Levator palpebralis superioris muscle histopathologic findings in congenital ptosis and surgical outcome after its resection: Is there any association?

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Research Article

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Abstract

Purpose

To evaluate the histopathologic findings of Levator palpebralis superioris (LPS) muscle biopsy after LPS resection for treatment of congenital ptosis and its possible relation with surgical outcomes.

Methods

Congenital ptosis patients were enrolled in this retrospective study. All of them underwent full ophthalmologic examination included of Margin-reflex distance 1 (MRD-1) and LPS function measurement preoperatively. The patients were followed for three months for the postoperative period and after that the measurements were repeated. Histologic parameters including percentages of fat, striated and smooth muscle, and fibrous tissue. The histopathologic findings and their possible correlation with the measurements are analyzed.

Results

67 patients with unilateral congenital ptosis were enrolled. 45 patients (67.2%) were males. The mean age of patients was 16.10 ± 11.18 years. The patients' MRD-1 was improved significantly from 0.82 ± 1.26 mm to 3.85 ± 1.25 mm after LPS resection (P = 0.000). The success rate was 80.3%. There were no correlations between MRD change and histopathologic tissue percentages but significant correlation was found between success of surgery and fibrous tissue percentage of resected sample (P = 0.033).

Conclusions

The histopathology of the LPS may be useful in prediction of surgical outcome after LPS resection in congenital ptosis patients. The percentage of fibrous tissue play an important role.

Introduction

Blepharoptosis is defined as a lowered upper eyelid margin [1] which could be categorized as congenital or acquired based on age and other examination findings [2]. Simple congenital ptosis (SCP) is the commonest type of congenital ptosis. Infrequently congenital ptosis may be related to blepharophimosis epicanthus inversus syndrome or Marcus Gunn jaw winking phenomenon (MGJWP) [3]. Generally, congenital type is considered as a myogenic form of ptosis in which the main pathology is related to the levator palpebralis superioris (LPS) muscle [4]. But some types such as MGJWP is thought to have a neurogenic base [3]. Clinically, SCP classified as a muscular dysgenesis as it is a stationary noninheritable condition and previous histopathologic studies have also supported this classification [5]. The recurrence of blepharoptosis or its poor improvement after LPS resection surgery is reported in many ptosis patients [6]. That might be due to observed pathologic changes on the LPS muscle and its aponeurosis.

In this study, the histopathologic results of the LPS muscle were evaluated in congenital ptosis patients who underwent LPS resection, trying to find any possible linkage between these findings and the surgical outcome.

Methods

This retrospective study was conducted in Farabi Eye Hospital, Tehran University of Medical Sciences, between November 2018 and December 2021. The study was approved by the ethics committee and all reports adhered to ethical principles outlined in the Declaration of Helsinki. An informed consent was obtained from all the patients before enrollment in the study.
Unilateral blepharoptosis was defined as an asymmetric marginal reflex distance 1 (MRD-1, corneal reflex distance to the upper eyelid margin) in which the affected upper lid is 1.5 mm or more lower than the normal side. Congenital ptosis was defined as a simple congenital ptosis without any other myopathy. Also, findings such as lid lag in downgaze, poor or absent upper lid crease and previous childhood or younger age photographs were evaluated for more precise diagnosis and ruling out the other types of ptosis. Exclusion criteria were other types of ptosis, any history of eyelid trauma or surgery, and less than 3 months postoperative follow-up. Patients underwent full ophthalmologic examination and their demographic data such as age and gender and specific ptosis findings e.g. pre- and post-operative MRD-1, and preoperative LPS (levator palpebrae superioris) function were registered.

LPS resection was done by external approach for all patients under either local or general anesthesia, depending on patients’ age and cooperation. After marking the future eyelid crease, based on the opposite eye in unilateral ptosis, all had local injection of lidocaine 2% (2 cc) + adrenaline (1/200000). For local anesthesia cases, intraoperative adjustments were made, and for general anesthesia patients, a 1mm overcorrection compared to the opposite eye (in the unanesthetized position) was implemented. The LPS muscle resection was performed by suturing the muscle to the tarsus, using three 5.0 vicryl sutures (Surgicryl PGA, Polyglycolic acid, SMI, Belgium), and then resecting the excess part which is embedded in the formalin solution for later histopathologic investigation. The skin was closed with 6.0 nylon sutures (Supalon, Supa, Iran), incorporating the LPS muscle for crease formation. Erythromycin ointment was applied twice daily and artificial tears were administered freely.

For histopathologic evaluation, LPS muscle samples immediately were fixed in 10% neutral buffered formalin and fixed for 24 hours in pathology department. All specimens were processed and embedded in paraffin blocks. Multiple 5 micrometer tissue sections were prepared, stained with hematoxylin and eosin (H/E) and Masson's trichrome and examined by light microscopy. Specimens composed of various amounts of striated muscle, adipose and fibrosis tissue. also, in some samples smooth muscle tissue was identified. Two or more sections were obtained from each specimen based on the size of the excised tissue. H/E-stained slides evaluated for muscle fiber pathology and pattern of myopathy then trichrome stained slides were examined for determination of fibrosis, adipose and muscle tissue percentage. The reported values were averages, due to the evaluation of several sections from each patient’s specimen by Imagej software (Imagej 1.53m, National Institute of Health, Bethesda, Maryland, USA) (Fig. 1).

Patients were examined on one week, one month and three months follow-up visits postoperatively. Success was defined as post-op MRD-1 ≥ 3 mm or MRD-1 difference between the affected side and the normal side ≤ 1 mm.

The statistical analysis was done by SPSS version 23 (SPSS Inc., Chicago, IL). A p-value of less than 0.05 was considered significant. The possible correlation between pre and post-operative MRD-1 changes or surgical success and the histopathologic findings was examined using Spearman correlation coefficient. The results are expressed as mean ± standard deviation.

**Results**

67 congenital ptosis patients were enrolled. 45 patients (67.2%) were males and 22 of them (32.8%) were females. The mean age of patients was 16.10 ± 11.18 years. The patients’ MRD-1 was improved significantly from 0.82 ± 1.26 mm to 3.85 ± 1.25 mm after LPS resection (P = 0.000). The MRD-1 improvement percentage were 264.44 ± 160.51% in males and 262.12 ± 163.71% in females (P = 0.055). The pre-operative LPS function was 6.28 ± 3.45 mm.

The histopathologic findings and their correlation with MRD change and surgical success are summarized in Tables 1–3. There were no correlations between histopathologic findings and amount of MRD change. The correlation scatter plots are shown in Fig. 2. But the amount of fibrous tissue was positively correlated with the success of surgical procedure (P = 0.033).
Table 1
Histopathologic findings among congenital ptosis patients

<table>
<thead>
<tr>
<th></th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrous tissue percentage (%)</td>
<td>.00</td>
<td>95.00</td>
<td>46.4627</td>
<td>20.98364</td>
</tr>
<tr>
<td>Fat tissue percentage (%)</td>
<td>.00</td>
<td>80.00</td>
<td>31.4848</td>
<td>18.55905</td>
</tr>
<tr>
<td>Smooth muscle tissue percentage (%)</td>
<td>.00</td>
<td>45.00</td>
<td>3.5606</td>
<td>7.88207</td>
</tr>
<tr>
<td>Striated muscle tissue percentage (%)</td>
<td>.00</td>
<td>70.00</td>
<td>18.5672</td>
<td>17.43405</td>
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</table>

Table 2
MRD change and tissue percentage Spearman's correlation among the patients

<table>
<thead>
<tr>
<th></th>
<th>Fibrous tissue percentage</th>
<th>Fat tissue percentage</th>
<th>Smooth muscle tissue percentage</th>
<th>Striated muscle tissue percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRD change Correlation Coefficient</td>
<td>0.174</td>
<td>-0.155</td>
<td>-0.121</td>
<td>-0.044</td>
</tr>
<tr>
<td>P value (2-tailed)</td>
<td>0.158</td>
<td>0.215</td>
<td>0.331</td>
<td>0.723</td>
</tr>
</tbody>
</table>

Table 3
Surgical success and tissue percentage correlation among the patients

<table>
<thead>
<tr>
<th></th>
<th>Fibrous tissue percentage</th>
<th>Fat tissue percentage</th>
<th>Smooth muscle tissue percentage</th>
<th>Striated muscle tissue percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success Correlation Coefficient</td>
<td>0.273</td>
<td>-0.181</td>
<td>-0.200</td>
<td>-0.087</td>
</tr>
<tr>
<td>P value (2-tailed)</td>
<td>0.033</td>
<td>0.162</td>
<td>0.126</td>
<td>0.503</td>
</tr>
</tbody>
</table>

Discussion

In evaluation of the blepharoptosis patients, amount of ptosis and the levator function are the two important factors that determine the clinical outcome [6]. The first histologic report of LPS muscle showed degeneration and fibrosis in postmortem levator muscle complex [4]. Although some reports have been published about LPS muscle histology [4, 6–8] no unit consensus has been provided about its relationship with levator function or surgical outcomes. Berke et al [8] evaluated 82 eyes (64 eyes with congenital ptosis) and reported that the higher number of striated muscles in the specimen correlated with less pre-operative ptosis and higher surgical success. Some other studies reported a relation between a decrease in the striated muscle and an increased fibrosis of the LPS muscle in histopathologic evaluation and the decreased LPS function in both congenital and acquired ptosis [3, 9, 10]. On the other hand, another study on 22 congenital ptosis samples revealed that fat amount in the levator muscle is not related to age, sex, ptosis degree or levator muscle function [11]. In our study, neither the striated muscle nor the fibrofatty changes of the LPS muscle related to the amount of preoperative ptosis or the improvements which were yielded from the levator resection surgery.

In this study, the mean of striated muscle percentage was less than twenty percent of the entire tissue and fibrofatty tissues consisted about 78 percent of the sample. That is consistent with observations of a prior study reporting that the etiology of congenital ptosis is more likely due to muscle dysgenesis [12]. In another study by Surve et al., it is reported that fibrocollagenous tissue predominated in all the congenital ptosis samples, and muscle fibers found correlated inversely with the severity of ptosis [3]. The predominancy of fibrous tissue is in favor with our findings but we found no such correlation with MRD change. But on the other hand, in our study the amount of fibrous tissue was positively correlated with surgical success. This may show the importance of fibrous tissue percentage in the levator muscle aponeurosis instead of fat tissue and fatty degeneration which could severely compromise the muscle and its aponeurosis function. In the other words, fibrous
tissue could be a positive cooperator with muscle tissue in levator function. In Surve study, the absence of degenerating, regenerating fibers and inflammatory cells reinforced the theory of dysgenesis of muscle. Though, internalization of nucleus seen in all the subtypes is a feature favoring dystrophy [3, 13]. In another study, the fatty infiltration of the Müller and anterior levator muscle was reported during surgery in 9 out of 115 patients with either congenital or acquired ptosis. In the same study, the fatty infiltration was also found in 5 other patients in microscopic examinations, albeit not evident at the surgery. Fatty infiltration seemed to be a degenerative change found in adults with congenital or acquired ptosis. The favorite postoperative results were attained with standard external levator resection. The fatty appearance may cause difficulty in identifying normal anatomical landmarks during surgery [14]. These changes in LPS muscle histopathology could be the main factor for the recurrence of blepharoptosis [6, 15] after surgery in some patients, either congenital or acquired. That recurrence could be more acceptable for patients, provided the histopathology report of the LPS indicated the microscopic fatty infiltration of the muscle.

A limitation of our study was that the LPS biopsy has been done from different parts of the muscle in each patient according to the desired length of muscle which should be resected. in some patients, the biopsy was taken from the more aponeurotic part but in some other the muscular part is more involved. Another limitation of the study was the limited histopathologic evaluation of samples for subcellular changes which may have more effects on the process of this abnormality.

In conclusion, observations made in this study indicated that the histopathology of the LPS muscle could not directly predict the MRD1 changes after levator muscle resection in unilateral congenital ptosis patients but more studies with larger samples and more precise pathologic evaluation could be planned.

Declarations

Consent to participate: Written informed consent was obtained from the patients for participation in the study.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

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References


Figures
Figure 1

Histopathologic evaluation of LPS muscle samples; a. H & E-stained slide (x400) showing atrophic striated muscle (Blue arrow), fibrosis (Orange arrow) and adipose tissue (Green arrow); b. Masson’s trichrome stained slide (x100) showing atrophic striated muscle (Blue arrow), fibrosis (Orange arrow) and adipose tissue (Green arrow); c. Masson’s trichrome stained slide showing atrophic striated muscle (Blue arrow) and fibrosis (Orange arrow). H& E: hematoxylin and eosin.
Figure 2

Scatter plots indicating no obvious correlation between MRD change and tissue percentages in histopathologic evaluations.