Early cardiac iron overload in children with transfusion-dependent anemias

by Juliano Lara Fernandes, Antonio Fabron Jr, Monica Verissimo

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Early cardiac iron overload in children with transfusion-dependent anemias

Quantitative magnetic resonance imaging (MRI) heart iron assessment has been an important advance in the follow-up of patients with transfusion-dependent anemias.1 Few longitudinal data are available on the natural history of cardiac iron overload.2 We refer this letter to the manuscript by Wood et al.3 where they recently reported that in pediatric patients with thalassemia major (TM) no detectable cardiac iron overload was observed in children under the age of 9.5 years. Another study showed that cardiac iron loading in patients with increased transfusion requirements occurred only after at least 13 years of chronic transfusion therapy.4 These facts are important in determining the appropriate age to start screening for increased iron in the heart with an expensive technique such as MRI. However, as published in recent guidelines,5 it has been hypothesized that these observations should only be true if chelation therapy has started early and been received regularly as well as there has been no increases in transfusion needs. To evaluate if cardiac iron overload might occur in younger children that do not satisfy these requirements, we assessed pediatric patients from 7-18 years of age with chronic transfusion therapy undergoing MRI to detect cardiac iron loading. Cardiac T2* assessment was performed on a 1.5T Siemens Symphony scanner using previously described validated techniques.6

A total of 23 patients were scanned (61% male, mean age of 12.6±3.1 years) with thalassemia major being the most frequent diagnosis (78%), followed by thalassemia intermedia (13%), sideroblastic anemia (4%) and sickle cell disease (4%). In this cohort, there were four patients diagnosed with cardiac iron overload, three of them males under the age of 10 (Table 1). The fourth patient was 17 years of age (older than the age reported for the first findings of cardiac iron overload in previous studies) and was not included in the analysis (heart T2* of 17.2msec). All other patients had normal heart T2* with no other cardiac findings (27.3±6.5msec).

In common, the three patients under the age of 10 with cardiac iron overload reported suboptimal chelation therapy prior to the MRI scans, either due to irregular use of the prescribed chelator or late access to chelation early in the course of the disease. Chelation history for these patients included late start for patient 1 and 2 (17 and 28 months gap between transfusions and desferrioxamine use, respectively) and irregular use for patient 3. All patients had adequate prescriptions for subcutaneous desferrioxamine at the time of cardiac iron overload diagnosis, with deferiprone added after heart involvement diagnosis. It is interesting to notice that the mean transfused iron input for these patients were 189.1±98.5 mg/kg/y, a total iron dose not too different compared to previous reports.7 Moreover, in all these patients the degree of cardiac iron overload was always severe with only one patient already showing symptoms of heart failure (patient number 3). This patient in particular showed signs of heart failure (shortness of breath while playing with other children and premature ventricular complexes in the ECG) already at the age of 3 with no other etiologies besides cardiac siderosis being found.

Regarding the other 20 patients in the cohort, chelation therapy included subcutaneous desferrioxamine only in 15 patients, desferrioxamine plus deferiprone in one patient and deferasirox in the remaining four. Compared to the three patients described, all these patients reported good adherence to chelation therapy, defined as correct intake of the prescribed medication more than 90% of times.

In this letter, we showed that increased cardiac iron deposition can occur even at a younger age than previously predicted by previous studies. The main reason for this occurrence seems to be inadequate compliance with chelation therapy as has been reported in unchelated adult patients with myelodysplastic syndromes.8 Other reasons for the results observed, such as anemia as a potential factor for iron overload, were not assessed in this study. Although chelation therapy is mentioned in previous reports with young patients, the compliance status of the population described was not portrayed,9 leaving the possibility that all patients were well chelated or that poorly compliant subjects were not included. Nevertheless, it seems prudent to recommend starting MRI screening as early as seven years of age if poor chelation is assumed, even in the absence of symptoms of heart disease. Cardiac MRI can be performed with no need of sedation in children at this age and normal reference ranges have been extensively studied for comparisons of heart function.10 While cost and availability should be considered, especially if one assumes that patients with difficult access to chelation will also have the same problems with MRI, these patients are the patients that should benefit most from precocious screening.

Table 1. Characteristics of study patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>All other patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>9.7</td>
<td>7.4</td>
<td>9.8</td>
<td>12.6±3.1</td>
</tr>
<tr>
<td>Diagnosis (see text)</td>
<td>TM</td>
<td>TM</td>
<td>Sideroblastic anemia</td>
<td>Varied</td>
</tr>
<tr>
<td>Age at start of transfusion therapy (m)</td>
<td>6</td>
<td>12</td>
<td>1</td>
<td>9.4 (1-18)</td>
</tr>
<tr>
<td>Age of initial chelation therapy (y)</td>
<td>1.9</td>
<td>3.3</td>
<td>0.7</td>
<td>1.4 (0.6–3.3)</td>
</tr>
<tr>
<td>Serum ferritin range (ng/dL)</td>
<td>2008-2568</td>
<td>1313-2316</td>
<td>1299-3076</td>
<td>957 (340–4211)</td>
</tr>
<tr>
<td>Transfusional iron input (mg/kg/y)</td>
<td>143.6</td>
<td>121.5</td>
<td>302.1</td>
<td>133.7 (76–403)</td>
</tr>
<tr>
<td>Cardiac T2* (ms)</td>
<td>8.1</td>
<td>6.9</td>
<td>3.2</td>
<td>27.3±6.5</td>
</tr>
<tr>
<td>Liver iron concentration (mg/g)</td>
<td>8.4</td>
<td>16.7</td>
<td>12.7</td>
<td>6.4 (1.2 – 18.9)</td>
</tr>
</tbody>
</table>

Data for all group reported as mean±SD or (range).

Juliano Lara Fernandes; Antonio Fabron Jr; Monica Verissimo

1. University of Campinas (Unicamp), Campinas, Brazil; 2. Faculdade de Medicina de Manhã, Manhã, Brazil; 3. Centro Infantil Boldrini, Campinas, Brazil

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Key words: iron overload, young children, transfusional requirements.

Correspondence: Juliano Lara Fernandes, R. Antonio Lapa 1032, Campinas, SP, 13025-292, Brazil. Phone: international +55-19.3579-2023, Fax: international +55-19.32522923. E-mail: jlaraf@fcm.unicamp.br
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