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Original Research Article

Synovial Biopsy in Joint Diseases: A Morphological Study

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Abstract

Introduction: Synovium is the primary site of inflammation and is affected in variety of joint diseases. Examination of synovial tissue can assist in diagnosis of some joint diseases, and in several atypical and rare synovial disorders. This study aims to describe the histomorphological changes in synovium and to evaluate the clinical presentation and radiological findings in various joint diseases. *Aim of the study:* To describe the clinical presentations, radiological findings and histomorphological changes in various synovial lesions. *Materials and Methods:* This was a prospective, descriptive type of study done over a period of two years. All synovial biopsy specimens sent from department of Orthopaedics in the study period were subjected to routine histopathological processing. The clinical and radiological details were collected. The radiological and histopathology findings were compared and the morphological features in various synovial/joint diseases were studied. *Results:* A total of 120 synovial tissue specimens were studied. The age group in this study ranged from 3 years to 77 years. The male to female ratio was 1.4:1. The most common joint involved was knee joint (74 cases, 61.7%). Common clinical features were of pain and swelling of the affected joint. Majority of cases had no significant radiological abnormality (72.5%). Others showed nonspecific findings (10.8%), degenerative changes (10%), and loose bodies (6.7%). The most common morphological change was synovial hyperplasia. (92 cases, 76.7%). The most common inflammatory infiltrate was lymphocytes (45 cases, 37.5%). The most common lesion found in synovial biopsy was non-specific synovitis (33 cases). *Conclusion:* Synovial pathology is common in 41–50 years males and presents often with pain and swelling. The most commonly involved sites are large joints like knee and hip and majority of cases do not show significant radiological abnormality. The most common synovial lesion in our study was non-specific synovitis. Inflammatory lesions have various etiologies. Degenerative changes show varied morphology. Tumor and tumor-like conditions can also be encountered.

Keywords: Synovial biopsy; Joint disease morphology; Synovitis; Rheumatoid arthritis.

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Introduction

Synovium is the primary site of inflammation and a major effector organ in variety of joint diseases. Examination of synovial tissue can assist in diagnosis of some joint diseases, and in several atypical and rare synovial disorders.[1]

It is used to diagnose many conditions like rheumatoid arthritis, tuberculous arthritis, septic arthritis, degenerative joint diseases, synovial cyst, synovial lipomatosis, synovial hemangioma, synovial sarcoma, pigmented villonodular synovitis, and synovial chondromatosis. An early diagnosis in patients presenting with arthritis is important to provide information about prognosis and to initiate treatment.

Synovial biopsy is now widely practiced in arthritis research. Multiple tissue samples can be readily obtained using closed needle or arthroscopy biopsy, usually from the suprapatellar pouch. This source may be suitable for many clinicopathological studies. Needle arthroscopy is considered more expensive, but provides larger samples which can be selected under direct vision. European synovitis study group convened some years ago, evaluated arthroscopy and synovial biopsy for tissue analysis. The procedure is simple and can be performed on an out-patient basis and it is confirmatory in many joint diseases.[2] Hence more studies are needed on this topic. This study aims to describe the histomorphological changes in synovium and to evaluate the clinical presentation and radiological findings in various joint diseases.

Aims and Objectives

To describe the clinical presentations, radiological findings and histomorphological changes in various synovial lesions and joint diseases and also to categorize the synovial lesions based on histopathological diagnosis.

Materials and Methods

This was a prospective, descriptive type of study done over a period of two years from August 2008 to July 2010 in the department of Pathology at Government Medical College, Thiruvananthapuram, Kerala, India.

Inclusion criteria

All synovial biopsy specimens sent from department of Orthopaedics in the study period were included.

Synovial biopsy specimens were received in the department of pathology, Medical college Thiruvananthapuram over a period of two years. The clinical history and radiological features were noted from the test request forms. The tissue samples were fixed in 10% buffered neutral formalin. Gross examination of the specimens was done. Representative bits were given for routine histopathological processing. The sections were cut at five-micron thickness and were stained with hematoxylin and eosin stains and were examined by light microscopy. In case of diagnostic problem special stains and immunohistochemical studies were done. Finally, based on the histopathological diagnosis synovial lesions were categorized.

Observations and Results

The present study included 120 cases of synovial biopsy. The histomorphological changes in synovium in various joint diseases were studied.

Age: The age group in this study ranged from 3 years to 77 years. The most common age group involved in synovial pathology was between 41–50 years (28 cases, 25.8%). (Fig. 1).

The most commonly involved age group in septic arthritis was 41–50 years (46.2%).

Gender: In this study, synovial lesions were predominantly seen in male population (71 cases, 59.2% males and 49 cases, 40.8% females). The male to female ratio was 1.4:1.

Site: The commonly involved joint, biopsied for synovial pathology was knee (74 cases, 61.7%) (Fig. 2).

Clinical feature: In this study majority of the patients presented with pain (81 cases, 67.5%) and 15 patients presented with both pain and swelling (12.5%), pain and deformity were present in 11.7% cases, only swelling in 7.5% cases and only deformity in 0.8% cases.

Radiological features: In our study majority of cases had no significant radiological abnormality (72.5%). Others showed nonspecific findings (10.8%), degenerative changes (10%), and loose bodies (6.7%) (Fig. 3).

Non-specific findings included joint effusion, soft tissue swelling and calcifications.

Gross features: Out of 120 cases, 110 cases (88%) were small synovial biopsies. Only 10 cases (12%) were received as intact gross specimens. These included 2 cases of synovial chondromatosis

showing multiple nodules of varying sizes studded on thickened synovium, 3 cases of synovial sarcoma showing grey to yellow colour with fleshy consistency and areas of hemorrhage and necrosis, 1 case of pigmented villonodular synovitis showing villous frond like synovial projections with tan and reddish colour, 1 case of synovial hemangioma showing a nodular mass with cut section showing brownish areas and 3 cases of loose bodies with synovial tissue.

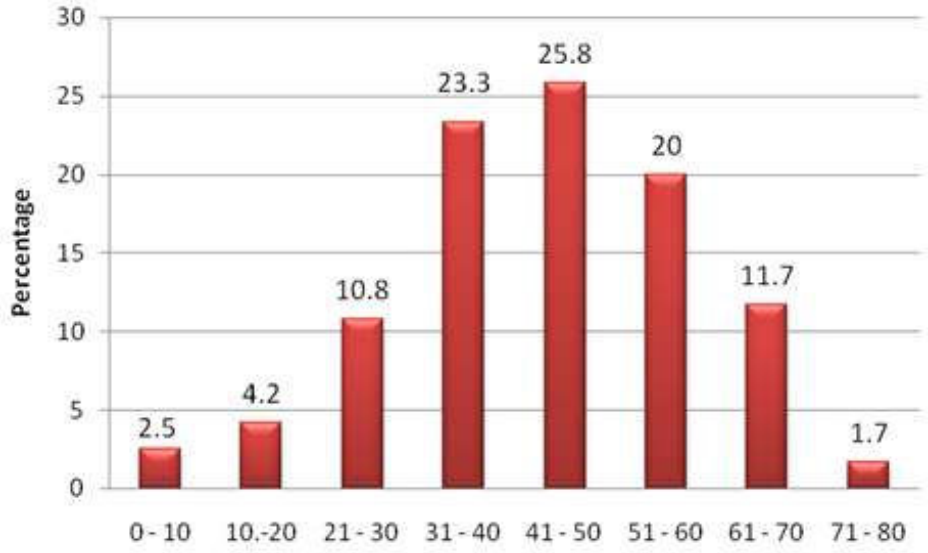

Fig. 1: Age-wise distribution of cases

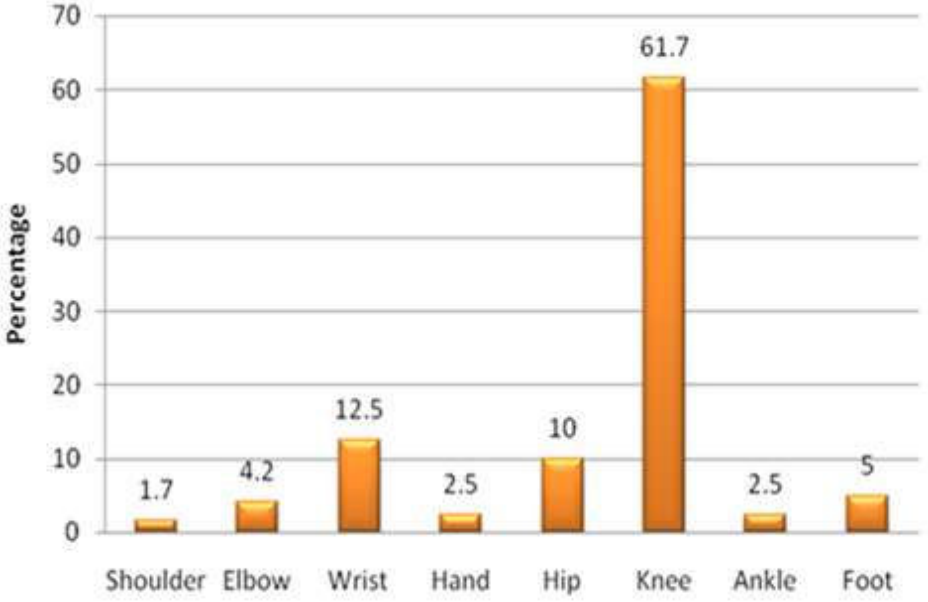

Fig 2: Site-wise distribution of cases

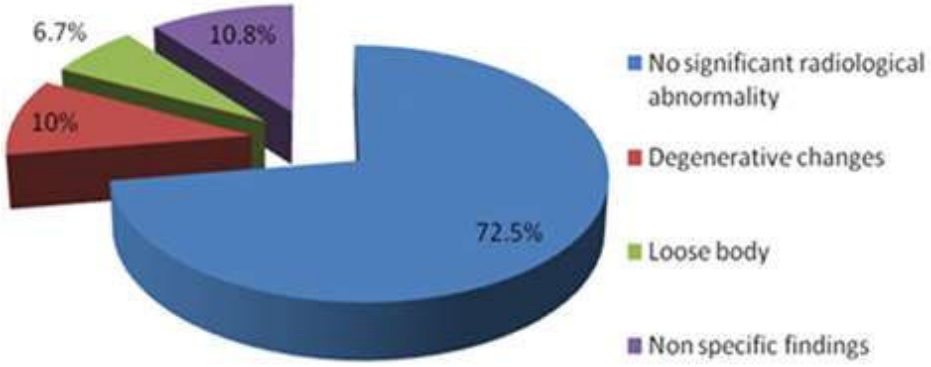

Fig. 3: Distribution of cases according to radiological features

Table 1: Changes in synovium on histopathology

Changes in synovium		Number of cases	Percentage (%)
Synovial hyperplasia		92	76.7
Inflammatory infiltrate	Lymphocytes	45	37.5
	Neutrophils	15	12.5
	Lymphoid follicle	11	9.2
	Granuloma	11	9.2
	Lymphoplasmacytic	8	6.7
	Hemosiderin laden macrophages	4	3.3
	Palisaded histiocytes	2	1.7
Necrosis	Suppuration	16	13.3
	Fibrinoid	12	10
	Caseation	11	9.2
Vascular changes	Granulation tissue	12	10
	Proliferated vessels	10	8.3
	Pannus	6	5
	Others	1	0.8
Fatty infiltrate		3	9.2
Metaplasia	Chondroid	18	15
	Osteoid	1	0.8
Loose bodies		9	7.5
Degenerative changes	Calcification	3	2.5
	Hyalinization	1	0.8
	Cholesterol clefts	1	0.8
	Myxoid change	1	0.8

The most common morphological change in synovial biopsy was synovial hyperplasia. (92 cases, 76.7%).

Type of Inflammatory infiltrate: Inflammatory infiltrate was noted in 86 cases of synovial biopsies. The most common inflammatory infiltrate was lymphocytes (45 cases, 37.5%). (Fig. 4).

Distribution of cases according to necrosis: In the present study 16 cases showed suppuration (13.3%). It was followed by fibrinoid necrosis in 12 cases (10%), and caseation necrosis in 11 cases (9.2%)

Distribution of cases according to vascular changes: Vascular changes were noted in 29 cases. Granulation tissue was seen in 12 cases (10%). Excessively proliferated vessels were seen in 10 cases (8.3%), and pannus was noted in 6 cases (5%). Others included 1 case of synovial hemangioma.

In our study the most common lesion found

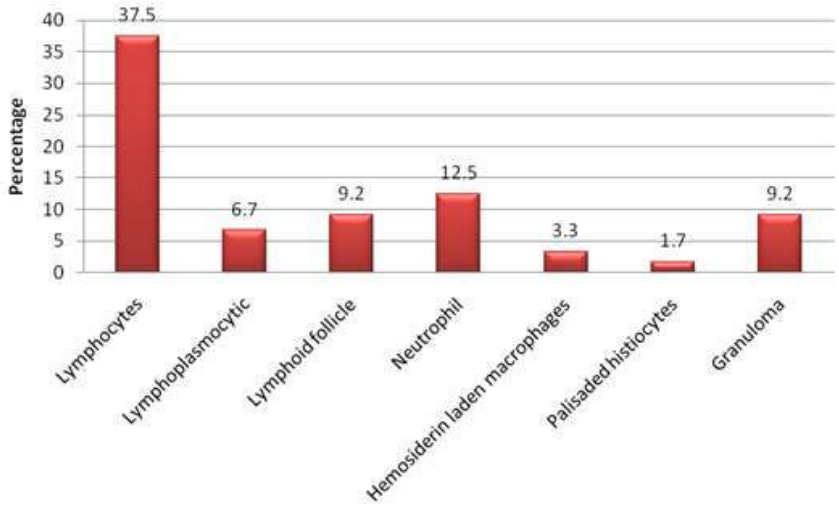

Fig. 4: Distribution of cases according to inflammatory infiltrate

Table 2: Distribution of cases according to histopathological diagnosis.

Diagnosis		Number of cases	Percentage (%)
Nonspecific degenerative changes		10	8.3
Inflammatory arthritis	Nonspecific synovitis	33	27.5
	Rheumatoid arthritis	18	15
	Septic arthritis	13	10.8
	Tuberculous arthritis	12	10
Tumour like conditions	Primary synovial chondromatosis	16	13.3
	Pigmented villonodular synovitis	4	3.3
	Synovial cyst	3	2.5
	Synovial lipomatosis	3	2.5
Tumours	Synovial sarcoma	4	3.3
	Synovial haemangioma	1	0.8
Other lesions	Chronic synovitis with foreign body giant cell reaction	2	1.7
	Chronic hypertrophic synovitis	1	0.8

in synovial biopsy was non-specific synovitis (33 cases). There were 12 cases of tuberculous arthritis (Fig. 5).

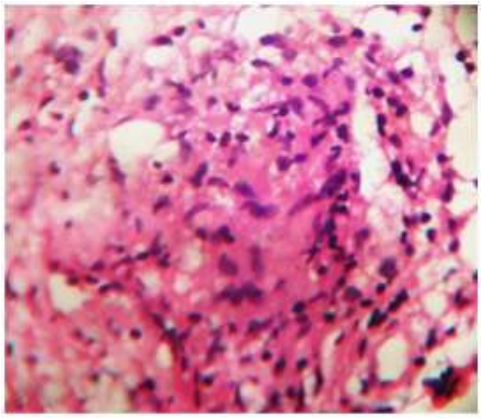

Fig. 5: Epithelioid cell granuloma in synovial tissue. (Hematoxylin and eosin stain, 100X)

Rheumatoid arthritis

The most common morphological change in rheumatoid arthritis was fibrinoid necrosis (66.67%), followed by lymphoid follicles (61.1%), and synovial hyperplasia (39.3%). Pannus was seen in 33.3% cases (Fig. 6).

Non-specific synovitis: In our study the most common morphological change in synovium in nonspecific synovitis was lymphocytic infiltrate (97%), followed by granulation tissue (15.1%), synovial hyperplasia (1%) and proliferated vessels (1%).

Primary synovial chondromatosis: Out of 16 cases of primary synovial chondromatosis, loose bodies were seen in 7 cases (77.8%).

Degenerative changes in synovium: In our study the most common degenerative change in

synovium was calcification (60%). Others changes included metaplasia (30%), myxoid change (30%), hyalinization (30%), cholesterol clefts (10%), and loose bodies (10%). In the present study out of 10 cases of degenerative changes in synovium, 3 cases showed metaplasia (30%) table (3). Among the 3 cases 2 cases showed chondroid metaplasia (66.7%) and 1 case showed osteoid metaplasia (33.3%).

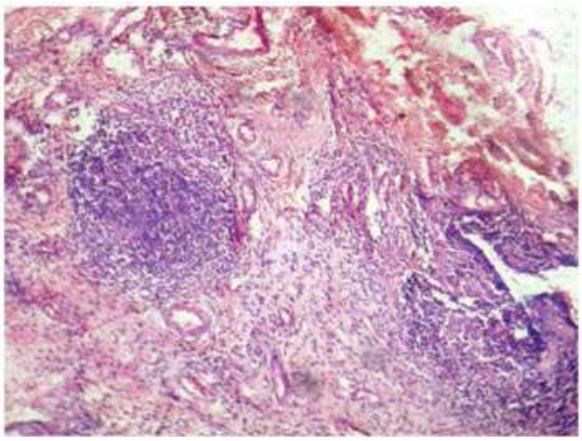

Fig. 6: Synovium from Rheumatoid arthritis showing lymphoid follicles and rich lymphoplasmacytic infiltrate. (Hematoxylin and eosin stain, 40X)

Distribution of metaplasia among non-specific degenerative changes: Of the 10 cases, 7 (70%) had no metaplasia and 3 (30%) had metaplastic changes. Osteoid metaplasia was seen in 33.3% cases and chondroid metaplasia in 66.7% cases.

No significant radiological abnormality was seen in 87% cases. All these cases were diagnosed histopathologically as seen in table 3.

Table 3: Comparison between radiological findings and histopathological diagnosis

Radiological feature	Histopathological diagnosis
No significant radiological abnormality (87 cases)	Non-specific synovitis (32 cases, 36.8%)
	Rheumatoid arthritis (14 cases, 16.1%)
	Septic arthritis (12 cases, 13.8%)
	Tuberculous arthritis (9 cases, 10.3%)
	Synovial chondromatosis (8 cases, 9.2%)
	Synovial cyst (3 cases, 3.4%)
	Pigmented villonodular synovitis (3 cases, 3.4%)
	Non-specific degenerative changes (2 cases, 2.3%)
	Synovial lipomatosis (1 case, 1.1%)
	Other lesion (3 cases, 3.4%), 2 cases of chronic synovitis with foreign body giant cell reaction and 1 case of chronic hypertrophic synovitis.

Clinically 12 cases were diagnosed as degenerative arthritis. Majority of cases (8 cases, 66.7%) were histopathologically also diagnosed as degenerative arthritis, 3 cases were diagnosed as rheumatoid arthritis and remaining 1 case was diagnosed as nonspecific synovitis.

Loose bodies were seen in radiology in 8 cases. All these cases were diagnosed as primary synovial chondromatosis with loose body formation on histopathology.

Non-specific findings in radiology were seen in 13 cases. All these cases were histopathologically diagnosed as seen in table 4.

Table 4: Comparison of non-specific changes on radiology with histopathology

Radiological feature	Histopathological diagnosis
Non-specific changes (13 cases)	Synovial sarcoma (4 cases, 30.8%)
	Rheumatoid arthritis (1 case, 7.7%)
	Tuberculous arthritis (3 cases, 23.1%)
	Synovial lipomatosis (2 cases, 15.4%)
	Synovial hemangioma (1 case, 7.7%)
	Pigmented villonodular synovitis (1 case, 7.7%)
	Septic arthritis (1 case, 7.7%)

Discussion

A total of 120 cases were studied which included various conditions primarily affecting synovium. The most common synovial lesion in the present study was inflammatory arthritis (63.5%). This is comparable with study conducted by Schumacher *et al.*[3] They also showed that 92% of synovial biopsies were diagnostic of inflammatory arthritis.

Age: In our study the most common age group involved in synovial pathology was between 41–50 years (25.8%). Karateev DE *et al.*[4] in his study the median age group of patients was between 40–50 years. In the present study the most commonly affected age group in septic arthritis was between 41–50 years (46.2%). This is in contrast with study conducted by Shetty AK *et al.*[5] in which peak incidence was observed in children under 3 years of age. Lee MKS *et al.*[6] in his study showed that median age group affected by pigmented villonodular synovitis was between 20–40 years as seen in the present study.

Synovial hemangiomas are generally seen in children and young adults. In the present study a case of a three years old child with synovial hemangioma was reported. Alaoui M *et al.*[7] reported a case of synovial hemangioma in a 7 years old child

who after excision was recurrence free for a follow up period of 36 months.

Synovial sarcomas are seen in adolescents and young adults. In the study conducted by Cadman *et al.*[8] 85% patients with synovial sarcoma were between 10–15 years of age which is similar to our finding.

Gender: Inour study male predominance was noted for synovial lesions (59.2%). Karateev DE et al.[4] in his study showed that women were affected 3 times more often than men in Rheumatoid arthritis. Other lesions showed no gender preference except in synovial lipomatosis and septic arthritis in which males were preferentially affected as seen in a study conducted by Hallel T *et al.*[9] and Shetty AK *et al.*[5]

Site: The most commonly involved site in synovial pathology was knee (61.7%) which is comparable with various studies. (Table 5)

Table 5: Comparison with other studies for site of synovial involvement studies

Study	Year	Diagnosis	Joint affected
Murphy *et al.*[10]	1962	Synovial chondromatosis	Knee
Shetty AK *et al.*[5]	1998	Septic arthritis	Knee
Devaney K *et al.*[11]	2000	Synovial sarcoma	Knee
Esteban PL *et al.*[12]	2004	Tuberculous arthritis	Hip and knee

In the present study small joints were involved in 7.5% of cases. Karateev DE *et al.*[4] in his study showed that the joints of hands and feet are nearly always involved in rheumatoid arthritis.

Clinical Features: Majority of the patients presented with pain (67.5%) followed by pain and swelling (12.5%). Only 0.8% of patients presented with deformity. Literature says only untreated cases progresses to deformity and the initial presentation of a joint lesion is pain followed by swelling.[5]

Radiological features: In our study majority of the cases had no significant radiological abnormality (72.5%) which is comparable with various studies. 10.8% of cases showed non-specific findings which include joint effusion, soft tissue swelling and calcification. Degenerative changes were seen in 10% of cases which include joint space reduction, osteophyte formation, subchondral sclerosis and bone erosions.

Buckwalter JA *et al.*[13] in his study described the typical radiological findings of osteoarthritis and same were seen in our study.

Our study showed loose bodies in 6.7% of cases. 77.8% cases of synovial chondromatosis showed loose bodies in their X-rays which are seen as innumerable calcified intra articular chondral bodies.

Calcification and soft tissue swellings were seen in a case of synovial sarcoma. Murphey MD *et al.*[10] in his study proved that although radiographic features of these tumors are not pathognomonic findings of a soft tissue mass, particularly if calcified is suggestive of the diagnosis.

Changes in synovium on histopathology: The most common morphological change in synovial pathology was synovial hyperplasia (76.7%).

Inflammatory infiltrates were noted in 80.1% of cases. The most common inflammatory infiltrate was lymphocytes.

In our study three types of necrosis were seen in synovial lesions, suppuration (13.3%), fibrinoid necrosis (10%) and caseation necrosis (9.2%). All cases of septic arthritis and tuberculous arthritis showed suppuration and caseation necrosis respectively.

Only 66.7% cases of rheumatoid arthritis showed fibrinoid necrosis. (Fig 11). Chapuy-Regaud S et al.[14] showed that fibrin deposition in the synovial tissue is a general phenomenon associated to any synovitis and not specific for rheumatoid arthritis.

24.1% of cases showed vascular changes. The most common vascular change was granulation tissue (10%). Neovascularization is one of the hall-mark of synovitis as noted by Canete JD *et al.*[15]

Rheumatoid arthritis: Rheumatoid arthritis was diagnosed in 15% patients. The most common morphological change in rheumatoid arthritis was fibrinoid necrosis (66.7%) followed by synovial hyperplasia (61.7%) and lymphoid follicle (61%)

Study of Karateev DE *et al.*[4] showed that the most common morphological changes were synovial hyperplasia (82.6%), lymphoid follicle (64.1%) and fibrinoid necrosis (60.9%) which is comparable with our study.

Fonseca JE *et al.*[16] described 6 histological features of rheumatoid arthritis as seen in our study which includes synovial hyperplasia, fibrosis in sub synovial layer, proliferating blood vessels, perivascular infiltrate of lymphocytes, focal aggregates and diffuse infiltrates of lymphocytes.

Palisaded histiocytes were seen in 5.6% of cases. Koizumi F *et al.*[17] observed in their study that 20% of rheumatoid arthritis patients had rheumatoid nodules, which are composed of necrotic center impregnated with fibrin, surrounded by palisaded

histiocytes.

Tuberculous arthritis: 10% of cases were diagnosed as tuberculous arthritis. All cases showed granulomas. (Figure 5)

Atypical Mycobacteria and fungal infection can also produce granulomatous synovitis as noted by Ling Mah *et al.*[18] These were excluded in our study by doing AFB and methenamine silver stains. They described tin their study that synovial biopsy is an important and diagnostic method to ascertain the causative agent. The gold standard for confirming TB diagnosis probably will remain cultures in addition to early utilization of molecular TB diagnostics.[19]

Septic arthritis: 10.8% of cases showed septic arthritis in their biopsies. Microscopy of all cases showed polymorphonuclear infiltrate and suppuration.

Non-specific synovitis: 27.5% of cases showed non-specific synovitis. Lymphocytic infiltrate (97%) was the most common morphological change in synovium. Others included granulation tissue 15.1%, synovial hyperplasia 1%, and proliferated vessels 1%.

Palmer *et al.* DG[20] have revealed various patterns in synovium of non-specific synovitis which include mild synovial proliferation, occasional vascular congestion and diffuse infiltrates with lymphocytes and histiocytes.

Primary synovial chondromatosis: 13.3% of cases were diagnosed as primary synovial chondromatosis. Gross features showed numerous nodules in the synovium giving a cobble stone appearance. Microscopy showed osteocartilagenous metaplasia beneath the thin lining of synovial membrane. Similar findings were observed by Frank P *et al.*[21]

Loose bodies were seen in 77.8% cases of primary synovial chondromatosis. Grossly they appeared as nodules of size ranging from 2 mm to more than 1 cm and were firm on cut section. Microscopically they were seen as nodules of osteocartilagenous masses.

Murphey MD *et al.*[10] described that secondary synovial chondromatosis can be distinguished from primary disease both pathologically and radiologically by its association with underlying joint abnormality and fewer chondral bodies of variable size and shape.

Pigmented villonodular synovitis: In the present study 3.3% cases were diagnosed as pigmented villonodular synovitis. Gross features showed many villous or frond like synovial projections with a characteristic tan or reddish colour. Microscopy showed hyperplastic synovium with intra and extracellular hemosiderin lying in a fibrous stroma.

Lee MKS *et al.*[6] in his study described the gross and microscopy of pigmented villonodular synovitis as seen in the present study. He also described that absence of hemosiderin does not exclude the diagnosis as hemosiderin deposition is also seen in rheumatoid arthritis, post traumatic synovitis, haemophilic and amyloid arthropathy and synovial osteochondromatosis.

Synovial cyst: Three cases of synovial cyst were diagnosed. Histopathology showed cyst lined by synovial membrane and wall showed fibrocollagenous tissue. These cysts arise as a collection of fluid secreted by inflamed synovial sheath of the tendon extending from the synovium of joint.

Synovial lipomatosis: Three cases of synovial lipomatosis were diagnosed. Microscopy of these cases showed reactive synovial cells and infiltrate of mature adipocyte in the sub synovial connective tissue. Chronic synovitis can also show fatty infiltration of synovium but for the diagnosis of synovial lipomatosis there should be complete replacement of subsynovial tissue with mature adipocytes.[7]

Hallel T *et al.*[9] in his study described 5 cases of synovial lipomatosis with histology showing similar features as seen in our study.

Synovial hemangioma: One case of synovial hemangioma, cavernous type was reported. Devaney K[11] studied 20 cases of synovial hemangioma. In his study the most common histological pattern was cavernous type.

Synovial sarcoma: Four cases were diagnosed as synovial sarcoma. Gross features showed grey to yellow colour with fish flesh consistency and areas of hemorrhage and necrosis. Two cases were diagnosed as monophasic type with microscopy showing spindly cells in diffuse sheets and fascicular interlacing pattern. Other 2 cases were diagnosed as biphasic type, microscopy of which showed both epithelial and mesenchymal component. The diagnosis was confirmed by immunohistochemical markers such as cytokeratin and vimentin.

Murphey *et al.*[10] described 3 histological sub-type monophasic, (50–60%), biphasic (20–30%) and poorly differentiated (15–20%). Poorly differentiated synovial sarcomas are generally epithelioid in morphology and have high mitotic activity and geographic necrosis.

Degenerative joint disease: Degenerative changes

were seen in 8.3% of cases. In our study the most common degenerative change in synovium was calcification (60%). Myxoid change was seen in 30% cases. Cholesterol clefts were seen in 10% of cases. Loose bodies were seen in 10% cases of degenerative joint disease. Microscopically they were seen as nodules of acellular masses possibly fibrinous type loose body. Murphy FP *et al*.[21] described the diseases giving rise to loose bodies other than primary synovial chondromatosis which include degenerative joint disease, osteochondritis dissecans, neurotrophilic arthritis, tuberculous arthritis and osteochondral fractures.

Metaplasia was seen in 30% cases (chondroid in 66.7% and osteoid in 33.3% cases). Gardner DL and Salter DM[22] in their study showed that metaplasia of the synovium in osteoarthritis may occur. As seen in our study the most common metaplasia in their study was also chondroid metaplasia.

Comparison between radiological findings and histopathological diagnosis: Any significant radiological abnormality was absent in 87 cases. Among these 63.2% cases were histopathologically diagnosed and 36.8% cases were diagnosed as non-specific synovitis.

Radiology showed non-specific findings in 13 cases. All these cases were also histpathologically diagnosed. Bresnihan B *et al*.[23] in his study proved that examination of synovial tissue can assist in diagnosis of joint infections and in several atypical and rare synovial disorders.

Finally based on the histopathological diagnosis synovial lesions were categorized as follows:[24]

1. Degenerative: with or without metaplasia.
2. Inflammatory:

   Acute-septic arthritis

   Chronic-Nonspecific synovitis

   Specific synovitis-Tuberculous arthritis, Rheumatoid arthritis
3. Tumor like conditions: synovial cyst, synovial lipomatosis, pigmented villonodular synovitis, primary synovial chondromatosis
4. Tumors: Benign-synovial haemangioma

   Malignant-synovial sarcoma

Conclusion

Synovial pathology is common in 41–50 years males and presents often with pain and swelling. The most commonly involved sites are large joints like knee and hip and majority of cases do not show significant radiological abnormality. The most common synovial lesion in our study was non-specific synovitis. Inflammatory lesions included rheumatoid arthritis, tuberculous arthritis and septic arthritis. Degenerative changes seen in synovium were calcification, myxoid change, hyalinization and cholesterol clefts. Loose bodies were seen in primary synovial chondromatosis and degenerative joint disease. Tumor like conditions include synovial cyst, synovial lipomatosis, pigmented villonodular synovitis and primary synovial chondromatosis. Tumors in the study include synovial hemangioma and synovial sarcoma. Synovial lesions can be categorized as degenerative, inflammatory, tumour like conditions and tumours based on histopathological diagnosis.

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