Case Report

Hypersensitivity reaction with deferasirox

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ABSTRACT

Thalassemias comprise a group of hereditary blood disorders. Thalassemia major presents with anemia within the first 2 years of life requiring frequent blood transfusions for sustaining life. Regular blood transfusions lead to iron overload-related complications. Prognosis of thalassemia has improved because of the availability of iron-chelating agents. Oral iron chelators are the mainstay of chelation therapy. Deferasirox is a new-generation oral iron chelator for once daily usage. We herein describe a patient of beta thalassemia major who developed an allergic manifestation in the form of erythematous pruritic skin rashes to the oral iron chelator deferasirox. This is a rare adverse reaction reported with deferasirox that led to a therapeutic dilemma in this particular case.

Key words: Deferasirox, rash, thalassemia

INTRODUCTION

Thalassemia major clinically presents between 6 and 24 months of age. Infants become progressively pale and fail to thrive. If untreated or poorly transfused, the clinical picture is characterized by growth retardation, pallor, jaundice, hepatosplenomegaly and skeletal changes resulting from expansion of the bone marrow. On the other hand, transfused patients may develop complications to iron overload. Complications related to iron overload may result in growth retardation, dilated cardiomyopathy, hepatitis, liver cirrhosis and endocrine dysfunction such as diabetes mellitus, hypogonadism, hypothyroidism, hypopitutarism, osteoporosis etc., with cardiac complications being the most common cause of death.[1,2] Some may also suffer from transfusion-related complications such as HIV and Hepatitis B and C. Survival of individuals with proper transfusion and chelation is beyond 40 years. Iron chelating agents like deferoxamine, deferiprone and deferasirox have dramatically improved the outlook in beta thalassemia. Among these, deferiprone and deferasirox are used orally.[2,3]

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CASE REPORT

A 22-year-old female, a case of thalassemia major, was undergoing treatment at our thalassemia day care center. She was on oral iron chelator deferiprone 3000 mg/day in three divided doses for the past 8–9 years and was diagnosed as a case of deferiprone-induced arthropathy of the right knee and hip joint as other causes of arthropathy were ruled out. Rheumatoid factor and ANA were negative. The findings were further confirmed on magnetic resonance imaging. As a result of the pain due to arthropathy, she used to come limping all the way into the thalassemia day care ward and was advised to start with the alternative, oral iron chelator deferasirox. Despite this

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adverse effect, she was continuing on deferiprone because of nonaffordability of the drug. It was only after the availability of the drug at our pharmacy that she was started on deferasirox at a dose of 750 mg once a day. On day 6 of initiation of therapy, she started with pruritic skin rash that started from the neck and spread downwards to involve the whole body. She reported to us on day 11. On history taking, the patient reported that there was an increase in the number and severity of lesions since then. There was no history of breathlessness, difficulty in breathing or any episode of loss of consciousness. There was no family history of any allergic disease or bronchial asthma. On examination, she was having diffuse erythematous and palpable urticarial lesions all over the body. The lesions were more prominent on the dorsal surfaces. On physical examination, except for mild splenomegaly, the rest of the examination was normal. Laboratory investigations revealed low Hb (10.6 g/dL), normal leukocyte count and platelets. Liver function and renal functions were within normal limits. Oral deferasirox was stopped and the patient was started on oral antihistaminics. The rashes subsided gradually and the patient recovered completely by the 9th day after the discontinuation of deferasirox and initiation of antihistaminic therapy. In order to confirm the cause and type of hypersensitivity, we approached the patient for the skin prick and patch tests, for which she refused to give consent.

DISCUSSION

The three forms of iron chelation available are deferoxamine, deferiprone and deferasirox. Deferiprone and deferasirox are the ones used orally. Deferoxamine is given parentrally, and compliance has been a major issue. Our patient was taking deferiprone as an iron chelator and had developed arthropathy. The association of arthritis and deferiprone is known, and the incidence varies from 4% to 30–40%. The large joints are more commonly affected.[3,4] Despite all her odds, she was still continuing on deferiprone because she was not able to afford deferasirox. Oral deferasirox is the new weapon in the armamentarium for the fight against iron chelation. In a developing country like India, where managing patients in resource-constraint settings is a challenge, the availability of drugs from the hospital pharmacy is a welcome step. Deferasirox is a new-generation oral iron chelator with once daily usage.[5] As we started our patient on deferasirox, she developed urticarial rash as described. The common adverse effects of deferasirox are gastrointestinal events (15.2%), skin rash (10.8%) and transient increase in serum creatinine (38%).[6] On extensive literature search, we came across a single similar case report in a thalasemic patient.[7] A maculopapular rash with deferasirox has also been reported in a 75-year-old female, a case of acute myeloid leukemia who had received frequent blood transfusions.[8] On causality assessment, the association between the offending drug and the suspected adverse drug reaction was found to be probable on the WHO-UMC scale because, on dechallenge, the reaction subsided and rechallenge was not attempted because of the fear of possible anaphylactic reaction. According to the Hartwig severity assessment scale, the reaction was found to be level 3 (moderate) in severity. Our patient, who was already suffering from an adverse effect, landed into further trouble after changing the form of iron chelation. This situation can be aptly described as caught between the deep blue sea and the devil. Management of this patient has become a challenge, with the only form of iron chelation left as deferoxamine. The patient was started on deferoxamine; however, compliance now remains an issue.

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