Late spontaneous recovery of chronic thrombocytopenia

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Abstract
Five cases are reported of spontaneous remission of chronic childhood thrombocytopenia four or more years after diagnosis. Other than typical features of chronic idiopathic thrombocytopenic purpura there were no obvious markers predictive of late remission, although a slow progressive recovery was common to four of the patients. In light of this experience splenectomy is not recommended in clinically mild thrombocytopenia. (Arch Dis Child 1993; 68: 680–681)

Childhood idiopathic thrombocytopenic purpura commonly has an acute onset and lasts for a few months. Ten to twenty per cent of patients may have long term disease and resist treatment with steroids, immunosuppressive drugs, and intravenous immunoglobulin. Several centres have reported patients who have gone into remission after many years, even as late as 20 years after diagnosis (table 1), but no published series gives precise details which can identify such patients. We report the clinical details of five children, seen at Booth Hall and the Royal Manchester Children’s Hospitals, who did not show any sustained response to treatment but spontaneously went into remission at four, five, six, six, and 10 years after diagnosis. There were no common features which might have enabled us to identify these patients.

Case reports
Table 2 gives the salient features of the five children with late spontaneous remission of chronic idiopathic thrombocytopenic purpura. All were girls and presented between the ages of 5 and 13 years. Only one, patient 2, had a recognised preceding infection (rubella) and haemorrhage was present for less than one week before diagnosis. In the other four cases there was no precipitating factor and symptoms preceded diagnosis by three to eight weeks. The lowest recorded platelet counts ranged from 5 to 19×10⁹/l and in each instance bone marrow findings were consistent with a diagnosis of idiopathic thrombocytopenic purpura. In all patients the symptoms at diagnosis and throughout the course of the thrombocytopenia were never severe, consisting of minor bruising, petechiae, epistaxis, and in the older girls mild menorrhagia. Patient 2 had a chronic frequently relapsing course whereas the others, once the platelet count had started to improve, had a gradual progressive recovery with resolution of symptoms several years before the platelet count returned entirely to normal.

Discussion
Childhood idiopathic thrombocytopenic purpura is uncommon. The incidence is estimated to be less than 10/100 000 children each year. Most cases resolve quickly either with or without a short course of steroids or intravenous immunoglobulin. Only 10–20% persist for longer than six months and are classified as chronic idiopathic thrombocytopenic purpura. In acute idiopathic thrombocytopenic purpura the sexes are equally affected, but chronic idiopathic thrombocytopenic purpura appears to be two to three times more common in girls and more prevalent in older children. The peak incidence of acute idiopathic thrombocytopenic purpura occurs in children aged 2–5 years. Consequently, it is perhaps not surprising that our patients with late remission are all older girls. Also, the lack of any preceding infection and longer duration of symptoms before diagnosis in four of the five girls are recognised predictors of chronic disease.

Unfortunately, as our two hospitals’ experience of children with idiopathic thrombocytopenic purpura includes many referred from other districts because of a lack of remission, we cannot determine the total number of patients with acute and chronic disease occurring over the same 10 year period during which the five girls with late remission were observed. Therefore we are unable to estimate the percentage of patients with chronic idiopathic thrombocytopenic purpura who may be expected to eventually go into remission spontaneously. If the 658 cases from the five series in table 1 which give full numbers are analysed, however, 35 children (5–3% of all patients or 23% of patients with chronic disease) showed spontaneous remission after two years. It is also worth noting that over these five series a further 50% of patients with chronic disease were cured, usually remitting between six and 24 months or after splenectomy.

The partial unsustained response to steroids, seen in most of our cohort, is perhaps just a
Late spontaneous recovery of chronic thrombocytopenia

Table 2 Characteristics of five children with late spontaneous remission

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age at onset (years)</th>
<th>Indirect platelet antibody test</th>
<th>Lowest platelet count (x10^9/l)</th>
<th>Initial treatment</th>
<th>Course and duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>Weak positive</td>
<td>5</td>
<td>Steroids, poor response</td>
<td>Gradual recovery, six years</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>Positive*</td>
<td>5</td>
<td>Steroids, transient rise; iv IgG, transient rise</td>
<td>Chronic relapsing, 10 years</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>Negative</td>
<td>6</td>
<td>Steroids, transient rise</td>
<td>Gradual recovery, 4 years</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>Negative</td>
<td>19</td>
<td>Steroids, poor response</td>
<td>Gradual recovery, 5 years</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>Positive</td>
<td>9</td>
<td>Steroids, transient rise; iv IgG, no response</td>
<td>Gradual recovery, 6 years</td>
</tr>
</tbody>
</table>

*This patient, who had preceding rubella, also had a weakly positive test for antibodies to DNA; iv=intravenous.

marker of chronic disease, as are the mild symptoms which are often a feature of chronic idiopathic thrombocytopenic purpura.15 Bone marrow findings were not unusual and none had immunoglobulin deficiency. The only feature which seemed to herald late spontaneous recovery was the eventual slow increase in platelet count above the symptomatic threshold. This was seen in all but patient 2, who in many ways ran a different course and may potentially relapse in the future. We are therefore unable to identify markers specific to future spontaneous remission.

It is important to recognise that spontaneous remission can occur years after diagnosis and therefore patients should not be rushed into splenectomy, which has often been performed when remission has not been achieved six to 12 months after diagnosis. Admittedly this option will produce a successful response in 50–65% of patients with chronic disease12,14 but this responding group may include many who would have later remitted spontaneously. It should be remembered that the risk of sepsis after splenectomy is perhaps greater than the risk of intra-cranial haemorrhage due to thrombocytopenia.10 This risk is life long12 and often fatal, though it is anticipated that current vaccination practices and prophylactic antibiotic treatment, if complied with, will reduce the risk considerably.

Therefore, in view of our experience of several late spontaneous remissions in chronic idiopathic thrombocytopenic purpura we would concur with the current views that splenectomy is delayed until at least 12 months after diagnosis and perhaps be reserved for children with either life threatening haemorrhage or recurrent bleeding without local cause.11,17 Indeed, in clinically mild chronic idiopathic thrombocytopenic purpura it is best avoided as spontaneous remission may occur after many years.