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The Frequency of Signs of Meibomian Gland Dysfunction in Children with Epidermolysis Bullosa

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Purpose: To determine the frequency of meibomian gland dysfunction (MGD) in children with epidermolysis bullosa (EB).

Design: Hospital-based cross-sectional study.

Participants: One hundred five children with different forms of EB.

Methods: Prospective ophthalmic examination of children with EB presenting over seventeen months including meibomian gland assessment using a recognized classification.

Main Outcome Measures: Frequency of MGD.

Results: One hundred five children were recruited, 8.6% with junctional EB, 34.3% with simplex EB, 34.3% with autosomal recessive dystrophic EB, and 22.9% autosomal dominant dystrophic EB. Mean age was 7.42 years (range, 0.08−17.75 years). Ninety-two children (87.62%) demonstrated 1 or more features of MGD.

Conclusions: Most children with EB exhibit signs of MGD. To the best of our knowledge, this is the first prospective ocular surface evaluation in children with EB to include lid margin evaluation using a recognized classification system. Our findings help explain some of the ocular surface anomalies seen in children with EB. *Ophthalmology 2016;■:1−9 © 2016 by the American Academy of Ophthalmology.*

Epidermolysis bullosa (EB) describes a genetically and clinically heterogeneous group of inherited bullous disorders associated with abnormalities of the basement membrane zone of skin and mucous membranes. It is characterized by varying degrees of skin fragility and blistering and occasionally mucosa, after friction or mild mechanical trauma. Present at birth, EB does not discriminate as to race, ethnic origin, or gender and many times appears spontaneously because of a mutant gene.

More than 1000 mutations in more than 15 structural genes encoding several structural proteins within the epidermis and basement membrane zone have been documented, resulting in specific subtypes of EB.[1] These subtypes are based on the ultrastructural site of blister formation and include EB simplex (EBS); junctional EB (JEB), which includes Herlitz and other subtypes; dystrophic EB, comprising dominant (DDEB) and recessive (RDEB) variants; and Kindler syndrome, which recently was included in its own category because of its mixed levels of skin cleavage.[1]

Several publications have reported the ophthalmic findings in EB, but almost all have been retrospective.[2−7] Ocular features are thought to result from a lack of adherence and disruption of either the corneal or conjunctival epithelium, or both, in response to any friction or trauma. Repeated corneal and conjunctival blistering can lead to corneal abrasion, punctate keratopathy, symblepharon, ectropion, entropion, and corneal scarring, with reduced visual acuity and even blindness. The most severe[2] and most frequent[8] ophthalmic complications have been reported in the RDEB and JEB groups.

The degree of ocular involvement generally parallels the extent of the skin disease. Tong et al[2] performed a retrospective case review of 181 patients with JEB, EBS, and dystrophic EB. They reported that the incidence of ocular complications varies widely with subtype and occurred in 12% of patients with EBS, 40% with JEB, 51% with RDEB, and 4% with DDEB. The rate of meibomian gland dysfunction (MGD) was unreported.[9]

Meibomian gland dysfunction, as defined by the International Workshop on MGD, is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by qualitative or quantitative changes in glandular secretion, terminal duct obstruction, or both. This may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease.[10] It is a form of posterior blepharitis affecting the Meibomian glands and their ducts, to be distinguished from anterior blepharitis, which is confined to the lash line of the lid margin and its environs. Meibomian gland dysfunction subtypes include noncicatricial MGD, in which initially the meibomian orifices retain their position anterior to the mucocutaneous junction, and cicatricial MGD.[11,12] In the latter, submucosal connective tissue scarring leads to ductal exposure with posteriorization of affected orifices across the mucocutaneous junction. It may occur as a primary condition, in combination with noncicatricial MGD or in association with various forms of cicatricial conjunctivitis.[12]

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Table 1. Epidermolysis Bullosa Subtypes

Major Epidermolysis Bullosa Type and Subtype	No. of Patients (%)
EBS	**36 (34.3)**
DM	17 (16.2)
Localized	9 (8.6)
Superficialis	3 (2.9)
Recessive	3 (2.9)
Generalized other	2 (1.9)
Plakophilin-1 deficiency	2 (1.9)
JEB	**9 (8.6)**
Herlitz	5 (4.8)
non-Herlitz	4 (3.8)
DEB	60 (57.1)
RDEB	**36 (34.3)**
DDEB	**24 (22.9)**
Total	
Major type	105 (100)
Subtype	105 (100)

DDEB = dominant dystrophic epidermolysis bullosa; DEB = dystrophic epidermolysis bullosa; DM = Dowling-Meara; EBS = epidermolysis bullosa simplex; JEB = junctional epidermolysis bullosa; RDEB = recessive dystrophic epidermolysis bullosa.
Boldface indicates major subtypes.

Table 2. Frequency of Meibomian Gland Dysfunction

	All Subtypes	Epidermolysis Bullosa Simplex	Dominant Dystrophic Epidermolysis Bullosa	Recessive Dystrophic Epidermolysis Bullosa	Junctional Epidermolysis Bullosa
Frequency of meibomian gland dysfunction, no./total no. (%)	92/105 (87.62)	30/36 (83.33)	17/24 (70.83)	36/36 (100)	9/9 (100)

Meibomian gland dysfunction has not been reported previously to be a universal or high-frequency finding in EB in the published retrospective literature. Previous reports in lid abnormalities in these children is limited to the absence or presence of blepharitis,[13,14] which is reported to vary from 0.37% to 17.65%, depending on EB subtype.[8] The National EB registry reported blepharitis as an uncommon finding, with highest frequencies in RDEB inversa and severe generalized RDEB (approximately 18% in each) and in JEB subtypes (6%–7%).[8] Blepharitis was reported in approximately one fifth of RDEB patients in a study by Gans.[13] The cause of this and many other ophthalmic findings remains unexplained. A report by Bron et al[11] classified and described lid changes in MGD and stated that the condition is seen increasingly in cicatrizing conditions of the eye. Because EB may be considered to be a cicatrizing disease, we performed a cross-sectional study of all patients with EB using the grading and classification of Bron et al[11] to evaluate the frequency of MGD in children with EB of any type.

Methods

Patients were recruited from the Departments of Ophthalmology and Dermatology, Great Ormond Street Hospital for Children, and the offices of one of the investigators (K.K.N.). There is a dedicated team

Table 3. Features of Meibomian Gland Dysfunction Occurring in Each Epidermolysis Bullosa Subtype

Feature	Feature No. in Graph 5.4	All Subtypes	Epidermolysis Bullosa Simplex	Junctional Epidermolysis Bullosa	Recessive Dystrophic Epidermolysis Bullosa	Dominant Dystrophic Epidermolysis Bullosa
Lid margin						
Thickening	1	**11/105** (10.48)	**3/36** (8.33)	**2/9** (22.22)	**6/36** (16.67)	**0/24**
Rounding	2	**14/105** (13.33)	**3/36** (8.33)	**4/9** (44.44)	**6/36** (16.67)	**1/24** (4.17)
Telangiectasia	3	**36/105** (34.29)	**12/36** (33.33)	**5/9** (55.56)	**12/36** (33.33)	**7/24** (29.17)
Hyperkeratinization	4	**10/105** (9.52)	**1/36** (2.78)	**1/9** (11.11)	**8/36** (22.22)	**0/24**
Irregularity	5	**17/105** (16.19)	**6/36** (16.67)	**2/9** (22.22)	**9/36** (25.00)	**0/24**
MCJ						
Retroplacement	6	**19/105** (18.10)	**7/36** (19.44)	**1/9** (11.11)	**10/36** (27.78)	**1/24** (4.17)
Ridging	7	**15/105** (14.29)	**3/36** (8.33)	**1/9** (11.11)	**11/36** (30.56)	**0/24**
Meibomian orifices						
No. decreased	8	**13/105** (12.38)	**3/36** (8.33)	**4/9** (44.44)	**6/36** (16.67)	**0/24**
Duplication	9	**4/105** (3.81)	**3/36** (8.33)	**0/9**	**0/36**	**1/24** (4.17)
Capping	10	**25/105** (23.81)	**6/36** (16.67)	**3/9** (33.33)	**9/36** (25.00)	**7/24** (29.17)
Pouting/plugging	11	**61/105** (58.10)	**17/36** (47.22)	**9/9** (100.00)	**26/36** (72.22)	**9/24** (37.50)
Retroplacement	12	**8/105** (7.62)	**4/36** (11.11)	**0/9**	**4/36** (11.11)	**0/24**
Distichiasis	13	**4/105** (3.81)	**2/36** (5.56)	**2/9** (22.22)	**0/36**	**0/24**
Madarosis	14	**7/105** (6.67)	**2/36** (5.56)	**2/9** (22.22)	**3/36** (8.33)	**0/24**
Duct exposure	15	**5/105** (4.76)	**1/36** (2.78)	**0/9**	**4/36** (11.11)	**0/24**
Acini concretions or chalazia	16	**3/105** (2.86)	**1/36** (2.78)	**1/9** (11.11)	**1/36** (2.78)	**0/24**
Secretions	17	**4/105** (3.81)	**1/36** (2.78)	**0/9**	**3/36** (8.33)	**0/24**

MCJ = mucocutaneous junction.
Data are number/total number (%).