Lymphocytes bearing the T cell receptor γδ (TCR-γδ) in human early milk and peripheral blood

<table>
<thead>
<tr>
<th>Source of lymphocytes</th>
<th>No samples tested</th>
<th>Mean % (range) CD3+ cells</th>
<th>Mean % (range) TCR-γδ+ cells*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>15</td>
<td>68 (55-81) 11 (6-26)</td>
<td></td>
</tr>
<tr>
<td>Postpartum blood</td>
<td>15</td>
<td>72 (60-84) 5 (0-18)</td>
<td></td>
</tr>
<tr>
<td>Normal blood</td>
<td>15</td>
<td>72 (60-86) 6 (1-15)</td>
<td></td>
</tr>
</tbody>
</table>

*CD3+/TCRδ1+ cells.

Discussion

Although it is unlikely thatcolostrum TCR-γδ+ lymphocytes are merely contaminating blood borne T cells, their origin remains enigmatic. Human TCR-γδ+ cells populate organised lymphoid tissues (thymus, tonsil, lymph node, and spleen), as well as the gut and skin associated lymphoid systems, at similar frequencies without obvious tropism for epithelial microenvironments. The recent demonstration in experimen-
tal animal models that enterally administered human milk leucocytes adhere to the gut epithe-
lium or lie intramurally and persist in the intestine for at least 60 hours after a single breast feed, however, suggests that these cells may be involved in the host's local immune response. The problem of whether TCR-γδ+ cells play a part in the transfer of adoptive immunoprotection to the sucking infant remains unresolved. Now that some of the antigens these lymphocytes respond to have been defined, however, the way is open to search for the answer. Finally, because of the specificity (δ protein) of the monoclonal antibo-
dy (TCR δ 1) used in this study, the possibility that breast milk contains lymphocytes which express just one of the TCR-γδ chains cannot be totally ruled out.

Intravenous immunoglobulin in virus associated haemophagocytic syndrome

P Goulder, D Seward, C Hatton

Abstract

A 1 year old boy with virus associated haemophagocytic syndrome caused by cytomegalovirus infection is described. Persistent severe thrombocytopenia responded to repeated intravenous infusions of immuno-

globulin.

Virus associated haemophagocytic syndrome is known to occur in association with herpes virus infections. Although the mortality is high, complete recovery has been reported. Immunoglobulin infusions have been shown to increase platelet counts in chronic immune thrombocy-
topenia. This treatment was effective in a child with severe persistent thrombocytopenia com-
plicating virus associated haemophagocytic syn-
drome.

Case report

A boy aged 1 year presented with a one month history of intermittent fever and rash. Two days before presentation, he developed periorbital cellulitis, epistaxis, and a petechial rash.

He was the only child of healthy, unrelated parents. He had previously been well, had received no transfusions, and had been immunised with the full course of triple vaccine and oral polio. He was taking no medications.

On admission, he was febrile (39.1°C) with a diffuse petechial rash. There was generalised lymphadenopathy and appreciable hepatosple-


gnomegaly. Examination of the nervous and respiratory systems was normal.

An initial peripheral blood count showed a haemoglobin concentration of 120 g/l, platelets 57×10^11/l, and a white cell count of 8.3×10^9/l, with an absolute neutrophil count of 0.08×10^9/l. Within 18 hours the haemoglobin was 83 g/l, the platelet count 4×10^9/l, and the total white count 2.7×10^9/l. Red cells were hypo-

chroic and microcytic, and occasional reactive lymphocytes were visible. Clotting function was normal.

A bone marrow aspirate showed increased cellularity with active erythropoiesis, increased granulopoiesis, and plentiful megakaryocytes. Haemophagocytosis was present. There was no evidence of malignancy. A repeat bone marrow examination one month later was unchanged. An inguinal lymph node biopsy specimen showed reactive hyperplasia: the architecture

Discussion

The term 'virus associated haemophagocytic syndrome' (VAHS) was introduced to describe a disorder characterised by benign histiocytic hyperplasia and prominent haemophagocytosis associated with a systemic virus infection.\(^1\) Herpes viruses, in particular cytomegalovirus, have been most commonly implicated, although since the original description the syndrome has been expanded to accommodate associations with non-viral infections and with other underlying illness including immune deficiency states, and has been termed 'haemophagocytic histiocytosis'.\(^2\)

The clinical and histopathological features of this patient were consistent with the diagnosis of VAHS. Haemophagocytosis, histiocytic hyperplasia, and active cytomegalovirus infection were documented. There was no evidence of malignant proliferation of histiocytes, and serum lipids were not raised as may be found in other haemophagocytic syndromes, such as malignant histiocytosis and familial erythrocytic lymphohistiocytosis respectively.

There is no specific treatment for VAHS at present. Specific antimicrobial therapy has been used with success against bacteria associated with haemophagocytic syndrome and acyclovir in two patients with VAHS associated with Epstein-Barr virus.\(^3\) There are no reports of the use of ganciclovir in the treatment of VAHS associated with cytomegalovirus.

Other approaches to treatment of VAHS have included immunosuppression. Both splenectomy and the use of steroids or vinca alkaloids have met with temporary success at best, however, and some authors have advocated reduction in immunosuppression as critical in the management of such patients. Etoposide has been successful in controlling haemophagocytosis in both familial erythrocytic lymphohistiocytosis and VAHS associated with Epstein-Barr virus, but did not affect the outcome in the latter patient.\(^4\) Cyclosporin has been used in the long term treatment of haemophagocytic histiocytosis associated with Weber-Christian disease.\(^5\)

There are no published reports of the use of intravenous immunoglobulin in this condition. A trial of this treatment was initiated in view of potentially life threatening severe thrombocytopenia.

The mechanism by which immunoglobulin caused an increase in platelet count in this patient is uncertain. The precise immunoregulatory disturbance that occurs in VAHS is uncertain, but the platelet count response to immunoglobulin suggests that the mechanism of platelet destruction has features in common with that in idiopathic thrombocytopenic purpura.\(^6\) Low platelet counts precluded measurement of platelet associated immunoglobulin in this patient.

In conclusion, intermittent intravenous immunoglobulin has proved safe and effective...
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in the treatment of severe persistent thrombocytopenia complicating VAHS.

We are grateful to Dr R M Gardiner for encouragement and advice. D Seward was supported by the Wellcome Trust.


Do children need anticonvulsant treatment after a first fit?

The specious argument runs 'Epilepsy means recurrent fits. A single fit is therefore not epilepsy and does not require antiepileptic treatment'. The sensible argument depends on an assessment of the pros and cons of treatment. Estimates of recurrence risk after a first unprovoked seizure have varied from about 30% to 70%. A prospective study of 283 children in New York (Shinnat et al, Pediatrics 1990;85:1076-85) has given useful information. The overall risk of recurrence was 26% after one year, 36% after two years, 40% after three years, and 42% after four years. Factors increasing the risk were previous known cerebral pathology, abnormal electroencephalogram (EEG), and seizures of focal origin. Age at first seizure and duration of seizure did not influence the risk. Of 101 recurrences only two were status epilepticus and neither child suffered neurological sequelae.

The authors conclude that first unprovoked seizures should not lead to anticonvulsant treatment irrespective of risk factors.

The following table summarises the recurrence risks found in this study:

<table>
<thead>
<tr>
<th>% Recurrence risk (years)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>26</td>
<td>36</td>
<td>40</td>
<td>42</td>
</tr>
<tr>
<td>Previous known brain pathology</td>
<td>37</td>
<td>53</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td>24</td>
<td>33</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Normal EEG</td>
<td>15</td>
<td>23</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Abnormal EEG</td>
<td>41</td>
<td>54</td>
<td>56</td>
<td></td>
</tr>
</tbody>
</table>

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