CLINICOPATHOLOGICAL STUDY OF SYNOVIAL LESIONS

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ABSTRACT

Introduction: Synovium is a specialized mesenchymal tissue which reacts to wide variety of changes and noxious influences originating locally or elsewhere in the body. Histopathological examination of synovial biopsy plays a vital role in distinguishing between various possible etiologies such as infective, traumatic or crystal-induced arthropathy and neoplastic lesions. Clinical and radiological findings are also essential in arriving at an accurate diagnosis of synovial lesions. Aims and objectives: To study the spectrum of synovial lesions and correlate clinico-radiological findings of various lesions into degenerative, infective, inflammatory and neoplastic lesions. Methods: All the synovial biopsy specimens received in the Pathology laboratory, KIMS Hospital and Research Centre were studied. Detailed histopathological studies of the sections were done. Relevant clinical and radiological findings were analysed. Results: In the present study, the common age groups affected were between 2nd decade to 3rd decade (31.1%) and above 5th decade (31.1%). Females (56.6%) were more commonly affected. The knee joint (43.3%) showed a predilection for most synovial lesions. Among all the cases most common was tumour-like lesions (42.2%) followed by inflammatory lesions (19.9%), degenerative lesions (16.6%), infective lesions (9.9%), benign (9.9%) and malignant lesion (1.1%). Conclusion: Most synovial lesions have identical clinical findings classified into various subgroups by histopathological study. The study of synovial biopsy is a useful diagnostic tool in assessing various joint diseases.

KEYWORDS  Immunohistochemistry, Crystal Induced Arthropathy, Histopathology

Introduction

Synovial joints account for most body articulation and are the most commonly affected joints by disease in the body.[1, 2, 3] Synovium is a specialised mesenchymal tissue that reacts to a wide variety of changes and noxious influences originating locally or elsewhere in the body.[1-5] It is composed of an inner secretory zone lined by a discontinuous layer of specialized cells with both secretory and phagocytic functions. The synovial membrane behaves as a mirror to joint diseases, and examination of the synovial membrane often reveals many features suggestive of specific disease entities[4,5].

Lesions of synovial joints show typical pathological features but have identical clinical findings. The most common symptoms in synovial lesions include pain, swelling and stiffness of joints.[6] Various techniques have been implicated in synovial biopsies, of which arthroscopic synovectomy is the latest technique.[7] A systematic histopathological examination of synovial biopsies and clinical correlation is essential for arriving at an accurate diagnosis. In addition to routine H&E stained sections under light microscopy, special staining techniques, electron microscopy, and immunohistochemical techniques have evolved to diagnose synovial lesions accurately.[8,9,10]

Material and methods

This was a prospective study of 90 synovial specimens received in the Department of Pathology, KIMS Hospital and Research Centre, from July 2014 to July 2016. All synovial specimens were fixed in 10% formalin and routinely processed. Multiple serial sections of 3-5 micron thickness were obtained from
paraffin-embedded blocks. These sections were stained with Haematoxylin & Eosin. A detailed histopathological study of the sections was done. Special stains were done wherever required. Ziehl Neelsen staining was done in all suspected cases of tuberculosis. Immunohistochemical staining was done in relevant cases.

Clinical details and radiographic findings were maintained according to the proforma. Data for the study was collected from all those who fulfilled the inclusion and exclusion criteria on purposive sampling. The present study included all synovial biopsy specimens received in the Department of Pathology, KIMS. All autolyzed specimens and inadequate samples was excluded.

Results
In current study 90, synovial biopsy specimens were received in the Department of Pathology, KIMS, Bangalore for histopathological examination during a period of 2 years (July 2014 to July 2016), contributing to 0.9% of 9,962 surgical specimens. Histopathological examination of these specimens was done and categorized into degenerative, infective, inflammatory and neoplastic synovial lesions. (Table 1)

In the present study, the most common joint involved was the knee joint (43.3%), and the second most common joint involved was the wrist joint (33.33%). In the present study, synovial lesions were observed in 51 females (56.66%) compared to 39 males (43.33%) with a female to male ratio of 1.3:1. The swelling was the most common presenting symptom (94.4%) followed by pain (82.2%), 35 patients presented with fever (38.8%).

Osteoarthritis is the degenerative lesion of synovial joints. Radiological examination showed reduced joint space in 13 patients (86.66%), and osteophyte formation was noted in all patients. Grossly biopsy specimens appeared grey-white to grey-brown and ranged from 0.5 to 6 cm. 3-4 cartilaginous bodies were seen in 5 biopsies (33.33%). Cut section of cartilaginous bodies showed grey white to grey yellow areas. On histopathological examination, all the biopsies of osteoarthritis showed predominant synovial hyperplasia and chronic inflammatory infiltration. Villous hypertrophy and blood vessel proliferation were observed in 13 biopsies (86.66%).5 cases (33.33%) showed cartilaginous bodies, and 10 biopsies (66.66%) showed bone fragments.

Tubercular arthritis was seen in 2 patients, elbow joint was involved in one patient (50%), and in the other case, the ankle joint was affected. Grossly specimens were grey-white, and one of the biopsies showed cheesy white caseous necrotic material. On microscopy, well-formed granulomas with caseous necrosis were seen in both cases. (Fig -1).

Septic arthritis was encountered in 7 patients (7.77%) with knee joints commonly involved. On radiological examination, all seven cases showed joint effusion and narrowing of joint space. On microscopy, all cases showed acute inflammatory infiltrate comprising of neutrophils. Synovial hypertrophy and sub synovial fibrosis was observed 4 cases (71.42%). Blood vessel proliferation was noted in six cases (85.71%). One case (14.28%) showed necrotic debris. Fibrin deposition and cartilaginous tissue were noted in two cases (28.57%).

In the present study, chronic nonspecific synovitis was the second most common lesion comprising of 16 patients (17.77%)—all the patients presented with pain and swelling. On radiological examination, joint space reduction was observed in 14 patients (87.5%). Laboratory investigation revealed a raised ESR in 9 patients (56.25%), and in the remaining 7 patients (43.75%), ESR was within normal limits.

Gross examination showed grey-white to grey-brown, and size varied from 0.5 to 3 cm. (Fig 2). On microscopy, 12 biopsies (75%) showed synovial hyperplasia. Synovial hypertrophy and villous hypertrophy was observed in 8 cases (50%). Lymphocytic infiltration and blood vessel proliferation was observed in all biopsies, and plasma cells were observed in 8 (50%). Macrophages were seen in one case (6.25%).7 cases (43.75%) showed cartilaginous tissue, and bone fragments were observed in 2 biopsies (Fig 3).
### In the current study, there was the highest incidence of ganglion cysts comprising 33 patients (36.66%). Grossly ganglion cysts were grey-white masses measuring from 0.5 to 2 cm, and the cut section was cystic. Microscopically presence of fibro-collagenous cyst wall and myxoid degeneration was observed in all cases. Focal lymphocytic infiltration was seen in 5 cases (15.15%). Blood vessel proliferation was seen in 17 cases (51.51%) and cartilage in 5 (15.15%).

Grossly Baker’s cyst biopsy specimens were similar to a ganglion cyst. Microscopic findings in all 5 cases showed fibro-collagenous cyst wall lined by cuboidal to flattened epithelium. 3 cases (60%) showed cartilage and blood vessel proliferation was observed in 2 (40%).

Synovial lipomatosis was encountered as a very rare benign synovial lesion. Grossly multiple papillary projections were noted in all 3 specimens. Microscopic findings in all the 3 biopsies included synovial hyperplasia, synovial hypertrophy, vil-lous hypertrophy, lymphoplasmacytic infiltration, adipose tissue and blood vessel proliferation. (Fig 6&7)

In the present study total of 6 (6.66%) cases of giant cell tumours of tendon sheath were obtained. The second interphalangeal joint was involved in 5 patients (83.33%). Gross features were similar to rheumatoid arthritis. Microscopic findings in all cases included multinucleated giant cells admixed with spindle-shaped cells in a fibro-collagenous stroma with cleft like spaces. Hemosiderin laden macrophages were noted in 2 cases (33.33%).
Table 2 Comparison of incidence of synovial lesions

| Synovial lesions                  | Vijay P.M. et al[5] | Mamatha S.V. et al [7] | Kali et al [9] | Abhayankar et al [10] | Present study |
|-----------------------------------|---------------------|------------------------|----------------|------------------------|--------------|
| Osteoarthritis                    |                     |                        |                |                        |              |
| Tubercular Arthritis              | 1(3.33%)            | 10(20%)                | 8(26.6%)       | 85(42.5%)              | 2(2.22%)     |
| Septic Arthritis                  | 5(6%)               | 7(14%)                 | 2(6.66%)       | 15(7.5%)               | 7(7.77%)     |
| Chronic Non Specific Synovitis    | 59(71%)             | 12(24%)                | 9(30%)         | 6(3%)                  | 16(17.77%)   |
| Rheumatoid Arthritis              | 4(4.8%)             | 20(40%)                | 6(20%)         | 55(27.5%)              | 2(2.22%)     |
| Ganglion Cyst                     |                     |                        |                |                        | 3(3.33%)     |
| Baker’s Cyst                      |                     |                        |                |                        | 4(4.44%)     |
| Giant Cell Tumor Of Tendon Sheath |                     |                        | 1(3.33%)       |                        | 6(6.66%)     |
| Synovial Lipomatosis              |                     |                        |                |                        | 3(3.33%)     |
| Synovial Sarcoma                  |                     |                        | 1(3.33%)       |                        | 1(1.11%)     |
| TOTAL                             | 83(100%)            | 50(100%)               | 30(100%)       | 200(100%)              | 90(100%)     |

Figure 6 Irregular yellowish-white masses with multiple papillary projections.

Figure 7 Core of the villi showing mature adipocytes, proliferating vessels and chronic inflammatory cell infiltrate (H&E, 10X).

Synovial sarcoma was diagnosed in only one female patient (1.11%), and the age of the patient was 40 years—the patient presented with fever, loss of weight, pain and swelling of the knee joint. Grossly the specimen of synovial sarcoma appeared grey to grey-brown, measuring 6 cm in diameter. Cut surface showed multiple hemorrhagic areas. On microscopy, spindle-shaped cells were seen arranged in sheets and glandular patterns.

Individual cells were pleomorphic with hyperchromatic nuclei, prominent nucleoli and scant cytoplasm. 2-3 mitotic figures/10 hpf were seen. (Fig 8). The histopathological diagnosis was confirmed by Immunohistochemistry. IHC markers used were vimentin, cytokeratin and CD 99 (Fig 9,10 &11). Tumour cells were strongly positive for vimentin and cytokeratin and showed focal positivity for CD 99 (Fig 9,10 &11).

Figure 8 Glandular arrangement of tumour cells (H&E-10 X).

Figure 9 Strong cytoplasmic expression of cytokeratin (10 X).
1.3:1. In a study done by Mamatha. S.V et al. female to male ratio was 1.9:1 [7]. Vijay P .M . et al., M.SankaranKutty et al. observed peak incidence between 20 to 35 years (31,34.44%) and above 50 years (31,34.44%). Peak incidence was seen between 40 to 50yrs in the study done by Vijay P.M . et al.[5]. M.SankaranKutty et al. observed peak incidence between 20 to 50 years [6]. In our study, females were more commonly affected (56.66%) with a female: male ratio of 1.3:1. In a study done by Mamatha. S.V et al. female to male ratio was 1.9:1 [7]

The knee joint was the most common (43.33%), followed by the wrist joint (33.33%).In the study done by M.S. Sant et al., the knee joint was involved in 138 cases (55%).[8] In our study, swelling (85, 94.4%) was the major presenting symptom, followed by pain in 74 patients (82.2%).

Osteoarthritis is pathologically characterized by focal cartilage damage, bone sclerosis, and synovioapathy. There were 15 cases of osteoarthritis in the present study constituting 16.66% of total biopsies. Incidence was more when compared to the study by Abhayankar et al (12.5%) [10] and less when compared to Norman . S. Cooper et al (18.82%).[11]

In our study, knee joint was involved in 13 patients (14.44%), and wrist joint was affected in 2 (13.33%). On radiological examination, reduced joint space was observed in 13 patients (86.66%). In most studies, osteoarthritis cases showed a reduction in joint space (95%).[10,11,12]

Cooper et al., in their study, observed synovial hyperplasia (63.5%), villous hypertrophy(73%), chronic inflammatory cells (81%), fibrosis (68.9%), cartilage (12.2%) and bone fragments (12.2%) with no blood vessel proliferation. [11] Similar features were observed in the present study.

Tuberculous synovitis causes destruction of joints if not diagnosed early. Making an early diagnosis is often difficult, and treatment is therefore frequently delayed in clinical practice which results in significant morbidity and mortality. [13] The age group affected was between 11-30 years in the study done by Sant.M.S.et al.[8] The present study also showed incidence between 2nd to 3rd decade. Microscopic findings in our study are in concordance with the study by Mamatha.S.V.et al except for synovial hyperplasia. In present study Zeihl Neelsen staining for acid fast bacilli was done on both the histopathological sections. Acid fast bacilli were not seen in both the cases which was similar to in the studies done by Vijay.P.M.et al [5] and Mamatha.S.V et al[7]

The term chronic nonspecific synovitis was used for cases in which no specific histological features suggesting etiology were observed and revealed nonspecific histological changes. In present study chronic nonspecific synovitis was the second most common lesion comprising of 16 patients. Mamatha.S.V.et al [7] studied 12 cases (25%) of chronic nonspecific synovitis in which most common age of presentation was 32-65 years (25%) with male preponderance (50%) and was in concordance with present study. On radiological examination joint space reduction was observed in 14 patients (87.5%). In the study done by Vijay.P.M.et al, decrease in joint space was observed in 14 patients (72%).[5]

In the present study 2 patients had rheumatoid arthritis constituting 2.22% of total synovial biopsies. Mamatha.S.V et al in 2015 studied 20 cases (40%). Middle aged female preponderance is observed in many studies.[7]

In present study a total of 33 cases (33.33%) of ganglion cyst were diagnosed Ganglion cysts develop most frequently on dorsal aspect of wrist.[7] Over usage of wrist and fingers is cause for this frequent location. Ozkan et al in their study assessed the necessity of routine histopathologic examination of ganglion cysts. Most common age group affected in our study was 20-35 years constituting 16 patients (48.48%).[14] 21 patients (63.63%) were females with female to male ratio of 1.8:1. Aksbar Zubari et al studied 112 cases of ganglion cysts, with female predominance and incidence between 20 to 30 years. Similar observations were made by Ozkan et al.[14,15]

Herniation of synovium through a joint capsule produces synovial cyst. Synovial cyst in popliteal space secondary to inflammatory arthritis is Baker’s cyst. [16] Any joint disease will lead to increase in intra-articular pressure which results in the formation of Baker’s cyst. In the study of 17 cases (35.4%) of Baker’s cysts by W. Rauschning et al, histopathology showed fibrosis with thickening of bursal wall.[17] In present study all 5 cases showed fibrocollagenous cyst wall lined by cuboidal to flattened epithelium.

Lipoma arborescens commonly affects large joints with knee joint being the commonest. The exact etiopathogenesis is unknown but one of the hypothesis states that there is inverse relationship between adipose differentiation and osteogenic activity of bone marrow stromal cells. It possibly represents a
Table 3 Comparison of histopathological features of rheumatoid arthritis

| Microscopic features         | P.M.Vijay et al [5] | Mamatha S.V. et al [7] | Present study |
|------------------------------|---------------------|------------------------|--------------|
| Villous Hypertrophy         | 100%                | 100%                   | 100%         |
| Synovial Cell Hyperplasia   | 75%                 | 100%                   | 100%         |
| Diffuse Infiltration Of     |                     |                        |              |
| • Lymphocytes               | 100%                | 100%                   | 100%         |
| • Plasma Cells              | 100%                | 100%                   | 100%         |
| Lymphoid Aggregates         | 25%                 | 100%                   | 100%         |
| Blood Vessel Proliferation  | 75%                 | -                      | 100%         |
| Fibrin                       | 50%                 | -                      |              |

Table 4 Comparison of the incidence, age, site and sex distribution of synovial lipomatosis

| Present study         | Shalinee rao et al [18] | M de vleeschhouwer et al [19] |
|-----------------------|------------------------|-------------------------------|
| 3 cases (100%)        | 8 cases (100%)         | 1 case (100%)                 |
| 20-75 yrs             | 1 -73 yrs              | 30 yrs                        |
| M>f                   | M>f                    | M>f                           |
| Knee joint            | Knee joint             | Knee joint                    |

protective and adaptive response of the articular cartilage or metaplastic change in a chronically inflamed synovium.[18,19]

The giant cell tumour of the tendon sheath is benign and is the most common tumour in hand. It occurs at any age, with a peak incidence in 3rd to 4th decade. There is a high risk of recurrence, especially when a tumour invades the joint or tendon.

In the present study total of 6(6.66%) cases of giant cell tumours of tendon sheath were obtained. R. Lancigu et al. studied 96 cases of giant cell tumours of the tendon sheath.[20] Females were more commonly affected (59.5%, 1.5:1), and most of the patients were between 20 to 30 years of age in the present study. The index finger was commonly involved in most cases (30.2%). Multinucleated giant cells admixed with spindle-shaped cells was noted. Fibro collagenous stroma with cleft like spaces was observed. Hemosiderin laden macrophages were noted in 2 cases (33.33%). Cholesterol clefts and Touton type of giant cells were not encountered in our study, and similar findings were described in other studies.

Synovial sarcoma is a rare but distinctive soft tissue sarcoma that displays epithelial differentiation. It is the 4th most common sarcoma. The cell of origin has not been proven to date. The most common site is around knee and ankle joints.[21,22,23]In the present study included a case of a biphasic variant of synovial sarcoma of was studied in a 40-year-old female. Very few pieces of literature are there which describes biphasic synovial sarcoma[23]. In our study, also knee joint was affected in the single case.

A microscopic study of the biphasic synovial sarcoma showed short spindle cells separated by myxoid stroma.2 to 3 mitotic figures per 10 high power fields were seen. Similar features were observed in the study by Vijay. P.M et al. except for the mitotic figures.[21] Few studies show strong positive results for vimentin and cytokeratin.[22,23] In the present study, tumour cells were strongly positive for vimentin and cytokeratin and showed focal positivity for CD 99.

Conclusion

The histopathological examination of synovial tissue with a correlation of clinical and radiological findings aids in classifying synovial lesions into various subgroups. Early and specific diagnosis of various joint diseases is possible only by histological assessment of synovial biopsies.

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Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

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