CASE REPORT

Rapid iron loading in a pregnant woman with transfusion-dependent thalassemia after brief cessation of iron chelation therapy

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Abstract

In general, in women with transfusion-dependent thalassemia, during pregnancy, iron chelation therapy is ceased. We report a splenectomized patient, who was an excellent complier with chelation therapy, who before embarking on a pregnancy showed no evidence of iron overload, with normal cardiac, thyroid function and glucose metabolism. Laboratory findings showed ferritin 67 μg/L, myocardial T2* of 34 ms and liver magnetic resonance imaging (MRI) liver iron concentration of 1 mg/g dry weight. She became pregnant by in vitro fertilization in October 2006, delivery occurred in June 2007. She breast fed for 2 months. After 12 months without iron chelation, ferritin was 1583 μg/L. Quantitative MRI showed myocardial T2* of 27 ms, that the liver iron concentration had increased to 11.3 mg/g dry weight, indicative of moderate to heavy iron load. This case demonstrates that iron overload can develop rapidly and that physicians caring for patients with transfusion-dependent thalassemia should be particularly alert to any discontinuation of chelation therapy over time.

Key words thalassemia major; pregnancy; transfusion iron load; chelation therapy

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The marked improvement in survival and reduced morbidity in thalassemia major (TM) allows many patients to parent children (1, 2). For women, in many instances assisted reproduction methods in vitro fertilization (IVF) need to be used. In general, as pregnancies in TM patients are usually planned, iron chelation therapy is stopped before the patient enters the IVF programme (3). In the past, the impact of such cessation was not easily assessable except by serum ferritin levels. Liver biopsies, though valuable were relatively traumatic and had low acceptance from patients. With the advent of magnetic resonance imaging (MRI) techniques such assessments are more easily accessible (4). The patient, subject of this report was followed prospectively before and after a pregnancy to determine the impact of withholding chelation therapy for a period of 12 months.

Patient information

The patient is now 38 yr old. She commenced regular blood transfusion at 10 months of age and desferrioxamine iron chelation therapy at the age of 11 yr. In June 2001 with the availability of the oral chelator deferiprone, she commenced combination therapy with deferiprone at 60–80 mg/kg/d in three doses (25% in the morning, 25% in the afternoon and 50% at night) and desferrioxamine at 30–50 mg/kg/infusion/d. She was always very compliant with her chelation therapy.
did not show any cardiac complications, glucose and thyroid metabolism were normal. She was diagnosed as having primary amenorrhea at 16 yr of age and received hormone replacement therapy. She had osteopenia. In October 2006 with IVF she became pregnant. She delivered in June 2007 and breast fed for 2 months. She had ceased chelation therapy from October 2006 till the end of September 2007. She has given written consent to the anonymous publication of this report.

Liver R2* (reciprocal of T2*) is linearly proportional to total iron present in an organ and a calibration equation was derived from the least squares fit of liver R2* data of patients who subsequently underwent liver biopsy vs. linear ion concentration (LIC) determined by the liver biopsies. For liver R2 vs. LIC a non-linear calibration curve was determined and a calibration equation is also available (5). In order to use the calibration equations for liver R2* and R2 the same protocols for determining R2 and R2* must of course be used. Our R2* data were obtained with identical protocols as described from a Los Angeles group (6) but a different pulse sequence was used for determining R2, thus our R2 data can only be correlated to LIC in a qualitative way. For the period of the pregnancy all quantitative determinations are based on our R2* data.

Table 1 shows the mean ferritin levels, the red cell consumption, left ventricular ejection fraction (LVEF) as assessed by echocardiography, cardiac T2* and liver iron concentration. The initial and final LIC were determined from the MRI data of patients who subsequently underwent liver biopsy. For liver R2 vs. LIC a non-linear calibration curve was determined and a calibration equation is also available (5). In order to use the calibration equations for liver R2* and R2 the same protocols for determining R2 and R2* must of course be used. Our R2* data were obtained with identical protocols as described from a Los Angeles group (6) but a different pulse sequence was used for determining R2, thus our R2 data can only be correlated to LIC in a qualitative way. For the period of the pregnancy all quantitative determinations are based on our R2* data.

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Table 1 Iron load parameters over time

| Year | Annual mean ferritin | RCC | LVEF | T2* heart | LIC mg/g dw |
|------|----------------------|-----|------|-----------|-------------|
| 2001 | 1500                 | 230 | 77%  | 35.5      |             |
| 2002 | 126                  | 251 | 66%  | 39.6      |             |
| 2003 | 92                   | 210 | 69%  | 32.8      | 35.4        |
| 2004 | 105                  | 229 | 67%  | 38.0      | 35.3        |
| 2005 | 142                  | 257 | 61%  | 37.8      | 34.4        |
| 2006 | 67                   | 242 | 63%  | 38.3      | 34.1        |
| 2007 | 1481                 | 230 | 65%  | 33.8      | 27.3        |

RCC is the red cell consumption per annum in mL/kg.
LIC is expressed as mg/g dry weight and was assessed by magnetic resonance imaging T2 and T2*.
All T values are in milliseconds.
LVEF, left ventricular ejection fraction; LIC, liver iron concentration.

Discussion

This case report demonstrates the iron loading that occurred in one individual patient after the usual practice of cessation of iron chelation therapy for pregnancy. It would be valuable to have results from more patients. It would also seem that the policy of ceasing chelation therapy during the whole of pregnancy may be inadvisable and may be placing patients at risk of increased morbidity and ultimately mortality, especially during a period in which their cardiac function may need to be at its best. In the experience of one of the authors (VB), armed with the understanding that desferrioxamine is not teratogenic, recommencing regular chelation therapy with desferrioxamine after the 16th week of gestation did not result in any fetal abnormalities. In addition, a number of patients who became pregnant unexpectedly and did not stop desferrioxamine therapy until they were aware of the pregnancy had normal outcomes to their offspring. A case report of a patient who received desferrioxamine chelation therapy and gave birth to a normal...
child is also indicative of the safety of its use during pregnancy (7).

It is also likely that the free iron that results from the iron overload may be very avidly taken up in the liver and possibly the heart (8).

**Conclusion**

This case report shows clearly that pregnant women with TM should be monitored carefully for iron loading before they embark upon a pregnancy and afterwards and consideration should be given to offering desferrioxamine chelation therapy after the middle of the second trimester. The main message from this patient is that in some transfusion-dependent patients, cessation of chelation therapy allows rapid iron overload. Patients should be made aware of this risk in order to encourage them to maintain their chelation therapy consistently.

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