The symptomatic mediopatellar plica
(The Histological, Immunohistological and Clinical Characteristics)

Ph. D. DOCTORAL THESIS

Csaba Farkas MD.

Department of Orthopaedic Surgery University of Debrecen,
Medical and Health Science Centre

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1. INTRODUCTION

The knee joint is one of the large joints in the body, and the disease processes and trauma to it are being actively studied. Under normal circumstances, within the knee joint, you can find a pleat of mucosa membrane – a plica – which, under normal circumstances, is completely asymptomatic, but under certain circumstances, can become symptomatic and cause problems.

In the orthopaedic literature that deals with adult problems, you can find relatively few articles about the synovial septum. However, as Pipkin first showed, the plica can also be one of the causes of knee pain, in addition to the pain originating from the bone, the cartilage, the meniscuses or the ligament structures.

In daily orthopaedic practice, we see anterior knee pain frequently, and when we have occasion to examine the knee itself, we frequently hear and feel clicks, feel crepitation, and occasionally elicit tenderness. We also can be confronted with locking knees, knee instabilities and knee swelling. All these signs and symptoms can be found often in our patient population. Even though the diagnosis is difficult to ascertain, we owe it to our patients to establish the correct diagnosis, and to give each patient optimal treatment for his or her condition.

In the knee joint, we can find plicae- the suprapatellar, the infrapatellar, the medial and the lateral. Of these, the infrapatellar and the lateral never cause any problem, and the suprapatellar only rarely is the cause of knee pain. As we can see, then, the mediopatellar plica is the principal cause of knee pain among the plicae.

With this in mind, I decided to study and present this dissertation of this “insignificant” mucosa membrane fold, because of the fact that this plica is considered “insignificant”, it is easy to overlook it as the cause of knee pain, and in doing so, one will make a spurious diagnosis. If on the other hand, one takes it into account, a correct diagnosis can be established, and the patient can receive optimal treatment.

2. OBJECTIVES

1. What factors play a role in changing the anatomy of this area, and thereby causing pain?
2. Can the plica cause pain on its own, or does it need to be accompanied by femoral condyle and/or patellar chondropathy?
3. What are the histological and immunohistolgical changes in a plica which is painful?
4. Can other pathological changes influence the result of the treatment?
5. What are the operative indications, and which interventions are indicated for surgery?

1. MATERIALS AND METHODS

3.1 Test samples

Twenty-one patients were referred to the Department of Orthopaedic Surgery University of Debrecen, Medical and Health Science Centre in the period of January 1st 1996 and September 1st, 1997. The reason of referral of these patients was for a symptomatic mediopatellar plica. We performed arthroscopies on these patients, and we took tissue sampled during the operation. The study was approved by the Ethics Committee of the University of Debrecen, Medical and Health Science Centre (DOTE KEB 269/96), and we received financial support from the University of Debrecen, Medical and Health Science Centre Mecenatura Foundation (Mec 20/96).

The 21 patients consisted of 11 males and 10 females with an average age of 27.52 years (SD: 7.7 years). The control group consisted of 11 patient, 9 males and 2 females with an average age of 27.72 years (SD 6.18 years), who were treated for other conditions, for example, ACL repair, meniscus surgery or with chondropathia. In the symptomatic group, the right knee was involved in 12 cases, while the left knee was involved in 9 cases. In the control group, the right knee was involved in 7 cases, while the left knee was involved in 4 cases.

We diagnosed a “symptomatic plica” when, during arthroscopy we saw that the plica was thickened, expressed a loss of elasticity when it was moved with a probe, and in fact, it could be seen that the plica was taut. We could also see that either the femoral chondyle or the medial surface of the patella was depressed, and the cartilage was softened, which was attributed to the movement of the plica during extension and flexion of the knee.

The arthroscopies were performed in supine position by the patients, and a tourniquet was applied. The surgery was performed either under general anaesthesia or spinal anaesthesia. From a suprapatellar portal, the plica was resected completely in breadth and partially in length. We sent the plica specimen for analysis, the test group just like the control group.

3.2 Histological examination

All the specimens were subjected to routine histological examinations, using standard H&E and van Gieson staining. In addition, all sections were also examined with a polarising light microscope.

On the other hand, immunohistochemical examination was performed on each half of sample. 8% buffered formalin was used to fix the sample, and it was mounted in paraffin. Afterward, it was re-hydrated, and the endogene peroxidase activity was blocked using 3% H_2O_2/20 minutes, and the anti-genes were retrieved by using citrate buffer (10 mmol Na-citrát pH 6/2 min). After blocking the non-specific binding sites with normal goat serum for 20 minutes, monoclonal anti-Neurofilament antibodies (Clone 2F11, DAKO, USA 1:50), or anti-Synaptophysin (Clone SY38, DAKO, USA 1:10) as primary antibody were applied. . Following incubation at room temperature for an hour, the sections were washed in phosphate buffer (PBS, pH 7,4) for 3x5 minutes, and anti-Mouse IgG, marked with biotin was used as binding plasma. The reaction was then developed with avidin-biotin (ABC) method, marked with peroxidase (1:500, 45 minutes, room temperature). In order to show the antigenes mentioned above, peroxidase substrate KIT was used (Vector USA). Background staining was achieved by using Methyl-green.

The neuro-elements in the samples were counted in ten 10X10 magnification field in each case, in such a way that the examined area was magnified 100 times. The area examined was 7.77 mm^2 in each case.

3.3 Clinical examination

The symptomatic patients that complained of knee pain rated their pain on a 0 to 5 scale, 5 being the most intense. The severity of the existing arthritis was likewise evaluated by a 3-view x-ray, and categorized using the Kellgren method.

We recorded the patient's age, which knee was involved, the time that occurred between the original complaint and the surgery, the patient's sex, and finally if there was a history of trauma to the area. The follow-up time was between 9 and 24 months after the surgery. At this time, the patients once again classified their pain on a subjective scale from 0 to 5, where 0 was no pain at all, and 5 being the most intense. We then judged the results of the surgery, based on the patient's opinion as good, no change or bad.

3.4 Statistical analysis

After a positive test for normality a Student t-test was performed to compare the mean number of neuro-elements found in the samples of patient from the symptomatic and the asymptomatic groups, after Synaptophysis and Neurofilament plasma reactions. The Student-t test was also used to compare the symptomatic and unsymptomatic groups.

A variance analysis was used to find out if there was any correlation between the number of the neurofilaments found in the plica, the age, trauma, the result of operation, the subjective judgement of the pain before and after operation, the body weight, the time that transpired between the complaint and the operation, and the degree of arthritis.

All statistical analyses were carried out with the help of SAS System Rel. 6.04 with 0.95% of significance level.

We used the GLM (General Linear Model) to analyize the varience. We were interested in finding out which, if any, factors had any significance. We found a definite factor with a confidence limit of 0.95%.

During the analysis, we tried to correlate the number of the neurofibers with the patient's subjective judgement of the pain level before and after the operation. Here, we found that there was a wide range of numbers in both groups, therefore we arbitrarily chose cut-off values in each group, thereby rendering the numbers of groups into a manageable number. The analysis was the based on this new classification, which, once again, I would like to stress was arbitrary.

For the purposes of this study, we divided the groups up and classified the based on a few factors. The first classification was based on the number of neurofilaments. If the number of neurofilaments we saw per high-powered field was more than 10, we placed them in group 2, however, if it was less than 10, we placed them in group 1.We also classified the results by their age group. If the subject was below 38 years of age, they were placed in group 1, and if they were over this threshold, they were placed in group 2. Finally, we grouped the test subjects according to the time that had transpired between the original complaint and the surgery. Here, we arbitrarily classified the groups, placing the people who waited less than a year in group 1, the people who waited between 1 and 2 years into group 2, and finally, they were placed in group 3 if the time transpired was more than 2 years.

Based on our analysis, there was a definite relationship between the number of neurofilaments and the difference between the subjective assessment of the pain perceived prior to surgery, and the pain perceived after the surgery.

2. RESULTS

4.1 Histological results

Using H&E and van Gieson staining, synovial hyperplasia was observed in 80.9 % of the symptomatic plica (17 patients of the 21 examined). The synovial hyperplasia created papillary formations. The area poor in capillaries under the hyperplastic epithelium contained rich hyaline bundles of collagen fibres, where the polarising microscope revealed that the regular arrangement of the fibres had largely disappeared, and disorganised, irregularly oriented collagen fibre bundles developed. Chronic inflammatory infiltration was not significant as compared to the control samples.

In the control group, we found in 81.8% of the patients (9 out of 11 patients), that normal synovial membrane covered the surface but underneath, there was degenerated connective tissue, but wavy fibres were laid down and arranged normally.

When we examined the specimens under the polarizing microscope, we found two different types of specimens. In the last two cases, we could see unorganised collagen fibres. In a part of the specimen, we could see a proliferation of the capillaries near the endothelial surface, which was laid down in an unorganised manner. Here, we could find that the collagen fibres were chronically inflamed, a inflammation that also extended into the pericapillary areas.

In the substance of the plica, we also observed very few adipose cells which were normal.

We did not find any positive synaptophysin results by the immunohistochemical method either in the symptomatic nor asymptomatic group. However, in both groups we observed neurofilaments within the collagen fibres. These were primarily observed nestled in the perivascular area, where we observed oblong propagations of the nerve filaments.

In the symptomatic group, we observed an average of 6.9 (SD 2.9) nerve fibres in every 7.77 mm^2 field, whereas in the asymptomatic group, we only observed an average of 3.0 (SD 1.2) nerve fibers in the corresponding field, which translates to a significance of P=0.005.

4.2 Clinical results

The patient follow-up occurred at an average of 14.2 months after the surgical intervention (9-24months). There was no significant differences between the age of the patient, the sex of the patient nor the side either in the symptomatic nor asymptomatic group. The average classification of the pain prior to the operation was 3.8 (SD: 0.3), which diminished to an average of 1.6 (SD: 0.6), which was significant p=0.05.

The results after the surgery were rated as excellent in 7 patients (38.8%), good in 7 other patients (38.8%), while 4 patients reported that their pain was unchanged (22.4%).

In the symptomatic group, we found that there was a tear in the medial meniscus in 4 cases, whereas in the control group, we found longitudinal or collateral ligament tears in 6 patients, while 2 patients suffered from a ruptured ACL, and one patient had a PCL tear.

4.3 Statistical analysis

Variation analysis did not show a significance between different number of neurofilaments in the specimen. However, a significance was found in the subjective judgement in the following factors after the surgical intervention.

These are the follows:

-the time transpired between the original complaint and the surgery (table I.),

Table I.

C-S / mos	n	Subjective clasification
1	11	1.2
2	7	1.6
3	3	2.7

table legend:

C-S:	time transpired between the original complaint and the surgery
1:	< 12 months
2:	= 12 and 24 months
3:	> 24 months
n:	number of cases

Subjective classification: The subjective classification of the pain after the surgery, where 0 is the absence of pain, while 5 corresponds to the exact level of pain felt prior to the surgery.

-the role of trauma (table II.)

Table II.

Trauma	n	Subjective clasification
0	13	1.92
1	8	0.88

Table legend:

Trauma: 0 = no history of trauma
1 = history of trauma
n: =number of cases
Subjective classification: The subjective classification of the pain after the surgery, where 0 is the absence of pain, while 5 corresponds to the exact level of pain felt prior to the surgery.

- the relationship between the neurofilament number and trauma (table III)

Table III.

	Trauma	
NF	0	1
1*	# 9 _ 1.55	# 4 _ 1.25
2*	# 4 _ 2.75	# 4 _ 0.5

Table legend:

NF: Neurofilaments
1*: less than 10 neurofilaments
2*: more than 10 neurofilaments
Trauma: 0= no trauma in the medical history
1= a history of trauma in the medical history
#: The sample group number
_: The average post-op pain relief, where 0 is equal to complete relief of the pain and 5 is equal to the level of pre-operative pain.

The relationship between the number of neurofilaments, and the objective rating of the pre and post-operative pain levels is in the tabale IV.

Table IV.

	Neurofilament number	Preoperative pain	Postoperative pain	Diminishment of pain
Trauma	9.6	3.8	0.8	3.0
No trauma	5.2	3.7	1.9	1.8

5. DISCUSSION

Due to examinations under anaesthesia, we do not accept that pain is only caused by mechanical factors, since not only the taut, thickened mediopatellar plica causes pain, but we can also find pain where there is a thin, elastic plica. In addition, the incidence of impingement is quite rare. Furthermore, the plica that does not touch the femoral condyle can be symptomatic.

Likewise, chondromalatia is not likely to be a factor in the cause of the pain, for it is found in the minority of the cases, and many times here, you can see a maltracking of the platella. To complicate things, in some cases, you can see menicus problems and tears as well. In groups, the control as well as the test group, the softening of the cartilage of the majority of the groups could be found in Outerbridge I-II. We found that if the softening of the cartilage was such that it could not be treated conservatively, when an arthroscopy was performed, diffuse global softening of the cartilage was found. Inevitably, in all of these cases, there was pain.

However, we can state definitively here that a “symptomatic plica” was more painful when we found some alteration of its histology.

In a symptomatic plica, neither the propagation of the synovial mucosaa membrane nor a minimal inflammation of the connective tissue could explain the pain. In our series of patients, we did not see any macroscopic evidence of inflammation, either in the joint or the plica. We found this to be true not only in the test group, but in the control group as well. The one significant difference that we did find between the two groups was the number of nerve fibres found in the specimen. The difference was significant, and this fact could explain the pain in the test group, and the mechanism by which the plica became symptomatic.

When we analysed the variables, we looked for a relationship between the operative outcomes and the subjective values (in particular, a decrease in the pain levels) with respect to the number of nerve fibres. One definite factor that came to light during our analysis was trauma. In the patients that had a history of trauma, the decrease in the subjective pain felt after surgery was significant, being rated 0.8 instead of 1.9. When we examined the specimens taken from these patients, we found that the number of nerve fibres was noticeably increased. But the absolute number of nerve fibres didn’t explain the whole picture, for if we examined groups of patients that had the same average numbers of nerve fibres, we found that the decrease of the subjective pain felt was larger for the

group that had sustained trauma (3.0) than for the group that didn't (1.8). If we investigated further, we found in the group that had sustained trauma, we notice the best results were obtained when the amount of nerve fibres had increase 10 fold or more. A final observation was that when we looked at the group that had sustained trauma, the optimal time for performing an operative intervention from the standpoint of diminishing the pain, was when the surgery occurred within a year of the traumatic event.

In any case, when we speak of the trauma patients, the amounts of nerve fibres do indeed play a factor in the outcome, for we found that when there is a greater amount of nerve fibres in the specimen, the post-op pain relief is better. The optimal time for performing the surgical procedure is within a year of the traumatic event, for we believe that after this time, the proliferation of scar tissue is such that the results of the surgical intervention is not so good. In the delayed treatment patients, we think that the mechanical irritation also begins to play a factor in the pain sensation.

6.SUMMARY

In the evaluation of anterior knee pain, one should keep in mind the symptomatic mediopatellar ligament, or rather the accepted opinion of an interior joint mechanical damage and its continuing patho-physiolgical process. When we compared a group of patients with a symptomatic mediopatellar plica with a control group, we were looking for some type of damage we could see microscopically, which could be attributed as the cause of the pain. We sent 21 tissue samples from 21 symptomatic patients, and these samples were stained with either H&E or van Gieson stains, and subsequently examined under a microscope or a polarizing microscope. In the plica itself, we examined semi-quanitatively the amount of nerve fibres that were present. Then, using immuno-histological methods we did a quanitative analysis and determined the exact number of nerve fibres. Another group of 11 patients who went to the OR for other reasons (mescal tear, ACL rupture, etc.) served as controls, and samples were taken from them as well for that purpose and examined. When we looked at the two groups, there was no significant differences regarding the average age, the amount of time that transpired between the initial complaint and the surgery, the seriousness of the complaint, the side of the knee involved (right or left) or the sex. Upon examination of the specimens, we found that the structure of the tissue was different regarding the symptomatic and asymptomatic groups. In the symptomatic group, we found synovial hyperplasia was observed in 80.9 % of the symptomatic plica. The synovial hyperplasia created papillary formations. The area poor in capillaries under the hyperplasiatic epithelium contained rich hyaline bundles of collagen fibres, where the polarising microscope revealed that the regular arrangement of the fibres had largely disappeared, and disorganised, irregularly oriented collagen fibre bundles had developed. In both groups, we succeeded in identifying the nerve fibres. When identical visual fields were examined, we found that in the symptomatic group, an average 6.9 (SD 2.9) per field, whereas in the asympomatic group, only an average of 3.0 (SD 1.2) were observed. We also noticed that when there were more nerve fibres present in the tissue, the amount of pain relief in the post-operative period was unequivocally higher. Our investigations provide a basis that from the tightening of the plica, a mechanical irritation can arise, and in addition to chondromalatia and synovitis, the symptomatic mediopatellar ligament can cause knee pain, and the amount of knee pain can depend on the amount of nerve fibres in the plica. The amount of nerve fibres can be increased when one finds a history of trauma in the medical history, for it is very likely

that the proliferation of nerve fibres can be a consequence of the trauma, and in turn, can give rise to a symptomatic plica.

Publications related to the thesis

1. Farkas Cs., Gáspár L., Jónás Z: The pathological plica in the knee
   Acta Chirurgica Hungarica 1997:36(1-4):83-85

2. Ortutay Zs., Polgár A., Gömbör B., Géher P., Lakatos T., Glant T. T., Gay R. E., Gay S., Pállinger É., Farkas Cs., Farkas É., Tóthfalusi L., Kocsis K., Falus A., Buzás E.I.:
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   Arthritis & Rheumatism Vol. 48, No. 8, August 2003, 2163-2172
   Impact factor: 7,26

3. Farkas Cs., Hargitai Z., Gáspár L., Kuki A., Csernátony Z., Szepesi K.:
   Histological changes in the symptomatic mediopatellar plica
   The Knee 11, 2004, 103-108
   Impact factor: 0,25