Congenital Eyelid Ptosis: Onset and Prevalence of Amblyopia, Associations with Systemic Disorders, and Treatment Outcomes

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Objectives To determine the age at onset of amblyopia, the response to occlusion therapy, and the association with systemic disorders in children with congenital eyelid ptosis.

Study design Retrospective chart review of children seen at Seattle Children’s Hospital with moderate or severe congenital ptosis. Assessments were longitudinal visual acuity development using objective methods, definition of ptosis severity by eyelid margin to pupillary light reflex distance (margin reflex distance [MRD]), age at amblyopia diagnosis, correlation between amblyopia and MRD, and associated systemic disorders.

Results Eighty-four children with moderate-to-severe congenital ptosis met inclusion criteria; the mean longitudinal follow-up was 49.1 months. Fifteen (18%) of these children had amblyopia, of which 9 had deprivation amblyopia (mean age 17.3 months ± 11.2) and 6 had anisometropic or strabismic amblyopia (mean age 60 months ± 11.8). Eleven (73%) of the children with amblyopia were successfully treated with occlusion therapy. Amblyopia was not correlated with MRD. A systemic disorder was identified in 29 (35%) of the children, the most common being genetic, chromosomal, or neurologic conditions. Patients with systemic disorders and developmental delay have significantly lower visual acuity bilaterally compared with patients without systemic disorders (P = .003).

Conclusions Using longitudinal and objective visual acuity assessments, the incidence of amblyopia was 18% in children with moderate to severe congenital ptosis. Visual deprivation was the predominant risk factor that was reliably distinguished by its earlier onset in young children. The best indicator of amblyopia in children is visual acuity rather than MRD measurements. Systemic disorders are frequent in children with moderate to severe congenital ptosis. (J Pediatr 2014;165:820-4).

Congenital ptosis (droopy eyelid) is a conspicuous ocular finding that brings infants and young children to medical attention early in life. The ptosis most commonly occurs as an isolated unilateral abnormality in an otherwise normal child.¹ The severity of ptosis can be mild, moderate, or severe. Congenital ptosis can be associated with anomalies of extraocular muscle development and of innervation. Limitation of eyelid elevation occurs in 5%-16% of children owing to failure of the superior rectus and levator muscles to develop from their shared mesenchymal origins.² Anomalies of innervation include anomalous eyelid synkineses commonly referred to as the Marcus Gunn jaw-winking phenomenon and congenital oculomotor paresis. Normally, the eyelid tracks with eye position owing to neural connections between the eyelid and the ocular muscles. Misrouting of these connections can lead to a dyskinesis of the levator and jaw muscles resulting in ptosis in the resting phase and exaggerated elevation of the eyelid during activation of the jaw muscles. Oculomotor paresis is distinguished by the associated horizontal and vertical ophthalmoplegia, variable presence of ipsilateral pupillary dilation, and structural abnormalities of the central nervous system defined by neuroimaging.³

Ptosis also can be a manifestation of a genetic, craniofacial, chromosomal, or neurologic disorder.¹⁻⁴,¹² Children with these systemic disorders are likely to initially come to pediatricians’ attention because of ptosis. The pediatrician plays a central role in the early identification of an underlying systemic disorder. Furthermore, the presence of a systemic disorder may influence the laterality of ptosis and may impact visual acuity outcomes because of developmental comorbidities.

The eyelid margin encroaches on the visual axis in moderate and severe congenital ptosis, and predisposes the child to amblyopia. The overall prevalence of amblyopia because of deprivation, strabismus (eye misalignment), or anisometropia (unequal refractive error between eyes) ranges from 1.5%-12.0% across studies.¹³⁻²⁰ Previous large series of congenital ptosis have been retrospective reviews of visual acuity outcomes¹⁻⁰ or have focused largely on the surgical correction of ptosis.¹⁴,¹⁵,¹⁸,²¹ In most studies, visual acuity in preverbal children was estimated from visual fixation behavior. Treatment of amblyopia includes monocular patching (occlusion therapy), spectacles, and surgery. Few data have documented the efficacy of occlusion therapy in young children with congenital ptosis.

MRD Margin reflex distance

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We aimed to determine the incidence and age at onset of deprivation vs strabismic and anisometropic amblyopia, to characterize systemic disorders that occur with congenital ptosis, to compare visual outcomes and laterality of ptosis in isolated ptosis vs ptosis associated with a systemic disorder, and to document the efficacy of occlusion therapy in the treatment of amblyopia in children with congenital ptosis.

**Methods**

The study population comprises a retrospective chart review of 84 patients consecutively evaluated by a pediatric ophthalmologist (A.W.) for moderate to severe ptosis at Seattle Children’s Hospital. The research followed the tenets of the Declaration of Helsinki, and this retrospective chart review was approved by the institutional review board for patients seen from January 1992, to December 2009.

Unilateral congenital ptosis was defined as a decrease in the palpebral fissure height, margin reflex distance (MRD, upper eyelid margin to pupillary light reflex distance in mm), and decreased levator function of one eye. Bilateral congenital ptosis was defined as an asymmetric or symmetric decrease in palpebral fissure height, MRD, and levator function in both eyes. Inclusion into the study was the presence of congenital ptosis by history or examination prior to 6 months of age. The severity of ptosis was graded according to MRD and levator function. We classified severe ptosis as an MRD in the affected eye(s) of 0.5 mm or less and levator function of 4 mm or less, moderate ptosis as an MRD of 1.0 or 1.5 mm and levator function of 5–9 mm, and mild ptosis as an MRD of 2.0 mm or more and levator function greater than 10 mm. MRD was measured in primary gaze with the frontalis muscle fixed manually. Measurement of levator function represents the excursion of the upper eyelid margin going from maximum downgaze to upgaze with manual fixation of muscle. Both were recorded in increments of 0.5 mm using a metric ruler.

Children with jaw-wink syndrome were excluded from the study. A large number of patients with previously diagnosed craniofacial disorders having ptosis were excluded from this analysis to avoid biasing the population. All children with mild ptosis, or ptosis associated with myasthenia gravis, botulism, congenital cranial nerve III palsy, ophthalmoplegia syndromes, or ocular malformations (ie, microphthalmos, persistent fetal vasculature) were excluded. Children with mild ptosis were excluded because the age at detection occurs much later and is a cosmetic concern only.

Patients younger than 3 years of age had binocular or monocular visual acuity assessments using the Teller acuity cards (Vistech Consultants, Dayton, Ohio). In patients older than 3 years of age, distance visual acuity with full optical correction was measured with the use of a computerized visual acuity tester. There is good agreement between preferential looking grating acuity and recognition acuity in children. Patients older than 3 years of age were tested with optical correction only if their refractive error was greater than or equal to 3.00 D of hyperopia, greater than or equal to 1.0 D of myopia, or greater than or equal to 1.5 D of astigmatism. In patients younger than 3 years age, visual acuity was adjusted for age-related improvements in acuity by reporting the relative deficit from the mean value for age-matched control patients.

Amblyopia was defined as 2-fold difference in visual acuity between eyes or from age-matched normals on 2 consecutive visits. Anisometropic amblyopia was defined as visual loss because of a refractive difference between eyes of at least 1 D of myopia, 2 D of hyperopia, or 1.5 D of astigmatism. Strabismic amblyopia was defined as visual loss because of a microtropia (8 D or less) with subnormal stereoacuity or any larger heterotropia. Eye alignment was measured using standard cover-uncover testing at both distance and near. Deprivation amblyopia was defined as visual loss because of complete or partial obstruction of the pupillary aperture by the ptotic eyelid on 2 consecutive visits. Deprivation amblyopia was an exclusionary diagnosis made in the absence of strabismus or significant anisometoria.

After confirming the presence of amblyopia, all patients with deprivation, strabismic, and anisometropic amblyopia were treated with optical correction and part-time occlusion therapy. Surgery was performed before the age of 4 years for failure to adopt compensatory mechanisms, interference of the chin-up posture with locomotion, or noncompliance with amblyopia therapy.

**Results**

Eighty-four patients met inclusion criteria, 53 had unilateral ptosis, and 31 bilateral ptosis. The average age of presentation was 18.5 (range 0.5–90) months. Mean longitudinal follow-up was 49.1 (3–196) months. Fifteen (18%) of the 84 patients met our criteria for amblyopia (9 with unilateral ptosis and 6 with bilateral ptosis). Of the 84 patients, 9 had deprivation amblyopia, 4 had strabismic amblyopia, and 2 had anisometropic amblyopia. Of 9 patients with deprivation amblyopia, 2 had a systemic disorder. Of the 6 patients with strabismic or anisometropic amblyopia, 3 had a systemic disorder. All except for 3 patients with severe ptosis adopted either a chin-up posture, used their frontalis muscle, or both at some time.

Figure 1 (available at www.jpeds.com) shows the visual acuity of the affected and unaffected eyes in patients with unilateral ptosis, respectively, compared with young controls. Development of visual acuity is similar between eyes and demonstrates the relative infrequency of amblyopia in unilateral ptosis. Figure 2 (available at www.jpeds.com) shows the visual acuity of the nonpreferred and preferred eyes in patients with bilateral ptosis, respectively, compared with controls. Both patients with unilateral and bilateral ptosis who have developmental delay and systemic disorders have significantly lower visual acuity in both eyes compared with patients without systemic disorders (P = .002 for unilateral ptosis; P < .0001 for bilateral ptosis).

The mean age at amblyopia onset derived from the longitudinal data was 17.4 months (SD = 15.2) for deprivation
Patients with craniosynostosis were excluded to avoid biasing the data.

Eleven (73%) of the 15 patients with amblyopia recovered normal visual acuity following occlusion therapy of the non-
amblyopic eye. Each of the 4 patients who remained ambly-
opic was nonadherent to occlusion therapy. Of these, 2 of 3
patients ceased occlusion therapy after early surgical correc-
tion of the ptosis and one had ipsilateral high myopia.

At presentation, MRD difference between eyes ranged
from 0.0-5 mm. Figure 3, A (available at www.jpeds.com)
shows noncompensatory eyelid height (minimum MRD
without the contribution of the frontalis muscle) and
interocular acuity ratio. Figure 3, B shows compensatory
eyelid height (minimum MRD with the contribution of the
frontalis muscle) and interocular acuity ratio. The shaded
area depicts amblyopia indexed by an interocular ratio of
\( \leq 2 \) or higher. In both the noncompensatory and
compensatory conditions, there is a nonsignificant trend
amongst amblyopia in the subset of children with the lowest
eyelid height (\( r^2 \leq 0.13 \)).

Systemic disorders were identified in 29 (35%) of the 84
patients (Table). The most common abnormality was a
defined genetic syndrome, followed by a neurologic
disorder, and a chromosomal alteration as detected by
ekaryotyping or comparative genomic hybridization. Of the
29 patients with systemic associations, 16 (55%) had
bilateral ptosis and 12 (41%) had unilateral ptosis.

Thirty-six children (43%) had corrective surgery for
congenital blepharoptosis at an average age of
4.6 \pm 1.6 years (0.5-9 years). Twenty-one patients had a fron-
talis sling procedure, and 15 patients had either a graded or
maximal levator resection. The indications for surgery
\( \geq 4 \) years were for cosmesis, brow ache, and limitations
imposed by a constant chin-up posture. Thirty-one of the
36 surgeries were performed \( \geq 4 \) years. Of the 5 cases per-
formed at a younger age, 3 had unilateral ptosis with ambly-
opia. Two of the 5 patients with early surgery had bilateral
ptosis with developmental delay, severe hypotonia, and
inability to adopt a compensatory chin-up posture that pre-
vented them from walking.

### Table. Systemic associations

<table>
<thead>
<tr>
<th>Chromosomal (n = 7)</th>
<th>Chr. 7 deletion (2)</th>
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<tbody>
<tr>
<td>Chr. 3 pericentric inversion</td>
<td>Mosaic gain Chr. 9</td>
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<tr>
<td>Chr. 5q microreplication (2)</td>
<td>Chr. 18p deletion</td>
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<tr>
<td>Genetic (n = 12)</td>
<td>Mowat-Wilson syndrome</td>
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<tr>
<td>Blepharophimosis-like syndrome (3)</td>
<td>Nooran syndrome (3)</td>
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<tr>
<td>Trisomy 21</td>
<td>Polycystic kidney disease</td>
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<td>Neurofibromatosis Type 1</td>
<td>Costello syndrome</td>
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<tr>
<td>Joubert syndrome</td>
<td>Neurologic (n = 8)</td>
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<tr>
<td>Microcephaly with severe developmental delay</td>
<td>Merosin positive muscular dystrophy</td>
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<tr>
<td>Congenital-fiber type I disproportion</td>
<td>Arthrogryposis (2)</td>
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<tr>
<td>Moderate developmental delay with hypotonia (2)</td>
<td>Severe cystic encephalomalacia with hydrocephalus</td>
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<tr>
<td>Craniofacial (n = 2)</td>
<td>Cleft lip and palate (2)</td>
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Chr. chromosome, total numbers of patients noted in parentheses if more than 1.
*Patients with craniosynostosis were excluded to avoid biasing the data.

Discussion

This study documents the incidence and age of onset of
amblyopia because of visual deprivation, anisometropia,
and strabismus in children with severe or moderate congen-
tal blepharoptosis. A major strength of this study was the
longitudinal measurement of visual acuity in preverbal chil-
dren using the Teller Acuity Card procedure, which provides
objective visual acuity in pediatric eye disorders.

The overall incidence of deprivation amblyopia in patients
with congenital ptosis was low (11%) despite the congenital
presence of moderate to severe ptosis. The low prevalence of
deprivation amblyopia was attributed to the ability to reverse
the occlusion of the visual axis by using the frontalis muscle
to raise the eyelid, and by adopting a chin-up posture. The
initiation of compensatory behaviors is delayed until 2-
3 months of age when the neonate is more visually attentive
and has improved head control or can sit independently
(6 months). Therefore, it is our practice to delay assessment
of the potential impact of upper eyelid position on visual acu-
ity until 2-3 months of age and of head position until 6 months of age. Of note, the muscular effort required to
raise the eyelid continuously is demanding and likely ac-
counts for the failure of some children to adopt these strate-
gies or to abandon them at an older age. Likely as a result of
this variability in compensatory behaviors, we found no
consistent relationship between interocular MRD differences
and amblyopia.

Clinically, the presence of deprivation amblyopia is sus-
pected on the basis of the relationship between the upper
eyelid margin and the pupillary center. That is, the presence
of asymmetry of the MRD or bilateral presence of a small
MRD prompts concern for amblyopia. However, our data
showed that recruitment of the frontalis muscle to increase
the MRD with or without a chin-up posture provided adequate compensation in 89% of patients. These compensatory behaviors provided a visual experience that enabled normal visual acuity development. We conclude that the most reliable means to detect deprivation amblyopia in this population is based on objective measurement of visual acuity.

We found a high prevalence of reduced visual acuity bilaterally in children with systemic disorders irrespective of ptosis laterality. Bilateral visual deprivation alone is not amblyogenic because there is no competitive advantage of one eye’s input vs the other eye’s input at the level of striate cortex. Therefore, the bilateral presence of reduced visual acuity in a child with systemic disorder and bilateral symmetric ptosis is more consistent with the associated developmental comorbidities. We postulate that the subset of children with systemic disorders and developmental delay have reduced visual acuity because of underlying defects in visual cortical processing.

Previous studies have focused on the amblyogenic potential, therapeutic interventions, and associated ocular abnormalities. Only 2 large series and several case reports have focused on the relationship between congenital ptosis and systemic disorders. In this study there was a high prevalence (35%) of an underlying chromosomal, genetic, or neurologic disorder. The higher incidence of systemic disorders in our study likely reflects 2 biases. One is the tertiary nature of our referral practice. In an attempt to overcome this referral bias and to capture the population that a pediatrician would encounter, we excluded a large number of patients with craniofacial and neurologic disorders. Second, we routinely take a developmental history and perform a general evaluation emphasizing systemic, neurologic, and dysmorphic features. This practice is based on the underlying notion that congenital ptosis represents a malformation of the levator muscle or aponeurosis and like any ocular malformation can be associated with a systemic disorder. The history of systemic disorder, developmental delay, and bilateral ptosis should prompt a genetic consultation and chromosomal testing. Patients with systemic disorders having a higher incidence of developmental delay are more likely to have lower visual acuity in the unaffected eye or preferred eye.

Oclusion therapy recaptured normal visual acuity in 73% of the patients with amblyopia. The only patients who did not recapture normal visual acuity failed to adhere to occlusion therapy. Surgical correction of the ptosis was performed electively in 41% of subjects at 4 years of age or older. This criterion was selected because it represents the age at which growth of the frontonasal complex and upper face is complete. Five patients underwent surgical correction of ptosis prior to age 4 years for specific reasons. Two patients without amblyopia, 1 with severe hypotonia, and 1 with arthrogryposis, underwent a bilateral frontalis sling procedure because somatic motor involvement interfered with the ability to walk. Three others underwent frontalis sling procedure prior to the age of 3 years for deprivation amblyopia because of failure to maintain compensatory mechanisms (2 patients) or to adhere to occlusion therapy. In all cases, the parents were advised that frontalis sling procedures in this age group have a limited half-life because of continued growth of the frontonasal complex.

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References

23. Louwagie CR, Jensen AA, Christoff A, Holleschau AM, King RA, Summers CG. Correlation of grating acuity with


Figure 1. Development of visual acuity in patients with unilateral ptosis for A, the affected eye and B, the unaffected eye. The gray area is the 95% normative range for Teller card acuity. Filled circles plot both longitudinal and cross-sectional visual acuity for patients with normal development. Open triangles plot both longitudinal and cross-sectional visual acuity for patients with systemic disorders and delayed development. Longitudinal data comprise 45 of the 55 patients.

Figure 2. Development of visual acuity in patients with bilateral ptosis for A, the nonpreferred eye and B, the preferred eye. The gray area is the 95% normative range for Teller card acuity. Filled circles plot both longitudinal and cross-sectional visual acuity for patients with normal development. Open triangles plot both longitudinal and cross-sectional visual acuity for patients with systemic disorders and delayed development.
Figure 3. A, The relationship between noncompensatory lid height and interocular visual acuity ratio. A negative eyelid height indicates the upper eyelid margin was below the pupillary center. B, Compensatory lid height (with the contribution of the frontalis muscle) and interocular visual acuity ratio. The shaded area in both plots depicts amblyopia indexed by an interocular ratio of 2.0 or higher. The line in each graph is the linear regression (nonsignificant) of their relationship.