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ORIGINAL STUDY

Histopathological Changes of Levator Palpebrae Superioris Muscle in Different Degrees of Congenital Ptosis

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Abstract

Objectives: To evaluate the Histopathological changes in specimens of levator palpebrae superioris muscle of patients with different degrees of congenital Ptosis.

Background: Ptosis, also called blepharoptosis, is known as the drooping of the upper eyelid. Simple congenital ptosis is the most prevalent form of congenital ptosis. Levator palpebrae superioris (LPS) and Muller’s muscle are two muscles of the upper eyelid responsible for its elevation. The levator palpebrae superioris is a triangular-shaped muscle located in each upper eyelid.

Patients and methods: This prospective analysis included a total of 30 eyelids of patients with different degrees of ptosis eligible for the study who underwent levator resection through a skin approach and then sent for assessment by a histopathologist. Patients presented with ptosis were examined and enrolled from March 2022 to June 2023, from the outpatient ophthalmic clinic of Menoufiya University Hospital.

Results: There was a statically significant difference between the studied cases regarding percentage of muscle fiber components, percentage of fatty tissue components and percentage of fibrosis. The presence of muscle fibers correlates with the degree of ptosis and levator muscle function. The severity of congenital ptosis correlates positively with the degree of histopathological changes in the levator muscle.

Conclusion: Examination of all cases with different degrees of congenital ptosis show significant correlation between histopathological findings and grades of ptosis as follows: Increasing fatty tissue infiltration and fibrosis in severe congenital ptosis more than moderate more than mild ptosis. The presence of muscle fibers in mild ptosis is more than moderate than in severe ptosis.

Keywords: Congenital ptosis, Levator, Muscle, Palpaberae, Superioris

1. Introduction

Ptosis, also called blepharoptosis, is known as the drooping of the upper eyelid, and the patient usually presents with the complaint of the defect in vision and cosmesis. It can decrease or even occlude the vision completely. It can be congenital or acquired, or it can be neurogenic, myogenic, aponeurotic, mechanical, or traumatic in origin [1].

Among all cases of ptosis, congenital ptosis is the most common type which seems to be more prevalent in males. Simple congenital ptosis is the most prevalent form of congenital ptosis. Among acquired cases, aponeurotic ptosis is the most common type which usually presents in late adulthood [2].

The levator palpebrae superioris is a triangular-shaped muscle located in each upper eyelid. The primary function is elevation and retraction of the upper eyelid, it is supplied by the superior branch of the oculomotor nerve, any problem in levator muscle lead to blepharoptosis [3].
Levator muscle dystrophy causes simple congenital ptosis. On the other hand, involutional changes in the eyelid are the most common pathogenesis in adult ptosis. Deceasing tone and thinning of the levator muscle, due to aging, results in abnormal position of the eyelid. Disinsertion of the levator aponeurosis, or its dehiscence, after any trauma or surgery, can also lead to ptosis.

Proper diagnosis and management of blepharoptosis require assessment of the following measurements: Levator muscle function, Margin-reflex distance, Palpebral fissure height and Margin crease distance [4].

Surgical correction of ptosis include Levator muscle resection; Levator muscle gets shortened by resecting the muscle if it is not paralyzed completely with mild (2 mm) to moderate (3–4 mm) ptosis.

There are different approaches for this purpose: Everburnsch; approach through the skin, Blaskovics; approach through palpebral conjunctiva. And Fasannella-Servat: a portion of the tarsal plate, palpebral conjunctiva and Muller’s muscle get excised along with levator resection. It is usually a proposed option in minimal ptosis [1].

The aim of the work was to evaluate the Histopathological changes in specimens of levator palpebrae superioris muscle of patients with different degrees of congenital ptosis.

2. Patients and methods

This prospective analysis included a total of 30 eyelids of patients with different degrees of ptosis eligible for the study who underwent levator resection through skin approach then sent for assessment by histopathologist. Patients presented with ptosis were examined and enrolled from March 2022 to June 2023, from the outpatient ophthalmic clinic of Menoufia University Hospital. The study was approved by the Ethical Committee of Menoufia Faculty of Medicine and in accordance with the Declaration of Helsinki. As congenital ptosis is an uncommon condition compared with other types of ptosis, sample size will be estimated according to rate and time, all eligible patients from those attending the Ophthalmology Department at the University Hospitals for at least 6 months; will included in this study. The rate estimation is about five patients/month, so it is expected to include 30 patients in the study.

‘Inclusion criteria included patients with different degrees of ptosis, above 2 years of age, in whom it will be possible to accurately calculate levator function (LF). No previous surgery performed to correct the ptosis’, and ‘Exclusion criteria included age below 2 years, patients with Marcus Gunn Jaw Winking syndrome, patients with acquired ptosis, patients with any eyelid scar and patients with any previous ptosis surgery, Co-existence of Ocular Pathology other than ptosis’.

The details of the study and the procedure were explained to eligible patients and informed consent was obtained from their guardians.

History (Patients were evaluated for age, gender, family history, medical history, surgical history, ocular history including previous ophthalmic surgeries, history of trauma and presenting symptoms (onset and diurnal variability). Also, any congenital anomalies or syndromes were recorded if present.

Examination (all the patients underwent full preoperative ophthalmologic examination including general ophthalmological examination and detailed physical examination was done and relevant investigations in preparation for general anesthesia were obtained in correspondence with an anesthesiologist).

Classification of ptosis: According to the Beard technique, ptosis is classified as mild with a drop of 1–2 mm in the lid margin from its normal position (cover upper 2 mm of superior limbus), moderate with a drop of 3 mm, and severe with a drop of 4 mm or more. By another way, mild ptosis is when the lid margin is between its normal position and the upper margin of the pupil in normal daylight, moderate ptosis is when the lid margin covers the upper margin of the pupil but does not block the visual axis, and severe ptosis is when the lid margin blocks the visual axis and may even cover the entire cornea.

Evaluation of ptosis: the following preoperative eyelid measurements were taken for every case: (levator muscle function and its grade (according to Berke’s method), degree of ptosis (Margin reflex distance, palpebral fissure height (PFH), Upper lid crease position if present, Margin crease distance and some of photographs of the eyes with different degrees of ptosis were taken after proper consent and were included in the patient's record for documentation.

Procedure Most of surgeries were done under general anesthesia and some under local anesthesia. In cases of general anesthesia we also used local anesthesia 1–2 ml of 2 % lignocaine with 1 : 200 000 adrenalin to obtain adrenalin effect. Local anesthesia is directly injected at subcutaneous with avoiding deep penetration to the muscle area and then massage is done for 5 : 10 min prior to operation. If the patient is awake as in local anesthesia, the lid height and contour are examined after two additional temporarily 5/0 Vicryl are tied.
Under aseptic conditions. The eyelid crease line was marked with a marker. If the eyelid crease line was absent, it was made using a caliber and a marker at a distance of 6–10 mm from the lid margin or by matching the contralateral eyelid crease. Two toothed forceps hold the two edges of skin incision at the center upwards and a central cut in orbicularis oculi was done with Wescott scissors. The rest of orbicularis was then opened horizontally with Wescott scissors. The skin-muscle flap was then dissected superiorly exposing the orbital septum and underlying preaponeurotic fat pad. The septum was opened horizontally throughout the entire length of the incision and the preaponeurotic fat pad was exposed which was retracted superiorly to display the levator aponeurosis, Whitnall’s ligament and levator muscle (Fig. 1).

The edge of levator aponeurosis was identified and dissected off the tarsus throughout the entire length of the incision, avoiding the superior tarsal vascular arcade. The levator aponeurosis was dissected from underlying Müller’s muscle or it dissected along with Müller’s from the conjunctiva and the levator muscle is exposed above Whitnall’s ligament. Caliber was used to measure the amount of aponeurosis to reject it. The measurement began at the superior tarsal border and passed superiorly. The superior 3–4 mm of tarsus was exposed by dissecting away the overlying pretarsal orbicularis. Three double-armed mattress sutures of 5–0 Vicryl were passed in a lamellar fashion at the upper 1/3 of the tarsus in a transverse orientation (partial thickness) taking care to protect the underlying globe. The central suture was placed just above fourth silk traction suture to ensure the maximum peak was at this position. Both arms of the 5/0 Vicryl suture were passed through the levator aponeurosis at the desired distance from the tarsus and tied in a loop fashion. The two additional 5/0 Vicryl suture were passed through the tarsus and through the aponeurosis.

Postoperative outcome was assessed as functional and cosmetic result. Functional outcome: Corneal protection, Eyelid elevation and Symmetric eyelids. Cosmetic outcome: The lid was inspected for any abnormality that would affect the cosmetic outcome. Eyelid crease, contour and lid margin are examined.

All the resected levator muscles were sent for examination by the Pathologist, the specimens varied from 10 to 25 mm in length were immediately fixed for at least 24 h in 10 % buffered neutral formalin. Once the paraffin block was obtained, serial sections of 4 micron thickness were obtained, and routine staining by: Hematoxylin—eosin (H and E) stain (Figs. 2 and 3).

The principle investigator will be responsible for obtaining the participants’ approval and written informed consent.

2.1. Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number percent. The Shapiro–Wilk test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5 % level. Kruskal Wallis test for abnormally distributed quantitative variables, to compare between more than two studied groups, and post hoc (Dunn’s multiple comparisons test) for pairwise comparisons.

3. Results

This table showed Distribution of the studied cases according to demographic data (n = 30). They are 18 male and 12 female. The age of the patients in this study ranged from 4 to 20 years with mean 12 years (Table 1).

This table showed the distribution of the studied cases according to ages of patients with different degrees of ptosis (n = 30). Cases with mild ptosis are
10 and their ages range from 4 to 9 years, moderate ptosis are 14 and their ages range from 6 to 12 years and severe ptosis are 6 cases and their ages range from 11 to 20 years (Table 2).

This table showed Mean $\pm$ SD of the percentage of muscle fiber components was 46.0 $\pm$ 18.73, percentage of fatty tissue components was 27.33 $\pm$ 13.31, and percentage of fibrosis was 25.0 $\pm$ 14.32. There was no presence of infection or skeletal muscle atypia between studied cases (Table 3).

This table showed that there was a statistically significant difference between the studied cases regarding percentage of muscle fiber components as $P$ value was (0.001), percentage of fatty tissue components as $P$ value was (0.044), and percentage of fibrosis as $P$ value was (0.046) (Table 4).

4. Discussion

Congenital ptosis is an idiopathic condition that often appears only in the affected eyelid. Anterior approach levator resection (ALR), which preserves the physiological vector of the levator muscle, is regarded as an effective treatment, even for severe cases with poor levator function [5].

Congenital blepharoptosis represents a cosmetic and functional issue. Deprivation amblyopia is the most significant surgical surgery indication. The aims of treatment, the underlying diagnosis, and the level of levator function all affect the method of repair. Although the repair is mostly performed for functional reasons, the surgeon has the chance to create symmetry in the height, contour, and crease of the eyelids to achieve better cosmesis [6,7].

Clinically, dystrophy is characterized as a hereditary condition that causes progressive muscular wasting while dysgenesis is characterized as a non-progressive, non-heritable abnormality in the muscle. Variable fibers size, hypertrophy, fibrosis of endomysia connective tissue, regenerating or degenerating muscle fibers, and an increase in internalized nuclei are hallmark histological findings of skeletal muscle dystrophies [8].

In our study, regarding to histopathological changes of levator muscle in different degrees of congenital ptosis, 30 patients (18 male and 12 female) with different degrees of congenital ptosis (mild 33.3 %, moderate 46.7 %, sever 20 %) underwent to levator resection then sent for histopathological
assessment showing a clinical degree of severity of congenital ptosis correlates positively with the degree of histopathological changes of the levator muscle, in agreement with Iljin et al. [9].

In contrast with Leite and colleagues who disagreed with our study, to determine whether there might be a correlation between the amount of fat and age, sex, the severity of the ptosis, and the function of the levator muscle, 22 samples of levator muscle from patients with congenital ptosis were examined, the amount of fat or atrophy in the levator muscle from congenital ptosis did not appear to be related to either age or levator muscle function [10].

In our study regarding to muscle fibers, we found inverse relation between muscle fibers and severity of ptosis, that is similar to study of Leite et al. [7], who reported in his study that muscle fibres were detected significantly more in cases with mild and moderate ptosis as compared with severe ptosis and there is direct correlation between normal muscle fibres and presence of eyelid crease and eyelid fold, that is also supported by our study [7,10,11].

In our study regarding fatty tissues infiltration, we proved that there is positive correlation between fatty infiltration and severity of ptosis, this is agreed with Cahill et al. [12] who reported in his study which included 115 patients with congenital ptosis submitted to levator muscle resection sent for histopathological evaluation showing a marked fatty tissues infiltration in group of severe ptosis compared with group of mild ptosis. By using light microscope, these macroscopic data were confirmed where fatty infiltration appeared as a degenerative changes affecting the muscle fibers [12].

In our study regarding to changes of levator muscle (fatty infiltrations and fibrosis) in severe congenital ptosis we agreement with Quaranta-Leoni et al. [13], myofibers identified in specimens of levator muscle obtained after levator resection for congenital ptosis showed characteristics of a degenerative process as fatty infiltration and fibrosis and this appears to demonstrate that degeneration of the muscle tends to be more obvious in older children with severe congenital ptosis as histology shows signs of more severe degeneration of levator muscle in these cases [13].

In our study, the percentage of normal muscle fibers and abnormal muscle components depend on severity of congenital ptosis as following; 10 specimens of cases with mild congenital ptosis shows 50–70 % of normal muscle fibers, 10–30 % of fatty tissues infiltration as well as fibrosis. 16 specimens of cases with moderate congenital ptosis shows 30–60 % of normal muscle components, 10–40 % of fatty tissues infiltration and 10–50 % of fibrosis. 4 specimens of cases with sever congenital ptosis

Table 3. Descriptive analysis of the studied cases according to Histopathological findings (n = 30).

<table>
<thead>
<tr>
<th>Histopathological findings</th>
<th>Min. – Max.</th>
<th>Mean ± SD.</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of Muscle fiber components</td>
<td>50.0–70.0</td>
<td>30.0–60.0</td>
<td>10.0–20.0</td>
</tr>
<tr>
<td>Median</td>
<td>47.50</td>
<td>45.50</td>
<td>17.50</td>
</tr>
<tr>
<td>Sig.bet. Grps</td>
<td>$P_1 = 0.008^<em>$, $P_2 &lt; 0.01^</em>$, $P_3 = 0.009^*$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of fatty tissue components</td>
<td>10.0–30.0</td>
<td>10.0–40.0</td>
<td>10.0–60.0</td>
</tr>
<tr>
<td>Median</td>
<td>30.0</td>
<td>30.0</td>
<td>40.0</td>
</tr>
<tr>
<td>Sig.bet. Grps</td>
<td>$P_1 = 0.04^<em>$, $P_2 = 0.027^</em>$, $P_3 = 0.550$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of fibrosis</td>
<td>10.0–30.0</td>
<td>10.0–50.0</td>
<td>20.0–70.0</td>
</tr>
<tr>
<td>Median</td>
<td>20.0</td>
<td>20.0</td>
<td>30.0</td>
</tr>
<tr>
<td>Sig.bet. Grps</td>
<td>$P_1 = 0.152$, $P_2 = 0.014^*$, $P_3 = 0.166$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Relation between grade of ptosis and histopathological findings (n = 30).

<table>
<thead>
<tr>
<th>Histopathological findings</th>
<th>Grade of ptosis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (n = 10)</td>
<td>Moderate (n = 14)</td>
<td>Severe (n = 6)</td>
</tr>
<tr>
<td>Percentage of Muscle fiber components</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min–max.</td>
<td>50.0–70.0</td>
<td>30.0–60.0</td>
</tr>
<tr>
<td>Median</td>
<td>65.0</td>
<td>47.50</td>
</tr>
<tr>
<td>Sig.bet. Grps</td>
<td>$P_1 = 0.008^<em>$, $P_2 &lt; 0.01^</em>$, $P_3 = 0.009^*$</td>
<td></td>
</tr>
<tr>
<td>Percentage of fibrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min–max.</td>
<td>10.0–30.0</td>
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</tr>
<tr>
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<td>30.0</td>
</tr>
<tr>
<td>Sig.bet. Grps</td>
<td>$P_1 = 0.04^<em>$, $P_2 = 0.027^</em>$, $P_3 = 0.550$</td>
<td></td>
</tr>
</tbody>
</table>

p: P value for comparison between the studied categories.
$P_1$: P value for comparison between mild and moderate.
$P_2$: P value for comparison between mild and severe.
$P_3$: P value for comparison between moderate and severe.
*Statistically significant at $P$ less than or equal to 0.05.
shows 10–20 % of normal muscle components, 10–60 % of fatty tissues infiltration and 20–70 % of fibrosis. There is no evidence of atypia or infection in all cases in our study, that is agreed with Iljin et al. [9].

4.1. Conclusion

Examination of all cases with different degrees of congenital ptosis shows significant correlation between histopathological findings and grades of ptosis as followings: Increasing of fatty tissues infiltration and fibrosis in sever congenital ptosis more than moderate more than mild ptosis. Presence of muscle fibers in mild ptosis more than moderate more than sever ptosis, so there is positive correlation between histopathological findings (fibrosis and fatty tissues infiltration) and severity of ptosis, and there is inverse relation between muscle fibers of levator muscle and severity of ptosis.

Conflicts of interest

No conflict of interest.

References