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Case Report

Maculopathy Following Intravenous Deferoxaminemesylate in a Multi Transfused African Child

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Abstract

Deferoxamine is a chelating agent used to treat iron overload in multi transfused patients. Overdose of Deferoxamine may lead to loss of vision from possible toxicity to the retina. Maculer changes from Deferoxamine and the resulting visual loss can be very severe. It has not yet been reported in the literature in West African children. We present a case report of macular mottling presenting similar to a bull's eye maculopathy in a West African child resulting in vision loss. Adjustments in dosing may reduce the disability associated with Deferoxamine associated retinal changes. It is important that ophthalmologists are aware of this condition and recommend dosage adjustments when patients on this drug complain of loss of vision.

Keywords: Deferoxamine; Blood transfusions; Ocular toxicity; Bulls eye maculopathy; Toxicity; Retina

Introduction

Deferoxaminemesylate is a drug used as a chelating agent in the management of patients with acute iron poisoning and aluminium toxicity, it is also used for treating chronic iron overload. It is used regularly in children to treat haemochromatosis and iron overdose following multiple blood transfusions. It is thought to be associated with ocular toxicity which is dose and duration related [1]. The main ocular manifestation is maculopathy, which may present similar to a bull's eye maculopathy. The maculopathy may be reversible if the treatment with Deferoxamine is discontinued or reduced. Other ocular manifestations that may occur include optic atrophy, pigmentary retinopathy and vitelliform retinopathy [2,3].

The condition is rare and usually mild, but it can be severe and lead to severe loss of vision. Physicians may delay ophthalmic consults if they do not have protocols for routine regular eye screening of patients receiving high doses of intravenous or subcutaneous Deferoxamine therapy [4]. The Maculer changes is postulated to be due to the direct effect of Deferoxamine, chelation of ions (iron, copper, aluminium) on the retinal pigment epithelial with resultant dysfunction or due to defective vasoregulation [5]. Loss of vision can be prevented if it is recognised early and the Deferoxamine dosage is adjusted appropriately.

To the best of our knowledge Deferoxamine maculopathy has not been previously reported in the literature in West African children. This case study adds to the existing information on ocular manifestations of Deferoxamine toxicity within an African context.

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Case Presentation

We present the case of a 13-year-old girl who was seen at a teaching hospital after being referred from a district hospital as a case of query pancytopenia of unknown cause, with a differential of "bone marrow failure" and "febrile neutropenia". She had reported to the district hospital with a four months' history of dizziness, palpitation, breathlessness and syncopal attacks. At the teaching hospital her initial findings were the absence of associated night sweats, cough or abdominal pains. Her menarche was at 12 years old .She had menorrhagia for three months prior to presentation. She had no history of long term chloroquine ingestion. She was very ill, lethargic, severely pale, febrile, no lymphadenopathy and well hydrated. She had a subconjunctival haemorrhage on her right eye. Pulse rate was 166 beats per minute regular, rapid and of weak volume. Her blood pressure on admission was 84/40 mmHg. Other systems were within normal limits. An initial impression of severe anaemia secondary to pancytopenia was made, with a differential of neutropenic fever and bleeding disorder. Her initial haematology workup results showed remarkably low haemoglobin of 1.8 g per dl, Haemoglobin electrophoresis was negative for sickle cell disease with a phenotype of AA. The cause of the severe anaemia was undetermined by the paediatricians.

She was initially transfused with 3 units of blood and subsequently 5 more units over the next one week. Because of the multiple transfusions, she was started on subcutaneous deferoxaminemesylate 50 mg per kg throughout all periods of blood transfusions.

One week later she started complaining of blurred vision in both eyes at which point she was sent for an ophthalmic consult The history from this initial Ophthalmology consult revealed that she had indicated that her vision had been good a week earlier. On examination, her Visual acuity was 6/12 in both eye and did not improve with pinhole. There was a moderate amount of subconjunctival haemorrhage in both eyes. Other ocular structures seemed to be within normal limits. There was clearly no retinopathy and no maculopathy a cause for the blurred vision was not found at this time and Deferoxamine toxicity was not considered.

After four weeks on admission she had received more transfusions and subcutaneous Deferoxamine, she complained that her visual

acuity had become worse and a second ophthalmic consult was requested.

Her vision was now Hand Motions in both eyes. There was a moderate amount of subconjunctival haemorrhages seen on both eyes. She had good red reflex in both eyes, the pupils reacted briskly to light and there was no relative afferent pupillary defect. She had no strabismus and had full ocular movements in all directions of gaze.

Fundus examination with the indirect and 78D fundus lenses showed a central macular hyper pigmented lesion surrounded by concentric hypo pigmented and hyper pigmented rings of up to 2.5 disc diameters in size surrounded by a circinate exudate and some optic disc haemorrhages. Right eye and Left eye Electroretinogram (ERG), Electrooculograms (EOG), Optical Coherence Tomography (OCT) and Fundus Fluorescein Angiography (FFA) tests were not done because of their unavailability at the teaching hospital at that time.

A diagnosis of Deferoxamine related maculopathy was made. A dosage adjustment of the Deferoxamine was made by the paediatrician.

Over the next 5 months she was discharged and readmitted multiple times from frank haematuria and active bleeding from the gums receiving more multiple transfusions before she eventually expired at home. The underlying cause of the bleeding disorder remained undetermined.

She remained blind. Her vision did not improve from Hand Motions in both eye throughout and the maculopathy remained unchanged whilst the patient was alive.

Discussion

Despite multiple blood transfusion being a common practice in paediatrics units across West Africa, it is of interest that to the best of our knowledge there hasn't been any documented published report of retinal changes from Deferoxamine overdosing occurring in the region. The three possible reasons for this may be that the retina of African children are resistant to Deferoxamine or Deferoxamine is not regularly given to West African children to prevent iron overload or retinal toxicity does occurs but is not unrecognised and not reported.

As illustrated by this case, patients on Deferoxamine can present with sub-acute loss of vision. There may not be any retinal findings during the early stages of the condition. Also if there is delay in diagnosis and severe retinal toxicity occurs, resolution may not occur readily even when the dosage is adjusted. This emphasises the importance of early diagnosis. Other ocular side-effects of Deferoxamine that have been described in the literature such as cataract, retro bulbar optic neuritis, pigmentary retinopathy [6-8] were not found in this patient. In this case the pathology was in the macular area. Other Case reports indicate that the pigmentary retinopathy is classically macular but can present rarely at the periphery. It can also present in the paramacular, papillomacular or peripapillary areas [8,9]. Existing literature suggests that those with lower iron loads and Deferoxamine dosage higher than 50 mg/kg/day are at increased risk for developing retinal toxicity [5,10] . This patient received repeated doses at the limit of 50 mg/kg/day. The subconjunctival haemorrhage that was consistently observed may be as a result of the generalised undetermined bleeding disorder that the patient had. Admittedly the maculopathy may be due to a combination of both the unknown bleeding disorder and the Deferoxamine that the patient had for multiple transfusions. Other case reports indicate that in some cases of Deferoxamine toxicity, it may be difficult to differentiate between ocular manifestations of the underlying disease from the actual toxicity of the drug [11]. As ocular toxicity can be asymptomatic during the early stages of toxicity, all patients on Deferoxamine should have baseline visual acuities, colour vision, visual fields done. Even when the patients are symptomatic, there may not be any frank retinal lesions to see as was the case in the initial evaluation of this patient. In such situations, Fundus Fluorescein Angiography (FFA), Electro-Oculography (EOG) and Electro Retinography (ERG), if available, help in the diagnosis. During the follow-up phase, diffuse outer retinal fluorescence on FFA is a useful marker for ongoing disease activity whilst EOG and ERG are helpful in monitoring the retinal dysfunction. Other authors have suggested that Fundus Autoflourecence (FAF) may be a useful non-invasive tool for the evaluation of the clinical course of Deferoxamine retinopathy [9] Regular ophthalmic screening at three-monthly intervals along with monthly monitoring of serum ferritin levels and maintenance of the therapeutic index level of Deferoxamine (daily dose per body weight (mg/kg) divided by serum ferritin (microgram/l)) at levels <0.025 can help in prevention and reversal of ocular toxicity [12,13]. It is also interesting to observe that a presenting therapeutic index level of Deferoxamine below 0.04 can be indicative of better visual prognosis [6,7].

It is interesting to note that the clinical picture of this case shows exudates and some hemorrhages at the disc margin that suggests that unlike what the literature suggests, the lesion may be a vasculopathy rather than a toxicity. The Pathophysiology of this condition is poorly understood and the role of vasculopathy may have to be explored.

Conclusion

Ophthalmologist need to be aware of this condition. Even though it is uncommon, a heightened awareness amongst physicians and regular ophthalmic screening is required in all patients receiving multiple blood transfusions who are given intravenous Deferoxamine for managing iron overload. This will avoid delayed diagnosis and needless loss of vision in these patients.

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