Serum ferritin in juvenile chronic polyarthritis

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SUMMARY Six children with juvenile chronic polyarthritis were studied and their disease activity correlated with haematological values including serum ferritin. The latter is often raised above reference values, but even when within them appears to fluctuate significantly and correlates more closely with disease activity than any of the other parameters measured. We conclude that the serial measurement of serum ferritin may be a useful guide to the management of such children.

Moderate anaemia is often found in adult patients with rheumatoid arthritis and may be associated with a low serum iron concentration which is inversely related to the disease activity (Engskedt and Strandberg, 1966). Serial measurements have been suggested as a means of following the course of the disease (Whittingham et al., 1967). Changes in iron are thought to be characteristic (Turnbull, 1971) and, in spite of the low serum iron, total body iron is increased as evidenced by greater amounts of haemosiderin in the marrow, particularly in those with active disease (Hill and Greenbury, 1959). Furthermore, the amount of haemosiderin correlates well with the quantity of iron that can be chelated with desferrioxamine (Wardle et al., 1968). More recently the serum ferritin has been shown to be an accurate index of body iron stores in health (Walters et al., 1973), and Bentley and Williams (1974) have shown a close relationship with stainable bone marrow iron in adult rheumatoid patients, some of whom had raised serum ferritin levels. Similar changes in iron kinetics are thought to occur in children with juvenile chronic polyarthritis but these are not well documented. We have therefore studied a small group of children with this condition and correlated changes in iron and ferritin with alterations in disease activity.

Patients and methods

Six children, 4 male, 2 female, aged from 6 to 15 years who satisfied the criteria of Ansell and Bywaters (1959) for the diagnosis of juvenile chronic polyarthritis, were studied. All were Rose-Waaler negative and blood was taken at varying intervals during the course of the disease for estimation of haemoglobin, ESR (Westergren), serum iron, and serum ferritin (immunoradiometric method of Addison et al., 1972). Clinical disease activity was assessed by the method of McConkey et al., (1972): an arbitrary score of 100 was given at entry into the study and on each subsequent occasion was scored +10 if the patient was worse, 0 if unchanged, and −10 if improved from the previous visit. Assessment was a composite of the mother’s, child’s and doctor’s (A.W.C.) opinion and was made before any laboratory findings were known. 4 of the children were receiving treatment with corticosteroids, D-penicillamine, and benorylate, and the other 2 with salicylates alone.

Results

Laboratory investigations at entry into the study are shown in Table 1. The references values for ferritin were obtained from 10 healthy children aged 2–16 years. The Fig. shows the course of one patient’s clinical score and laboratory findings over a 7-month period, and the correlation between clinical rating and serum ferritin has been calculated (for each patient) using Spearman’s Rank Correlation Coefficient for nonparametric measurements (Table 2). A similar correlation coefficient for the other parameters studied was calculated for individual patients and a mean of the separate coefficients calculated by Z transformation (Table 3).

Neither the negative correlation between serum iron and clinical rating/ferritin/ESR nor the positive correlation between ESR and clinical rating/ferritin was significant. The significance between ferritin and clinical rating at the 5% level would possibly be greater if more observations had been performed on Cases 5 and 6.

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Table 1 Mean values (+ range) at entry into study

<table>
<thead>
<tr>
<th></th>
<th>Study group</th>
<th>Normal</th>
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<tbody>
<tr>
<td>Ferritin (µg/l)</td>
<td>822 (120-2000)</td>
<td>35-155</td>
</tr>
<tr>
<td>Iron (mmol/l)</td>
<td>3.8 (2.7-5.4)</td>
<td>4.8-27.4</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>68 (38-104)</td>
<td>1-15</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>10.5 (8.2-11.8)</td>
<td>11.7-16.2</td>
</tr>
</tbody>
</table>

Conversion: SI to traditional units—Iron: 1 mmol/l ≈ 5.8 mg/100 ml.

Table 2 Ferritin vs. clinical rating

<table>
<thead>
<tr>
<th>Case no.</th>
<th>n</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>0.965</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>0.936</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>0.928</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>1.000</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>0.900</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>0.550</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 Mean correlation coefficients

<table>
<thead>
<tr>
<th></th>
<th>Clinical rating</th>
<th>Ferritin</th>
<th>Iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferritin</td>
<td>0.954*</td>
<td>0.47</td>
<td>0.226</td>
</tr>
<tr>
<td>Iron</td>
<td>-0.197</td>
<td>0.74</td>
<td></td>
</tr>
</tbody>
</table>

*P<0.05.

Discussion

Our most difficult problem was to find a satisfactory measure of disease activity. Other methods have been used in adult studies, for example, joint score, joint size, and duration of morning stiffness, but these are unsatisfactory and even less applicable to children. Lee et al. (1974) have suggested that the patient's impression of his clinical state is the most valuable indicator of the disease activity and although this is clearly influenced by many factors, we have found the method used to be simple and satisfactory.

There was an overlap between our patients' measurements and the reference values at entry into the study, and because of the wide variation in results we have concentrated on analysis of changes within individual patients as this will be the most useful clinically. Of the parameters studied, serum ferritin appears to be the most useful, and even in one patient whose levels remained within the reference values throughout the study, a marked alteration occurred during the course of the disease. This is in contrast to healthy people in whom the serum ferritin does not alter during the day or from day to day (Siimes et al., 1974). However, raised levels of serum ferritin are found in many conditions, e.g. haemolysis, liver disease, leukaemia, and do change within the course of some infective illnesses (E. J. Eastham, unpublished observations, 1976). Interpretation should be guarded, therefore, but in our patients there was no evidence of these other factors.

It is unlikely that the changes seen in serum ferritin were due to the drug treatment, as corticosteroids do not have any effect on iron in health (Mowat et al., 1969) and penicillamine has no significant effect on serum iron (Walsh and Patston, 1965) or iron excretion (W. Lyle, personal communication, 1976).

Our findings confirm that changes in iron kinetics similar to those in adults with rheumatoid arthritis occur in children with juvenile chronic polyarthritis. The marked increase of the reticuloendothelial system in active disease creates a larger iron storage pool and it seems that in some way the iron is preferentially taken up by these cells and not made available for normal haemopoiesis until the disease regresses. The serum ferritin is the most reliable laboratory reflection of disease activity that we have measured, and might be of value in those conditions where a more accurate assessment of clinical activity is needed, e.g. drug trials, and would also serve as an indicator as to when iron replacement may benefit the haemoglobin status of the patient.

Fig. Clinical and laboratory course of one child.
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References


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