

Starry-like Cornea: A Case of Ocular Cystinosis

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ABSTRACT

Ocular cystinosis is a rare autosomal recessive disorder caused by mutations in the CTNS gene, which encodes a lysosomal cystine transporter protein. This results in the accumulation of cystine crystals in various ocular structures, leading to a range of ocular manifestations. The incidence of cystinosis is estimated to be 1 in 100,000 to 200,000 live births, with a higher prevalence in certain populations such as those of European descent. We report the case of a 5-year-old child with ocular cystinosis. The ophthalmological examination revealed a photophobic child with a visual acuity of 3/10 in both eyes (Pigassou scale), and diffuse stromal crystal deposits over the entire cornea in both eyes. The rest of the examination was unremarkable. The patient was referred to pediatrics for work-up of storage disease and was diagnosed with ocular and nephrological cystinosis. The patient was able to start general treatment with Mercaptamine with improvement in renal function, but was unable to obtain local treatment due to lack of funds. The patient is still being followed in our clinic with stable corneal involvement. Ocular cystinosis is a very rare genetic disorder. There are three main types of cystinosis: nephropathic cystinosis and non-nephropathic cystinosis. Nephropathic cystinosis divides further on infantile and intermediate. The most common ocular manifestation of cystinosis is corneal cystine crystal deposit, which typically presents in the first year of life and can lead to photophobia, tearing, and decreased visual acuity. The corneal crystals can also cause recurrent erosions, which can be very painful. The severity of corneal involvement can range from mild punctate deposition to severe confluent crystal accumulation that can lead to corneal scarring and vision loss. Cysteamine drops, which are a form of cysteamine hydrochloride, can help dissolve the cystine crystals and improve corneal clarity, prevent further vision loss, and reduce the frequency of recurrent erosions.

Early diagnosis and treatment are crucial in preventing further ocular damage in individuals with cystinosis. Regular ophthalmologic examinations should be conducted to monitor for ocular manifestations and initiate treatment as early as possible. A multidisciplinary approach is necessary, involving ophthalmologists, nephrologists, and other specialists, to manage the systemic manifestations of cystinosis.

Keywords: Cysteamine hydrochloride, cystine crystal, corneal deposit, nephropathy, ocular cystinosis.

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I. INTRODUCTION

Ocular cystinosis is a rare genetic disorder that affects the eyes and other organs in the body. It is caused by a buildup of the amino acid cystine in various tissues due to a defective cystine transporter protein. This buildup can alter the cornea, leading to cloudiness and decreased visual acuity. Other symptoms of ocular cystinosis may include sensitivity to light, involuntary eye movements, and increased risk of glaucoma. Ocular cystinosis is usually diagnosed in childhood and can be managed with medications that reduce cystine levels in the body. Early detection and treatment can help to prevent or minimize vision loss.

II. CASE REPORT

We report the case of a 5-year-old child with no medical history.

The parents consulted because they had noticed photophobia and severe blinking in their child. The ophthalmological examination revealed a photophobic child with a visual acuity of 3/10 in both eyes (Pigassou scale), and diffuse stromal crystal deposits over the entire cornea in both eyes (Fig. 1, 2, 3). The fundus examination was unremarkable. There was no similar case in the family. He was referred to the pediatric ward for a check-up of overload diseases. He was diagnosed with nephrotic cystinosis with ocular involvement. The patient had a moderate renal impairment, and was able to start general treatment with Mercaptamine with improvement in renal function, but was unable to obtain cysteamine eyedrops due to lack of funds.

The patient is still being followed in our clinic with stable corneal involvement.



Fig. 1 OD crystal corneal deposit.



Fig. 2 OS Crystal corneal deposit.



Fig. 3 Stromal corneal deposit on slit lamp.

III. DISCUSSION

Ocular cystinosis is a very rare genetic disorder, with an estimated incidence of approximately 1 in 100,000 to 200,000 individuals [1], [2].

It affects both males and females equally and is most commonly diagnosed in childhood, typically between the ages of 1 and 7 years. Ocular cystinosis is caused by mutations in the CTNS gene, which encodes a protein that transports cystine out of cells. The condition is inherited in an autosomal recessive pattern. Ocular cystinosis is more common in individuals of European descent, but it has been reported in people of all ethnic backgrounds. Unfortunately, we're still lacking epidemiological data concerning its incidence in regions with a high rate of consanguinity [1].

There are three main types of cystinosis: nephropathic cystinosis and non-nephropathic cystinosis. Nephropathic cystinosis divides further on infantile and intermediate (juvenile onset), as for ocular cystinosis (non-nephrotic) there

is no systemic manifestations only corneal deposits, and it's usually diagnosed in adulthood [2], [3].

Ocular involvement can occur in both types of cystinosis (nephropathic and non-nephropathic cystinosis), but the severity and progression of ocular symptoms can vary.

Nephropathic cystinosis is the most frequent (95%) and severe form of cystinosis and is characterized by the accumulation of cystine crystals in various organs, including the eyes, kidneys, liver, muscles, and brain [1].

Ocular involvement in nephropathic cystinosis is common and usually occurs early in life (usually visible at 16 months on the corneal periphery and evolves in a centrifugal manner) [4].

The most common ocular manifestation is corneal cystine crystal deposit, which can lead to photophobia, tearing, and decreased visual acuity. Ocular symptoms tend to worsen over time and can lead to significant vision loss if left untreated.

Non-nephropathic cystinosis, also known as ocular cystinosis, is a milder form of the disorder that primarily affects the eyes. In this type of cystinosis, cystine crystals accumulate only in the eyes and do not affect other organs. The ocular symptoms of non-nephropathic cystinosis are similar to those of nephropathic cystinosis and can include corneal cystine crystal deposit, photophobia, and decreased visual acuity. However, the severity and progression of ocular symptoms tend to be milder in non-nephropathic cystinosis than in the nephropathic form [5].

In ophthalmology, the ocular manifestations of cystinosis can affect various structures of the eye, including the cornea, conjunctiva, anterior chamber, lens, and retina. The accumulation of cystine crystals in these structures can lead to various symptoms, which can range from mild discomfort to significant vision loss.

Corneal cystine crystal deposition is the most common ocular manifestation of cystinosis and can cause photophobia, tearing, and decreased visual acuity. In advanced cases, corneal crystals can become large and confluent, leading to opacification of the cornea, which can severely impair vision [3], [4].

Conjunctival deposit is another common ocular manifestation of cystinosis and can lead to chronic irritation, redness, and discharge. In some cases, conjunctival cystine crystals can be visible on the surface of the eye [4].

Cystine crystals can also be deposited in the iris, ciliary body, choroid and retinal pigment epithelium (RPE), and lens capsule [2], [4].

Retinal involvement in cystinosis is less common. Retinal cystine crystals can lead to pigmentary retinopathy, with vision loss and visual field deficit. Treatment with cysteamine drops can slow the progression of retinal degeneration and preserve vision [1], [2], [4].

It is important for individuals with cystinosis to have regular ophthalmologic examinations to monitor for ocular manifestations and initiate early treatment to prevent further damage.

The standard treatment for ocular cystinosis is oral and eyedrops based cysteamine, both approved by the US Food and Drug Administration (FDA) for the treatment of cystinosis. Cysteamine works by reducing the accumulation of cystine crystals in the tissues. However, the use of

cysteamine can be associated with adverse effects such as vomiting, diarrhea, which resolve when the drug is withdrawn. To mitigate these side effects, newer formulations of cysteamine have been developed, such as delayed-release cysteamine bitartrate (PROCYSBI®) and cysteamine hydrochloride CH (Cystadrops® Cystaran®) eye drops.

Recent studies have shown that cysteamine eye drops can effectively reduce the corneal cystine crystals and improve visual outcomes in patients with ocular cystinosis [6]. In a study by [3], cysteamine eye drops were found to be effective in reducing corneal crystals in all study participants, with a significant improvement in visual acuity observed in those with significant corneal disease.

Another study by [7] showed that 0.55% cysteamine hydrochloride eye drops were well-tolerated and effective in reducing corneal cystine crystal deposition and improving visual acuity in patients with ocular cystinosis.

CYSTADROPS® (0,55%-5,5mg/mL CH) is the first drug approved in the European Union for the treatment of corneal crystal deposits in adults and children aged >2 years with cystinosis. Recently CYSTARAN (0.44%-6,5mg/mL of CH) is the only FDA approved eyedrop drug for ocular cystinosis. Both requires multiples administration per day [2], [8], [9].

A study by [2] demonstrated that corneal cystine crystals can clear out after administration of 0,55% of CH eyedrop within 8 to 40 months when used 10 times a day. Due to the strain associated with eye drops, Cysteamine pre-loaded lenses are being researched.

In addition to cysteamine therapy, corneal transplantation may be necessary in cases of advanced corneal damage or in patients who do not respond to medical therapy. However, the success of corneal transplantation may be limited by the risk of recurrent cystine crystal deposition in the donor cornea [3].

Overall, the management of ocular cystinosis requires a multidisciplinary approach involving ophthalmologists, nephrologists, and other healthcare professionals. Further research is needed to develop new treatments that can prevent or mitigate the ocular complications associated with this disease.

IV. CONCLUSION

Early diagnosis and treatment are crucial in preventing further ocular damage in individuals with cystinosis. The corneal involvement in our patient may for now be tolerated but if left untreated, given the lack of means, can result in severe visual impairment. Ophthalmologists should be aware of the potential ocular manifestations of this disease and work closely with nephrologists to ensure timely intervention and optimal outcomes. A multidisciplinary approach is necessary, involving ophthalmologists, nephrologists, and other specialists, to manage the systemic manifestations of cystinosis.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

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