PEDIATRIC OPHTHALMOPLAGIA AND PTOSIS WITH EPIDERMOLYSIS BULLOSA SIMPLEX-MUSCULAR DYSTROPHY (EBS-MD)

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Introduction

Epidermolysis bullosa (EB) is a genetic disorder of the skin and mucous membranes which causes blisters in response to minor trauma. The 4 types of EB are simplex (EBS), junctional EB, dystrophic EB, and mixed EB (Kinder syndrome). These are differentiated by the level at which the epidermis splits. EBS is the most common and involves blister formation at the intra epidermal layer. EBS encompasses all subtypes of EB having mechanical fragility and blistering confined to the epidermis. EBS can be further separated into suprabasal and basal subgroups, based on the histopathologic site of cleavage within the epidermis.1-3

Plectin is a giant multifunctional cytoplakin protein and plays a crucial role in stabilizing and orchestrating intermediate filament networks in cells. Mutations in the human plectin gene result in multiple diseases manifesting with muscular dystrophy, skin blistering, and signs of cardiomyopathy.4-6 Mutations in the gene for plectin (PLEC) cause three distinct subtypes of basal EBS: EBS with muscular dystrophy (EBS-MD), EBS with pyloric atresia (EBS-PA), and EBS Oghna. EBS-MD is the most common type and is an autosomal recessive disorder with neonatal skin blistering and delayed, progressive muscular weakness.7-9 In all cases, skin fragility seems to be mild and improvement of skin involvement with time is described.10-11 The Muscular dystrophy associated with EBS has been described by Shimizu et al.10 None of the 10 patients in their cohort had ocular motility manifestations. There is only one case in the ophthalmic literature of plesctin and epidermolysis in a patient with EBS-MD described by Auringer et al.12

Methods

Billing records and an institutional clinical database were searched for all patients with EBS evaluated from 2000 to 2015. Medical records of patients identified with EBS were retrospectively reviewed and 6 patients with EBS-MD and documented eye exams were identified. Three of the 6 patients had ocular abnormalities and will be presented in more detail.

Results

Subject 1: An 11-year-old African-American boy with EBS was referred to the pediatric ophthalmology clinic at Cincinnati Children’s Hospital Medical Center to screen for ocular surface issues. A diagnosis of EBS was made during infancy by skin biopsy in an evaluation of skin blistering at birth. The patient had a history of intellectual disability but no motor developmental delays. Uncorrected visual acuity was 20/25 in each eye. Blepharitis was present bilaterally but the ocular surface was normal. Bilateral symmetric ptosis was noted however no anomalous head position was present and margin-reflex distance was not documented. Ocular motility was moderately limited in side gazes and severely limited in upgaze and downgaze. Alternating exotropia of 40-45° was present in primary gaze. The remainder of the exam was unremarkable. The patient’s family declined strabismus surgery. The patient returned at age 13 with a complaint of decreased vision. Examination revealed normal visual acuity but increased ptosis with compensatory chin up head position. Ophthalmoplegia was severe in all gazes and exotropia was unchanged. His vision was stable and he was then lost to follow up for 4 years. He was later seen after being admitted to the hospital at age 17 to the Pediatrics service for poor oral intake, malnourishment and progressive muscle weakness. His parents reported his inability to climb stairs starting at age 14 and the need for a wheelchair at age 16. He was found to have left ventricular non-compaction cardiomyopathy. During the hospitalization, ocular findings were unchanged as compared with the eye exam performed 4 years prior. Muscle weakness and dysphagia progressed despite proper systemic management and improved nutrition. He was evaluated for muscular dystrophy and found to have homocysteine mutations for PLEC1 confirming a diagnosis of plectin deficiency EBS-MD. At age 21, ptosis, exotropia and ophthaloplegia had improved compared with his findings at age 13 years (Figure 1). Chronic blepharitis and recurrent chalazia remained his chief ocular complaint.

Subject 2

A 4-year-old Caucasian female patient was an EBS patient with in the prior diagnosis of plectin deficiency EBS-MD. EB was diagnosed at age 5 months. She had delays in gross motor development which was initially attributed to her extreme prematurity but she was later evaluated for muscular development and found to have PLEC1 mutations. She sat alone at about 18 months and walked at age 2 years old. Parents reported chronic neck weakness, difficulty bending over and standing up, fine motor delay and language delay. Family history was significant for a 1 year old sister with the same PLEC1 mutations. The patient’s initial eye exam at 4 years of age was normal with the exception of periorbital crusted skin blisters. When she returned 2 years later, she had developed bilateral ptosis with compensatory chin up head position and bilateral limitation of abduction (Figure 2). Trichiasis was present but not sufficient to require treatment. The patient’s younger sister had normal eye exams at age 1 and age 4 and no signs of developmental delays or muscle weakness yet.

Subject 3

A 6-year-old boy with EBS and mutations in PLEC1 presented for ocular surface evaluation. Examination revealed age-appropriate hyperopia and was otherwise unremarkable. When he returned at age 12 years, mild acquired ptosis was present without a compensatory chin-up head position. Ocular motility and the remainder of the exam were unremarkable. The patient and his family denied symptoms of muscle weakness or developmental delay.

Conclusions

Our series is the largest to evaluate ocular manifestations of EBS-MD and demonstrated ptosis in 3 of 6 patients and ophthaloplegia in 2 of 6 patients. Ptosis and ophthaloplegia may develop early in the course of EBS-MD while muscle weakness becomes evident.

References


The authors of this study do not have any financial interests in the material presented.