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CASE REPORT

Ocular Cystinosis-Bilateral Corneal Crystals and Macular Atrophy in a Child

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ABSTRACT

Introduction: *Cystinosis is a rare autosomal-recessive lysosomal storage disorder caused by CTNS gene mutations, leading to cystine accumulation in multiple organs. Ocular involvement often precedes systemic disease and provides critical diagnostic clues.* ***Case Presentation:*** *We describe a 7-year-old child presenting with photophobia, bilateral corneal crystals, and visual decline. Slit-lamp examination revealed dense, refractile stromal deposits, while fundus evaluation showed macular atrophy and mild optic disc pallor. Systemic evaluation identified growth retardation and rickets-like deformities, consistent with nephropathic cystinosis. Laboratory and genetic testing confirmed the diagnosis.* ***Discussion:*** *This case emphasizes the correlation between ocular and systemic manifestations in cystinosis. Corneal and retinal findings serve as accessible biomarkers for disease burden and treatment adherence. Early ophthalmic recognition enables timely initiation of cysteamine therapy and systemic management, mitigating renal and skeletal complications.* ***Conclusion:*** *Ocular cystinosis, though rare, offers a unique diagnostic window for systemic disease. Routine slit-lamp screening in children with photophobia or growth failure and interdisciplinary management can significantly improve visual and systemic prognosis.*

Keywords: *Cystinosis, Corneal crystals, Macular atrophy, Pediatric ophthalmology, Lysosomal storage disorder*

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INTRODUCTION

Cystinosis is a rare, autosomal-recessive lysosomal storage disorder caused by mutations in the *CTNS* gene, which encodes cystinosin—a transmembrane lysosomal transporter responsible for cystine efflux [1]. Defects in this protein result in intralysosomal accumulation of cystine crystals within multiple organs and tissues, ultimately leading to progressive multisystem damage [2]. The estimated global incidence ranges from 1 in 100,000 to 1 in 200,000 live births, though under-diagnosis and late recognition remain common due to variable phenotypic expression [3]. Three main clinical variants are recognized: infantile nephropathic (≈95 % of cases), juvenile or late-onset nephropathic, and ocular or non-nephropathic cystinosis [4]. The infantile form is the most severe, typically presenting within the first year of life with renal Fanconi syndrome, metabolic acidosis, and growth retardation. The ocular form, by contrast, may remain isolated to the eyes for years before systemic abnormalities become apparent.

The pathophysiology of ocular cystinosis reflects widespread lysosomal deposition of cystine crystals in the cornea, conjunctiva, iris, ciliary body, and retina [2]. In the cornea, crystal accumulation begins at the anterior peripheral stroma and progresses centrally and posteriorly with age [5]. Progressive deposition produces increased light scatter, glare sensitivity, and ocular surface irregularities. Patients frequently present with photophobia, blepharospasm, and recurrent erosions due to epithelial disruption [6]. These symptoms typically develop by 12 to 18 months in infantile nephropathic cases, often serving as the first clinically recognizable sign of the disease [7]. The severity of corneal involvement usually correlates with systemic cystine load, making ophthalmic findings a useful biomarker for disease progression and treatment response [2].

Posterior segment changes, although less common, have important implications for visual prognosis. Studies using fundus photography and in vivo confocal microscopy have documented pigment epithelial mottling, chorioretinal atrophy, and macular involvement resulting in reduced visual acuity and field constriction [7]. Histopathologic analyses show cystine crystals in the retinal pigment epithelium (RPE) and choroid, confirming that cystinosis affects both anterior and posterior ocular structures [8]. Persistent photophobia and visual decline are often exacerbated by these posterior changes. Recent advances in imaging, such as optical coherence tomography (OCT), have enhanced the ability to monitor posterior involvement and quantify crystal burden non-invasively, aiding early therapeutic intervention [2].

Although ocular changes may dominate the early clinical course, cystinosis is fundamentally a systemic disease. In its nephropathic form, patients develop generalized proximal tubular dysfunction leading to renal Fanconi syndrome, with polyuria, aminoaciduria, and phosphate wasting. These abnormalities cause rickets, growth failure, and skeletal deformities [9]. The accumulation of cystine crystals in bone,

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muscle, and endocrine tissues further contributes to stunted growth and metabolic imbalance [10]. Importantly, ocular findings such as bilateral corneal crystals often appear before overt renal manifestations, sometimes preceding systemic diagnosis by several years [11]. This temporal relationship underscores the ophthalmologist's pivotal role in early detection. A slit-lamp examination revealing the characteristic refractile, needle-shaped crystals can guide clinicians toward confirmatory testing, including leukocyte cystine quantification and genetic analysis.

Early ophthalmic identification of cystinosis is particularly vital because timely systemic therapy with cysteamine can substantially delay progression of renal and extra-renal complications [3]. Delay in diagnosis often results in irreversible systemic damage, including chronic kidney disease and growth impairment. Hence, interdisciplinary collaboration between ophthalmologists, pediatricians, and nephrologists is critical to improving outcomes [12]. Recent reviews emphasize that ocular monitoring should be integrated into long-term management, as corneal and retinal findings not only indicate local disease but also reflect systemic therapeutic efficacy [2,10].

The relationship between ocular and systemic disease in cystinosis also exemplifies shared embryologic and molecular pathways between the eye and kidney. Both organs rely on lysosomal and tubular transport systems, making them vulnerable to metabolic derangements [13]. Studies of ocular–renal syndromes reveal common mechanisms involving oxidative stress and the renin–angiotensin–aldosterone system, which may amplify tissue injury [14]. Consequently, detailed ophthalmic examination serves not only diagnostic but also prognostic functions, providing insight into systemic disease status.

In summary, cystinosis represents a rare but instructive metabolic disorder linking ocular and systemic pathology through a unifying lysosomal mechanism. Corneal and retinal changes, often detected long before systemic manifestations, make the eye a natural window to diagnosis. Awareness of these characteristic findings allows ophthalmologists to play a central role in early recognition, multidisciplinary coordination, and preservation of both visual and systemic function. This case adds to the expanding literature emphasizing that ocular cystinosis, though visually disabling, is diagnostically invaluable for identifying a life-threatening systemic disease in its earliest and most treatable stages.

CASE HISTORY

A 7-year-old boy named Raj Dev, the second child of non-consanguineous, healthy parents from Sylhet, presented to the ophthalmology outpatient department with complaints of poor growth since age two, bowing of both legs since birth, inability to run properly, and loss of appetite. He was fully immunized according to the national schedule, and there was no family history of similar illness or inherited disorders.

Systemic History

The child's caregivers denied any urinary abnormalities, such as polyuria, polydipsia, or nocturnal enuresis. There was no history of diarrhea, constipation, vomiting, convulsions, or respiratory distress. There was no record of prolonged drug intake, including vitamin D or anticonvulsant therapy.

General Examination

The child appeared short and stunted for his age, with an overall thin habitus. His vital signs were within normal limits: temperature 98.5 °F, pulse 82 bpm, respiratory rate 22 breaths/min, and blood pressure 90/60 mm Hg. Physical examination revealed frontal bossing and a box-shaped head. Skeletal changes were evident, including widened wrists and ankles, enlarged costochondral junctions (rachitic rosary), and bowing of both lower limbs with knee deformity, consistent with features of rickets. The abdomen was soft with mild hepatomegaly. Cardiovascular and respiratory system examinations were unremarkable. Cognitive evaluation indicated mild mental retardation.

Ocular Examination

On ocular inspection, both eyes were orthophoric with no evidence of strabismus or ptosis. The anterior segment of each eye showed bilateral hazy corneas containing multiple fine, refractile crystalline deposits throughout the entire stromal thickness. The density of crystals was greater in the peripheral cornea and relatively sparse centrally. The iris details appeared indistinct, but the anterior chamber depth was normal, pupillary light reflexes were brisk and equal, and the lenses were clear bilaterally.

Best-corrected visual acuity (BCVA) was 6/36 in both eyes.

Fundus Findings

Due to anterior corneal haze, the media were mildly hazy, limiting fine visualization. The optic discs showed mild pallor with normal retinal vasculature. The maculae exhibited chorioretinal atrophy with absent foveal reflex, suggestive of early macular degeneration secondary to cystine deposition. No active retinal hemorrhage or exudate was observed.

Clinical Impression

Based on the combination of growth retardation, skeletal deformities suggestive of rickets, and ocular crystalline keratopathy with macular atrophy, the child was provisionally diagnosed with ocular cystinosis associated with systemic features of infantile nephropathic cystinosis. The presence of corneal crystal deposition and posterior segment involvement indicated advanced ocular disease, while the skeletal abnormalities implied systemic metabolic dysfunction, possibly due to renal Fanconi-type pathology.

Initial Management and Counseling

The child and caregivers were counseled on the probable diagnosis and the need for multidisciplinary evaluation. Baseline investigations including urinary amino acid analysis, serum electrolytes, and renal function tests were recommended to assess systemic involvement. Cystine crystal deposition was explained as a hallmark of cystinosis, and referral to pediatric nephrology was advised for confirmation through leukocyte cystine quantification and genetic testing for *CTNS* mutation.

Ophthalmic management was planned to include topical cysteamine hydrochloride drops (0.44 %) to reduce corneal crystal density and regular follow-up for visual acuity, photophobia, and ocular surface integrity. The parents were educated on protective measures against light exposure and the importance of systemic therapy initiation to prevent further ocular and systemic deterioration.

Figure – 1: Ocular cystinosis

The findings in this child illustrate the classical ocular phenotype of cystinosis-related crystalline keratopathy, together with systemic stigmata of a generalized lysosomal storage disorder. Early ophthalmologic recognition is crucial, as the ocular signs often precede severe renal and skeletal manifestations, allowing timely initiation of multidisciplinary management.

DISCUSSION

The present case highlights the diagnostic and clinical relevance of ocular cystinosis in a pediatric patient presenting with bilateral corneal crystals, macular atrophy, and systemic features including growth retardation and rickets-like skeletal deformities. Cystinosis is an autosomal-recessive lysosomal storage disorder caused by mutations in the CTNS gene, which encodes the lysosomal cystine transporter cystinosin. The resultant cystine accumulation leads to progressive cellular dysfunction and multisystem involvement encompassing renal, skeletal, endocrine, neurological, and ocular systems [1,3]. While nephropathic cystinosis typically presents in infancy with renal Fanconi syndrome, ocular manifestations can precede systemic symptoms by several years, serving as a critical window for early detection [10].

Ocular findings in this child, particularly bilateral corneal crystal deposition, mirror classical descriptions of cystinosis-related keratopathy where crystals initially appear in the peripheral anterior stroma and progressively extend centrally and posteriorly [5,7]. This deposition disrupts stromal architecture, increases light scatter, and contributes to photophobia and reduced visual acuity [2]. The presence of macular atrophy and mild optic disc pallor further indicates posterior segment involvement, a feature less frequently reported in pediatric ocular cystinosis but associated with disease progression and chronic oxidative stress in the retinal pigment epithelium [7]. Similar retinal degeneration and chorioretinal atrophy have been noted in advanced cases, reinforcing the link between cystine accumulation and photoreceptor damage [15].

From a pathophysiologic standpoint, oxidative stress and lysosomal dysfunction play pivotal roles in tissue damage. Excess cystine promotes apoptosis and collagen disorganization within the corneal stroma, compromising transparency and structural integrity [2]. The degenerative macular changes in the present case are consistent with cumulative oxidative damage and cystine deposition in the RPE [16]. These mechanisms illustrate how local ocular findings may mirror the systemic burden of cystine, underscoring their utility as biomarkers of overall disease activity.

The coexistence of ocular and skeletal abnormalities in this patient further exemplifies the systemic reach of cystinosis. Growth failure and rickets-like deformities observed here are compatible with renal Fanconi syndrome, a hallmark of nephropathic cystinosis [3]. Comparable pediatric reports describe ocular signs preceding or paralleling systemic metabolic bone disease, highlighting the diagnostic value of early ophthalmic evaluation [9]. Consequently, routine slit-lamp screening in children presenting with photophobia or unexplained growth retardation should be prioritized to facilitate timely referral and systemic evaluation [11].

Management in this case followed established recommendations involving topical cysteamine hydrochloride (0.44%) for reducing corneal crystal density and systemic cysteamine therapy to lower intracellular cystine levels. While systemic therapy effectively mitigates renal and endocrine complications, its limited corneal penetration necessitates concurrent topical administration [2,5]. Regular monitoring using slit-lamp biomicroscopy and optical coherence tomography (OCT) remains essential to assess both anterior and posterior segment response [17].

This case underscores the multidisciplinary dimension of cystinosis management, integrating ophthalmology, nephrology, and pediatrics. It demonstrates how characteristic ocular findings—corneal crystals and macular changes—can provide critical diagnostic cues for a systemic lysosomal disorder. Furthermore, it reinforces that ophthalmic surveillance not only detects disease early but also reflects systemic treatment adherence and efficacy [10,13]. Therefore, enhancing clinical awareness of ocular cystinosis among pediatric and ophthalmic practitioners is vital for preventing irreversible visual and systemic sequelae.

CONCLUSION

This case reinforces the diagnostic and prognostic value of ocular findings in pediatric cystinosis. The coexistence of bilateral corneal crystals, macular atrophy, and systemic features such as growth retardation and skeletal deformities highlights the systemic nature of this lysosomal storage disorder. Recognizing the characteristic refractile corneal crystals on slit-lamp examination remains essential for early diagnosis, particularly when renal or systemic manifestations are subtle or delayed. Timely initiation of combined systemic and topical cysteamine therapy, along with regular ophthalmic monitoring using slit-lamp and OCT, can slow progression and improve quality of life. This report underscores the critical role of ophthalmologists as front-line detectors of systemic metabolic disease and advocates for multidisciplinary collaboration among pediatricians, nephrologists, and ophthalmologists to optimize outcomes. Increased awareness and early screening in children with photophobia or unexplained growth failure may prevent irreversible ocular and systemic sequelae.

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