News Release

Title

Retinal ferroptosis as a critical mechanism for the induction of retinochoroiditis during ocular toxoplasmosis

Key Points

- The iron concentration in the vitreous humor of OT patients is reduced
- Retinal ferroptosis was observed in T. gondii-infected mouse eyes
- Deferiprone prevents OT by reducing iron accumulation in the retina

Summary

Toxoplasma is a widespread disease, affecting approximately one-third of the global population, primarily concentrated in South America. One of the prominent clinical manifestations of this infection is ocular toxoplasmosis (OT), which presents a significant visual impairment. Approximately 24% of patients with OT experience a loss of vision in at least one eye, often to the extent of legal blindness.

Detecting toxoplasma remains a challenge; the most reliable detection method for toxoplasma is polymerase chain reaction (PCR) test of intraocular fluid and the current detection rate of toxoplasma using PCR is only 30%. This limitation reveals the urgent need for the development and implementation of more accessible diagnostic and therapeutic approaches, especially in developing countries where medical resources may be scarce.

In this study, the iron concentration in the vitreous humor of patients with OT was decreased compared to patients with other ocular diseases. Retinal sections from patients with OT and the eyes of toxoplasma-infected mice showed increased iron uptake into the retina, which is not typically observed in normal donor eyes. Moreover, the involvement of ferroptosis, a form of cell death associated with iron, were found in this abnormal iron accumulation within the retina. In addition, deferiprone, an iron chelator, not only reduced the iron uptake but also ameliorated the toxoplasma-induced retinochoroiditis by reducing retinal inflammation.

Research Background

Toxoplasma is a widespread parasite, affecting approximately one-third of the global population. Ocular toxoplasmosis (OT) is one of its major clinical manifestations. Toxoplasmic retinochoroiditis is characterized by acute

necrotizing retinochoroiditis and accounts for 28%–50% of all cases of posterior uveitis. The diagnosis of OT is based mainly on the clinical observation of a retinochoroiditis and the combination of clinical findings and biochemical tests is conducted to achieve a precise diagnosis. However, while being one of the most reliable diagnostic methods, the detection rate of PCR analysis is only about 30%. Since differences in the quality of medical care may affect the control of infectious diseases, it becomes essential to improve the diagnostic rate without relying on highly specialized equipment.

Research Results

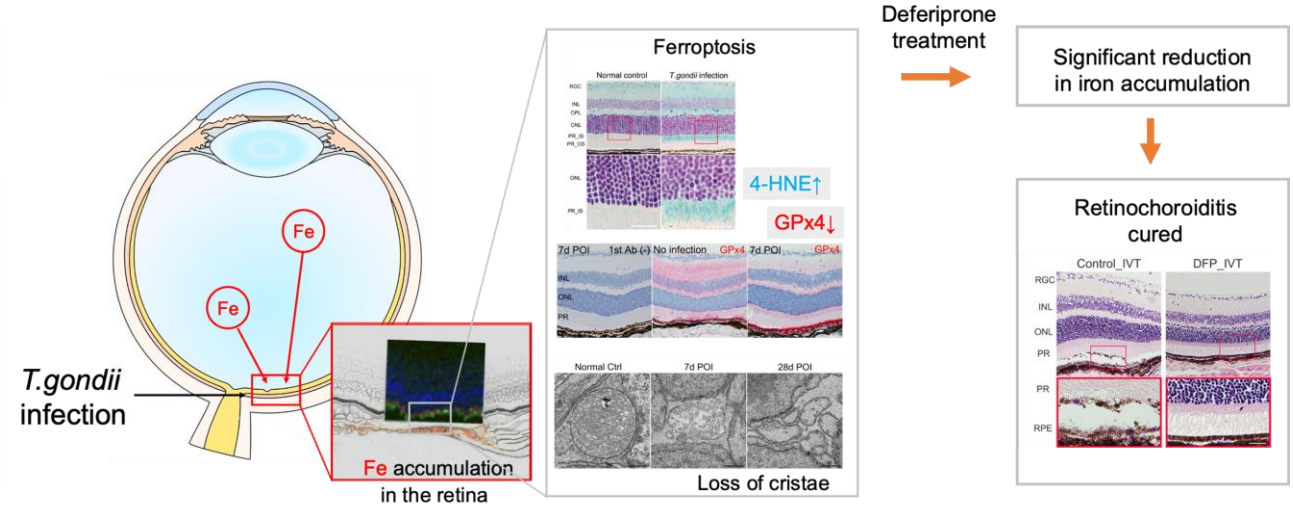
Iron concentrations in the vitreous fluid of patients with OT were decreased comparing to those in patients with macular hole, proliferative diabetic retinopathy, and acute retinal necrosis caused by viral infection. LA-ICP-MS also confirmed the presence of increased iron uptake within human retinal sections from OT, a phenomenon that is not typically observed in normal donor eyes.

Furthermore, the administration of ^{57}Fe, a rare isotope present in only 2% in nature, were conducted via intravitreal and intravenous injections into toxoplasma-infected mice. This intervention led to the accumulation of ^{57}Fe in the middle and outer retinal layers, providing additional evidence of altered iron dynamics in toxoplasmosis.

Subsequent investigations into the retina of toxoplasma-infected mice revealed several interesting observations. These included increased levels of lipid peroxidation markers such as 4-HNE and MDA, reduced levels of glutathione peroxidase (GPx4), and a reduction in the size and a loss of cristae in mitochondria. Collectively, these findings suggested the involvement of ferroptosis in OT.

To assess potential therapeutic interventions, we administered vitreous injections and oral doses of deferiprone. These treatments led to significant improvements in the retinochoroiditis of OT.

Figure 1.



Research Summary and Future Perspective

The result of this study revealed decreased iron level in the vitreous humor of patients with OT and intraretinal accumulation of iron in the toxoplasma-infected mouse eyes. LA–ICP–MS revealed that intravitreal iron was taken up in the retina following infection. Biological examinations demonstrated increased oxidative stress, decreased GPx4, and mitochondrial changes in the toxoplasma-infected mouse retina, indicating the involvement of ferroptosis. Furthermore, deferiprone successfully ameliorated toxoplasmic retinochoroiditis. Understanding the pathological role of ferroptosis in OT can potentially advance future diagnostic methods and treatment strategies.

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