Journal of Pharmaceutical Care
jpc.tums.ac.ir

Leg amputation following intramuscular injection of iron dextran in a 32 year old woman

Gloria Shalviri [1*], Kheirollah Gholami [2], Naghmeh Javidnikou [1]

[1] Iranian Adverse Drug Reaction Monitoring Center, Ministry of Health and Medical Education, Tehran, Iran
[2] Clinical Pharmacy Department, Faculty of Pharmacy and Research Center for Rational Use of Drugs, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article type:
Case Report

Keywords:
Iron-Dextran Complex
Amputation
Drug Toxicity
Adverse Drug Reaction Reporting Systems

ABSTRACT

To inform healthcare professionals of a rare serious reaction leading to leg amputation following intramuscular injection of iron dextran and report comments for preventing such reactions.
A case of leg amputation following intramuscular injection of iron dextran reported to Iranian Pharmacovigilance Center was reviewed. Patient and reaction data was collected by assessing the reported yellow card, patient chart review and interviewing with patient and physicians. World Health Organization definition for serious reactions was used to determine the seriousness of the reaction. Naranjo algorithm was used to determine probability scale. The probability of the reaction was determined based on questionnaire of Schumock et al. The studied case is classified as a rare and serious but preventable reaction induced by intramuscular injection of iron dextran in a 32 year old woman. The probability of the reaction is appeared to be "probable" based on Naranjo algorithm. It seems that Iron dextran could cause serious and life threatening adverse effects. It is necessary for healthcare professionals to be informed of such rare but serious reaction in order to apply preventive actions.

J Pharm Care 2013; 1(2): 74-76.

► Please cite this paper as:
Shalviri G, Gholami K, Javidnikou N. Leg amputation following intramuscular injection of iron dextran in a 32 year old woman. J Pharm Care 2013; 1(2): 74-76.

Introduction

Hypersensitivity reactions following administration of iron dextran is not uncommon in the literature. However, few cases of hypersensitivity vasculitis have been reported. We report the case of a woman whose legs were amputated after intramuscular injection of iron dextran.

Despite of allergic reactions induced by intravenous injection of iron dextran mentioned in the literature (1-3), there are limited data on such a reaction with intramuscular injection of the product. A symmetrical allergic purpura of the lower limbs due to hypersensitivity vasculitis has been observed in a child following intramuscular injection of iron dextran (4). Also there are evidence on amputation of the limb following vascular calcification and skin necrosis known as calciphylaxis, which has increased during last decade because of number of possible factors, including more widespread use of parenteral vitamin D and iron dextran (5-7). Some studies show that iron dextran therapy are associated with higher risk of hypersensitivity reactions in comparison with newer parenteral iron products such as iron sucrose and sodium ferric gluconate (8) and life-threatening adverse events appear to be lower with the use of non-dextran iron formulations (9). To the best of our knowledge there is no published report of iron dextran-induced vasculitis leading to amputation in the literature.

Case Presentation

A 32-year-old woman referred to physician because of general weakness. The patient had no history of underlying

* *Corresponding Author*: Dr Gloria Shalviri
Address: Food and Drug Organization, Fakhr_e_Razi Ave., Enghelab Street, Tehran, Iran. Tel:+982166963862
E-mail: shalviri_g@yahoo.com

diseases or any allergic reaction to medicines. Iron dextran injection (100 mg per 2 ml) was prescribed with the probable diagnosis of anemia. Laboratory information to confirm anemia was not performed prior to iron dextran prescribing. A few hours after intramuscular injection of the first dose of iron dextran, the patient developed fever, dyspnoea, nausea, flushing, fatigue, rash, ecchymosis and severe tenderness in hands and lower limbs leading to hospitalization.

On admission to hospital, laboratory findings were as follows: HBS Ag:(negative), HCV Ab: (negative), HIV Ab: (negative), Calcium: (9.1 µ/l), Phosphorus: (2.8 mg/dl), WBC:(11600 cell/mm^3), Hemoglobin: (13g/dl), Platelet: (125000 cell/mm^3), Prothrombin Time (PT): (normal), Partial Thromboplastin Time (PTT): (normal), Urea: (23 mg/dl), Creatinine: (0.8 mg/dl), Uric acid: (5 mg/dl), Blood Sugar: (111 mg/dl), Sodium: (142 mmol/L), Potassium: (3.5 mmol/L), Bilirubin: (1.4 mg/dl), Cholesterol: (130 mg/dl), Triglyceride: (404 mg/dl), Aspartate aminotransferase (AST): (34 IU/L), Alanine aminotransferase (ALT): (16 IU/L), Lactate dehydrogenase (LDH): (519 IU/L), Alkaline phosphatase (ALP): (65 IU/L), Creatine phosphokinase (CPK): (173 mg/dl), Rapid Plasma Reagin (RPR): (negative), C-Reactive Protein (CRP): (negative), Reumatoid Factor: (negative), Anti-nuclear antibodies (ANA): (negative), C3/C4/CH50: (normal), Anti-neutrophil cytoplasmic antibody (ANCA): (negative), Lupus anticoagulant: (negative), Anti-ds DNA: (normal), Anti-phospholipid: (normal), Cold-agglutinin: (negative), Cryo-glubulin: (negative), Erythrocyte Sedimentation Rate (ESR): (47). Echocardiography: (normal), Brain CT scan: (normal).

Bilateral upper and lower extremities after Doppler showed totally occlusion in the right pedis dorsalis artery from its proximal portion at dorsal aspect of the right foot.

She received prednisolon 1g for 5 days and heparin infusion. Plasma exchange was started on the third day of hospitalization and continued for 5 days, it followed by 750 mg cyclophosfamide on the last day. Thereafter, Intravenous immunoglobulin (IVIG) 25 g daily for 5 days administered for the patient. The symptoms in hands got better but in legs worsened resulted in amputation due to gangrene. The probable differential diagnosis was necrotizing vasculitis.

Discussion

Based on questionnaire of Schumock et al. (10), studied reaction is categorized as a preventable one. The probability of the reaction is estimated to be “probable” according to Naranjo algorithm (with the estimated score as 7) (11).

In evaluation of this case, we found that it could be categorized as a preventable reaction. So, in order to prevent such serious adverse reactions, we issued a dear doctor letter to health care professionals emphasizing the following notes (1);

1. There are limited indications for administration of parenteral form of iron preparations. These limited indications include iron-deficiency in which one of the following dose exist:
   a. The patient is unable to use oral forms.
   b. The oral forms are ineffective e.g. secondary to poor absorption, Gastro- intestinal disease or intolerance.
   c. The rapid replenishment of iron stores is necessary as in hypochromic anemia of infancy or the last trimester of pregnancy.
   d. Patients with chronic renal failure receiving epoetin alfa, because of the dramatic decrease in iron stores associated with erythrocyte formation.
2. Since fatal anaphylactoid reactions are reported following administration of iron dextran, a significant indication should be confirmed by laboratory tests before using the product.
3. Administration of Iron dextran will not get more rapid hematologic response compared to orally iron preparations.
4. There is no priority in hematologic response to iron dextran comparing other parenteral iron preparations.
5. It is necessary to give a test dose before administration of the first therapeutic dose of iron dextran.
6. Necessary equipment and trained personnel for managing serious allergic reactions must be available wherever the test dose and subsequent doses of iron dextran are administered.

In addition to issuing alerting letter, iron dextran was not reapproved to be included in our national drug list because of more frequency and severity of its adverse reactions compared to other parenteral iron preparations.

New Alerts with old medicines

On 16 December 2009, American Regent and the US Food and Drug Administration (FDA) issued a warning on anaphylactic type reactions, including fatalities, following parenteral administration of iron dextran injection (12). According to this warning, the Boxed Warning has been modified to recommend a test dose prior to the first therapeutic dose and observing for signs or symptoms of anaphylactic-type reactions during administration of Dexferrum. It has been reported that despite of tolerating the test dose, fatal reactions have occurred in some cases. History of drug allergy or multiple drug allergies could be considered as risk factors for anaphylactic-type reactions following iron dextran injection.

In conclusion, safety monitoring of medicinal products is an eternal and unavoidable need in the area of science and activities related to medicinal products. As far as a product is available on the market, its safety profile should

be reviewed for newly established signals. It is necessary for healthcare professionals to be informed of such rare but serious reactions to apply preventive actions.

References

1. McEvory G. AHFS drug information. American Society of Health System Pharmacists, 2011.
2. Koda-Kimble MA, Young LY, Kradijan WA, Guglielmo JB, Allfredge BK, Corelli RL (eds). Applied Therapeutics, The Clinical Use of Drugs. Eight Edition 2005. Lippincott Williams and Wilkins: Maryland, USA 71-83.
3. Bielory L. Serum sickness from iron-dextran administration. Acta Haemotol 1990; 83(3):166-8.
4. Choulis NH, Dukes MNG. Metals. In: Dukes M.N.G., Aronson J.K. Meyler's Side Effects of Drugs. 14th ed. Amsterdam, PA: Elsevier Science B.V.; 2000:700.
5. Lin P, Goldberg L, Phillips T. Calciphylaxis. Available from: URL: http//www.medscape.com/viewarticle/438054_print.
6. Calciphylaxis. Available from: URL: http://www.mayoclinic.org/calciphylaxis.
7. Nunley JR. Calciphylxis. Available from: URL:http://www.emedicine.com/derm/topic555.htm
8. Bailie GR, Clark JA, Lane CE, Lane PL. Hypersensitivity reactions and deaths associated with intravenous iron preparations. Nephrol Dial Transplant 2005; 20 (7): 1443-9.
9. Chertow GM, Mason PD, Vaage-Nilsen O, Ahlmen J. Update on adverse drug events associated with parenteral iron. Nephrol Dial Transplant 2006; 21 (2): 378-82.
10. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm 1992; 27: 538.
11. Naranjo CA, Busto U, Sellers EM. A method for estimating the probability of adverse drug reactions. Clin Pharmacother 1981; 30: 239-45.
12. Dexferrum (iron dextran injection)-Labeling Change. Available from: URL: www.fda.gov/safety/MedWatch/SafetyInformation.