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A rare occurrence of intrauterine death following an allergic reaction to iron sucrose

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Abstract:

During pregnancy, iron-deficiency anemia if untreated can affect the mother and child and hence iron is supplemented. Intolerance to oral iron therapy and malabsorption are common indications for parenteral iron therapy. The regularly used intravenous iron preparations are iron sucrose, sodium ferric gluconate, and iron dextran, of which iron sucrose has a satisfactory safety profile. We report a case of iron sucrose causing rare reaction with generalized edema in the mother, which was followed by intrauterine death. The oxidative stress due to immune-mediated mechanisms or adjuvant used in iron sucrose could cause mild rashes to severe anaphylactic reactions. This case report warns us toward the use of parenteral iron preparations in pregnant women, as one of the safe formulations could lead to an unusual fatal outcome in the fetus.

Keywords:

Anemia, intrauterine death, iron sucrose, pregnancy

Introduction

Pregnancy is associated with medical diseases, with the most common being iron-deficiency anemia. The maternal deaths (20%) are unswervingly related to anemia, and more so 50% are related to its complications.^[1] The Centers for Disease Control and Prevention and Indian guidelines recommend screening for iron-deficiency anemia among pregnant women and universal iron supplementation to meet the iron requirements in pregnancy. Oral iron preparations are commonly used when compared to parenteral preparations which are indicated when Hb is ≤ 8 g% and failure of 14 days of oral therapy. Among the parenteral preparations, newer drugs such as iron sucrose are effective with minimal side effects.^[2,3] We report a

rare reaction to iron sucrose in a pregnant woman with moderate iron-deficiency anemia.

Case Report

A 35-year-old multigravida of 28-week gestation with moderate iron-deficiency anemia was advised to take tablet Orofer XT (Emcure Pharmaceuticals Limited) containing ferrous sulfate 100 mg + folic acid 1.5 mg once daily. She complained of on and off episodes of nausea and severe gastric irritation during the treatment, but continued taking oral preparations for 2 months. In spite of this treatment, there was no raise in hemoglobin (Hb) levels. Before conception, her Hb was 9 g% and serum ferritin was 58 ng/ml. The peripheral smear was suggestive of microcytic hypochromic anemia. The Hb during 16th week was 8 g%, which had improved to 8.5 g% at the end of 2 months. The dose and frequency of oral iron

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preparation was not increased due to intolerance to the drug. Hence, she was administered two doses of iron sucrose (Ferimax-SR and Micromax 5 ml, 1 ml = 20 mg) diluted in 500 ml normal saline infused over 5 h in a private hospital after the test dose (0.1 ml intravenous). One hour after infusion, she developed generalized edema with mild itching. The itching reduced after administering injection chlorpheniramine maleate 10 mg intravenously. On day 2, she experienced reduced fetal movements. She had no history of receiving parenteral iron preparation in the past. Ultrasound abdomen reported that reduced movement was due to the hyperextension position of the fetus, and cardiac activity was normal. The patient continued to have reduced fetal movements, so she consulted her obstetrician again after 4 days. On examination, her pulse rate was 84 beats/min, blood pressure was 110/60 mm Hg, and respiratory rate was 21 breaths/min with pallor and generalized pitting edema. During the fetal Doppler test, cardiac activity was not recorded, and the patient was reassured and advised adequate rest. In spite of taking adequate rest, she continued to have reduced fetal movements. On consultation after 2 weeks, the ultrasound abdomen was done. Ultrasound abdomen revealed the absence of fetal heart beat with signs of fetal death of 2-week duration as depicted in Figure 1. The previous ultrasounds done for nuchal thickness at 12 weeks and anomaly scan at 20 weeks were normal with no growth lag. The uteroplacental blood flow was normal. On investigation, the total blood count, thyroid profile, lipid profile, and random blood sugar were normal. The occult blood in stools was negative. The serological tests done during 8 weeks of pregnancy for human immunodeficiency virus infection, syphilis, and hepatitis B were negative. She had no history of fever, diarrhea, abdominal discomfort, burning micturition, and cough before the iron sucrose injection. Pregnancy was terminated by induction with tablet misoprostol, and the patient was counseled. On examination of the fetus, no congenital defects were observed.

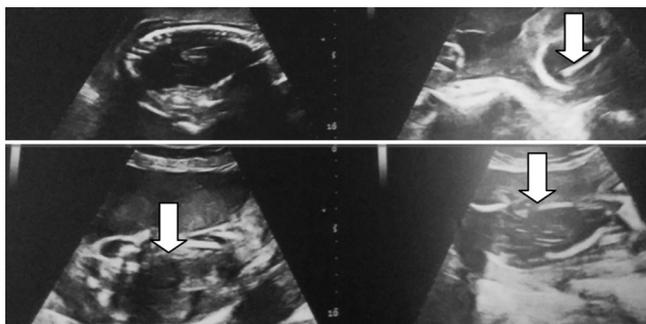


Figure 1: Ultrasound abdomen done at 28 weeks of gestation showing signs of fetal death. The arrow shows Spalding's sign (the overlap of fetal skull bones caused by collapse of the fetal brain)

Discussion

In pregnant women, the occurrence of anemia is estimated to be 39.9%–43.8% globally and 43.9%–52.5% in Southeast Asia. One of the most common types of anemia in pregnant women is iron-deficiency anemia. The prevalence of iron-deficiency anemia in developed countries is only 18% compared to developing countries, i.e., between 35% and 75%.^[4-6] In India, the recommended preventive strategy for iron-deficiency anemia is supplementation of oral ferrous sulfate 100 mg for 100 days. If pregnant women cannot tolerate the oral preparation or no raise in Hb level, parenteral iron therapy is considered.^[5] India contributes to a major extent in maternal deaths among South Asian countries. According to a survey done by the Indian Council of Medical Research, the highest prevalence of anemia was in pregnant women in India, and majority had moderate (Hb: 5–8 g%) and severe (Hb: <5 g%) anemia.^[7] The commonly available intravenous (parenteral) iron preparations are iron dextran, sodium ferric gluconate, and iron sucrose. The adverse reactions to parenteral iron are metallic taste, dizziness, nausea, vomiting, abdominal pain, and rarely anaphylactic reactions. The anaphylactic reactions can comprise breathlessness, chest pain, dizziness, urticaria, and hypotension. The basis for allergic hypersensitivity reactions is not clearly understood. Among the intravenous iron preparations, iron dextran has the highest incidence of hypersensitivity reactions followed by sodium ferric gluconate and least with iron sucrose. The highest risk of hypersensitive reactions is reported with iron dextran (85/100,000 persons), followed by ferric gluconate and ferumoxytol, and had risks of 47 and 34/100,000 persons, respectively.^[8] Iron sucrose (16 per 100,000 persons) relatively has less risk compared to other parenteral iron preparations. Hence, it is recommended for use in pregnant women with severe anemia even in the government hospitals.^[9,10]

In our patient, the generalized edema with mild itching had appeared after 1 h of infusion. The itching subsided with the administration of injection chlorpheniramine maleate. As there were no other symptoms and the patient was comfortable, the complete dose of iron was received by the patient. Only on day 2, she complained of reduced fetal movement. The reason for reduced fetal movements could be maternal hypovolemia, hypoxia, uterine hypoperfusion, and umbilical vessel vasoconstriction.^[11] The immediate scan done after observing reduced fetal movements was normal. The repeat scan was done after 2 weeks and, as a result, these maternal pathophysiological changes due to the presence of histamine could have gradually led to the impairment of fetal regulation of cerebral flow and induced neurological damage.^[12] The intrauterine death in this

patient cannot be explained by any other reason, as all the prior laboratory investigations and ultrasound scan reports were normal. The World Health Organization causality assessment scale suggests the reactions to be possible with a causative drug being iron sucrose. The Naranjo Adverse Drug Reaction Probability Scale was applied, and a score of +6 was obtained, which makes the reaction probable.^[13]

To conclude, treating physicians should be cautious even to the mildest reactions to parenteral iron, especially in pregnant women, as it can cause adversity in the fetus as well. When parenteral iron is administered to pregnant women, they should be advised to monitor fetal movements and consult the obstetrician immediately if the movements are decreased. This is a case report, but it may serve as signal detection. The parenteral iron to be advised in pregnant women with at most caution as even the safest preparations could cause such untoward outcomes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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