Deferasirox induced optic neuritis in thalassemia major child – a case report

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Abstract

Here, we describe the ocular side effects of the drug deferasirox in a patient who developed optic neuritis following high-dose deferasirox administration. A 14 year old boy receiving repeated blood transfusions for beta thalassemia since childhood, presented with sudden loss of vision. He was taking tablet deferasirox as chelating agent. Clinical and investigative findings were consistent with deferasirox induced optic neuritis. Recovery was partial following cessation of deferasirox. This report highlights the ocular side effects of the drug deferasirox which is the rarest complication and the need to be vigilant in patients on long duration deferasirox usage.

Keywords: deferasirox, optic neuritis, thalassemia, drug induced blindness.

Introduction

Thalassemia major is a hematological condition characterized by imbalance in synthesis of alpha and beta subunits of hemoglobin. It is estimated that worldwide there are over 20,00,000 transfusion dependent people with thalassemia major with the majority of cases in South East Asia[1]. These patients require repeated blood transfusions from an early age to meet oxygen demand, resulting in systemic iron overloading. Deferasirox is a bis-hydroxyphenyl-triazole benzoic acid derivative.Deferasirox is an orally active chelator that is highly selective for iron. It is a tridentate chelator that mobilizes iron stores by binding selectively to the ferric (Fe3+) form of iron[2]. The recommended starting daily dose is 20 mg per kg body weight. Dose adjustments should be made in increments of 5 or 10mg/kg[3]. Deferasirox can lead to many adverse affects[4]. The most frequent reactions reported during treatment with Deferasirox in adult and pediatric patients included gastrointestinal disturbances in about 26% of patients (mainly nausea,vomiting, diarrhea, or abdominal pain), and skin rash in about 7% of patients[5]. About the 11-14% of patients with thalassemia major (TM) treated with deferasirox (DFO) develops retinopathy, optic neuritis and/or lens opacities with an unclear pathogenesis but with a clear age related pattern.[6,7] This report discusses about one of the rare side effects of deferasirox

Case report

A 14 year old boy with a diagnosis of transfusion dependent beta thalassemia major from last 13 years was admitted with the complaints of sudden loss of vision. He had been taking tablet deferasirox everyday with dosage 30 -40mg per kg per day, His recent ferritin level was 5309ng per ml. On examination no neurological deficits were noted. On ophthalmic examinations, visual acuity was counting finger at 2 meters for right eye and perception of light was negative for left eye. The intraocular pressure measurement and anterior segment examination yielded normal results for both eyes. The fundus examination revealed disc appearing pink and superior and inferior margins were elevated on right side (Figure 1). Disc margins were blurred and showed dilated tortuous vessels on left side (Figure 2). CSF analysis was found to be normal. MRI of brain and cerebral venogram were normal but MRI of orbit was suggestive of left focal optic neuritis. Deferasirox induced optic neuritis was suspected, and drug dose was reduced to minimum dose. One year later, there was partial recovery.

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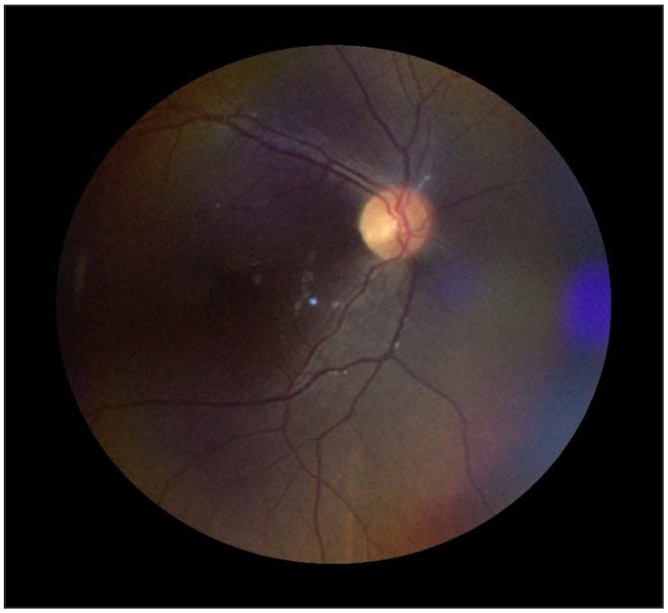

Figure 1. Right side fundus

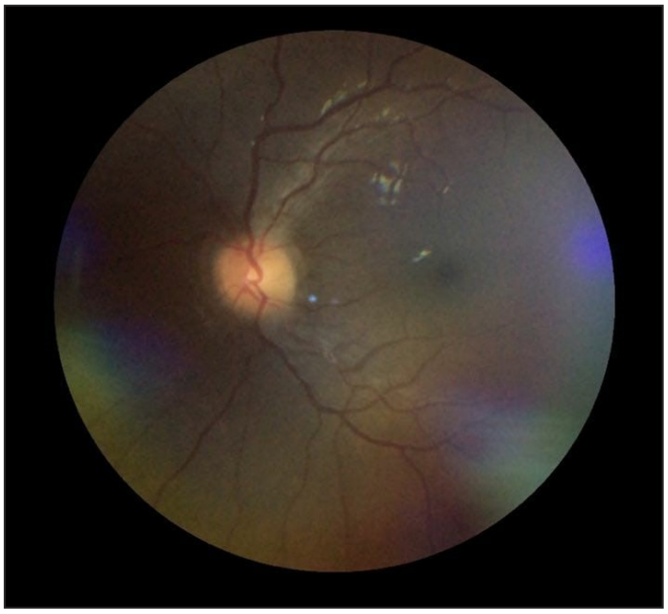

Figure 2. Left side fundus

Discussion

Deferasirox is a widely used chelating agent in managing patients with chronic iron overload.. As illustrated by this report, patient on Deferasirox can present with acute/sub-acute deterioration in visual acuity and colour vision, night blindness, scotomas or constricted fields.

Pathophysiology

Deferasirox related retinopathy is a recognised clinical entity, its pathophysiology remains unclear. It is thought that deferasirox – iron complexes form and induce mitochondrial calcifications. These calcifications then induce a loss of retinal pigment epithelium (RPE) microvilli and subsequently a thickening of Brusch's layer,ultimately impairing RPE function. Alternatively, a trace mineral depletioncan result from chelator therapy which then promotes oxidative stress in the RPE cell membranes and defective vasoregulation.[8] This ultimately impairs neurotransmission. Ocular side-effects include cataracts, retro bulbar optic neuritis, pigmentary retinopathy, bull's eye maculopathy and vitelli form maculopathy.[9-11] The pigmentary retinopathy is classically macular or peripheral but can rarely present in the Para macular, papillomacular or peripapillary pattern.[10] It is still unclear whether ocular toxicity is dose-dependent or not; however, existing literature as well as our experience with this patient shows that those with lower iron loads and Deferasirox dosage higher than 30 mg/kg/day are at increased risk for developing systemic toxicity.[8,12]

Management

As ocular toxicity can be asymptomatic, all patients on Deferasirox should have baseline visual acuities, colour vision, visual fields, fundus fluorescein angiography (FFA), electrooculogram (EOG) and electroretinogram (ERG). During the follow-up phase, diffuse outer retinal fluorescence on FFA is a useful marker for ongoing disease activity[10] whilst EOG and ERG are helpful in monitoring the retinal dysfunction. Regular ophthalmic screening at three-monthly intervals along with monthly monitoring of serum ferritin levels can help in prevention and reversal of ocular toxicity[13,14].

Conclusion: Heightened awareness amongst paediatrician and ophthalmologists and regular ophthalmic screening is required in patients receiving deferasirox to avoid delayed diagnosis and management of deferasirox - related optic neuropathy and retinal dysfunction.

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