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# BULL'S EYE MACULOPATHY POSSIBLY DUE TO IRON OVERLOAD IN A CHILD WITH THALASSEMIA MAJOR: A CASE OF POSSIBLE "FERRITIN RETINOPATHY"

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**Purpose:** To report a case of bull's eye maculopathy probably caused by iron overload in a child with thalassemia major.

**Methods:** Case report.

**Results:** A 6-year-old girl with thalassemia major who was on chronic multiple blood transfusions since 2 years of age presented with blurred vision in both eyes for 2 months. Blood reports showed very high serum ferritin levels in the range 400 to 2,250 ng/mL (checked every 3 months) since 4 years of age. She was on oral iron chelator deferasirox for 2 years, which was stopped a month ago. Fundus examination of both eyes showed a characteristic bull's eye macula with a purplish hue in the outer ring probably due to iron deposition. The center of the bull's eye had a beaten bronze appearance.

**Conclusion:** Careful history-taking is important in children with bull's eye maculopathy because all such retinopathies need not be hereditary fundus dystrophies. Further progression can be arrested by identifying and removing the cause vision loss.

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Bull's eye maculopathy is a term given to describe the appearance of the macula as a target or bull's eye. Degeneration of the retinal pigment epithelium (RPE) in the macular area causes alternating ring-like light and dark zones of pigmentation. This is the first case described to the best of our knowledge of bull's eye maculopathy probably caused due to serum iron overload in a child with thalassemia major.

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## Case Report

A 6-year-old girl of Indian origin, diagnosed to have beta thalassemia major at birth, presented with gradual decrease in vision in both eyes, especially for distance since 2 months. She had undergone multiple blood transfusions, and on repeated testing, her serum ferritin levels were between 400 ng/mL and 2,250 ng/mL checked every 3 months (normal range 7–140 ng/mL). She was using oral iron chelators deferasirox at 125 mg/day for 2 years, which was stopped a month back. Serum ferritin levels did not reach normal despite oral chelators.

On examination, best-corrected visual acuity was 20/100, N18 in the right eye and 20/40p, N8 in the left eye. Anterior segment examination was unremarkable. Fundus examination of both eyes showed a bull's eye pattern in the macula with a ring of purplish hue outside a circular bronze-colored zone of possible RPE atrophy (Figures 1 and 2). Optical coherence tomography of both eyes showed foveal thinning, more in the right eye, photoreceptor atrophy, and increased RPE reflectivity (Figures 3 and 4). Electroretinography showed extinguished photopic response while scotopic response was minimally affected.

There was no history of family members affected with hereditary fundus dystrophies.

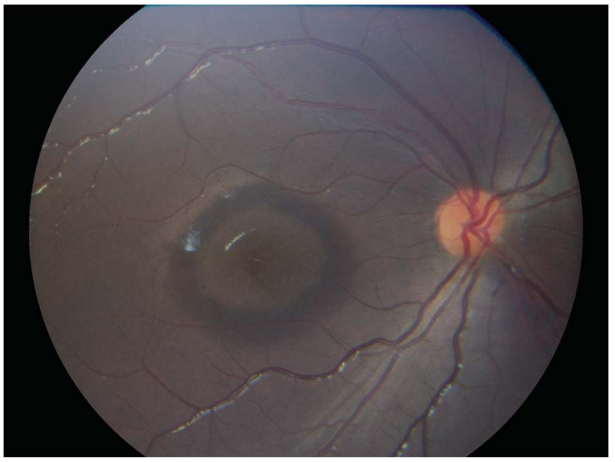

**Fig. 1.** Fundus image of the right eye showing a purple-colored bull's eye maculopathy.

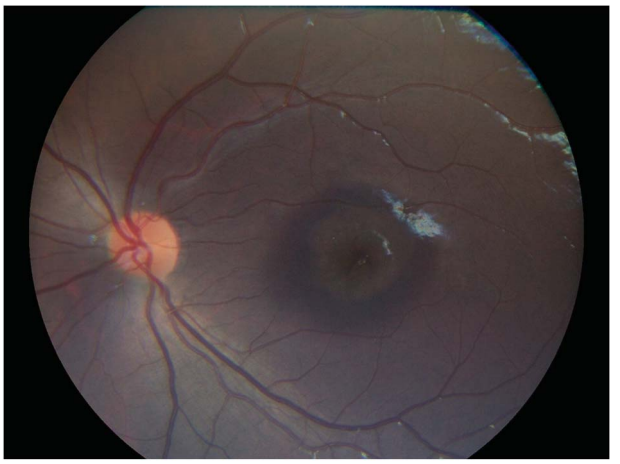

**Fig. 2.** Fundus image of the left eye showing a purple-colored bull's eye maculopathy.

## Discussion

Common causes of bull's eye maculopathy are progressive cone dystrophy, rod cone dystrophy, Stargardt dystrophy, benign concentric macular dystrophy, Batten disease, and drug-induced toxicity as in chloroquine and hydroxychloroquine retinopathy. In cone dystrophy, it is common to see a drop in visual acuity much earlier than fundus changes. Photophobia and loss of color vision are evident. With advancing age, visual acuity drops further with marked RPE atrophy in the fovea and temporal disk pallor. A bull's eye maculopathy in cone dystrophy presents as a lighter ring of RPE atrophy surrounding a dark center. In rod cone dystrophy, increased disk pallor, arteriolar attenuation, and pigmentary changes are seen in the retinal periphery, giving an appearance similar to that of retinitis pigmentosa. Night blindness occurs early in life. In Stargardt dystrophy, a beaten bronze–appearing fovea is seen with surrounding lighter RPE changes. This condition presents later in life and is rare in early childhood. Drug-induced toxicity is known to cause acquired bull's eye maculopathy.

β-Thalassemia major is a hereditary haemolytic anemia that is treated with multiple blood transfusions.[1] In this condition, blood transfusions, ineffective erythropoiesis, and increased gastrointestinal iron absorption lead to iron overload in the body. Iron overload can be determined by serum ferritin measurement. In these patients, iron deposition in parenchymal tissues begins within 1 year of starting the regular transfusions.[2]

Although blood transfusions are important for patients with anemia, chronic transfusions inevitably lead to iron overload because humans cannot actively remove excess iron. The cumulative effects of iron overload lead to significant morbidity and mortality, if untreated. A unit of erythrocytes transfused contains approximately 250 mg of iron, while the body cannot excrete more than 1 mg of iron per day. As iron loading progresses, the capacity of serum transferrin, the main transport protein of iron, to bind and detoxify iron may be exceeded. Thereafter, the non–transferrin-bound fraction of iron within plasma may promote generation of free hydroxyl radicals, propagators of oxygen-related damage.

Excess iron is extremely toxic to all cells of the body and can cause serious and irreversible organic damage, such as cirrhosis, diabetes, heart disease, and hypogonadism.[3] Normal values of serum ferritin for men and women are 12 to 300 ng/mL and 12 to 150 ng/mL, respectively. The distribution of iron and ferritin has been characterized in the adult rat retina.[3] Proton-induced X-ray emission identified the largest amounts of heme and nonheme iron in the inner segments of photoreceptors, the RPE, the choroid, the inner nuclear layer, and the ganglion cell layer. Iron was present in somewhat lesser, but still significant amounts in the photoreceptor outer segments. Interestingly, immunohistochemistry studies have demonstrated a similar distribution pattern of retinal ferritin. The exception is that iron, but not much ferritin, is contained in the photoreceptor outer segment.

Iron has an affinity for melanin in the RPE.[4] Accumulation of iron in the RPE causes RPE atrophy and hence foveal and photoreceptor atrophy. The purplish hue in the outer ring of the bull's eye maculopathy seen in this child could possibly be due to iron accumulation. The center shows foveal atrophy, suggesting a loss of RPE due to previous iron accumulation.

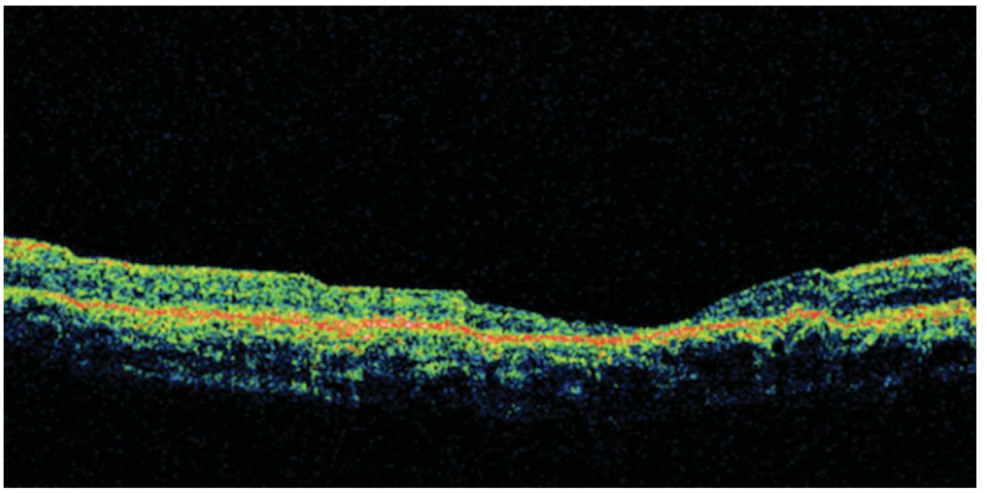

**Fig. 3.** Optical coherence tomography of the right eye showing foveal and photoreceptor atrophy with underlying hyperreflectivity of the retinal pigment epithelium.

Our patient was using oral chelator deferasirox at a dose of 125 mg/day for 2 years before she presented to us. This drug is known to cause reversible retinopathy and improvement of vision on drug withdrawal.[5] This drug did not help lower the ferritin levels, which were persistently high for 2 years. Our patient had stopped oral chelators a month ago and yet noticed progressive loss of vision in both eyes. Optical coherence tomography showed foveal and photoreceptor atrophy in our patient causing permanent vision loss.

Although we do not have any conclusive evidence that suggests iron overload as the cause for the purplish hue and bull's eye appearance of the macula, we do believe this discoloration could be due to ferritin accumulation.

We feel it is important to consider raised serum ferritin as a possible cause for vision loss as correcting this can prevent further visual loss.

## Conclusion

Although bull's eye maculopathy in children and young adults points to a diagnosis of hereditary degenerations in most cases, a careful examination of the pattern of bull's eye in the macula and history-taking is essential. In this case, the outer zone of the bull's eye has a classic purple hue with a central bronze zone. A careful systemic history and history of drug intake are necessary. Although oral chelators may be harmful to the RPE, it is important to note that persistently raised serum ferritin may be more harmful.

**Key words:** ferritin retinopathy, bull's eye maculopathy, raised serum ferritin, thalassemia major, blood transfusions.

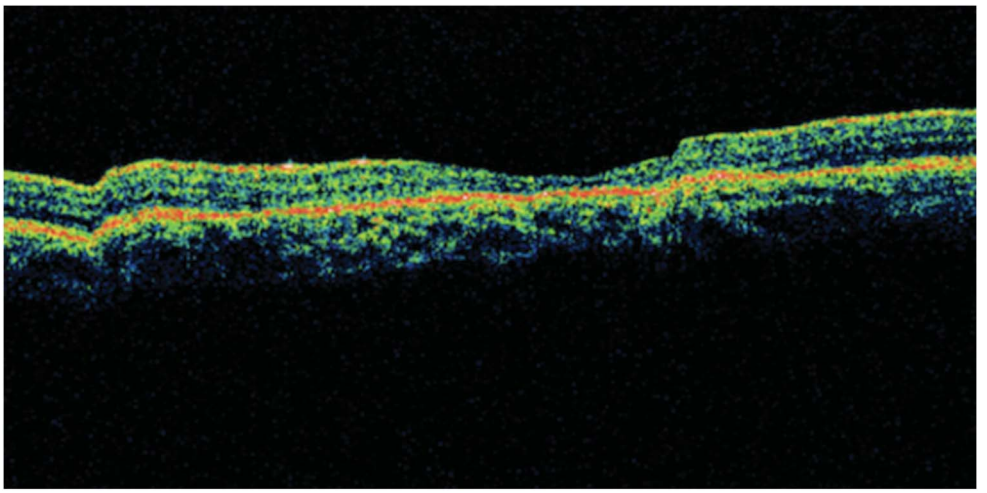

**Fig. 4.** Optical coherence tomography of the left eye showing foveal thinning with underlying hyperreflectivity of the RPE.

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