Tendinopathy of the long head of the biceps tendon is a difficult medical issue. Its pathogenesis and etiology is multifactorial and unclear. Tendinopathy is thought to be primarily degenerative in nature, as tendons are characterized by impaired regeneration and healing. Thirty-five patients with preoperatively diagnosed tendinopathy of long head of the biceps tendon were referred to the Orthopedics Department. All patients underwent an arthroscopic-assisted biceps tenodesis or tenotomy, according to techniques described previously [7]. Shoulder arthroscopy was performed in the beach chair position in general anesthesia. During the arthroscopy the physical examination performed by a specialist in orthopedic surgery, one day before shoulder arthroscopy was performed. Portions of intra-articular tissue were obtained from each of the patients who underwent arthroscopy. A macroscopic and microscopic evaluation of biceps tendon samples revealed degeneration among all specimens. This study demonstrates the prevalence of the degeneration process and the presence of marginal inflammation process in tendinopathy of the long head of biceps tendon. The role, that inflammation process plays in tendinopathy is important in the early phase and gradually becomes secondary to the developing degeneration. The inflammatory cells, occasionally seen in pathological tendons, could be an evidence of re-injury and recent healing response. 

Key words: biceps tendinopathy, anterior shoulder pain, the long head of the biceps tendon, tendon inflammation, tendinopathy.

Introduction

Tendons are hierarchically organized structures optimized for transfer of loads in the locomotor system. Since they are subjected to repetitive loads of various magnitudes, their main components: tenocytes and extra-cellular matrix (ECM) need to adapt to changing mechanical conditions. Tenocytes play the main role in maintaining tendon matrix and synthesis of the collagen molecules, they maintain the homeostasis of ECM and continuously remodel it to optimize the fibrous structure with respect to loads applied to the tendon [1]. This mechano-biological response requires a constant interaction between ECM and tenocytes which is efficient at physiological ranges. However repetitive application of loads exceeding these values result in pathological alterations in tendon’s structure and are one of main causes of their chronic failure [2]. Tendon after injury is repaired during three-step process, divided into inflammation, formative and remodeling phase [3]. The trigger factor – injury, promotes inflammatory process, which lasts about 7-8 days and is characterized by formation of hematoma in damaged area. In this time, the zone of injury, is rich in inflammatory cells: neutrophils, macrophages and platelets. After the inflammatory phase, the proliferative phase lasts up till about 21th day. In this period of time, there is a gradual reduction of inflammatory cells and progressive domination of tenocytes. In contrast to acute injuries, which can result in healing, repetitive overloading leads to degeneration of tendinous tissue, which results in deterioration of biomechanical properties of the affected tendon. This process is called tendinopathy, and as demonstrated by several studies seems to be predominantly a result of mechanical damage associated with very limited inflammatory response. Tendinopathy is characterized by increased matrix remodeling, elevated activity and expression of metalloproteinases (MMPs), increased type III collagen contents, collagen degeneration and increased proteoglycans contents [2]. Chaotic production of ECM components by tenocytes and chaotic expansion of new capillary correlates to clinical symptoms such as chronic pain and spontaneous partial or full rupture. The etiology of tendinopathy is poorly understood and multifactorial. The most common hypothesis is divided into two parts: extra-articular and intra-articular [2]. The extra-articular part of the LHBT is prone to degeneration due to its exposition to tear, compression and friction forces [2]. Interestingly, there is surprisingly little data regarding histological findings in this common condition. Moreover several reports indicated, that LHBT tendinopathy may be asymptomatic or associated with mild pain, and currently there is no clear link between microscopic changes within affected tendon and clinical symptoms. The aim of this study is to conduct a histopathological analysis of intra-articular parts of long head of the biceps tendon, compare chaotic nature of tendinopathy among them and architectural defects of tendinous tissue, which results in deterioration of biomechanical properties of the affected tendon.
35 subjects. The two asymptomatic cases were a 52 years old male with complete medial dislocation of LHBT (Bonar score 8), and a 65 years old male with complete LHBT rupture (Bonar score 11).

Arthroscopic investigation of the affected shoulders revealed that only three patients had isolated LHBT lesion (Bonar score 5, 5, 8 points respectively), in other cases we found concomitant pathologies, such as rotator cuff tears (RCTs) in 24 patients, subacromial impingements in 18 patients and labral defects in 2 patients. During shoulder arthroscopy 7 patients underwent the tenotomy procedure and 27 patients underwent the tenodesis procedure, there was one sub resection due to previous the LHBT complete rupture. There was no different anatomic variants of LHBT origin’s found in the study.

Microscopic evaluation of the LHBT samples showed signs of degeneration among all specimens: visible tears, fraying, widening and flattening, gray – yellowish discoloration of the tendons (Fig. 1). Mean length of samples was 12.3 mm (range 3.2-20 mm) of the length and , their mean diameter was 6.8 mm (range 3.15 mm).

Microscopic evaluation of H&E staining slides showed advanced degeneration in all specimens (Figs. 2 and 3). After examination according to Bonar scale, grades 2 and 3 in tenocyte morphology were identified in 24 of 35 samples (Table I). In these patients the morphology of tenocytes was altered; there was an increased number of enlarged, rounded cells, with enlarged nuclei and decreased amount of cytoplasm (Fig. 3C, 3D). In these samples tenocytes were randomly scattered in the tissue, their organized distribution typically seen in healthy tendons was lost. Grades 2 and 3 in collagen bundle characteristics were identified in 30 of 35 samples (Fig. 3A, 3B). Overwhelming disorganization of the longitudinal alignment of collagen fibers was found. We not identified separation of collagen bundles, loss of characteristic “crimping pattern”, and disorientation of the fibers. Degeneration of the ground substance (Grade 2 and Grade 3 ) was identified in 34 of 35 specimens (Fig. 3A-D). Ground substance was accumulated mainly between collagen bundles, separating them. Neovascularization was present in 28 of 35 samples with Grade 2 and 3 found in 23 specimens (Fig. 2B, 2C, 2D). Groups of capillary vessels were distributed randomly and chaotically. One sample demonstrated abundant granulation tissue with blood vessels consolidated in clusters.

In the examined cohort, mean Bonar score was 8.2 (range 4-11 and SD – 2). In three samples we noted presence of modest infiltration of inflammatory cells around blood vessels cells: in two patients the infiltration consisted of lymphocytes, in one patient of neutrophils. Despite the invasion of inflammatory cells, microscopic analyze of LHBT samples revealed advanced degenerative response of tissue – Bonar 7, 10, 11 points respectively.

This group included three patients: a 52 years old male with SST and SSC tendon lesions and LHBT thickening (symptoms since 1 year, Bonar score 7), a 60 years old female with SST tear and LHBT degeneration (symptoms since 1 year, Bonar score 10), and a 49 years old male with subluxation of thickened LHBT (symptoms since 6 months, Bonar score 11). Based on data from medical history, clinical and microscopic examination we were unable to explain the cause of inflammatory infiltration in these patients (Table II). All control samples included in this study had a macroscopic appearance of healthy tendons with brilliant white color. Microscopically all samples were characterized by low density of elongated, spindle–like tenocytes; characteristic “wavy configuration” of collagen fibers with their axial orientation and non-separation of bundles; few capillary vessels were found, with no visible vascular expansion. The Bonar score for these samples was 0 and inflammatory cells were absent (Fig. 4).

Discussion

Although damage to tendinous tissue related to mechanical overload is typically referred to as tendi-
nnosis, this term may be misleading, since the inflammatory process implied by the name is usually mildly marked, and the degenerative process seems to play the main role [4, 10, 11, 12, 13]. Most authors described pathological tendon tissue as amorphous, grey or yellow, locally thickened, with deteriorated structure, and reported several microscopic features, such as disorganized ECM, presence of neovascularization and rounded tenocytes (Fig. 5) [2, 5, 14]. Interestingly, there is relatively little data regarding histology of LHBT degeneration and the relationship between microscopic findings or clinical symptoms. In this study we examined a series of LHBT tendons resected during shoulder arthroscopies to verify presence of microscopic signs of inflammation and degeneration, additionally link these findings with clinical symptoms.

Similarly as previous reports regarding tendinopathy, in humans, our study is limited in several ways. The most important limitation comes from the fact that our group is not homogenous, since we included patients with different shoulder pathologies; moreover in some patients pathological changes may also be related to old age [15]. This could have biased our results, since it is possible that patients with isolated LHBT pathology the extent of degeneration could be different than in this study, however since isolated cases of LHBT pathology are rare, most studies regarding this tendon included a group of patients similar to ours [2, 9]. Due to ethical reasons we included hamstring tendons from healthy individuals as controls. These samples had microscopic characteristics of healthy tendons, however we cannot exclude, that in patients with asymptomatic and macroscopically intact LHBT tendons some pathologies could be detected at microscopic examination. Previous studies were also limited this way; some authors included samples from cadavers, however in such cases microscopic findings may be biased by post mortem tissue degeneration, it was also impossible to verify clinical symptoms. Lastly, our study was based on semiquantitative scoring system which can be affected by subjective differences between observers. In order to avoid this samples were examined by three authors, similarly as in other studies.

Currently two main classifications are being used to evaluate histopathological alterations in tendinopathies: Bonar and Movin scores [16]. The most important difference between these systems is the evaluation of hyalinization, in the Movin scale, which was primarily designed for Achilles tendon pathology, where hyalinization is often seen. This criterion is not included in Bonar scale used in this study, however this choice is unlikely to bias our results, since hyalinization is rare phenomenon in LHBT tendinopathy. Moreover, Bonar score was also validated by authors studying tendons of the upper and lower extremity [10]. The utility of Bonar score was also demonstrated in SST and patellar tendon pathology [8, 17].

Table I. Distribution of scores according to Bonar scale

<table>
<thead>
<tr>
<th>Variable/Grade according to Bonar score</th>
<th>0</th>
<th>1 point</th>
<th>2 points</th>
<th>3 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenocytes</td>
<td>11 samples</td>
<td>21 samples</td>
<td>3 samples</td>
<td></td>
</tr>
<tr>
<td>Ground substance</td>
<td>1 sample</td>
<td>16 samples</td>
<td>18 samples</td>
<td></td>
</tr>
<tr>
<td>Collagen disorganization</td>
<td>5 samples</td>
<td>17 samples</td>
<td>15 samples</td>
<td></td>
</tr>
<tr>
<td>Neovascularization</td>
<td>7 samples</td>
<td>5 samples</td>
<td>10 samples</td>
<td>15 samples</td>
</tr>
</tbody>
</table>

**Table II. Comparison of subjects with inflammation and degeneration**

<table>
<thead>
<tr>
<th>Pathology recognized in microscopic examination</th>
<th>Number of subjects</th>
<th>Mean Bonar score in a group</th>
<th>% of positive clinical test</th>
<th>Additional pathologies found during arthroscopic investigation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation with degeneration</td>
<td>3</td>
<td>9.3</td>
<td>100</td>
<td>2 RCTs, 1 SI</td>
</tr>
<tr>
<td>Alone degeneration</td>
<td>32</td>
<td>8.1</td>
<td>94</td>
<td>22 RCTs, 17 SI, 2 LD</td>
</tr>
</tbody>
</table>

LD – lateral defect; SI – surgical incision
Inflammation is of a lesser importance. It is thought, driven by an inflammatory process, which results in expression of certain proteins such as collagen III new capillary vessels [2]. Since these authors focused ground substance accumulation and expansion of the tendon. [25, 24]. Our study demonstrated advanced neovascularization process among 80% of specimens and positive clinical test among 90% of subjects, despite absence of any inflammatory process. Similarly Streit et al. did not find the correlation between pain in inflammation and degeneration of the LHBT due to limited inflammatory response [10].

Summary

Biceps tendinopathy is not a very common issue in literature, although it is a widespread phenomenon and medical problem. The development of shoulder arthroscopy put the phenomenon of the chronic tendinopathy in a new light and allowed the non-invasive treatment of the LHBT disease. Morphological and histological analysis of the LHBT portions obtained from patients, revealed advanced tendinopathy in each case. We showed, that inflammation is not the only factor. Similarly Streit et al. noticed, that in chronic tendinopathy, the predominant angio-ﬁbroblastic response often correlates with painful conditions [4, 23, 24]. During capillary vessels expansion, nerves endings penetrate the tendon’s tissue – with a predominance of the sensory and autonomic nerves fibers [14, 23, 25]. Our study demonstrated advanced neovascularization process among 80% of specimens and positive clinical test among 90% of subjects, despite absence of any inflammatory process. Similarly Streit et al. did not find the correlation between pain in inflammation and degeneration of the LHBT due to limited inflammatory response [10].

The authors declare no conflict of interest.

References

2. Joseph M, Maresh CM, McCarthy MB, et al. Histological and histochemical analysis of the LHBT portions obtained from patients, revealed advanced tendinopathy in each case. We showed, that inflammation is not the only factor. Similarly Streit et al. noticed, that in chronic tendinopathy, the predominant angio-ﬁbroblastic response often correlates with painful conditions [4, 23, 24]. During capillary vessels expansion, nerves endings penetrate the tendon’s tissue – with a predominance of the sensory and autonomic nerves fibers [14, 23, 25]. Our study demonstrated advanced neovascularization process among 80% of specimens and positive clinical test among 90% of subjects, despite absence of any inflammatory process. Similarly Streit et al. did not find the correlation between pain in inflammation and degeneration of the LHBT due to limited inflammatory response [10].