RESULTS OF GENETIC, METABOLIC, AND INFECTIOUS EVALUATION OF BILATERAL PEDIATRIC CATARACTS

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INTRODUCTION

- **BACKGROUND:** Congenital cataracts (CCs) are a rare, but important cause of visual impairment and treatable blindness affecting 191,000 children worldwide.[1] CCs have a diverse spectrum of etiologies including genetic mutations, metabolic disease, and congenital infection (TORCH infections).[2-4] At this time there is not a standardized approach to the work-up of these cataracts and it is common practice at many institutions for all young children with unexplained cataracts to undergo extensive testing. However, the results of such testing, particularly the infectious and metabolic work-up, appear to have low diagnostic yield. Given this, the Pediatric Eye Disease Investigator Group (PEDIG) has recommended reevaluation of the standard-of-care testing ordered in the evaluation of these cataracts.[5]

- **STUDY OBJECTIVE:** To evaluate the results of laboratory testing performed in the work-up of pediatric cataracts at our institution in order to determine how frequently such tests identified the cause of a child's cataracts.

METHODS

- A Colorado Multiple IRB approved retrospective case series was conducted using the Children's Hospital Colorado database.
- From March 2006 to December 2022, we identified all patients under 18 years old who underwent cataract surgery.
- We reviewed the available clinic and surgical records of each child to identify patients with bilateral cataracts without a known cause at the time of first ophthalmologic examination.
- We recorded the results of laboratory testing ordered by the pediatric ophthalmologists as part of the work-up for the child's cataracts, including tests for genetic, infectious, and metabolic etiologies.
- Test results were excluded if they were ordered by providers from a specialty other than ophthalmology or clinical genetics, as such testing may have been ordered as part of the work-up for co-morbid congenital anomalies other than specifically cataracts.

RESULTS

TABLE 1: Demographics and Testing Ordered

Characteristic	Mean (SD)
Age at Diagnosis (Years)	1.47 (2.26)
Sex	**Number (%), n = 44**
Male	27 (61.4%)
Female	17 (38.6%)
Testing Ordered	**Number (%), n = 44**
Genetic	35 (79.5%)
Infectious	34 (77.3%)
Metabolic	37 (84.1%)

TABLE 2: Genetic and Metabolic Testing Results

Genetic Test Results	Number (%), n = 35
Positive Result	16 (45.7%)
Result of Uncertain Significance	3 (8.6%)
Negative Result	16 (45.7%)
Galactosemia Testing	**Number (%), n = 35**
Positive Result	3 (8.6%)
Positive Confirmatory Testing	0 (0.0%)
Urine Reducing Substances	**Number (%), n = 17**
Positive Result	2 (11.8%)
Positive Confirmatory Testing	0 (0.0%)

TABLE 3: Infectious Testing Results

Overall TORCH Titers	Number (%), n = 34
Positive Screening	23 (67.6%)
Positive Confirmatory Testing	0 (0.0%)
CMV	**Number (%), n = 28**
Positive IgG	10 (35.7%)
Positive Confirmatory Testing (CMV IgM or CMV PCR)	0 (0.0%)
Rubella	**Number (%), n = 23**
Positive IgG	7 (30.4%)
Positive Confirmatory Testing (Rubella IgM)	0 (0.0%)
Toxoplasma	**Number (%), n = 28**
Positive IgG	0 (0.0%)
Positive Confirmatory Testing (Toxoplasma IgM)	0 (0.0%)
HSV	**Number (%), n = 28**
Positive IgG	6 (21.4%)
Positive Confirmatory Testing (HSV IgM or HSV PCR)	0 (0.0%)
Syphilis	**Number (%), n = 27**
Positive RPR/VDRL	0 (0.0%)
Positive Confirmatory Testing (FTA-ABS)	0 (0.0%)

TABLE 4: Cataract Etiologies

Etiology	Number (%), n = 44
Genetic	16 (36.4%)
Metabolic	0 (0.0%)
Infectious	0 (0.0%)
Idiopathic/Unknown	28 (63.6%)

KEY FINDINGS

- Genetic testing had the highest diagnostic yield, identifying a pathogenic mutation in 45.7% of the patients for which it was ordered.
- Twenty-three (67.6%) patients who were evaluated for TORCH infection were found to be positive on screening for IgG. However, no patients were found to be positive for congenital infection on confirmatory testing.
- No patients were found to have a metabolic etiology for their cataracts.
- Twenty-eight (63.6%) patients had no cataract etiology identified after extensive genetic, metabolic, and infectious evaluation.

CONCLUSIONS

- Pediatric Ophthalmologists should consider ordering more targeted work-ups for their patients with unexplained bilateral cataracts.
- Genetic testing should be strongly considered in all cases given its high diagnostic yield.
- While metabolic testing may be justified by the rare possibility that cataract may be the first clinical sign of a metabolic disorder.
- Pediatric ophthalmologists should not routinely order TORCH titers in otherwise healthy children – In particular, testing for IgG should be avoided in patients young enough to still carry maternal IgG.

DISCLOSURES

- The authors have no conflicts of interest.

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