Clinicopathological study of synovial biopsies at tertiary care hospital and its diagnostic utility

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Abstract

Introduction: Arthritis, an important cause for morbidity, is commonly found in clinical practice. Diseases such as tuberculous synovitis and gout need treatment directed towards specific diagnosis which can be achieved by the use of relatively simple technique of arthroscopic synovial aspiration and biopsy.

Aim and Objectives: To study the histomorphological spectrum of different clinically suspected synovial lesions and to assess diagnostic utility of synovial biopsies.

Materials and Method: The present study comprises analysis of 100 biopsies of clinically suspected synovial lesions during period of 4 years. Relevant clinical details were obtained. Synovial biopsy specimens were processed routinely and wherever necessary special stains like Z-N stain for AFB, Prussian blue stain for haemosiderin and immunohistochemical studies were carried out.. Wherever necessary the available clinical and radiological findings were taken into consideration to categorize the lesions. Lesions were classified under main categories of inflammatory joint diseases, degenerative joint disease, tumor and tumor like conditions.

Results: In our study, the common age groups affected were between 40-60years. Both sexes were equally affected. Most common symptoms were pain and swelling. Knee was the commonest joint involved. Most common histopathological diagnosis made among the clinically suspected synovial lesions was chronic nonspecific synovitis followed by rheumatoid arthritis, septic arthritis& tuberculous synovitis. Also cases of benign tumors including synovial lipoma arborescence, chondromatosis, pigmented villonodular synovitis and malignant tumors like synovial sarcoma and clear cell sarcoma were noted in present study.

Conclusion: Histological analysis of synovial biopsies proves to be a valuable tool in establishing an early and specific diagnosis.

Keywords: Synovial biopsy, Histopathology, Synovial sarcoma, Clear cell sarcoma

Introduction

Arthritis, an important cause for morbidity, is commonly found in clinical practice. It is seen to affect all age groups and either sex.[1]Trauma and infective etiology results in monoarticular arthritis. However, rheumatoid pathology leads to polyarticular arthritis. There is seen generous use of NSAIDS by the general practitioners for symptomatic treatment in arthritis. Diseases such as tuberculous synovitis and gout need treatment directed towards specific diagnosis which can be achieved by the use of relatively simple technique of arthroscopic synovial aspiration and biopsy.[1] Arthroscopic biopsy has the advantage over closed needle biopsy being minimally invasive, less destructive to normal tissue, quicker recovery and rehabilitation leading to minimal hospital stay and less infection rate.[2]

We have attempted to study the histopathological spectrum of synovial biopsies which were referred to us from the orthopedic department.

Materials and Method

This cross sectional study consisted of 100 cases of synovial biopsies sent to the histopathology department during a study period of four years (Jan 2013 – Dec 2017). Clinical records were reviewed. Special stains and immunohistochemical studies were performed wherever necessary. The cases were divided into three classes of inflammatory and degenerative joint disease, and tumor and tumor like conditions.[3]

Results

Table1: Distribution of various synovial lesions according to etiology

Sr. No.	Lesion		Number of cases(%)	Male	Female
I	Inflammatory Joint Disease				
a	Infectious	Septic arthritis	9	5	4
		Tubercular synovitis	10	1	9
b	Autoimmune	Rheumatoid arthritis	14	6	8
c	Others	Chronic nonspecific synovitis	49	27	22
II	Degenerative Joint Disease	Osteoarthitis	5	3	2
		Gout	1	1	-
		Pseudogout	1	1	-

		Avascular necrosis	1	1	-
III	Tumor and Tumor like lesions				
a	Benign	Synovial chondromatosis	3	1	2
		GCT Tendon sheath	2	-	2
		PVNS	2	1	1
		Synovial lipoma arborescence	1	-	1
b	Malignant	Synovial sarcoma	1	1	-
		Clear cell sarcoma	1	-	1

Table 2: Age distribution of inflammatory joint disease

Age group	Number (62)
1-10	3
11-20	13
21-30	12
31-40	9
41-50	8
51-60	8
61-70	6
71-80	2
81-90	0
91-100	1

Table 1 describes distribution of various synovial lesions in the present study according to the etiology with sex distribution. In the present study, histopathological changes in 49% of the cases were not specific for any specific disease entity. These cases showed fibrocollagenous tissue with increased vascularity and variable chronic inflammatory infiltrate composed of lymphocytes. These cases were diagnosed as chronic non-specific synovitis. There were ten cases of tuberculous synovitis in our study. There were nine female and one male patient. Age range was 18 to 68 years. In six cases site of biopsy was knee and in 4 cases it was wrist. Two cases showed rice bodies grossly. All the cases showed granulomas with Langhan's type of giant cells. (Fig. 1a) In 3 cases caseous necrosis was noted. Modified ZN staining was done in all cases; however acid fast bacilli could not be demonstrated. There were 14 cases of rheumatoid arthritis in the present study. Microscopically synovial cell hyperplasia and moderate lymphoplasmacytic cell infiltrate was noted in 13/14 (92%) cases.(Fig. 1b) Lymphoid follicle formation was seen in 85% (12/14) cases. (Fig. 1c) Pannus formation and ulceration was observed in 35% (5/14) of cases. Increased vascularity was seen in 71% (10/14) of cases and fibrin deposition was noted in 57% (8/14) of cases. Giant cells were noted in one case. There was neutrophilic infiltrate with ulceration of synovial lining in all the cases of septic arthritis. Age distribution of inflammatory synovial lesions is shown in Table 2.

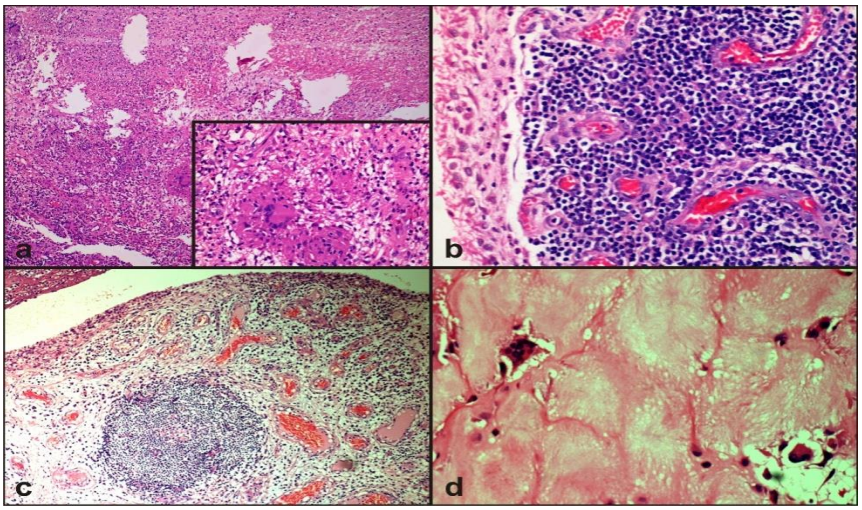

Fig. 1

a. **Tuberculous synovitis : Photomicrograph showing granulomas with caseous necrosis (H&E,100X), Inset – Photomicrograph showing Langhan's type of giant cells (H&E,400X)**

b. **Rheumatoid synovitis: Photomicrograph showing Pannus formation (H &E,400X)**

c. **Rheumatoid synovitis : Photomicrograph showing Lymphoid formation with increased vascularity (H&E,100X)**

d. **Gouty arthritis: Photomicrograph showing tophaceous deposits with giant cell reaction (H &E,400X)**

There were five cases of osteoarthritis showing features of degenerative changes. Majority cases were in sixth decade. Microscopically degenerating cartilage with minimal inflammation and granulation tissue was noted. One case each of gouty arthritis and pseudogout was noted. Microscopically there was deposition of amorphous pink tophaceousmaterial surrounded by giant cell reaction and chronic inflammatory cell infiltrate in gout(Fig. 1d) and granular appearance without giant cell reaction in pseudogout. There were three cases of synovial chondromatosis of which two were females and one male. In two cases it involved knee and in one case it was seen in wrist. Number of loose bodies was one in two cases and three in one case. Grossly these were round, globular and whitish in color. These were decalcified and then sectioned. Microscopically they show nodules of hyaline cartilage with enchondral ossification. (Fig. 2a)There were two cases of giant cell tumor of tendon sheath (TSGCT) of knee. Both were females of age group 48 and 46 years. Microscopically lobulated well circumscribed tumor composed of synovial mononuclear cells with numerous multinucleated giant cells and foam cells was seen in both the cases. (Fig. 2b)There were two cases of pigmented villonodular synovitis of knee. Microscopically there was villous proliferation of synovium. Subepithelial tissue showed moderate infiltration by foamy histiocytes, hemosiderin laden macrophages, pseudoglandular spaces lined by synovial cells. (Fig. 2c) Mitotic figures were absent. Prussian blue stain done in all cases showed presence of blue granules of hemosiderin pigment.(Fig. 2c,inset)There was one case of lipoma arborescence in present study. Microscopically there was infiltration of mature adipose tissue in the subsynovial tissue. (Fig. 2d)There was one case of Monophasic synovial sarcoma of knee in our study. Grossly there were multiple grayish white tissue bits aggregating to 10 cc. Microscopically there were spindle cells arranged in hemangiopericytoma like pattern. (Fig. 2e) Abnormal mitotic figures were noted. Surrounding areas show hemorrhage and necrosis. Immunohistochemistry done in this case showed vimentin, CD 99 and EMA immunoreactivity with negative CK7, CK19, desmin and S100. Ki67labelling index was 60% confirming its malignant nature. There was one case of clear cell sarcoma of synovium of knee. The patient was 56 year female. Microscopically there were sheets of round to polygonal cells (Fig. 2f) with prominent nucleoli and moderate amount of eosinophilic cytoplasm. (Fig. 2f,inset)Few abnormal mitotic figures were noted. An Immunohistochemical study showed immunoreactivity for HMB45 and melan A and was negative for EMA.

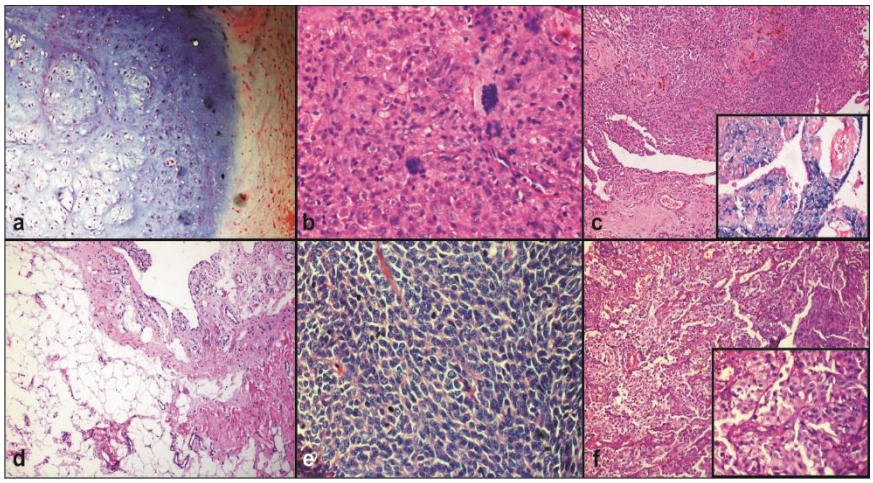

Fig. 2

a. Synovial chondromatosis: Photomicrograph showing lobules of mature hyaline cartilage (H&E,100X)

b. Giant cell tumor of tendon sheath: Photomicrograph showing sheets of mononuclear cells with giant cells (H &E,400X)

c. Pigmented villonodular synovitis: Photomicrograph showing proliferation of synovium with hemosiderin deposition (H&E,100X), inset- positive Pearls Prussian blue(PPB) reaction with bluish granules of hemosiderin (PPB ,400X)

d. Lipoma arborescence: Photomicrograph showing mature adipose tissue in subsynovial tissue (H&E,100X)

e. Synovial sarcoma: Photomicrograph showing Spindle cells with many abnormal mitotic figures(H &E,400X)

f. Clear cell sarcoma: Photomicrograph showing round to polygonal cells (H &E,100X), inset- tumor cells with prominent nucleoli (H &E,400X)

Discussion

Diseases related to synovium constitute major part of orthopedic outpatient department management. Diagnosis includes clinico-radiological and serological investigations. In cases were these findings are equivocal, specific tests become mandatory for appropriate management.[2] It has been documented in literature that cases presenting as chronic synovitis of the knee could benefit by undergoing synovial membrane biopsy.[4,5] In the present study knee joint was the common joint involved by synovial lesions.

In our study, inflammatory synovial lesions predominated. Maximum cases occurred in the age group of 11 to 30 years. Chronic non-specific synovitis (49/100, 49%) was the commonest inflammatory synovial lesion followed by rheumatoid arthritis (14%) and tubercular synovitis (10%). In a study by Vijay PM et al chronic non specific synovitis (71%, 59/83) was the commonest inflammatory synovial lesion followed by tuberculous synovitis (18%, 15/83) whereas in Abhyankar et al study tuberculous arthritis was the commonest lesion followed by rheumatoid arthritis and degenerative joint disease.[6,7] In cases where no specific etiology was identified, a diagnosis of chronic non specific synovitis was offered. Higher distribution of such cases was found in most studies in literature.[6,8] These could be either early stages of rheumatoid arthritis or early osteoarthritis not showing the characteristic histomorphological and radiological features required for its diagnosis. These cases when followed up could evolve showing distinctive histopathological features on synovial biopsy or might undergo complete therapeutic resolution due to its self limiting nature.[4] In our study 10 cases of tuberculous synovitis were encountered. Non caseating granulomas (70%) predominated over caseating granulomas (30%). Higher incidence of non-caseating was observed in a study by Vijay PM et al. All the cases showed presence of Langhan's giant cells in the present study. Various studies mention values ranging from 6.7% to 18% of cases showing giant cells.[4,9] Epithelioid cell reaction has been found to be predominant feature in many studies in literature.[10,11] Septic arthritis may be caused by hematogenous infection or direct inoculation of joint following trauma or surgery. It is usually seen in neonates and infants.[12] In the present study, 9 cases were encountered with male preponderance and age range of 1 to 69 years. Maximum cases (6/9) were seen in 1-15 age group with predominantly knee joint (6/9) involvement. One study mentions 6.02% of such cases with majority in age group of 0-10 years. In another study, 20% of the cases were of septic arthritis in an age range of 1-55 years with male predominance.[13] Rheumatoid arthritis mainly involves peripheral joints such as small joints of hands and feet with peak age incidence in 20-40 years. In present study, the age range was 18 to 72 years with maximum cases in the range of 20 to 45 years. Female preponderance was seen with M:F ratio of 1.3:1. Literature mentions that rheumatoid arthritis is 2-3 times more common in females than males.[14-16] In present study, knee and hip joints were affected. A study done by Abhayankar et al documents involvement of knee and wrist joints in majority of the cases. In our study sero-negativity was observed in 50% of cases. One study has quantified the degree of histologic variation in synovial membranes in rheumatoid arthritis taking into consideration parameters such as synovial hyperplasia, fibrosis, vascular proliferation and inflammation (perivascular, focal and diffuse).[17] In our study synovial hyperplasia with lymphoid cell aggregates were most consistently seen in synovial biopsies of clinically suspected rheumatoid arthritis.

Pigmented villonodular synovitis (PVNS) is a nodular and villous thickening of the synovial membrane that affects males and females equally with knee being the most commonly involved joint as seen in present study.[18] Synovial chondromatosis is characterized by multiple nodules of metaplastic hyaline cartilage most often showing endochondral ossification.[17] The degree of cellularity and nuclear atypia sometimes may lead to suspicion of malignancy. However a triad of clinical, radiological and histomorphological diagnosis helps rule out well differentiated chondrosarcoma.[17]

Crystal arthropathies are systemic disorders and show presence of crystals within synovium, articular cartilage and periarticular soft tissue. Clinical features may range from asymptomatic synovial deposits to chronic destructive arthropathies.[19,20] The three endogenously formed crystals that produce disease are monosodium urate, calcium pyrophosphate dihydrate, and calciumhydroxyapatite. 1 each case of gout and pseudogout were seen in males with characteristic histopathological features in present study.

Lipoma arborescence is characterized by fatty infiltration of the subsynovial connective tissue. It is one of the rarest of the synovial proliferative lesions.[21] Grossly, the entire synovium assumes a bright yellow, nodular, papillary appearance. It is considered non-neoplastic and represents an excessive accumulation of fat in the subsynovial space.[21] Treatment is synovectomy and recurrence is rare. Synovial sarcoma occurs at any age but maximum cases occur between 10-35 years with slight male predominance. More than 60% occur in lower limb especially thigh, knee and ankle joints.[22] 1 such cases is reported in the present study. Clinical suspicion and detailed immunohistopathological workup is extremely essential in the diagnosis of such lesion.

Arthroscopic guided synovial biopsies help in direct viewing of the synovial membrane which reveals primary diagnosis especially in neoplastic and infective pathology, to understand follow up changes related to targeted therapies (when fluid analysis fails to give clear picture of etiopathogenesis) and provides material for

advanced proteomic studies which could eventually lead to better patient management.[23]

Conclusion

Arthroscopic synovial biopsy is a simple and easy to perform technique. It offers specific diagnosis of various joint diseases. Synovial biopsy may give conclusive diagnosis where clinical diagnosis and synovial fluid analysis is equivocal.

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