

Lymphoscintigraphic and morphometric study of synovial membrane in the osteoarthritic knee

Etude morphométrique et lymphoscintigraphique de la membrane synoviale de genoux ostéoarthritiques

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SUMMARY

The present work reports the study of 53 synovial membranes using histology and morphometry.

The synovial membrane was collected in osteoarthritic knee which presented lymphoscintigraphic abnormalities. The morphometric study showed inflammatory infiltrate, congestive vessels and fibrosis. The articular lymphoscintigraphy, with ^{99m}Tc labelled dextran, demonstrated that tracer disappeared at 24 hours more slowly from the abnormal joint but accumulated more intensely in regional lymph nodes on the pathological side. The statistical analysis of the morphometric and lymphoscintigraphic data shows a significant correlation between the lymphatic dysfunction and the synovial membrane fibrosis. There is no significant correlation between other morphometric data (vessels and inflammatory infiltrate) and articular lymphoscintigraphic results.

RÉSUMÉ

Le présent travail porte sur l'étude morphométrique et histologique de 53 cas de membranes synoviales obtenues au niveau de genoux ostéoarthritiques présentant des anomalies à l'étude lymphoscintigraphique.

L'étude morphométrique montrait : infiltrat inflammatoire, vaisseaux congestifs et fibrose. La lymphoscintigraphie articulaire au dextran technétié démontrait : une disposition retardée du traque au niveau de l'articulation pathologique mais une accumulation ganglionnaire plus marquée du même côté. L'analyse statistique des données morphométriques et lymphoscintigraphiques démontre une corrélation significative entre la dysfonction lymphatique et le degré de fibrose. Aucune autre corrélation significative n'a pu être établie.

KEY WORDS : Articular Lymphoscintigraphy, Morphometry of Synovial Membrane, Osteoarthritis of the Knee, Chronic Synovitis, Degenerative Knee Arthropathy.

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1. INTRODUCTION

The relationship synovial-osteoarthritis is not completely clarified. That's why the author tried to settle a correlation between the data obtained by the morphometry of the synovial and the articular lymphoscintigraphy. It was necessary to know the histological behavior of the synovial corresponding to the lymphatic dysfunction of the osteoarthritic joints - subject already explained in a former paper (1).

2. MATERIAL AND METHODS

The study group included 53 pathologic knees (35 male patients) with degenerative arthropathy. The diagnosis of joint disease was made clinically, radiographically, and verified by notable cartilage damage at time of arthrotomy*. The range in age was from 19-74 years (mean 44). During the operatory procedures** the synovial tissue is collected. The specimens were taken from the condilar part of the knee joint at the attachment of the condilar fibrous capsule in the compartment of the knee where the degenerative disease was more visible. The synovial was fixed in 10 % neutral buffered formalin and embedded in paraffin wax. Sections for light microscopy were prepared from all the specimens (5 μ m), stained with hematoxylin-eosine, Mac Manus and Van Giemsa methods and used for histological and morphometrical analysis. With the morphometric study was determined the volume percentage (VV %) of fibrosis, vascularization and inflammatory infiltrate, according to Weibel (2) - point counting was used for mesured volume percentage. A multipurpose test was superimposed on a TV screen on microscopic image-magnification X 400.

A previous lymphoscintigraphic articular study was made in all the patients studied according to the method described in a former paper (1).

(*) According to this data the studied knees were classified in three groups :

Initial Chondropathy (cartilage edema - n = 11) ;

Advanced Chondropathy (cartilage fissuration - n = 18)

and Osteo-arthritis (cartilage erosion - n = 23).

(**) Meniscectomy, ligamentoplasty, synovectomy, shaving of the cartilage with retinaculum elongation or Maquet procedure, arthrotomy or prosthetic substitution

3. RESULTS

The synovial samples studied, showed always a moderate chronic synovitis (fig. 1). The presence of a chronic irritative process of the synovial was substantiated by the presence of lymphocytes and plasma cells. The infiltrate was diffused with a little agglomeration of lymphoides all over the vessels. Add to this infiltrate there were always the other typical aspects of chronic nonspecific synovitis, that is to say the vascular ectasia, and an increase of synovial fibrosis. But, if the histologic study not quantitative, was enough to show clearly structural changes, it did not allow to determine the real depth of the articular injury. Trying to prevent this kind of difficulties, it was made a morphometric study of the cellular populations of the inflammatory infiltrate in order to find additional and more clear information concerning the type of histological changes. With this purpose the morphometric parameters studied in the synovial samples were the fibrosis, the vascularization and the inflammatory infiltrate. The values obtained in this study are presented in Table I.

The lymphoscintigraphic study (fig. 2) shows that in contrast to the normal knee, the radiopharmaceutical disappeared more slowly from the pathologic joint (tracer retention $86,9 \pm 3,3\%$ - $p < 0,01$ - in the studied pathologic knees (vs $77,44 \pm 4,6\%$; $p < 0,01$ in the normal knee (1). The tracer also accumulated more in the regional nodes draining the studied pathological knees ($4,74 \pm 2,7\%$; $p < 0,01$) as compared to the normal side (vs $1,88 \pm 0,209\%$; $p < 0,01$ in the normal side (1).

The statistical analysis showed no correlation among values of the 24 hours lymphoscintigraphic articular quantification and the histological morphometric parameters of the infiltrate and vessels. In the fibrosis case, the results allowed us to conclude a linear relationship between the morphometric fibrosis values - indicated on fig. 3 by y - and the lymphoscintigraphic values of the lymph node accumulations - indicated on fig. 3 by x.

4. DISCUSSION

In spite of the lack of interest manifested in orthopaedics towards the lymphatic system, we consider that it plays an important role in joint function and its study might clarify some pathological findings (3). This is why we have tried to find more satisfactory

means of displaying possible abnormalities of joint function. Even though in the osteoarthritis the synovial reaction was rarely severe in all the studied cases, the presence of light or mild synovial changes was expressed as an unspecific chronic synovitis with edema and lymphoplasmocitary infiltration (4). In the course of time, this inflammatory reaction of the synovial ends to consolidate causing a structural alteration with congestion and fibrosis, most of the times with perivascular organization. According to some authors opinion, there are an existence of low oxygen tension on the articular fluid (5) and an abnormal protein pattern in osteoarthritis (6) suggesting an increased capillary permeability in the synovial membrane owing to capillary dilatation and stasis. These synovial changes may be relevant in the joint and determinative concerning the future compromise of articular cartilage.

Would it be the articular lymphatic dysfunction described by us (1, 7) strictly connected to the cellular populations alterations morphometrically verified in the knee arthropathy? The answer to this question can be found in the morphometric quantified data found. The statistic analysis showed to the fibrosis a significant correlation between articular lymphoscintigraphy-synovial morphometry, when the lymph nodes accumulation values were considered. No correlation could be demonstrated among the values of synovial vascularization or synovial cellular infiltrated and articular lymphoscintigraphy.

It seems obvious that the failure of lymphatic articular system causes an increase of the articular interstice fibrosis. This is in agreement with the findings concerning the lymphatic function in other organs.

5. CONCLUSIONS

- 1) In patients with knee osteoarthritis, the histological examination of the synovium shows a picture of a moderate inflammatory reaction with edema, lymphoplasmocitary infiltration, venous stasis and fibrosis.
- 2) The synovial fibrosis seems to correlate with the lymphoscintigraphic accumulation values obtained in the regional nodes draining the pathological knees.

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PAT.			Synovial Morphom.			Articular Lymphoc. 24 H. Quant.		SURGICAL PROCEDURE	
NAME	AGE	SEX	Infiltr.	Fibrosis	Vessels.	Knee	Inguinal	Type of surgical intervention	Cartilage lesion see during surgical arthroscopy
CAS	45	F	5,60	16,70	22,20	84,99	3,28	Valgus Osteotomy	Advanced Chondropathy
HA	65	M	11,10	33,30	8,30	81,03	4,26	Valgus Osteotomy	Osteo-arthritis
JRM	40	M	16,70	16,70	2,80	83,93	3,12	Varus Osteotomy	Advanced Chondropathy
JIP	48	M	11,10	22,20	16,70	89,78	3,92	Shaving + Ret. Elong.	Advanced Chondropathy
MEDR	51	F	2,80	5,60	5,60	81,03	2,05	Varus Osteotomy	Osteo-arthritis
MAC	36	M	16,70	38,90	13,90	89,39	2,63	Valgus Osteotomy	Advanced Chondropathy
LMRD	29	F	8,30	13,90	11,10	87,92	2,17	Meniscectomy	Initial Chondropathy
FB	24	M	2,80	13,90	5,60	84,68	2,35	Synovectomy	Initial Chondropathy
FLPL	32	F	8,30	16,70	5,60	88,31	2,62	Shaving + Maquet	Advanced Chondropathy
JMN	69	M	2,80	22,20	5,60	93,28	11,92	Valgus Osteotomy	Osteo-arthritis
MAN	60	F	5,60	44,40	22,20	92,34	8,06	Valgus Osteotomy	Osteo-arthritis
MLM	49	F	2,80	11,10	8,30	85,34	2,85	Valgus Osteotomy	Advanced Chondropathy
LM	69	F	8,30	36,10	2,80	93,73	8,12	Valgus Osteotomy	Osteo-arthritis
MSS	50	F	11,10	16,70	16,70	83,10	2,23	Synovectomy	Initial Chondropathy
ARJ	32	M	8,30	14,70	8,30	89,38	3,28	Shaving + Ret. Elong.	Advanced Chondropathy
AASP	35	M	22,20	11,10	2,80	84,35	2,39	Meniscectomy	Initial Chondropathy
CMFM	19	M	2,80	13,90	2,80	87,38	2,03	Ligamentoplasty	Initial Chondropathy
AG	69	M	8,30	38,90	2,80	95,86	8,80	Varus Osteotomy	Osteo-arthritis
SSMS	44	F	16,70	33,30	8,30	96,45	5,48	Ligamentoplasty	Initial Chondropathy
CAP	24	F	16,70	5,60	2,80	88,21	2,92	Meniscectomy	Initial Chondropathy
JE	65	M	5,60	16,70	22,20	89,84	6,48	Varus Osteotomy	Osteo-arthritis
APL	25	F	11,10	27,80	22,20	88,08	3,15	Shaving + Maquet	Advanced Chondropathy
ERG	51	M	8,30	33,30	16,70	91,23	6,90	Valgus Osteotomy	Osteo-arthritis
MCMG	26	F	5,60	5,60	16,70	89,95	2,07	Meniscectomy	Initial Chondropathy
MJEL	53	M	11,10	16,70	5,60	83,99	2,96	Meniscectomy	Initial Chondropathy
ACR	26	M	11,10	22,20	11,10	86,39	3,24	Shaving + Maquet	Advanced Chondropathy
AMPV	25	M	8,30	22,20	22,20	81,71	3,35	Shaving + Ret. Elong.	Advanced Chondropathy
AGMO	37	M	5,60	44,40	5,60	89,11	12,19	Prosthetic Replacement	Osteo-arthritis
MHSV	33	M	2,80	18,70	8,30	87,22	4,03	Varus Osteotomy	Osteo-arthritis
JPT	46	M	2,80	11,20	22,20	85,67	2,53	Valgus Osteotomy	Advanced Chondropathy
AJL	48	M	5,60	44,40	11,10	84,75	3,34	Varus Osteotomy	Advanced Chondropathy
MPMC	28	M	11,10	5,60	16,70	82,70	2,05	Ligamentoplasty	Initial Chondropathy
AMRV	27	M	11,10	8,30	2,80	85,05	2,13	Shaving + Ret. Elong.	Advanced Chondropathy
JARA	34	M	5,60	16,70	11,10	79,89	1,77	Shaving + Maquet	Advanced Chondropathy
CMCC	30	M	2,80	33,30	18,70	87,40	4,56	Valgus Osteotomy	Advanced Chondropathy
FPI	28	M	2,80	16,70	8,30	85,54	3,94	Valgus Osteotomy	Osteo-arthritis
GA	41	M	11,10	22,20	13,90	80,63	3,11	Synovectomy	Advanced Chondropathy
DSC	27	M	5,60	44,40	13,90	89,23	4,58	Varus Osteotomy	Osteo-arthritis
DT	62	M	16,70	44,40	22,20	79,98	6,18	Prosthetic Replacement	Osteo-arthritis
MSN	51	F	5,60	11,10	16,70	85,45	6,09	Valgus Osteotomy	Osteo-arthritis
LFM	35	M	16,70	24,20	2,80	83,21	10,63	Shaving + Maquet	Osteo-arthritis
CN	64	F	2,80	11,10	5,60	89,87	6,61	Varus Osteotomy	Osteo-arthritis
MAFM	69	F	5,60	22,20	5,60	86,17	5,16	Shaving + Ret. Elong.	Osteo-arthritis
IPF	24	F	11,10	22,20	16,70	84,05	2,53	Shaving + Maquet	Advanced Chondropathy
VMFP	26	M	2,80	8,30	2,80	91,47	3,61	Valgus Osteotomy	Advanced Chondropathy
MJV	69	F	11,10	33,30	2,80	91,87	8,95	Prosthetic Replacement	Osteo-arthritis
MR	63	M	5,60	16,70	16,70	87,31	4,93	Valgus Osteotomy	Osteo-arthritis
NC	48	M	11,10	22,20	5,60	86,63	8,84	Varus Osteotomy	Osteo-arthritis
EES	60	M	11,10	16,70	8,30	84,03	2,90	Varus Osteotomy	Advanced Chondropathy
AD	61	M	2,80	33,30	22,20	92,11	9,35	Valgus Osteotomy	Osteo-arthritis
MO	74	M	5,60	27,80	8,30	87,11	5,75	Valgus Osteotomy	Osteo-arthritis
LSS	60	F	5,60	22,20	8,30	88,16	5,72	Varus Osteotomy	Osteo-arthritis
JACC	36	M	2,8	5,60	5,60	82,44	2,09	Meniscectomy	Initial Chondropathy

TABLE I - TABLEAU I

A comparison between the values of synovial morphometry and the articular lymphoscintigraphy.
 Knee : Disappearing joint radioactivity - percentage of radioactivity which remained in the knee as a function of the amount initially injected.

Inguinal : Regional nodal uptake - percentage of activity accumulated in the nodes in relation to the tracer activity initially injected in the knee.

Comparaison entre les valeurs de la histomorphométrie synoviale et la lymphoscintigraphie.

Genou : Disparition de l'activité - pourcentage de l'activité retenue dans le genou comme fonction de la quantité injectée initialement.

Inguinal : Imprégnation ganglionnaire - pourcentage de l'activité accumulée dans les ganglions inguinaux en relation avec l'activité injectée initialement dans le genou.

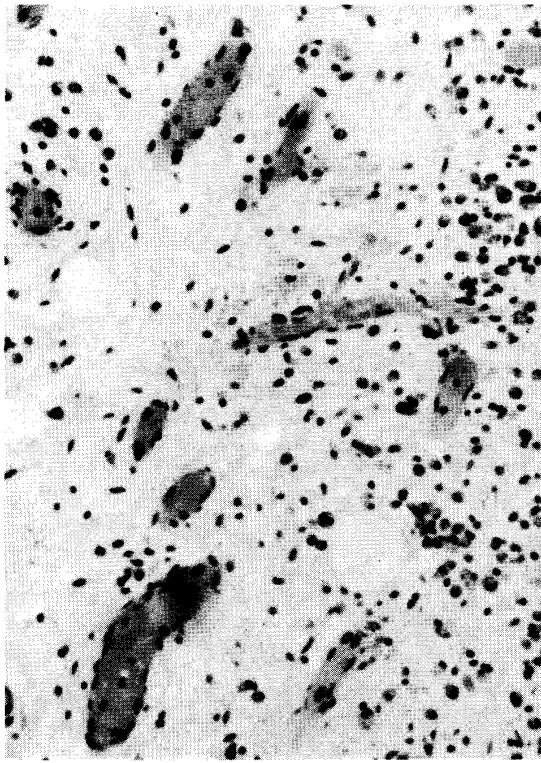


FIGURE 1

Long term chronic synovitis of the osteoarthritis.
 Synovial aspect : mononuclear cells infiltration ;
 marked venous stasis and capillary dilatation -
 (Patient : NC - hematoxylin and eosin - magnification $\times 100$).
 Synovitis chronique.
 Aspect histologique habituel : infiltrations par cellules
 mononucléaires ; congestion veineuse ; dilatation capillaire -
 (Malade : NC - hematoxiline eosine, $\times 100$).

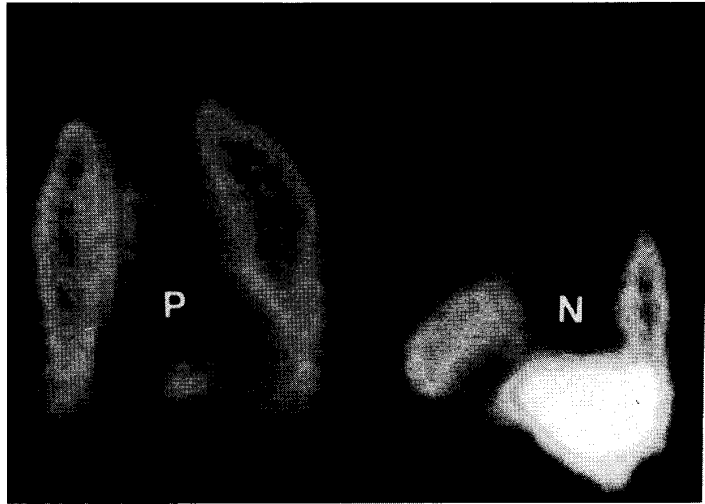


FIGURE 2

Articular lymphoscintigraphy (99 mTc-labelled dextran) :
 demonstrating images at 6 hours after tracer injection
 into the knee joint in a patient with degenerative arthropaty (P)
 and joint enlargement of the articular space after long term
 chronic synovitis (Patient JPL).
 P - Pathologic knee
 N - Normal joint.

Etude lymphoscintigraphique articulaire
 (Dextran marqué au 99mTc). Images obtenues 6 heures
 après l'injection du produit marqué dans les genoux.
 Augmentation de l'espace articulaire du côté malade (P)
 par synovitis chronique à longue durée
 (Malade JPL).
 P - Genou pathologique
 N - Genou normal.

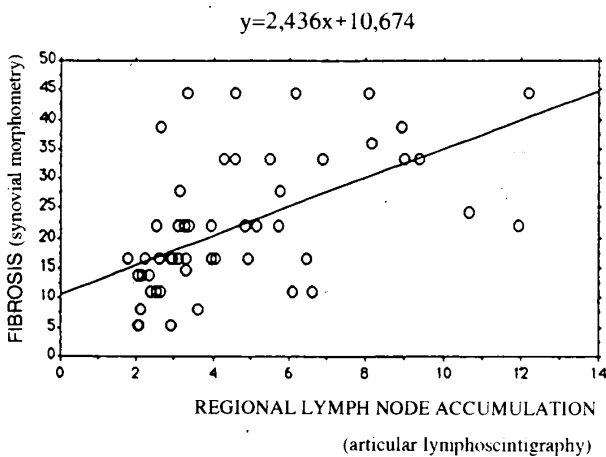


FIGURE 3

Linear regression represented by the straight line
 between the values of fibrosis
 and regional lymph node accumulation.
 Régression linéaire représentée par la ligne droite d'ajustement
 entre les valeurs de la fibrose et de l'accumulation ganglionnaire.