a four-day history of left shoulder tip and left pleuritic chest pain. At home, she had deteriorated despite antibiotics, and on arrival was unwell, dyspnoeic at rest, with a tachycardia of 130 beats/min. Her blood pressure was 140/70 mmHg and she had clinical evidence of consolidation throughout her left lung. Her blood gases showed a PO2 of 6.7 kPa, PCO2 of 5.21 kPa and her pH was 7.30. The chest X-ray showed extensive consolidation of her left lung and patchy changes in her right lung. She had no relevant medical history, no pre-existing clinical or laboratory evidence of immunosuppression, but she smoked 20 cigarettes a day. A diagnosis of pneumonia was made.

She was treated with high-dose intravenous broad spectrum antibiotics, including penicillin G, but she deteriorated rapidly and developed severe respiratory failure requiring intubation and ventilation. She was transferred to the intensive care unit, where she was noted to have a refractory hypoxia despite a FiO2 of 1.0, with 10 cm H2O PEEP and IPPV. Supplementary ventilation with the Hayek negative pressure oscillator was used and she required ionotropic support.

The causative agent was confirmed by blood culture to be Streptococcus pneumoniae (serotype 14) which was fully sensitive to penicillin G. Klebsiella was also grown in the sputum several days later. In addition to the investigations required for clinical management, blood was taken to assess her spleen function and specific anti-pneumococcal antibody levels as part of an ongoing study. Splenic function was assessed by counting pitted red blood cells (PRBC) in the circulation by direct interference microscopy. This method has been validated in many studies and a raised PRBC level is accepted as a marker of impaired splenic function. In our laboratory, a level

Causes of dysplasia
- trauma
- sickle cell disease
- malignancy
- alcoholism and drug addiction
- systemic lupus erythematosus
- HIV infection
- reticuloendothelial block

Box 1
Figure  Serum PRBC, alkaline phosphatase, and C-reactive protein levels during pneumococcal sepsis. The dotted lines indicate the upper normal levels.

Table  Serum anti-pneumococcal antibodies. Class and subclass specific antibody levels in serum (Units/ml)

<table>
<thead>
<tr>
<th>Time</th>
<th>IgM</th>
<th>IgG</th>
<th>IgG1</th>
<th>IgG2</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Days post-admission</td>
<td>13.9</td>
<td>ND*</td>
<td>1</td>
<td>ND*</td>
</tr>
<tr>
<td>20 Days post-admission</td>
<td>76.1</td>
<td>0.7</td>
<td>1.2</td>
<td>ND*</td>
</tr>
<tr>
<td>Post-vaccination</td>
<td>&gt;100</td>
<td>2.76</td>
<td>18.59</td>
<td>3.74</td>
</tr>
</tbody>
</table>

*ND*= not detected

greater than 2% is considered to indicate impaired splenic function.

Serum pneumococcal antibody levels were determined by enzyme-linked immunoassay, using the 23-valent Pneumovax (Merck Sharp & Dohme Ltd) as antigen.1 The acute phase of her illness was marked by a rise and fall in C-reactive protein as expected (figure). Subsequent to this there was a significant transient rise in PRBC and serum alkaline phosphatase, accompanied by increased levels of bilirubin and liver enzymes (gamma glutamyl transferase, alanine aminotransferase). Anti-pneumococcal antibody levels (table) demonstrated that she had made a good specific anti-pneumococcal IgM response but minimal specific anti-pneumococcal IgG, IgG1 and IgG2 responses.

After a 14-day stay in the intensive care unit and several weeks rehabilitation on a medical ward she has been at home for 16 months with no sequelae. The chest X-ray is now normal apart from minimal pleural thickening.


Box 2

Discussion

It is of interest that the PRBC increased transiently, and concurrently with an increase in alkaline phosphatase, which has been noted before by Parker et al to be associated with sepsis.6 Increased PRBC is an accepted means of assessing impairment of splenic function,2,3 Normally, the siderotic granules, Howell-Jolly bodies, Heinz bodies, etc, which form the PRBC pits are removed by the endothelial macrophages in the spleen, without destroying the red cells which return to the circulation. The transient rise in PRBC levels in the circulation indicates a reduced phagocytic potential or temporary blockade of the reticuloendothelial cells. The splenic cord macrophages are responsible for the uptake of microorganisms such as pneumococci and other antigens which are then delivered to immunocompetent cells in the lymphoid tissue (splenic white pulp). Even temporary failure of this system has serious implications for a patient with septicemia, since not only is the clearance of micro-organisms impaired, but also the ability to mount an adequate immune response.

One of the immune defects noted in patients with impaired splenic function is failure to mount satisfactory total IgG and IgG subclass responses to polysaccharide vaccines,4 although such patients have adequate IgM antibody responses. Our patient’s failure to switch from IgM to IgG antibody production further supports a diagnosis of temporary splenic dysfunction. It is of interest that, even after vaccination six months later, she mounted a predominantly IgM response (table).

The significance of these findings is not fully understood but it is probable that transient immunosuppression due to transient splenic dysfunction may sometimes go unrecognised. Transient raised PRBC levels have been observed in other patients with sepsis and further studies are underway. This observation has not been reported before.

Learning points

- pneumococcal disease is still a serious and prevalent condition
- in this case the organism was penicillin sensitive but the incidence of resistant strains is increasing
- transient hyposplenism occurs but, as yet, the clinical significance is unknown
- PRBC is an indicator of splenic dysfunction and may indicate mononuclear phagocyte blockade
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