Down Syndrome

14-month-old male with intermittently crossed eyes

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Chief Complaint: Eyes appear to cross inward

History of the Present Illness

A 14-month-old male diagnosed with Down syndrome presented for evaluation of intermittently "crossed eyes." His parents report that either eye intermittently appears to cross. The patient also has a prominent right head tilt, for which he is currently undergoing physical therapy. The parents feel he has appropriate vision and note that he reaches for toys, recognizes familiar faces, and follows objects across a room with both eyes.

Past Ocular History

None

Past Medical History/Problem List:

1. Trisomy 21 (Down syndrome)
2. Hypothyroidism
3. Tracheomalacia
4. Otitis media, recurrent
5. Language delay
6. Overweight (BMI 85-95 percentile)

Past Surgical History: Myringotomy with tube insertion August 2013. No ocular surgery.

Medications: Levothyroxine (oral, for hypothyroidism), ofloxacin (topical, for recurrent otitis media)

Family Ocular History: Paternal aunt with esotropia. Maternal grandfather with macular degeneration

Social History: Lives at home with his mother and father.

Review of Systems: All systems negative.

OCULAR EXAMINATION

Stereo testing: Unable to perform due to age

Pupils: No relative afferent pupillary defect OU

Extraocular motility: Normal versions

Visual acuity by toys

- OD - Distance: Central, steady, and maintained
- OS - Distance: Central, steady, and maintained
- OD - Near: Central, steady, and maintained
- OS - Near: Central, steady, and maintained

Equal objection to covering of either eye

Teller card testing OU: 9.8 cycles/cm at 55 cm (equivalent to 20/60)

Confrontation visual fields: No deficits OU by toys

Cycloplegic refraction

- OD: +3.00 diopters (D) sphere
- OS: +3.00 D sphere

External exam: Normal

Anterior segment exam

- **Lids:** Normal OU
- **Conjunctiva/Sclera**: Clear and quiet OU
- **Cornea**: Clear OU
- **Anterior chamber**: Deep and quiet OU
- **Iris:** Normal OU
- **Lens**: Clear OU
- **Vitreous**: Normal OU

Posterior segment exam

- **Discs:** Small cup:disc ratio with extra branching vessels OU
- **Macula**: Normal OU
- **Vessels**: Normal OU
- **Periphery:** Blonde fundus OU

Strabismus Exam

- Method: Alternate cover
- Near: 12 prism diopter (PD) intermittent esotropia
- Distance: 6 PD intermittent esotropia, no vertical deviation in all gazes including head tilts
- No nystagmus
- Right head tilt 20 degrees, does not resolve with monocular occlusion

DIAGNOSIS: Intermittent esotropia in the setting of Down syndrome

The patient had a higher magnitude esotropia at near than distance, suggesting that there may be an accommodate component to his esotropia. The patient's parents were advised to fill the glasses prescription to try to correct the accommodative component. In a subsequent visit 2 months later, the parents report that the patient is not tolerating the glasses well and does not wear them much. Esotropia without correction is improved at this follow-up visit, however, to a slight esotropia. His parents understand that the patient may ultimately require surgical correction if the strabismus does not correct with glasses alone.

Considering his anomalous head position, it was noted that the measured strabismus did not appear to change with varied head positions and the head tilt persisted with monocular occlusion, making the etiology non-ocular torticollis. As the torticollis is presumed to be musculoskeletal in origin, the patient is undergoing physical therapy, and the parents have noted some improvement with this intervention.

DISCUSSION

Down syndrome has been associated with many ocular manifestations. A review article published by Creavin et al. in 2009 compiled the results from 23 studies with sample sizes varying between 18 – 524 patients with confirmed Down syndrome in order to determine the most common ophthalmic disorders affecting this patient population (1). The prevalence of a visual acuity deficit was most common, and it ranged in prevalence from 30-62%. The second most common ophthalmic disorder was strabismus, noted in 3-57%, depending on the cut-off criteria for significant strabismus, with the majority of studies reporting 20-40% prevalence. Esodeviation far outweighed exodeviation. Variation in measurement of hyperopia and astigmatism was accounted for by varying criteria for diagnosis. Regarding hyperopia, a cut-off value of greater than +0.75 D yielded a prevalence of 59%, whereas a cut-off of +2.00 D yielded a prevalence of 10%. Similarly for astigmatism, a cut-off value of +0.50 D yielded a prevalence of 60%, and a cut-off value of +3.00 D yielded a prevalence of 10%. Cregg et al. proposed that children with Down syndrome are less likely to undergo emmetropization with age; 86% of children with Down syndrome maintain significant hyperopia, while only 39% of children without Down syndrome maintained +3.00 D of hyperopia by 20 months (7).

Although screening efforts have lead to earlier diagnosis of strabismus in this patient population, the deviation is often not clinically significant, and correction is unnecessary.

Other disorders relevant to this patient population are listed below, in order of prevalence.

1. Visual acuity deficit (30-62%)
2. Strabismus, particularly esodeviation (3-57%)
3. Astigmatism (6-60%)
4. Hyperopia (4-59%)
5. Myopia (8-41%)
6. Lacrimal duct obstruction (17-36%)
7. Nystagmus (10-20%)
8. Amblyopia (~ 20%)

9. Blepharitis (~ 9%)
10. Keratoconus (5 studies – none; 3 studies – 1-12%)

Less common diagnoses, but with serious implication, include cataracts and glaucoma, with one source suggesting the prevalence of cataracts to be as high as 15% in children with Down syndrome. Other readily identified ophthalmic features include slanting palpebral fissures, prominent epicanthal folds, hypertelorism, microphthalmos, and epiblepharon. Retinal abnormalities varied greatly.

Pseudostrabismus is a common finding in Down syndrome patients. Due to prominent epicanthal folds and a flat nasal bridge, there is often less sclera apparent on the nasal aspect of both eyes, giving the appearance of esotropia when in fact the child is orthophoric. Any child suspected of pseudostrabismus or true strabismus should be referred to a pediatric ophthalmologist who is best able to make the distinction.

There was great variation in the identification of Brushfield spots, attributed to ethnic variability. Brushfield spots are more easily seen in light-colored irides, and as such, studies in Hong Kong and India indicated an extremely low prevalence, while studies with a Caucasian base indicated a more significant prevalence, between 35-78% (1).

Akinci, et al. identified statistically significant differences between ophthalmic findings in Down syndrome patients (77 children with mean age 8.5 ± 3.7 years; age range 1-17 years) and an age-matched control group (151 children with mean age 8.9 ± 2.4 years; age range 3-15 years) including nystagmus, strabismus, hyperopia, astigmatism, and congenital cataracts (2). See Table 1. The total prevalence of any ocular findings in Down syndrome patients was 97.4%, whereas the control group had a prevalence of 42.4% ($P < 0.0001$). The prevalence of myopia and anisometropia was found to be similar in both groups. Hyperopia was not more common in children with Down syndrome who had a coinciding diagnosis of esotropia than in children with Down syndrome who did not have an esotropia diagnosis.

Ophthalmic findings in Down syndrome patients			
Ocular Finding	**Down Syndrome Group (n = 77)**	**Control Group (n = 151)**	**P value**
Nystagmus	19.4% (15)	0	< 0.0001
Strabismus	32.5% (25)	1.3% (2)	< 0.0001
Hyperopia	62.3% (48)	15.9% (24)	< 0.0001
Astigmatism	59.7% (46)	25.2% (38)	< 0.0001
Congenital cataract	5.1% (4)	0	< 0.01
Myopia	7.8% (6)	17.2% (26)	0.17
Anisometropia	9% (7)	4% (6)	0.13

Table 1. The prevalence of ophthalmic findings in Down syndrome patients compared to an age-matched control group (2).

Another important finding in this case was the presence of a head tilt. An abnormal head position may be due to non-ocular causes such as torticollis, or ocular causes such as strabismus, nystagmus, or ptosis. Investigation is crucial as identification of the underlying cause allows for proper treatment of the abnormal head position. Dumitrescu et al. identified the prevalence of abnormal head posture (AHP) in the Down syndrome population

to be 24.7%, based on a retrospective study that reviewed charts of 259 children with Down syndrome, 64 of which had AHP (3). The AHP developed around 3-3.5 years of age, on average. The most frequent causes of AHP were incomitant strabismus in 17 patients (26.6%), nystagmus in 14 (21.8%), undetermined causes in 12 (18.8%), and multiple causes in 9 (14.1%). Other causes for AHP in this study included refractive error, ptosis, unilateral hearing loss, and neck and spine musculoskeletal abnormalities (such as muscular torticollis and scoliosis). The odds of developing an AHP was increased with both Down syndrome and strabismus diagnoses, and it was increased even further if the patient's strabismus was incomitant. The purpose of head posturing in patients with strabismus-induced AHP is to adopt a head posture that will minimize diplopia and achieve fusion of the image. Alternatively, patients may tilt their head to the affected side in order to exaggerate the distance between two images, so they can more readily ignore one of them. The purpose of head posturing in patients with nystagmus-induced AHP is to place the eyes in a position in which they have the smallest amplitude of nystagmus and therefore the best visual acuity. Patients with ptosis may adopt a chin-up position to maximize their visual field under their low-hanging eyelids.

Of the patients with AHP, 23 (35.9%) showed improvement with intervention – either glasses or surgery. Only 17 of the 64 patients (26.6%) elected for surgery, which can be attributed to the risks associated with general anesthesia for Down syndrome patients. In particular, Bai et al. identified bradycardia and decreased mean arterial pressure to be more prevalent in Down syndrome patients compared to age-matched controls (4). Additionally, atlantoaxial instability is a concern for anesthesiologists who care for Down syndrome patients. Surgery was successful in 14/17 cases (82.4%), defined as a significant improvement in AHP without recurrence at follow-up visits. An additional 6 patients (9.4%) improved spontaneously with no intervention – 3 of these patients had nystagmus-induced AHP, 2 had unclear reasons for AHP, and 1 had refractive error-induced AHP. The mechanism of refractive-error induced AHP is unknown.

The importance of early screening for ocular anomalies in Down syndrome patients cannot be overemphasized, as some of them may be amblyogenic, and early identification and treatment can prevent long-term vision loss. Comparisons between routine pediatric well-child screening efforts and ophthalmologic assessment have indicated that routine well-child screening alone is insufficient. Overall, 20% of disorders that were identified by ophthalmologists went undetected by pediatricians; strabismus and blepharitis were particularly problematic to diagnose (5). According to Roizen, et al., "the percentage of children with ophthalmic disorders increased with age, from 38% in the 2 to 12-month-old group to 80% in the 5 to 12-year-old group." Therefore, it is a general recommendation that children with Down syndrome be first evaluated by a pediatric ophthalmologist within the first 6 months of life, and then re-evaluated annually thereafter. Pediatric ophthalmologists at UIHC agree with this recommendation.

Vision has a great impact on activities of daily living. Children with Down syndrome already encounter large social, behavioral, and emotional obstacles in their daily living and prevention of impaired vision with early screening by an ophthalmologist has immeasurable benefit for a child's quality of life.

Diagnosis

Intermittent esotropia in the setting of Down syndrome

Epidemiology:	Signs:
Prevalence of esotropia (6): 3% of all children; 15-52% of children with Down syndrome. Risk factors for esotropia: low birth weight, retinopathy of prematurity, family history, neurologic and developmental problems (Down syndrome, cerebral palsy, hydrocephalus).	Intermittent or constant inward deviation of one or both eyes with corresponding abnormal results on red reflex, Hirschberg, Krimsky, and cover testing. Abnormal head position. Varying degrees of amblyopia. Abnormal results on stereoacuity and/or Worth 4-dot testing. Other ophthalmic manifestations of Down syndrome (1): visual acuity deficit, strabismus (most commonly esotropia), astigmatism, hyperopia, myopia, lacrimal duct obstruction, nystagmus, blepharitis, keratoconus, congenital cataracts, and glaucoma.
Screening:	Treatment:
Ocular screening recommendations for all children with Down syndrome include evaluation by a pediatric ophthalmologist within the first 6 months of life and annually thereafter.	Observation may be reasonable for small angles of deviation. Accommodative component may respond to hyperopic spectacle correction. Extraocular muscle surgery may be required for residual esotropia. Amblyopia should be treated prior to surgery.

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