



Original Research Article

Study of histomorphological features of synovial biopsy in joint diseases

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ARTICLE INFO

Article history:

Received 15-07-2019

Accepted 20-07-2019

Available online 22-11-2019

Keywords:

Synovitis

Arthritis

Synovial biopsy

Histomorphological features

ABSTRACT

Introduction: The histopathological examination of synovial biopsy plays an important role in arriving at correct diagnosis in joint disease presenting as unclassified arthritis, suspicious of granulomatous disease, deposition disease or infectious disease.

Objectives: To study the histomorphological features of synovial biopsy in joint diseases.

Materials and Methods: This was a prospective study conducted in the Department of Pathology, K V G Medical College and Hospital, Sullia, D.K. In the present study 50 cases of synovial lesions were evaluated histopathologically.

Results: Histomorphological examination of 50 synovial biopsies revealed the following lesions: Chronic non specific synovitis was the commonest synovial lesion encountered in 30 (60%) cases followed by 6 (12%) cases of Ganglion cyst, 4 (8%) cases of Septic arthritis, 3 (6%) cases of Baker's cyst, 2(4%) cases each of Synovial chondromatosis and Rheumatoid Arthritis and 1 (2%) case of Cavernous hemangioma.

Conclusion: It was concluded that most of the cases in our study was that of chronic nonspecific synovitis. This could be due to early stage of Rheumatoid arthritis, osteoarthritis and other seronegative arthritis. Hence, these patients should be closely followed up and repeat biopsies should be carried out as they may present with specific diagnostic features in their due course.

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1. Introduction

Synovium which lines the joint space is labile, reacts to wide variety of changes and noxious influences originating locally or elsewhere in the body.¹

Arthritis is frequently encountered in clinical practice and is an important cause of morbidity, affecting all ages and both sexes. It may present as a monoarticular or polyarticular lesion. Monoarticular lesion often follows trauma or infective etiology, while polyarticular lesion is commonly seen in rheumatoid pathology. The latter can be easily arrived at by using a fairly simple technique of arthroscopic synovial aspiration and biopsy and specific treatment be instituted in cases like tuberculosis. It has added advantage of being therapeutic in certain cases like early osteoarthritis wherein loosebodies etc, can be removed

earlier on in the disease process.²

Synovial fluid analysis and biopsy have been found to be a valuable adjunct to conventional investigations and are routinely advised in most cases of joint diseases.²

Combination of clinical, radiological, serological, biochemical and microbiologic findings along with synovial fluid and biopsy findings help in the diagnosis of specific inflammatory lesions of synovium and treating the particular condition.³

Synovial fluid examination and identification of the etiologic agent is of importance in treating septic arthritis patients to avoid destruction of synovial joint.³ Any synovial fluid with increase in polymorphs indicates joint pathology. Specific diagnosis on biopsy is lymphoid follicles and plasma cell infiltration in cases of rheumatoid arthritis and crystals in case of gout.³ Histopathological study of synovial biopsy is one of the most valuable means

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for diagnosis of joint disease.¹

Present work has been conducted to study the histomorphological features of synovial biopsy in joint diseases.

2. Materials and Methods

This prospective study was conducted in the Department of Pathology, K V G Medical College and Hospital, Sullia, D.K. Duration of study was November 2014 to June 2016. In the present study 50 cases of synovial lesions were evaluated histopathologically. Permission for the study was obtained from the College authorities prior to commencement.

2.1. Method of collection of data

Patients presenting with clinical features of various joint diseases with synovial involvement were selected based on our inclusion criteria and biopsy was performed. Synovial biopsy specimens received were fixed in 10% formalin and subjected to thorough gross examination. After routine processing, Hematoxylin and Eosin (H & E) stain was performed on all tissue sections. Other investigations like synovial fluid analysis, complete blood count, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), RA factor, serum uric acid, blood culture and X-ray findings were collected from the laboratory wherever necessary to categorize the lesions and for appropriate clinicopathological correlation.

2.2. Inclusion criteria

All synovial biopsies performed except in cases of traumatic arthritis and limb amputation were included in the study.

2.3. Exclusion criteria

Cases of Traumatic arthritis and Synovial tissue from amputated limb were excluded from the study.

2.4. Study design

All patients with joint diseases were evaluated clinically and detailed history were taken regarding the number of joints involved, complaints of pain, swelling, fever and restricted movements.

After thorough laboratory investigations wherever necessary synovial fluid aspiration was performed and the following parameters were assessed.

Synovial fluid was subjected to physical, biochemical and cytological analysis. The parameters studied in physical examination included color, mucin clot test, and wet preparation. The biochemical analysis included synovial fluid glucose and estimation of protein in synovial fluid. Cytology entailed estimation of the total leukocyte count and study of the centrifuged deposit to see predominant

white blood cells (WBCs) and the presence of red blood cells (RBCs). Air dried smears were prepared after centrifugation at 2000 rpm and stained with Leishman's stain

Synovial fluid analysis was categorized in to 4 groups

Noninflammatory effusions (Group I) - leukocyte count 0-5000 cells/ cumm with a minority of neutrophils.

Inflammatory effusions (Group II) - leukocyte counts between 0-50000 cells /cumm with neutrophils accounting for more than 50% of the population.

Purulent (infectious) effusions (Group III)- leukocyte counts greater than 50,000, of which 90% or more were neutrophils.

Hemorrhagic effusions (Group IV) -may be seen in association with pigmented villonodular synovitis, synovial hemangioma, neuropathic osteoarthropathy, joint prostheses, and hematologic disorders (hemophilia, thrombocytopenia, anticoagulant therapy, sickle cell disease or trait, myeloproliferative syndrome).

Histopathologically, various lesions were diagnosed by interpreting the following features: hypertrophy and hyperplasia of the synovium, proliferation of synoviocytes, proliferation of villi, type of inflammatory cells, capillary proliferation, vascular congestion, presence of bone and cartilage fragments with or without inflammation, subsynovial fatty tissue and fibrosis.

Finally the clinical diagnosis and laboratory findings were correlated with the histopathological diagnosis.

3. Results

Among 50 patients studied, the most common age group affected were 41 to 50 years of age with 15 patients (30%) followed by 13 patients in the age group 31 to 40 years. There were 8 patients in age group 21 to 30 years, 5 patients in age group 61 to 70, 4 patients in the age group 51 to 60 years and rest are shown in table-5. Osteoarthritis was commonly seen in the 5th and 6th decade, septic arthritis in 1st and 3rd decade, chronic non specific synovitis was commonly seen in 4th decade, rheumatoid arthritis in 4th and 8th decade, baker's cyst in 3rd and 4th decade, ganglion cyst in 1st to 4th decade, synovial chondromatosis was commonly seen in 3rd decade and cavernous hemangioma in 2nd decade.

Among 50 synovial lesions, male were commonly affected (56%) when compared to females (44%) with male to female ratio of 1:0.78.

Synovial lesions were categorized into 4 groups based on their histomorphological features. Majority of them were inflammatory in nature 64% followed by the second major group benign tumor and tumor like conditions which accounted for 24% of cases.

Infective and degenerative joint diseases occupied the third and fourth slots representing 8 and 4% each. Table 1

Table 1: Categorization of synovial Lesions in present study

Categories	No. of cases	Percentage
Degenerative	2	4%
Infective	4	8%
Inflammatory	32	64%
Benign tumor and tumor like lesions	12	24%
Total	50	100%

The commonest synovial lesions encountered was chronic non specific synovitis in 30 patients (60%) followed by Ganglion cyst in 6 patients (12%), Septic arthritis in 4 patients (8%), Baker's cyst in 3 patients (6%), Osteoarthritis in 2 patients (4%), synovial chondromatosis in 2 patients (4%), Rheumatoid Arthritis in 2 patients (4%), and least common lesions was Cavernous hemangioma (2%) seen in one case. Table 2

Table 2: Incidence of synovial lesions in present study

Histopathological Diagnosis	No. of patients	Percentage (%)
I. Degenerative		
Osteoarthritis	2	4%
II. Infective		
Septic Arthritis	4	8%
III. Inflammatory		
Chronic non specific synovitis	30	60%
Rheumatoid arthritis	2	4%
IV. Benign tumor and tumor like lesions		
Bakers cyst	3	6%
Ganglion cyst	6	12%
Synovial chondromatosis	2	4%
Cavernous haemangioma	1	2%
Total	50	100%

Out of 50 cases, 30 cases of chronic non specific synovitis showed Hyperplasia of synoviocytes was seen in 27 cases (90%), followed by synovial hypertrophy in 3 patients (10%). Presence of inflammatory cell infiltrate comprising of lymphocytes in all patients, plasma cells in 6 cases (20%) and neutrophils in 2 cases (4%) Vascular congestion was noted in 15 cases (50%), vascular proliferation in 6 cases (20%), fibrosis in 5 cases (16.6%) and sub synovial fat in 7 cases (23.3%).

Among 2 cases of Osteoarthritis, mild lymphocytic infiltrate, cartilage fragments and congested blood vessels were seen in all two cases followed by fibrosis in one case. There were 2 cases of rheumatoid arthritis which showed villous hypertrophy, hyperplasia of synoviocytes, dense infiltration of lymphocytes along with lymphoid follicle formation, plasma cell infiltrate and vascular proliferation.

4 cases of septic arthritis showed dense infiltration of neutrophils in all cases (100%) followed by hyperplasia

of synoviocytes and congested blood vessels in 3 patients, vascular proliferation in one patient, fatty tissue in 2 patients and fibrosis in 1 patient.

Out of 6 cases of ganglion cyst, synovial lining was present in two patients and flattened lining in 4 patients followed by lymphocyte infiltration in two patients and vascular congestion in 3 patients.

3 cases of baker's cyst showed synovial lining with cyst wall with mild lymphocytic infiltrate in 2 cases and vascular congestion in one case.

2 cases of synovial chondromatosis showed synovial lining with lobules of chondrocytes and foci of calcification. Fatty tissue was seen in one case

1 case of cavernous hemangioma showed large blood filled spaces with mild lymphocytic infiltrate. Table 3, Figures 1, 2 and 3

Rheumatoid arthritis

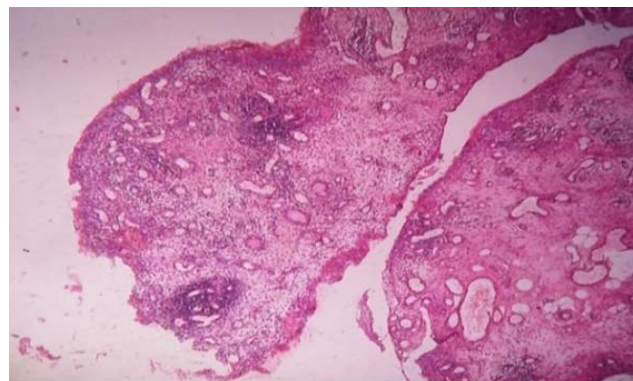
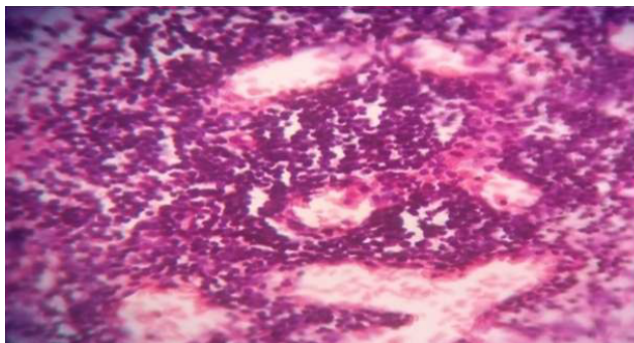
**Fig. 1:** Gross- Grey white to grey brown tissue mass measuring 2X1 cms**Fig. 2:** Photomicrograph showing Villous Hypertrophy (H&E 10X)

Table 3: Histomorphological features of synovial lesions

Microscopic features	Histopathological diagnosis							
	OA (n=2)	SA (n=4)	CNSS (n=30)	RA (n=2)	BC (n=3)	GC (n=6)	SC (n=2)	CH (n=1)
Cartilage	2	0	0	0	0	0	2	0
SH	0	0	3	0	0	0	0	0
VH	0	0	0	2	0	0	0	0
HS	0	3	27	2	0	0	0	0
N	0	4	2	0	0	0	0	0
L	2	0	30	2	2	2	0	1
P	0	0	6	2	0	0	0	0
Fib	1	1	5	0	0	0	0	0
CBC	2	3	15	0	2	3	0	0
Vas Pro	0	2	6	1	0	0	0	0
FT	0	2	7	0	0	0	1	0
Cw	0	0	0	0	3	6	0	0
LBFS	0	0	0	0	0	0	0	1
LF	0	0	0	2	0	0	0	0

OA-Osteoarthritis, SA-Septic Arthritis, CNSS-Chronic non specific synovitis, RA-Rheumatoid arthritis, BC- Baker's cyst, GC- Ganglion cyst, SC-Synovial Chondromatosis, CH-Cavernous Hemangioma.

SH- synovial hyperplasia, VH-villous hypertrophy, HS- hyperplasia of synoviocytes, N-neutrophils, L-lymphocytes, P- plasma cells, Fib-fibrosis, CBC congested blood vessels, Vas pro- vascular proliferation, FT-fatty tissue, CW-cyst wall, LBFS- large blood filled spaces, LF- lymphoid follicles.

**Fig. 3:** Photomicrograph showing well-formed lymphoid follicles (H&E 40X)

4. Discussion

Majority of the lesions occurred in the age group 11-70 years with a peak incidence between 41-50 years indicating that synovial lesions can occur almost in all age groups, but more common in adulthood. Similar observations were seen in the study done by P.M. Vijay *et al*¹ where the age group was between 10-80 years and peak incidence was between 40-50 years, Fletcher *et al*⁴ had maximum incidence between 12-88 years.

Males were most commonly affected than females in the present study with M:F ratio of 1:0.78. Similar observations were seen in the study done by P.M. Vijay *et al*¹ and Fletcher *et al*⁴ M:F ratio of 1:0.6 and 1:0.5 respectively

In our study, inflammatory arthritis comprising of chronic non specific synovitis was the most common synovial lesion, consisting of 30 patients (60%) from 50 synovial lesions. Similar observations were seen in the study done by Fletcher *et al*⁴ and Vijay *et al*¹

4.1. Chronic non specific synovitis

This was the most common synovial lesion in our study accounting for 60%. The high incidence of chronic non specific synovitis in the present study may represent early stage of rheumatoid arthritis or other seronegative inflammatory arthritis, in which the disease is still in the stage of evaluation without a full fledged clinical or serological picture and in some patients may be due to early osteoarthritis not satisfying histopathological and radiological features for its diagnosis.

In the present study, the term chronic non specific synovitis was diagnosed in absence of specific inflammatory etiological agent or related features and in absence of diagnostic features related to rheumatoid arthritis or other inflammatory joint diseases.

Among the 30 cases (60%) of chronic non specific synovitis, the most common age group affected was 41-50 years with male predominance. Similar incidence was seen in the study done by P.M Vijay *et al*¹ constituting 71%.

In the present study, X ray findings were normal in 21 out of 30 cases (70%) while 9 out of 30 (30%) cases showed decreased joint space. ESR was high in 60% (18) and was normal in 40% (12) cases. These observations were

in accordance with the study done by P.M.Vijay.¹

Synovial fluid analysis was available in 25 out of 30 cases of chronic non specific synovitis of which 19 cases showed inflammatory findings and the remaining 6 cases showed noninflammatory findings. Similar observations were seen in study done by Onis *et al.*²

On histological examination, most of the biopsies showed Hyperplasia of the synoviocytes followed by synovial hypertrophy. Presence of inflammatory cell infiltrate comprising of lymphocytes was the predominant inflammatory cell infiltrate in almost all the cases admixed with plasma cells in 6 cases and neutrophils in 2 cases. Similar observations was seen in study done by Mamatha *et al.*³ The other additional features in our study includes vascular congestion in 15 cases, vascular proliferation in 6 cases, fibrosis in 5 cases and sub synovial fat in 7 cases.

Histopathological criteria employed for diagnosis of rheumatoid arthritis were villous hypertrophy, synovial cell hyperplasia, dense inflammatory infiltrate consisting of lymphocytes, plasma cells and lymphoid follicle formation with vascular proliferation.

Morphologically synovial biopsy showed dense infiltration of neutrophils in all 4(100%) cases. These observations was in accordance with the study done by Sakhuja AC *et al.*⁵

4.2. Osteoarthritis

There were two cases of osteoarthritis in the present study constituting 4% of total synovial lesions. Incidence of osteoarthritis is less when compared to observations made by Fletcher *et al*⁴ where in it was 29%.

In the present study, osteoarthritis was commonly seen in the age group 51-70 years. According to the study done by Heidari B *et al*⁶ about 13% of women and 10% of men aged 60 years and older showed symptomatic OA of the knees.

Histopathologically, both the cases in our study showed mild lymphocytic infiltrate, cartilaginous fragments and congested blood vessels. Fibrosis was seen in one case. Similar features were seen in the study done by Onis singhal *et al.*²

4.3. Ganglion cys

In the present study ganglion cyst accounted for 12% of total synovial lesions. There were 2 male patients and 4 female patients. Wrist was the most commonly involved joint. Similar observations were seen in study done by Warren *et al.*⁷

Histologically 2 cases showed synovial lining and other 4 cases showed flattened lining. Similar observations were seen in the study done by Warren *et al.*⁷

4.3.1. Baker's cyst

There were 3 cases of baker's cyst encountered in the present study one in male and 2 in female patients

with maximum incidence seen between 41-50 years. Similar observations were seen in study done by Dennis. L.⁸ Histologically cysts are lined by synovium with fibrocollagenous tissue and mild lymphocytic infiltrate.

4.4. Synovial chondromatosis

Grossly, synovial biopsy was grey white to grey yellow in color with bony fragments m/s 4-5cms. Histological examination revealed synovial lining with normal chondrocytes arranged in lobules and clusters. Also seen are foci of calcification. Similar observations were seen in study done by. R.I. Davis *et al.*⁹

4.4.1. Cavernous hemangioma

Grossly biopsy specimen was grey brown in color measuring 4x3 cms. Microscopy showed tissue line by flattened synovium. The subepithelium shows large blood filled spaces lined by flattened endothelium along with mild lymphocytic infiltrate. This was in accordance with study done by Anosheh *et al.*¹⁰

5. Conclusion

It was concluded that most of the cases in our study was that of chronic non specific synovitis. This could be due to early stage of Rheumatoid arthritis, osteoarthritis and other seronegative arthritis. Hence, these patients should be closely followed up and repeat biopsies should be carried out as they may present with specific diagnostic features in their due course.

6. Source of funding

None.

7. Conflict of interest

None.

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Cite this article: Patil S, Rajesh G, Ranganath N. Study of histomorphological features of synovial biopsy in joint diseases. *Indian J Pathol Oncol* 2019;6(4):636-641.