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Major review

Congenital ptosis

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ABSTRACT

Congenital blepharoptosis presents within the first year of life either in isolation or as a part of many different ocular or systemic disorders. Surgical repair is challenging, and recurrence necessitating more than one operation is not uncommon. Not all patients with congenital ptosis require surgery, but children with amblyopia due to astigmatic anisometropia or deprivation may benefit from early surgical correction. A variety of surgical procedures to correct congenital ptosis have been described. The choice of procedure depends on a number of patient-specific factors, such as degree of ptosis and levator function, as well as surgeon preference and resource availability. We review the genetics, associated syndromes, and surgical treatments of congenital ptosis.

1. Introduction

Blepharoptosis, often abbreviated as ptosis, refers to an upper eyelid that is positioned lower than normal, which narrows the vertical dimension of the palpebral fissure. If present within the first year of life, it is considered congenital (Fig. 1). It may be either unilateral or bilateral and seen either in isolation or in conjunction with other ocular or systemic conditions.[70] In general, congenital ptosis is non-progressive, but it may be associated with abnormalities of visual development and function, including amblyopia. These complications may be minimized or avoided with early surgical correction.[70]

The eyelids are primarily elevated by the contraction of the levator palpebrae superioris (LPS) muscle, innervated by the superior branch of the third cranial nerve (CN3). The superior branch of CN3 also innervates the superior rectus muscle. Both LPS muscles receive innervation from a single, midline subnucleus in the rostral CN3 nucleus. Therefore, damage to the central subnucleus results in bilateral ptosis.

Epidemiological data regarding congenital ptosis are not widely available. One of the largest reports comes from China, published by Hu in 1987.[44] A population study of more than seven million people from multiple Chinese provinces, Hu's report provides information about a variety of genetic eye

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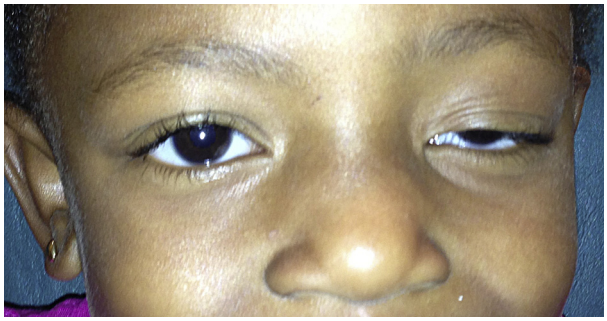

Fig. 1 – Congenital ptosis of the left upper eyelid.

diseases, including congenital ptosis. In that study, the prevalence of congenital ptosis was 0.18%. Pedigree analysis showed that the majority of cases were sporadic, although 18.4% were inherited in an autosomal dominant fashion and 14.5% in an autosomal recessive pattern. These findings cannot be extrapolated to other ethnic groups. In a more recent study from a tertiary hospital in Egypt, a retrospective review over a nine-year period found a total of 336 children with ptosis, 69% congenital.[28] Ptosis was unilateral in 65% of cases and the left side was more commonly affected (74%). Griepentrog et al reviewed all cases of childhood ptosis over a 40-year time period in Olmsted County, Minnesota. They identified 107 cases of ptosis, with an incidence of 7.9 per 100,000. Of these patients, 89.7% had congenital ptosis, although only 12% had a positive family history. The rate of congenital ptosis was 1 in 842 births. Only 3% were bilateral, and there was a slight predominance of left ptosis (55%).[36]

Many theories have been proposed regarding the pathogenesis of congenital ptosis. Historically, congenital ptosis has been thought of as a disorder of muscle development, but newer theories focus on disordered muscle innervation. Histopathologic studies have demonstrated a primary defect in the LPS muscle with fibrosis and decreased numbers of skeletal muscle fibers.[12,48] The exact mechanism of levator dysgenesis is poorly understood and could vary by condition. There are many other possible causes of congenital ptosis, including levator disinsertion secondary to birth trauma.[34] We shall review the etiology of congenital ptosis and options for surgical repair.

2. Genetics

In 1990, Vestal et al conducted a literature review investigating the concordance of congenital ptosis in monozygotic twins and found a heritability index of 0.75, indicating that 75% of the phenotype is attributable to genetic factors.[73] These data support a transmissible genetic defect contributing to this disorder. There are a variety of genes implicated in this process, with new loci being investigated and identified each year.

The first gene to be identified as a locus for isolated congenital ptosis was the PTOS1 gene.[29] Engle et al studied the DNA from 42 members of a family in which 20 members had isolated congenital ptosis in at least one eye. Fluorescent in-situ hybridization was performed and identified a 3 centi-Morgan (cM) region of chromosome 1 as being responsible for ptosis. For this gene, inheritance is autosomal dominant with incomplete penetrance.

In 2002, McMullan et al described an X-linked dominant form of isolated, bilateral congenital ptosis.[53] The family studied was noted to have a dominant inheritance pattern without male-to-male transmission. Genetic linkage studies identified the locus of interest as Xq24-q27.1.

The ZFH-4 gene was identified in 2002 after DNA analysis of a child with bilateral congenital ptosis who was found to have a balanced translocation of chromosomes 8 and 10.[54] The mutation in chromosome 8 was found to disrupt the ZFH-4 gene located at 8q21.12. This gene encodes a protein with a zinc-finger homeodomain that acts as a transcription factor. This protein has been shown to be prominently expressed in developing muscles and nerves.[47] The same gene product is also expressed in the developing midbrain and could affect the structure and function of the oculomotor cranial nerve nuclei.[38,57]

3. Associated syndromes

Normal extraocular muscle functioning depends upon normal innervation, which in turn requires normal cranial nerve development. Many well-characterized congenital syndromes display abnormal extraocular muscle innervation. Collectively, these syndromes are known as congenital cranial dysinnervation disorders (CCDDs), congenital disorders resulting from aberrant innervation of the ocular and facial musculature.[38] Many of these syndromes have associated ptosis. Ptosis can also be seen in association with dysfunction of the sympathetic nervous system, as in Horner syndrome, or with other forms of strabismus including congenital esotropia or exotropia.[39]

3.1. *Duane retraction syndrome*

Duane retraction syndrome (DRS) is the most common of the CCDDs. Type 1 DRS presents with limited abduction of the affected eye as well as contraction of both the medial and lateral rectus muscles upon attempted adduction, although adduction is intact or only slightly limited.[27] In type 2 DRS, abduction is usually intact but adduction is impaired in the affected eye. Type 3 DRS presents with limitations in both abduction and adduction. The contraction of the horizontal recti upon attempted adduction causes globe retraction, which leads to enophthalmos and resultant ptosis. Abnormal development of the motor neurons of the sixth cranial nerve leads to abnormal innervation of the lateral rectus.[43,57] Although the exact sequence and etiology is poorly understood, other cranial nerves can aberrantly innervate the lateral rectus.[43] This condition is usually sporadic and no single gene has been identified for DRS; however, various candidate genes have been mapped to chromosomes 2q31 and 8q13.[17,32]