



Synovitis as a concomitant disease in shoulder pathologies

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Abstract

Introduction Shoulder pathologies are often accompanied by rotator interval synovitis. This phenomenon is poorly described in the literature so far. The aim of the study was to analyze the occurrence of macroscopically visible synovial reaction in the rotator interval in patients with chronic shoulder pathologies and to perform a histopathological evaluation.

Materials and methods In this prospective cohort study, 167 consecutive patients undergoing arthroscopic shoulder surgery for chronic shoulder pathology were included (♀ = 45, ♂ = 122; 54.5 years ± 12.8). Included patients were divided into subgroups according to the encountered chronic shoulder pathology: (1) impingement syndrome with or without bursal sided partial rotator cuff tear (RCT); (2) articular sided partial RCT; (3) full-thickness RCT; (4) RCT that involves at least two tendons; (5) shoulder instability; and (6) cartilage damage. Standardized soft tissue biopsies from the rotator interval were taken. The synovitis score of Krenn/Morawietz was used for histopathological examination.

Results Extraarticular pathology (group 1) showed significantly decreased synovitis scores compared to all the other groups. Increased size of rotator cuff tears (group 4), as well as cartilage damage (group 6) showed significantly higher synovitis scores than group 3 ($p < 0.05$). Moreover, the synovitis score was significantly increased in patients with concomitant pathologies of the long head of the biceps ($p = 0.001$).

Conclusions This study suggests that chronic intra- and extraarticular shoulder diseases are very often accompanied by a histopathologically verifiable low-grade synovitis. Intraarticular pathologies seem to induce increased levels of synovitis. Furthermore, the increased size of rotator cuff tears is accompanied by a higher degree of synovitis.

Study design Cohort study, level of evidence, 2b.

Keywords Synovitis · Chronic shoulder disease · Rotator interval · Synovitis score · Rotator cuff tear · Synovial inflammation

Introduction

Chronic shoulder diseases are among the most common musculoskeletal disorders and are often accompanied by the presence of a macroscopically visible local non-arthrofibrotic synovial inflammation appearing with hyperemia, as well as hypertrophy of the synovial villi in the rotator

interval [8, 12, 13]. Rotator interval synovitis can frequently be observed as a concomitant pathology without arthrofibrosis of the affected shoulder.

Krenn et al. implemented a validated histopathological score as a classification system of synovitis. They differentiate between low-grade synovitis and high-grade synovitis whereas the latter was strongly associated with rheumatic diseases [9, 10].

Recently, Jo et al. were the first who compared macroscopically visible characteristics of synovitis with four different microscopic assessment tools in 54 patients suffering from rotator cuff diseases and thereby created a macroscopic assessment system [8].

Since pro-inflammatory cytokines in the synovium were upregulated in rotator cuff tears, synovial inflammation is suggested to be an intrinsic factor connected with joint diseases [5, 6, 19]. Moreover, researches in rheumatoid arthritis

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or osteoarthritis have shown that synovitis is accompanied by higher pain levels [11, 18].

However, so far the role of synovial inflammation as a concomitant pathology in patients suffering from chronic shoulder diseases remains incompletely understood.

Purpose

The aim of this study was to perform a histopathological evaluation of macroscopically visible synovial inflammation in the rotator interval and analyze its correlation with intra- and extraarticular chronic shoulder pathologies. The hypothesis was that intraarticular pathologies of the shoulder are accompanied by increased synovial inflammation in the rotator interval.

Materials and methods

Study design and patients

The study was approved by the institutional review board (EA1/351/16). In this prospective cohort study, 167 consecutive patients treated by a single surgeon who underwent arthroscopic surgery due to chronic intra- or extraarticular shoulder diseases were enrolled. There were 45 female and 122 male patients with an average age of 54.5 ± 12.8 years. Chronic was defined as pathologies that last for at least 6 months. Exclusion criteria were rheumatic diseases, adhesive capsulitis, previous surgeries or septic joints.

Demographic data were documented and the major diagnosis of the shoulder were divided into subgroups as follows: group (1) impingement syndrome with or without bursal sided partial rotator cuff tears, group (2) articular sided partial rotator cuff tears, group (3) full-thickness rotator cuff tears, group (4) rotator cuff tears that involved at least two tendons, group (5) chronic shoulder instability, group (6) chronic cartilage damage. All partial tears were classified according to Ellman [4]. Furthermore, concomitant intraarticular pathologies of the long head of the biceps were assessed. Therefore, tendinitis, partial or full-thickness tears or superior labral anterior posterior (SLAP) lesions were captured.

Surgical intervention

All patients gave their written consent for the procedure after risks and complications of the following surgery were explained. Intraoperatively, biopsy specimens of the synovial tissue were taken from the rotator interval between the middle glenohumeral ligament and the tendon of the musculus subscapularis after diagnostic arthroscopy was

performed (Fig. 1a, b). Subsequently, arthroscopic surgeries were performed according to the respective shoulder pathologies.

Histopathological assessment of synovitis

Histopathological assessment was carried out by just one pathologist according to the microscopic assessment system (synovitis score) as described by Krenn et al. [9, 10]. Therefore, the biopsy specimens were embedded in paraffin and subsequently stained with haematoxylin and eosin (H&E).

The synovitis score consists of inflammatory alterations of the three compartments of the synovial membrane (enlargement of the lining cell layer, cellular density of the synovial stroma, and leukocyte infiltrate). The alterations were evaluated separately in each compartment from none (0), slight (1) and moderate (2) to strong (3). The sum of these values provides the following synovitis score: 0 = no synovitis, 1–4 = low-grade synovitis, 5–9 = high-grade synovitis.

Statistical analysis

All statistical analyses were conducted with the SPSS 16.0 software (SPSS, IBM, Chicago, IL). Continuous variables were expressed as means \pm SD. First, all the continuous data were tested for normal distribution using the

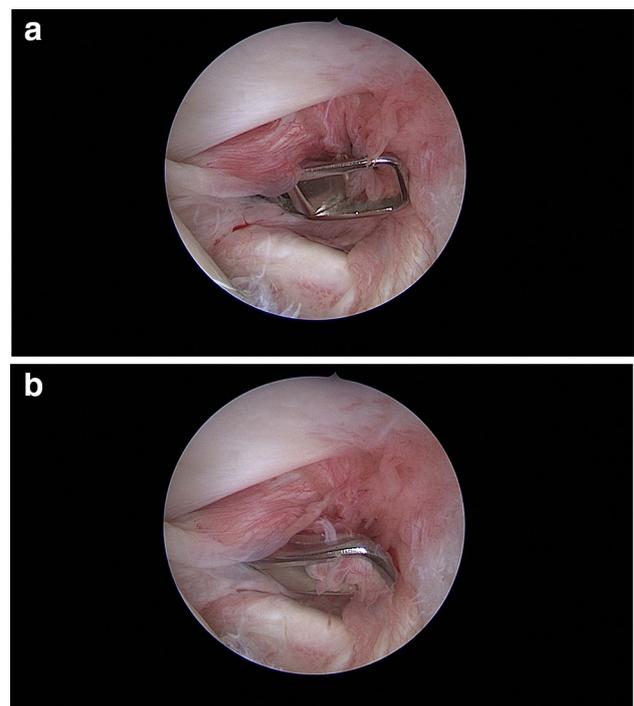


Fig. 1 a, b Biopsy of synovial tissue taken out of the rotator interval with macroscopically visible synovitis

Kolmogorov–Smirnov test. For comparison of more than two groups of the parametric continuous variables a one-way analysis of variance was employed. To compare more than two groups of ordinal scaled variables a Kruskal–Wallis test was performed. Differences between two groups for ordinal scaled samples were assessed with the Mann–Whitney U test for independent data. For comparison of categorical variables, the Chi square or Fisher’s exact test were used. If the null hypothesis could be rejected with $>95\%$ confidence, the differences were considered as statistically significant. Therefore, the level of significance was defined as two-tailed $p < 0.05$.

Results

Shoulder pathologies

The division of the 167 patients into subgroups revealed the following number of cases: group 1: $n = 41$, group 2: $n = 20$, group 3: $n = 24$, group 4: $n = 50$, group 5: $n = 21$, group 6: $n = 11$.

Overall, 117 patients were suffering from concomitant pathologies of the long head of the biceps.

Histopathological assessments

The microscopic evaluation of the synovitis score revealed a grade 0 in 21 patients, a grade 1 in 72 patients, a grade 2 in 48 patients, a grade 3 in 21 patients, a grade 4 in 3 patients,

a grade 5 in 1 patient and a grade 6 in 1 patient. None of the patients revealed grade 7–9.

Examples of macroscopic visible synovial inflammation in the rotator interval and the matching histological preparation are shown in Fig. 2a–d (synovitis score 0) and Fig. 3a–d (synovitis score 2).

Association between demographic data and histopathological assessments

Neither age nor sex showed any statistically association with the histopathological assessed synovitis score ($p > 0.05$).

Association between shoulder pathologies and histopathological assessments

Mean synovitis scores of all subdivided groups were: group 1: 0.93 ± 0.60 , group 2: 1.50 ± 0.76 , group 3: 1.29 ± 0.75 , group 4: 2.00 ± 1.28 , group 5: 1.52 ± 0.81 , and group 6: 2.09 ± 0.83 .

Group 1 showed a statistically significant lower synovitis score than group 2 ($p = 0.007$), group 3 ($p = 0.050$), group 4 ($p = 0.001$), group 5 ($p = 0.005$) and group 6 ($p = 0.001$). Furthermore, group 4, as well as group 6 revealed statistically higher grade of synovitis compared to group 3 ($p = 0.019/p = 0.020$). Between all other groups no statistically significant difference with regard to the synovitis score could be detected ($p > 0.05$).

Patients with observed intraarticular pathologies of the long head of the biceps tendon displayed a significantly

Fig. 2 **a** Intraoperative picture of synovitis grade 0. **b** Histological preparation ($\times 25$ magnification) of synovitis score grade 0. **c** Histological preparation ($\times 200$ magnification) of synovitis score grade 0. **d** Histological preparation ($\times 400$ magnification) of synovitis score grade 0

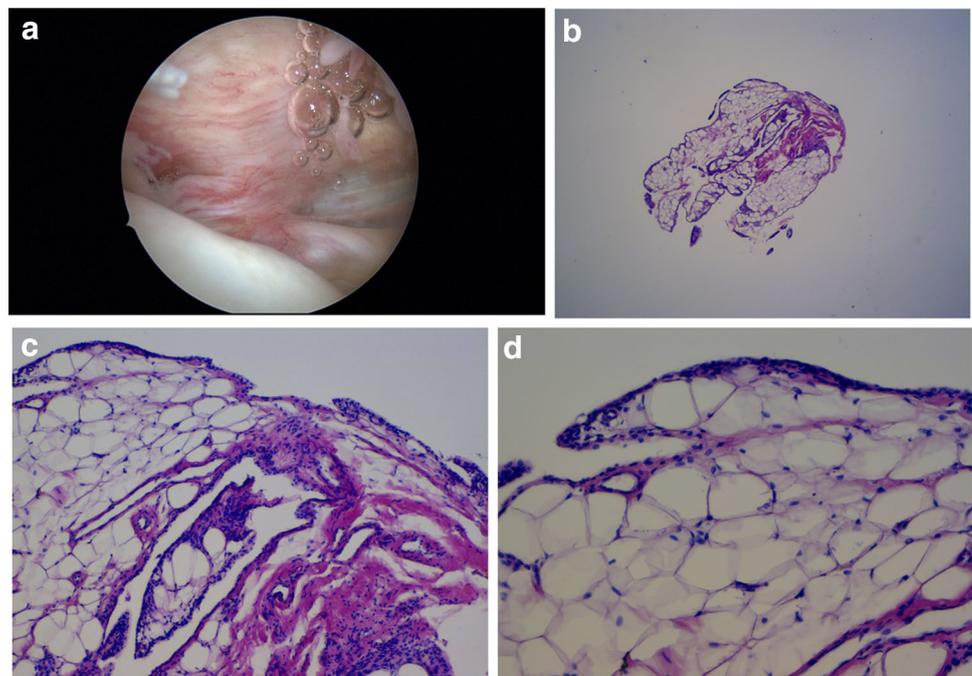
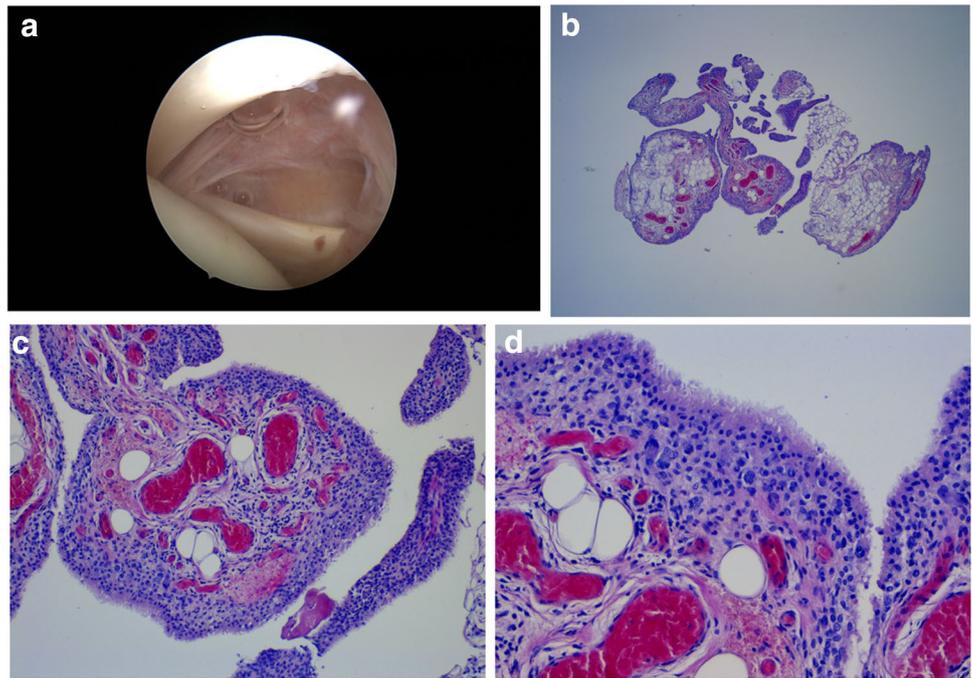


Fig. 3 **a** Intraoperative picture of synovitis grade 2. **b** Histological preparation ($\times 25$ magnification) of synovitis score grade 2. **c** Histological preparation ($\times 200$ magnification) of synovitis score grade 2. **d** Histological preparation ($\times 400$ magnification) of synovitis score grade 2



higher synovitis score compared to patients without biceps tendon pathologies ($p = 0.001$).

Discussion

This study investigated patients suffering from several different chronic shoulder diseases. A large amount of patients (87.6%) displayed microscopic synovitis. The most important findings of this study are that intraarticular pathologies show higher levels of synovitis than extraarticular pathologies. Furthermore, increasing size of rotator cuff tears result in higher synovitis scores. Moreover, pathologies of the long head of the biceps increase synovitis.

Synovitis is described as a commonly observed macroscopically visible local synovial inflammation appearing with hyperemia, as well as hypertrophy of the synovial villi [8, 12, 13]. However, synovitis of the shoulder as a concomitant pathology in shoulder diseases remains incompletely examined so far.

Recently, Jo et al. examined 54 patients with rotator cuff tear with regard to the level of synovitis to assess a macroscopic classification system. They determined different regions of interests (ROI) within the synovium and the subacromial bursa to take biopsies and to perform a macroscopic assessment. The most severe synovitis was found intraarticular next to the rotator cuff tear in the rotator interval [8]. This could be related to the findings of this study group that intraarticular diseases such as cartilage damage or pathologies of the long head of the biceps revealed significantly higher synovitis scores than subacromial diseases

such as impingement syndrome. But in comparison to this study it should be noted that Jo et al. only describe synovitis in rotator cuff tears. Furthermore, they did not differentiate between the different sizes of rotator cuff tears as analyzed in this study.

Rotator cuff tears are commonly reported to be accompanied by an inflammation of the subacromial bursa [6, 7, 16, 23]. The increasingly synovitis in greater rotator cuff tears found in this study could be due to the same inflammation process. The same applies to pathologies of the long head of the biceps, which are known to come along with pain [22]. So far, no study exists that has also shown that they are accompanied with increased synovitis in the rotator interval.

Moreover, synovial inflammation is suggested to elevate catabolic cytokines and degradative enzymes and to be an intrinsic factor connected with many joint diseases [2, 15, 20, 21]. The results of this study suggest that most of the patients with a chronic shoulder problem suffer from low-grade synovitis in the rotator interval as well. By now it remains unexplained whether synovitis is an influencing factor of chronic shoulder pathologies or synovial inflammation is a consequence of chronic shoulder diseases.

Moreover, researches in rheumatoid arthritis or osteoarthritis have shown that synovitis is accompanied by increased pain [11, 17, 24]. Further studies need to detect whether low-grade synovitis in chronic shoulder pathologies is associated with more pain as well.

Furthermore, synovitis in the knee is reported to be related to adverse effects such as cartilage damage, increased pain or decreased range of motion [1, 3, 14, 17]. Possibly these effects could be found in synovitis of the shoulder as

well. So far no consistent treatment strategy for synovitis in the rotator interval exists. Therefore, further studies need to be performed.

As suggested only 2 of the 167 patients without known rheumatic disease revealed a synovitis score ≥ 5 . This corresponds to the proposition that a synovitis score ≥ 5 is highly affiliated to rheumatic diseases [10].

Limitations of this study are that it did not consider pre- or postoperative clinical parameters such as pain, postoperative patient reported outcome or shoulder function or postoperative adhesive capsulitis. Furthermore, a macroscopic assessment of the synovitis would have been useful to compare macroscopic with microscopic assessments. To our knowledge this was the first study that compared different chronic pathologies of the shoulder regarding their degree of accompanying rotator interval synovitis.

Conclusions

This study suggests that chronic intra- and extraarticular shoulder diseases are very often accompanied by a macroscopically visible and histopathologically verifiable low-grade synovitis. Intraarticular pathologies seem to induce increased levels of synovitis. Furthermore, the increased size of rotator cuff tears is accompanied by a higher degree of synovitis. Further, studies need to assess the clinical relevance of synovitis in shoulder diseases with special regard to therapeutic strategies.

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Compliance with ethical standards

Conflict of interest No potential conflict of interest declared by the author.

Ethical approval This study was approved by the local ethical committee (EA1/351/16).

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