



A Rare Case Report of Toxic Epidermal Necrolysis with Iron Sucrose/first line Anti-tuberculosis Treatment Drugs

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Conflicts of Interest: Nil

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DOI: <https://doi.org/10.32553/ijmsdr.v6i5.940>

Abstract:

Toxic Epidermal Necrolysis [TEN] is life-threatening condition with mortality rate of 30-60%. Most common etiology of TEN is drug induced. Though Anaphylactic [Type I Hypersensitivity] reactions have been reported with Iron Sucrose, we present first case of TEN [Type IV Hypersensitivity], associated with Iron Sucrose along with Anti-tuberculosis treatment [ATT], to our knowledge. Iron Sucrose is considered relatively safer than other iron formulations. After 48 hours of administering Intravenous Iron Sucrose [20 mg in 200 ml N.S] infusion [first day], patient developed TEN symptoms [third day]. He was taking first line ATT drugs since past one month for Pulmonary Tuberculosis. On basis of history, 80-90% Body Surface area involvement, positive Nikolsky sign and laboratory findings, patient was diagnosed with drug induced TEN [fifth day]. For TEN management, ATT was withdrawn and patient was treated with intravenous Dexamethasone, Piperacillin/Tazobactam, Metronidazole, Pantoprazole, Intravenous fluids with dermatologically supportive local applications and patient was monitored. Patient died due to septic shock despite all resuscitative measures [seventh day]. Causality assessment (WHO UMC scale and Naranjo scale) was 'Possible' for both Iron Sucrose and ATT drugs. No improvement in patient's condition after withholding ATT and short duration between Iron sucrose and symptoms of TEN onset suggests an increased likelihood of TEN induction by Iron sucrose. However, either ATT or Iron Sucrose could trigger TEN in presence of other drug. Improved understanding by physicians of these relatively unknown life-threatening ADR's and interactions can aid in early identification and enhanced vigilance in future scenarios.

Keywords: WHO UMC Scale, SCORTEN score, Naranjo scale, Anaphylactic reactions

Introduction:

Toxic Epidermal Necrolysis [TEN] is life-threatening condition with mortality rate of 30-60% with most common etiology being drug induced.^{1 2} Anemia is critical global health issue with worldwide prevalence of 22.8%.³

Iron deficiency anemia [IDA] is most common cause in developing nations.⁴ Parenteral Iron Sucrose is fast and effective therapy to treat IDA.⁵

Most serious adverse reactions are observed with Iron dextran formulations while Iron sucrose is considered much safer.^{6,7}

First line ATT drugs can cause SJS/TEN, but no interaction with Iron Sucrose that might exacerbate or stimulate Steven Johnson Syndrome (SJS) / TEN has been documented.⁸⁻¹²

This case report aims to present probably the first case of drug induced TEN shortly after administration of parenteral Iron Sucrose with background of ATT therapy.

Case history

A 70-year-old male was diagnosed with Sputum positive Pulmonary Tuberculosis and was being treated with once daily fixed drug combination of Isoniazid [75 mg], Rifampicin [150 mg], Pyrazinamide [400 mg] and Ethambutol [275 mg] in the Intensive Phase since 26 July, 2021. One month later, on 23rd August, 2021 he presented to Community Health Center for generalized weakness. His blood tests revealed low Hb value [8.2 g/dl]. On same day, he was administered with Injection Iron sucrose [100 mg Iron sucrose (5 ml) in 200 ml 0.9 % Normal saline given as a slow infusion].

Two days later, on 25th August, 2021, a painless rash appeared over his trunk region which gradually spread to other areas of his body. On following day, [26th August, 2021] he developed bumps and blisters over his body. The blisters easily burst into painful sores with peeling of skin. On 27th August, 2021 he presented to Emergency of a Tertiary Care Hospital with extensive peeling of multiple skin areas. The patient had low Blood pressure [100/70 mm Hg], increased respiratory rate [23/min] & increased pulse rate [103bpm]. The patient was drowsy, obeyed verbal commands and his history was provided by his attendants. The dermatological examination revealed generalized maculopapular rashes with varying erosions of the skin [1×1 cm to 2×1 cm] and

relative sparing of scalp. Ocular, nasal, oral and genital mucosa was also involved. The Body surface area involvement was 80 – 90 %. Nikolsky sign was positive. The patient's SCORTEN score was 4 indicating mortality of 58%.

The patient did not have any history of fever or symptoms of infection prior to 23rd August, 2021. He didn't have any other chronic illness other than Tuberculosis or any organ transplantation. He was not reported to have any drug allergies or adverse reaction to any drugs in the past. His family members never experienced any similar episode in the past.

He was shifted to Cardiothoracic unit [non-covid ICU] and administered with supplemental oxygen. He was treated with intravenous Dexamethasone [1 ml (4 mg) BD], Piperacillin/Tazobactam [4.5 gm TDS], Metronidazole [100 ml (500 mg) TDS], Pantoprazole [40 mg BD], oral Pyridoxine Hydrochloride [40 mg OD], IV fluids and kept under monitoring. Local application of Fusidic acid cream over lips, paraffin gauze over body and other dermatologically supportive measures were provided.

The patient's condition had no significant improvement after stopping ATT drugs on 28 August 2021.

His investigations showed a normal TLC count [6980/mm³], decreased Lymphocyte count [8.3%], decreased Serum Sodium [127 mmol/L] but increased granulocyte count [74.3%], Blood urea [109 mg/dl], SGOT [97 U/L] and Alkaline Phosphatase [167 U/L] levels. Histopathological examination of patient's lesions was not done. On basis of detailed history, physical examination and laboratory findings he was diagnosed to be case of drug induced Toxic Epidermal Necrolysis. The Causality assessment (WHO UMC scale and Naranjo scale) was 'Possible' for both Iron Sucrose and ATT drugs.

Two days later, on 30th August, 2021, his condition deteriorated with sudden fall in blood pressure and rigors. Inotropic support was provided and intubation done, but patient could not survive. On evaluation, it was found that patient died due to septic shock.

Discussion

Intravenous Iron Sucrose can significantly increase Hemoglobin and other red cell indices.⁵ Its common side effects include headache, dizziness, nausea, vomiting, paresthesia, edema and muscle pain.^{9,13,14}

Though Anaphylactic reactions [Type I Hypersensitivity] have been reported, this is first case of TEN [Type IV Hypersensitivity], associated with Intravenous Iron sucrose to our knowledge. The Causality assessment (WHO UMC scale and Naranjo scale) was ‘Possible’ for both Iron Sucrose and ATT drugs. However, other factors include patient’s daily oral ATT intake since past one month before TEN onset, while it developed merely 48 hours after I/V Iron Sucrose. Studies done in various populations describe that risk of SJS/TEN is highest at beginning of ATT drug administration and decreases within 8 weeks and more.^{15,16}

Moreover, there was no improvement in condition of patient after withholding ATT drugs and patient died 2 days later due to Septic shock. This indicates increased likelihood of I/V Iron Sucrose inducing TEN. However, either ATT or Iron Sucrose could trigger TEN in presence of other drug.

The mortality rate in TEN is increased with factors like increased age, as in this case, and susceptibility for TEN is increased with specific HLA alleles. The limitations of this case report include lack of elaborate blood testing to rule out other infectious causes, lack of skin biopsy and lack of HLA antigen typing which could be used in correlating with any similar cases.

Since Iron Sucrose is very commonly administered drug due to high prevalence of Iron deficiency anemia — health care workers, pharmacovigilance officials and general public must be made aware and vigilant towards its adverse effects. Further studies are needed to explore the association between Iron Sucrose and TEN reaction.

Conclusion

The Causality assessment was ‘Possible’ for both Iron Sucrose and ATT drugs in inducing TEN. Either ATT or Iron Sucrose could trigger TEN in presence of other drug. However, adjunctive factors suggest an increased likelihood of Iron Sucrose inducing TEN.

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