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FROM DEFICIENCY TO OVERDOSE: IATROGENIC INTRAVENOUS IRON TOXICITY IN A PATIENT WITH IRON DEFICIENCY ANEMIA, A CASE REPORT

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Abstract:

Iron toxicity is less likely to occur with intravenous form; however it is commonly caused by excessive intake of oral form. Oral iron overdose usually takes place in the background of suicidal attempts or in children. Meanwhile, intravenous iron toxicity was seldom reported in literature. Intravenous iron toxicity may present with abdominal pain, diarrhea, hypotension, altered level of consciousness, muscular pain, and anaphylaxis. Moreover, serious complications may develop including multi-organ failure and possible fatality. The toxicity of iron starts at cellular level as it impairs mitochondrial function and oxidative phosphorylation. Once iron toxicity is suspected, serum iron levels should be measured within 2-6 hours from the time of administration. Initial management should be started by stabilizing the patient and iron chelating agents.

In this report, we present a rare case of iatrogenic IV iron sucrose toxicity in a 41-year-old female status post sleeve gastrectomy surgery known to have iron deficiency anemia presented with altered level of consciousness shortness of breath, and generalized body swelling. Her initial presentation was followed by hypotension and bradycardia hence she was managed provisionally as a case of anaphylaxis. Her serum iron level was 527 mcg/dL measured after five hours from IV iron sucrose administration. In present case, patient received a combination of IV Deferoxamine and oral Deferasirox. A day after admission, patient was discharged home on Deferasirox in a good condition.

Key words: *intravenous iron, iron toxicity, Deforoxamine, Deferasirox*

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INTRODUCTION:

Iron is commonly used for a wide-range of indications, varying from the most common form of nutrient deficiency, iron deficiency anemia, to more advanced and complicated conditions like chronic kidney disease and renal failure [1]. Moreover, iron is usually prescribed orally for most of its indications. Yet, in case of oral iron intolerability, parenteral iron is used [2].

In comparison to the effects attributed to the use of oral iron formulations, side-effects related to parenteral iron are relatively less common, less severe, and short-lasting [3]. Many cases were reported discussing the acute toxicity of iron, almost always in oral forms, most of which were either in children or as suicidal attempts [4-10]. Very rare cases of IV iron toxicity were reported in literature; although doses usually prescribed by physicians are insufficient to cause organ injury [11]. IV iron toxicity may present as gastrointestinal symptoms, alteration in mental status or anaphylaxis; with some reported cases of fatality [3,6]

In the following article, we report a rare case of iatrogenic intravenous iron toxicity in an adult female.

CASE SUMMARY:

A 41 year-old-female status post sleeve gastrectomy four years ago, cholecystectomy, and ovarian cystectomy.

She is a known case of iron deficiency anemia brought to the emergency department of King Fahad Hospital of the University by red crescent with shortness of breath, generalized body swelling, with a history of loss of consciousness for few seconds at home. Her symptoms started after she received a total of five ampules of IV iron sucrose (500 mg) within one day in a different hospital.

Upon examination, the patient was semi-conscious, sweating, and apparently pale with dry lips. Then patient became hypotensive 62/44 mmHg and bradycardic, thus patient was started on intravenous normal saline 0.9% along with Epinephrine 0.5 mg IM, Hydrocortisone 100 mg IVP, Promethazine 25 mg, and Ranitidine 50 mg IVP as a case of anaphylactic shock. The blood pressure improved to 94/57 mmHg and pulse normalized. Patient's hemoglobin level was 8.8, MCV 65.4, and serum iron level was measured to be 527 mcg/dL. Hence, diagnosis of iron overdose was established. Both renal and liver function tests, as well as coagulation profile and serum electrolytes, were all unremarkable. A total of 1000 mg IV Deforoxamine Mesylate, an iron chelating agent, regulated to consume for three hours. Not enough IV Deforoxamine was available, so 500 mg tablets of Deferasirox (Exjade) was given to continue management. Case was referred to the internal medicine department for further management and investigations.

Patient was admitted to the medical ward for one day and received Deferoxamine 200 mg IV infusion. Iron level dropped to 301 mcg/dL upon discharge. She was discharged on Deferasirox (Exjade) 500 mg PO BID for three weeks.

DISCUSSION:

Iron deficiency anemia (IDA) is a known common complication of gastric sleeve surgery, a weight reduction therapy that alters the anatomy and physiology of gastrointestinal tract [12]. As our patient was status post gastric sleeve surgery, four years ago, complicated by IDA. IDA is usually managed by either oral or parental iron supplements [13].

There are three different forms of IV iron: iron dextran, sodium ferric gluconate, and iron sucrose [14]. *Fishbane S.* reported differences in safety profiles among the former agents; with IV iron dextran linked to higher rates of morbidity and mortality [3,14]. In our case, patient received a total of five ampules of IV iron sucrose (500 mg) within one day in another hospital. However, according to Hinchingbrooke Health Care "Protocol for the use of Intravenous Iron Sucrose (Venofer)" the maximum dose is 200 mg not exceeding three times per week, so that each dose must be one day apart [15].

Multiple factors can contribute to the acute iron intoxication; patient age, dose given, kinetics and the general condition of the patient [4].

Acute iron intoxication mostly presents clinically as abdominal pain, diarrhea, intense muscular pain, altered level of consciousness and dizziness [6].

In adults, levels may not correlate well with the clinical presentation. However, mild-to-moderate toxicity generally manifests at levels of 350-500 mcg/dL. Persistently symptomatic patients with serum iron levels higher than 350 mcg/dL should be admitted and hepatotoxicity is usually observed at levels higher than 500 mcg/dL. Levels higher than 800 mcg/dL are associated with severe toxicity. Patients with serum iron levels higher than 1000 mcg/dL should be in a facility that can provide age-appropriate intensive case [16]. Thus, our patient can be classified as a case of mild-moderate iron intoxication. Iron intoxication can be complicated by serious multi-organ damage; involving the liver being the most commonly injured organ, along with other organs like the heart, kidney, lungs and hematological system [5, 6]. The suggested

mechanism by which iron causes its adverse effects is that on the cellular level, it causes injury resulting in impairment of oxidative phosphorylation and mitochondrial function; eventually leading to cell death [5].

Our patient had loss of consciousness, shortness of breath, generalized body swelling, along with hypotension and bradycardia. Anaphylaxis was considered and patient was managed accordingly.

Anaphylaxis is another possible risk of IV iron administration; although iron sucrose, the culprit in our case, and sodium ferric gluconate have lower potential risk of allergic and anaphylactoid-type reactions compared to dextran [14]. Nonetheless, lab results revealed a significantly elevated iron level, so a diagnosis of iron toxicity was established.

Timing of serum iron level measurement is curial in establishing the diagnosis of iron toxicity [4]. Serum iron should be measured in the first 2-6 hours after exposure for proper estimation, as serum iron levels would be found normal beyond this window period [6]. This is attributed to the fact that iron is distributed to the tissues which stabilizes the serum iron level [6]. When the serum iron is over 500 mcg/dl, Deferoxamine should be started, such as our case [16]. In present case, patient's serum iron level was measured after five hours of the last IV dose i.e. within the allotted period. Other indications of immediate Deferoxamine treatment include: metabolic acidosis, repetitive vomiting, lethargy, hypotension, or shock [5]. No guideline exists concerning the dosage and duration of therapy of Deferoxamine [4]. The recommended dose is fifteen mg/kg/hr as an IV infusion [4].

Skoczynska et al. described a very similar case; in which a 27-year-old female had clinical manifestations of acute iron poisoning following treatment with high dose oral and parenteral iron therapy. Like in our case, the initial presentation was altered mental consciousness, hypotension, and tachycardia. Both cases were managed by a combination of oral and parenteral chelating agents. Yet, the difference in management was that in present case, our patient was managed by intravascular Deferoxamine while in the other case, patient was managed by intramuscular Deferoxamine. The route of iron chelation should be tailored to the patient's condition where, like in our situation, intravenous is preferred in cases of hypotension or cardiovascular collapse [16].

CONCLUSION:

In conclusion, a high index of suspicion should be raised regarding acute IV iron toxicity in patients with IDA having altered level of consciousness and circulatory collapse. Since serious complications can occur, early diagnosis and management in intensive care setting is essential.

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