

Thyroid Eye Disease-Related Epiblepharon: A Comparative Case Study

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Purpose: This study describes the clinical features and management of epiblepharon as a manifestation of thyroid eye disease (TED). In addition, we compare the frequency and age in Asian and non-Asian patients, and discuss pathophysiologic implications.

Design: Retrospective case-control study.

Methods: This is a single-center retrospective review that identified 172 adult patients (age 19 to 83) with TED that were consecutively evaluated by 1 author (T.J.M.) between December 2015 and July 2018. Diagnosis of TED and epiblepharon was based upon clinical assessment as documented in the medical record.

Results: In a cohort of 172 patients (mean age 52; 138 female), 3 patients with acquired epiblepharon were identified, all of whom were Asian. The proportion of affected Asian patients (3 of 17, 17.6%) was significantly higher than that of non-Asian patients (0/155, $P < 0.001$). Patients with epiblepharon were also significantly younger than those without epiblepharon, 29.7 ± 2.1 versus 48.7 ± 13 years of age ($P = 0.026$). All 3 patients underwent surgical correction with lateral canthoplasty and anterior lamellar pretarsal fixation with successful outcomes.

Conclusions: Lower eyelid epiblepharon may occur in TED. In our clinic-based population, this finding was significantly more frequent in Asian patients and in younger patients. Relieving horizontal tension in conjunction with anterior lamella pretarsal fixation is an effective method of correcting TED-associated epiblepharon.

Key Words: Asian, epiblepharon, eyelid retraction, graves ophthalmopathy, thyroid eye disease

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Thyroid eye disease (TED) results from autoimmune inflammation of periocular tissues, most notably the extraocular

muscles and orbital fat.¹ Clinical manifestations are very heterogeneous. Common findings include eyelid retraction, proptosis, restricted ocular motility, and optic nerve compression.²

Lower eyelid malposition can occur in TED with retraction occurring in a large proportion of patients. Entropion is uncommon, almost exclusively occurring as a complication of surgery.² Lower eyelid epiblepharon is an under-recognized feature of TED, and is not included as a feature of TED in most ophthalmic textbooks including the Basic and Clinical Science Course.³ Epiblepharon is the inward rotation of the anterior lamella and eyelashes without malposition of the tarsus. Epiblepharon has been reported in TED within Asian populations and literature.^{4–9} The lack of published reports in non-Asian populations raises the question of an anatomic predisposition. There have been no previous studies comparing prevalence between patients of different race.

In this retrospective case-control study, we evaluated a clinic-based population for acquired lower eyelid epiblepharon as a consequence of TED. We describe key demographic and clinical features, and management.

METHODS

Demographic Assessment

This study was approved by the Institutional Review Board of the Johns Hopkins University School of Medicine and adheres to the requirements of the Health Insurance Portability and Accountability Act. A medical record database search was used to identify all adult patients with TED that were consecutively evaluated by 1 author (T.J.M.) between December 2015 and July 2018. Diagnosis was based upon clinical assessment as documented during the initial patient visit. Race assignment was based upon self-identification.

Surgical Technique

In each case, lateral canthoplasty with loosening of the lateral canthal tendon was performed in conjunction with anterior lamellar pretarsal fixation. The lateral canthoplasty consisted of a standard canthotomy and cantholysis. The lateral tarsus was allowed to retract medially to a position without abnormal tension. The eyelid was then secured to the cut edge of the lateral canthal tendon with a “hang back” suture. Pretarsal fixation was performed by removing a thin strip of orbicularis oculi through a subciliary incision. The skin was closed with 6–0 Vicryl sutures, placed in an interrupted fashion, with deep fixation to the inferior anterior tarsus. This portion of the surgery is similar to that commonly employed for congenital epiblepharon repair.

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TABLE 1. Thyroid Eye Disease: Patient Demographics

Ethnicity	No., %	Sex: %Male	Years of Age \pm SD
Asian	n = 17, 9.9%	n = 5, 29%	46.6 \pm 14
White	n = 86, 50%	n = 13, 15%	55.3 \pm 16
Black	n = 51, 30%	n = 11, 22%	51.4 \pm 14
Hispanic	n = 6, 3.5%	n = 0, 0%	45.9 \pm 12
Other*	n = 12, 7.0%	n = 6, 50%	43.8 \pm 15

*Remaining ethnicity was comprised of roughly equal numbers of patients from India and the Middle East.

Statistical Analysis

The data were entered and analyzed using Microsoft Excel, with a significance level of $P < 0.05$. Fisher exact test was used to compare the proportion of Asian patients with epiblepharon and non-Asian patients with epiblepharon. A 2-tailed student t test was used to analyze the difference in age of participants with epiblepharon and without epiblepharon.

RESULTS

Demographics

3 patients with acquired lower eyelid epiblepharon were identified within the 172 adult patients with TED. Table 1 summarizes patient demographics. All 3 patients with epiblepharon were Asian females, between ages 28 to 32 years. This contrasts the demographics of the entire group, with a mean age of 52 years (range 19–83). 34 patients were male and 138 were female.

A total of 17 Asian patients with TED were identified. The frequency of epiblepharon within this population was 17.6%, which was significantly higher than in the non-Asian population (0/155, $P < 0.001$, Fisher's exact test). Table 2 summarizes the demographics of Asian patients with and without epiblepharon. Patients with epiblepharon were significantly younger than those without epiblepharon, 29.7 ± 2.1 versus 48.7 ± 13 years of age ($P = 0.026$, Student t test).

Case Descriptions

Case 1

A 32-year-old Asian female with a history of hyperthyroidism presented for evaluation of TED. She had no previous history of eyelid or ocular surgery. Best-corrected visual acuity (BCVA) was 20/20 in both eyes, with no evidence of a compressive optic neuropathy. She had asymmetric proptosis, with exophthalmometry measurements of 18 mm OD and 21 mm OS. The right upper and lower eyelids were in normal position. The left upper eyelid

TABLE 2. Comparison of Asian Thyroid Eye Disease Patients With and Without Epiblepharon

	No., %	Sex: %Male	Years of Age \pm SD
With epiblepharon	n = 3, 17.6%	n = 0, 0%	29.7 \pm 2.1*
Without epiblepharon	n = 14, 82.4%	n = 5, 36%	48.7 \pm 13

*The difference in age was statistically significant ($P = 0.026$, student t test).

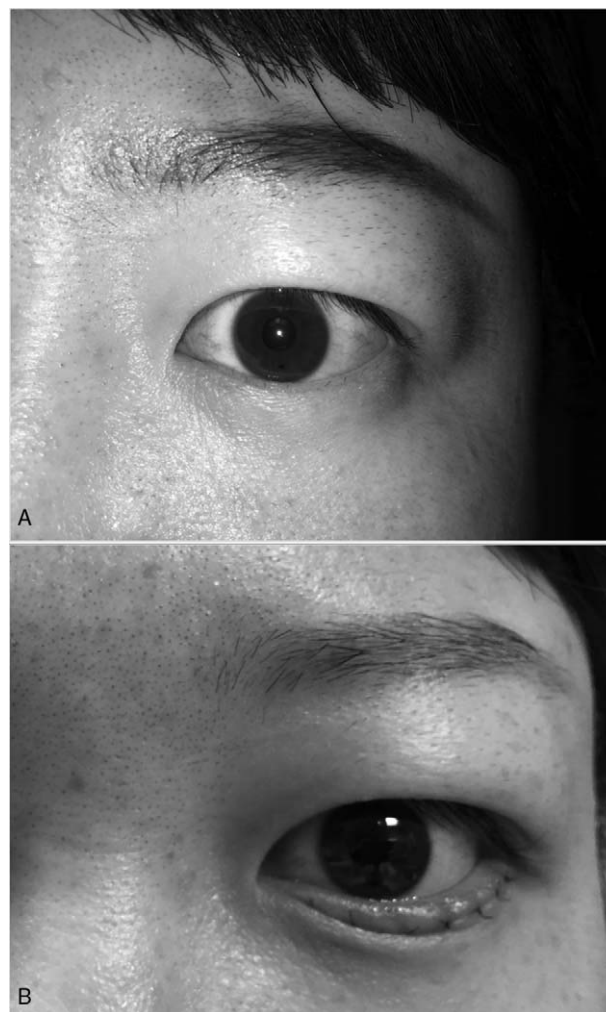


FIGURE 1. Thyroid eye disease-related epiblepharon: external photograph of involved left eye of patient 1 (A). The patient has cut the lashes to manage ocular irritation. The same eyelid 6 weeks after surgical repair with correction of epiblepharon (B).

was retracted with 1 to 2 mm of superior scleral show. There was epiblepharon of the left lower eyelid with lashes contacting the ocular surface, with associated conjunctival injection and superficial punctate keratopathy (SPK) (Fig. 1A). The left lower eyelid was mildly retracted to a slightly greater degree laterally than medially, with 1 mm of inferior scleral show. Her Clinical Activity Score (CAS) was 1. Surgical epiblepharon repair was performed with improvement in the ocular surface disease and resolution of foreign body sensation (Fig. 1B).

Case 2

A 29-year-old Asian female with a history of TED presented with bilateral lower eyelid epiblepharon. She had a history of previous left medial wall decompression and treatment with oral and intravenous steroids. She had also undergone electrolysis of the central lower eyelids to address contact of the eyelashes with the ocular surface. On initial presentation, BCVA was 20/25 in each eye. Exophthalmometry measured 26 mm OD and 21 mm OS. She had a left relative afferent pupillary defect of 0.3 log units and depressed visual field but normal-appearing optic nerve. There was bilateral upper eyelid retraction, and bilateral lower eyelid epiblepharon with moderate conjunctival injection and

inferior SPK. The lashes were sparse but not entirely absent from the central thirds of her lower eyelids, a consequence of the electrolysis. The remaining lashes were in contact with the corneas. There was also lower eyelid retraction with inferior scleral show of 1 mm OD and 2 mm OS. Her CAS score was 2. Initially, endoscopic left medial decompression of residual apical bone was performed, with resolution of the optic neuropathy. She then underwent bilateral lower eyelid epiblepharon repair with improvement in lower lid position and resolution of foreign body sensation. Months later, when clinically stable, she underwent bilateral upper lid retraction repair.

Case 3

A 28-year-old Asian female with findings suggestive of both TED and myasthenia gravis presented for evaluation. Systemic findings included hyperthyroidism and proximal muscle weakness. On initial presentation BCVA was 20/30 OD and 20/20 OS. She was noted to have near-complete ophthalmoplegia bilaterally with right hypotropia, largely attributable to myasthenia gravis. Exophthalmometry measured 19 mm OD and 15 mm OS. She had right lower eyelid epiblepharon with eyelashes contacting the ocular surface, resulting in marked injection, chemosis, and diffuse SPK. There was mild lower eyelid retraction with 1 mm of inferior scleral show, again more pronounced laterally. The reduced visual acuity OD was attributed to her ocular surface disease without evidence of an optic neuropathy. Her CAS score was 3. She underwent right lower eyelid epiblepharon repair with marked improvement in ocular surface disease.

DISCUSSION

This is the first study to assess and compare the occurrence rate of TED-related epiblepharon between races. TED related epiblepharon was seen exclusively in Asian patients, with an occurrence rate of 17.6%. This occurrence rate was significantly higher than non-Asian patients ($P < 0.001$). Of note, within this study, the mean age of Asian patients with epiblepharon was significantly younger than those Asian patients without epiblepharon (29.7 ± 2.1 vs 48.7 ± 13 years of age, $P = 0.026$). All patients were successfully managed surgically by reducing horizontal tension and fixating the anterior lamella to the tarsal plate.

Several factors may contribute to the development of epiblepharon in the setting of TED and explain the increased incidence in the Asian population. Possible anatomic considerations include fat hypertrophy, eyelid retraction, and proptosis. Age of onset also seems to play a critical role.

Hypertrophy of orbital fat is likely the primary cause of TED-related epiblepharon. Expansion of the lower eyelid fat compartment pushes the anterior lamella over a rigid and frequently retracted posterior lamella. Asian patients have relative anterior attachment of the orbital septum,¹⁰ and we postulate that this may predispose these patients toward the development of epiblepharon. There are important age-related differences in the proportion of fat versus muscle hypertrophy in TED. Younger patients have proportionally more fat than muscle hypertrophy.^{11,12} Orbital CT tomography of our 3 patients with epiblepharon and TED demonstrate mild to moderate muscle hypertrophy, with presumed disproportionate fat hypertrophy (Fig. 2). The relatively anterior attachment of the orbital septum combined with proportionally greater fat hypertrophy puts young

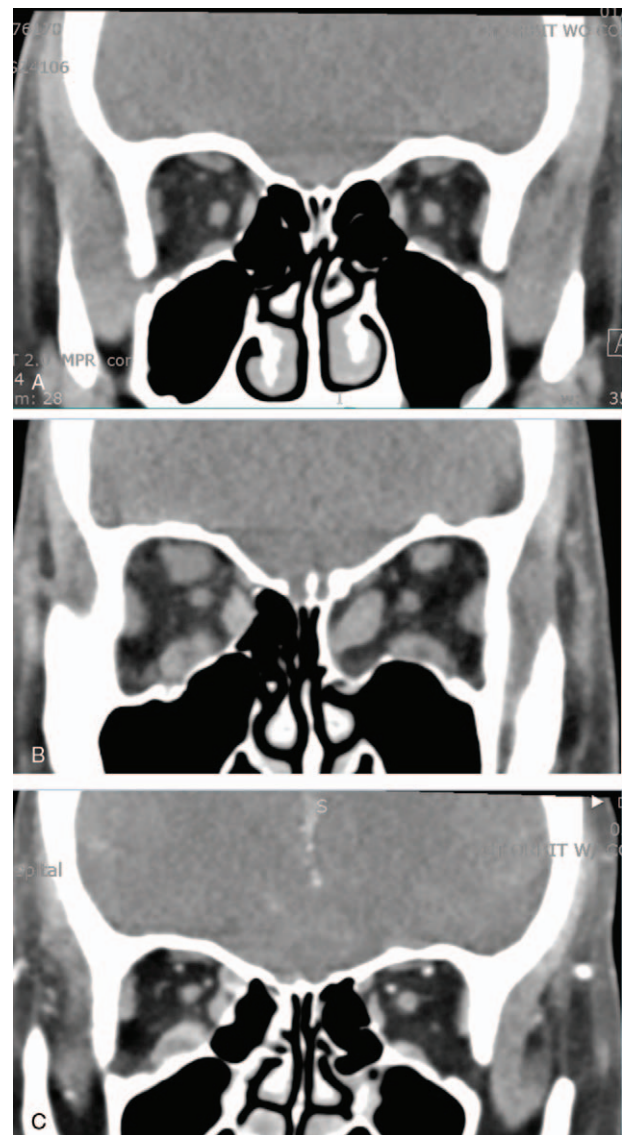


FIGURE 2. Computed tomography of patients 1 (A), 2 (B), and 3 (C). Note the relative mild muscle enlargement, suggesting that the proptosis related primarily to fat hypertrophy.

Asian patients at a disproportionately higher risk of developing TED-related epiblepharon.

Eyelid Retraction is the most common malposition of the lower eyelid seen in patients with TED. Epiblepharon is exacerbated by relative retraction of the posterior lamella, with consequential overriding of the anterior lamella. This was specifically assessed in the case series described by Park and colleagues, who found that eyelid retraction was more severe in TED patients with epiblepharon compared with those without.⁵ Variation in baseline eyelid anatomy and fat hypertrophy likely determine whether TED patients with lower eyelid retraction develop epiblepharon or not.

Globe proptosis contributes to the relative retraction of the eyelid. 2 of our patients had markedly asymmetric proptosis with epiblepharon on the more involved side. 1 patient had symmetric proptosis with bilateral epiblepharon. Anterior globe displacement in the setting of lower eyelid malposition may contribute to the relative inward position of the eyelashes, increasing ocular surface contact. Globe displacement also contributes to horizontal tightening leading to further inferior eyelid displacement. It is also

possible however that proptosis is simply another consequence of fat hypertrophy and therefore parallels but does not contribute to the development of TED related epiblepharon.

Age of onset also seems to be a pathophysiologic contributor. In the study by Park et al,⁵ the mean age of patients with epiblepharon in the setting of TED was 34.2 years, significantly lower than that of TED patients without epiblepharon, 46.5 years. The mean age of our cohort was similarly young at 29.7 years \pm 2.1 years, which was significantly lower than those without epiblepharon (Table 2). As discussed above, more pronounced fat hypertrophy in younger patients is a likely explanation. In addition, increasing eyelid laxity that comes with age may also be protective.

A racial predisposition in Asian patients is strongly supported by our data. It has been proposed that Asians are predisposed to entropion, due to anteriorly positioned orbital fat within the Asian lower eyelid.¹³ This allows fat to prolapse close to the lash line in Asian eyelids, predisposing patients to the development of TED-related epiblepharon. Previous reports of epiblepharon with TED are found almost exclusively in Asian populations.^{4–7} We identified only one study with mention of epiblepharon in non-Asian patients. In that case series of 9 patients, most were Asian, 1 was black, and 2 were white.⁸ The remaining literature is derived entirely from Asian populations. Park et al⁵ found a prevalence of 8.5% of acquired lower epiblepharon in 494 Korean patients with TED. Similarly, a study from Singapore reported a prevalence of 11.5%.⁴ The prevalence in our Asian patients was higher at 17.6%. This difference is likely reflective of our relatively small sample size and possibly a referral bias. The anatomic tendency for the anterior lamella to override the tarsus is likely the deciding factor in the development of epiblepharon as opposed to simple eyelid retraction in some Asian patients with TED.

TED-related epiblepharon is effectively managed surgically. This notion is supported by our experience and previous publications. Our technique and previously described techniques all involve a subciliary incision with fixation of the anterior lamella to the tarsus. The only significant variation is whether or not this is combined with canthoplasty. In the cohort of 53 TED patients described by Park et al,⁶ 12 underwent surgical repair. They describe repair with cilia-rotating tarsal fixation sutures performed in isolation without canthoplasty.⁶ Similar to our preferred technique, Sundar et al⁷ combined pre-tarsal fixation and canthoplasty. Although both techniques seem to be successful, we prefer eyelid loosening canthoplasty, as this also addresses mild retraction.

Nomenclature is deserving of brief discussion. Previous authors have applied the term acquired epiblepharon to the inward eyelid rotation encountered in patients with TED. Entropion refers to rotation of the entire eyelid including the tarsus or posterior lamella and we agree that epiblepharon is a more appropriate label. However, in the setting of TED, the pathophysiology is likely more complex than common epiblepharon, hence the use of our preferred label, TED-related epiblepharon.

Limitations of this study include its moderate sample size, and use of data from a single academic referral center. In addition, because of its retrospective design, we cannot exclude the possibility that the epiblepharon was present before diagnosis of TED. Although all 3 patients with epiblepharon attested that this finding was new. Furthermore, we have described only 1 surgical technique in correction of TED-related epiblepharon, and we acknowledge that there are various techniques, some of which may prove superior.

In conclusion, lower eyelid epiblepharon may occur in TED and occurs more frequently in the Asian population. Younger patients with TED are at higher risk of developing TED-related epiblepharon. Relieving horizontal tension in conjunction with anterior lamella pre-tarsal fixation is an effective treatment for TED-associated epiblepharon.

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