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Original Article

Clinicopathological Study Of Inflammatory Synovial Lesions

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ABSTRACT

Aims: The aim of the present study is to study the morphology of various clinically suspected inflammatory lesions of the synovial tissue and its diagnostic utility. Methods: The present study comprises analysis of 83 biopsies of clinically suspected inflammatory synovial lesions conducted at Department of Pathology, J.J.M Medical College, Davangere during period of 2 years from April 2002 to March 2004 contributing 0.75% of 10,954 total specimens received during the period. Synovial biopsy Specimens were processed routinely and stained with haematoxylin and eosin and wherever necessary special stains like Z-N stain for AFB, Prussian blue stain for haemosiderin were carried out and diagnosed histopathologically. Wherever necessary the available clinical, radiological and synovial fluid analysis findings were taken in to consideration to categorize the lesions. Results: In our study, the common age groups affected were between 40-50yrs. Males were commonly affected with M: F 1:0.6. Most common symptoms seen were pain & swelling. Knee was the commonest joint involved. Most common histopathological diagnosis made among the clinically suspected inflammatory synovial lesions was chronic nonspecific synovitis followed by T.B arthritis, septic arthritis & rheumatoid arthritis. Conclusion: High incidence of chronic non specific synovitis may represent smouldering infection where the causative agent was not demonstrable or represented an inflammatory response to local microtrauma or as an articular manifestation of a systemic disease. If these patients are closely followed up and repeat biopsies are performed, transition to definitive arthritis may occur. In rheumatoid arthritis the histopathological features may be non specific suggesting the diagnosis of chronic non specific synovitis. However in many early rheumatoid arthritis patients with strong clinical or histopathological features suggestive of rheumatoid arthritis; it is worthwhile to do serological test for rheumatoid factor to exclude rheumatoid arthritis.

1. Introduction

Joints are constructed to provide both movement and mechanical support. Their anatomy is complex and directly related to their function. [1, 2]. Joints are of two types, the solid (non synovial) joints known as synarthroses which provide structural integrity and allow minimal movement and lack a joint space. Synovial joints, in contrast have a joint space that allows for a wide range of motion [1, 3, 4]. Synovium which lines the joint space is labile, reacts to wide variety of changes and noxious influences originating locally or elsewhere in the body [5, 6].

Classification of Inflammatory Synovial Lesions:

1. Inflammatory joint disease: Infectious arthritis of known etiology.

a. Bacterial
b. Spirochetal
c. Mycobacterial or chronic granulomatous
d. Fungal
e. viral

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2. Inflammatory arthritides of unknown etiology
a. Rheumatoid arthritis
b. Stills disease /juvenile rheumatoid arthritis
c. Seronegative spondylo arthropathies
d. Psoriatic arthritis
e. Reiter's Syndrome
f. Enetropathic arthritis
g. sarcoidosis
h. Others

Common conditions, such as rheumatoid arthritis, rarely cause diagnostic problems when presenting typically and affecting the joints symmetrically. Difficulties arise when only one joint is affected; synovial biopsy is then helpful in distinguishing between various possible aetiologies such as infective, traumatic or crystal induced [7,8] .

The aim of the present study is to study the morphology of various clinically suspected inflammatory lesions of the synovial tissue and its diagnostic utility.

Although histopathological study of synovial biopsy is one of the most valuable means for diagnosis of joint disease, it has its own limitations. In many instances corroborating clinical, radiological, biochemical and serological examinations becomes essential making an accurate histopathological diagnosis [9].

2. Materials and Methods

The present study comprises analysis of 83 biopsies of clinically suspected inflammatory synovial lesions conducted at Department of Pathology, J.J.M Medical College, Davangere during period of 2 years from April 2002 to March 2004 contributing 0.75% of 10,954 total specimens received during the period.

Materials for study were obtained from Bapuji Hospital, Chigateri District Hospital, Woman and Children Hospital and from other well equipped private and Government Hospitals in and around Davangere.

The synovial biopsies were obtained by open method in the operation theater. After obtaining the specimens, detailed gross examination was done and salient morphological features were recorded and the whole biopsy material was fixed in 10% formalin for 12-24 hours. Finally representative bits were given. Tissues were processed routinely and paraffin blocks were prepared. 3-5µ thin sections were cut and stained with haematoxylin and eosin routinely and wherever necessary special stains like Z-N stain for AFB, Prussian blue stain for haemosiderin were carried out.

Histopathologically various lesions were analysed and diagnosed. Wherever necessary the available clinical, radiological and synovial fluid analysis findings were taken in to consideration to categorize the lesions.

3.Results

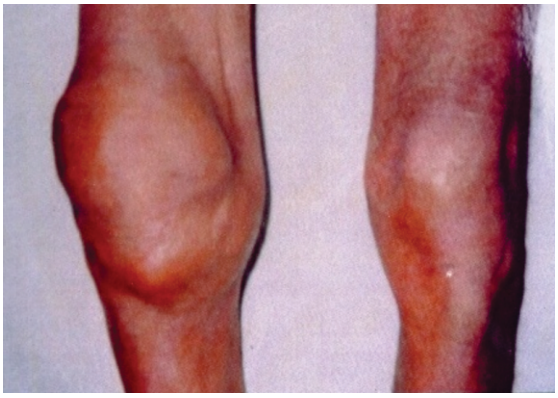
The incidences of various inflammatory synovial lesions in the present study are shown in table-1.

In our study, the inflammatory synovial lesion cases range from 1st decade to 8th decade. The common age group affected were between 40-50yrs. Males were commonly affected with M:F 1:0.6. Most common symptoms seen were pain & swelling. Knee was the commonest joint involved [Fig.1].

Table 1: Incidence of inflammatory Synovial Lesions

Pathological lesions	No. of Patients	Percentage
Inflammatory :		
a. Infectious arthritis of known etiology :		
• Tuberculous arthritis	15	18.07
• Septic arthritis.	5	6.02
b. Inflammatory arthritis of unknown etiology:		
• Chronic nonspecific synovitis	59	71
Rheumatoid arthritis	4	4.8
Total	**83**	**100**

Fig -1. Swelling over the Right knee joint



3.1.Chronic non specific Synovitis:

Only in 14 patients decrease in the joint space was noted radiologically. ESR value was increased in 28 patients and ranged from 29-46mm/hr and 29mm/hr in 1 patient and in the remaining 30 patients they were within normal limits.

Synovial fluid findings in 17 patients of chronic Nonspecific synovitis are shown in table -2.

Table 2. Synovial fluid findings in 17 patients of chronic Nonspecific synovitis

Findings	No. of Patients	Percentage
Colour : Straw yellow	15	88.2
Pale yellow	02	11.8
Mucin Clot: Fair	13	76.5
Good	4	23.5
Total Leukocytic count		
< 1000	01	5.9
>1000 < 20,000	16	94.11
Predominant cells :		
Neutrophils	16	94.11
Lymphocytes	01	5.9
Sugar level: Normal	11	64.7
Low	06	35.3
Protein Level: Normal	11	64.7
Moderate	01	5.9
High	05	29.4

3.2.Morphology: Gross Findings:

They appeared as grey white soft tissues in 35 patients' pearly white in 24 patients and grey white to grey yellow masses in 1 patient measuring between 2.5cms to 4.0cms in size.

The most persistent microscopic features encountered were diffuse and scattered infiltrates of lymphocytes in 30 patients, rest of the features are as shown in the microphotographs [Fig. 2, 3,4].

Fig -2.Chronic non specific synovitis : Villous hypertrophy (H&E.10X)

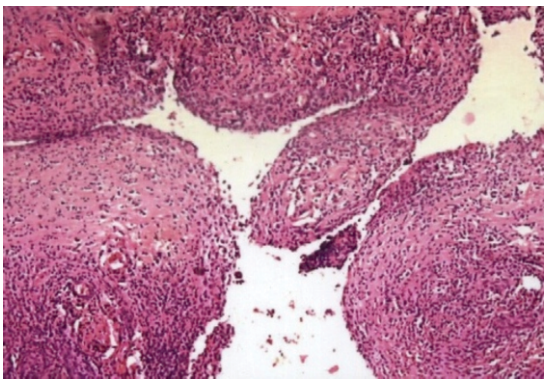


Fig – 3.chronic non specific synovitis: Diffuse infiltration of lymphocytes and blood vessel proliferation (H&E.10X)

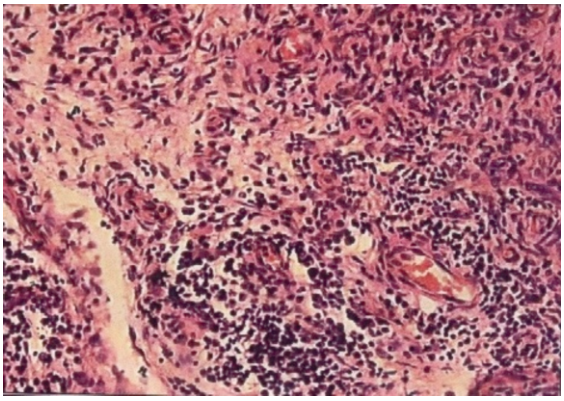
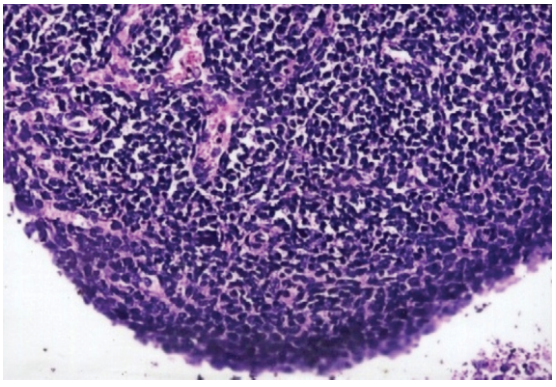


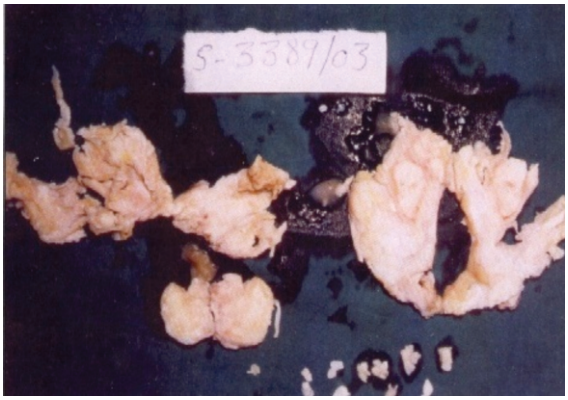
Fig – 4.Chronic non specific synovitis: Hyperplasia of synoviocytes and focal aggregates of lymphocytes (H&E.10X)



3.3. Tuberculous arthritis

Grossly in 13 patients synovial tissue were small multiple bits varying from 1cm - 3cm in diameter and were grey white, in other two pateints there were cystic masses with nodular surface containing grey white caseous necrotic material suggestive of tuberculosis [Fig.5].

Fig -5 : Irregularly cut opened synovial tissue in tuberculous synovitis showing large areas of caseous necrosis along with melon seed bodies

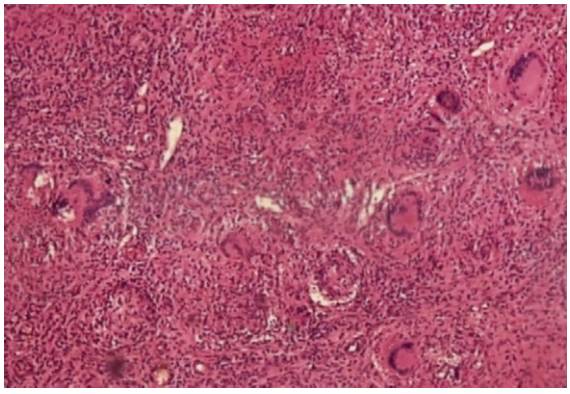


Histopathologically all 15 patients showed granulomatous lesion [Fig.6].

Z-N staining of histopathological sections for AFB was done in 6 patients. However AFB could not be demonstrated.

Decrease in joint space and gross osteoporosis was noted in 14 patients, incongrunity of articular surfaces was noted in 7 patients, osteophyte formation was seen in 5 patients and subluxation of tibia in 1 patient were noted radiologically. All the routine laboratory investigations were within normal limits except ESR which ranged from 30-48mm/hr in 13 patients (86%) and 28mm/hr in 2 patients.

Fig -6. Tubeculous synovitis : Epitheloid cell granulomas with Langhan's giant cells (H&E.10X)



Synovial fluid analysis was done in 2 clinically suspected patients. Grossly they were straw yellow in colour and mucin clot was fair in both, the total leukocytic counts were 16,418 and 17,204 cells/cu.mm respectively, neutrophil count was 82% in each,

lymphocytic count was 10% and 13% respectively and macrophage count was 8% and 5% respectively. Sugar and protein level was estimated in one patient in which Sugar level was 48mg% and protein level was 4.1g%. These 2 patients were diagnosed histopathologially as tuberculous synovitis. Of the 11 clinically suspected patients of Tuberculous arthritis histopathologically all patients showed features of Tuberculous synovitis. In the remaining 4 patients' clinical diagnosis were rheumatoid arthritis, Septic arthritis, Bursitis and chronic nonspecific synovitis which were also diagnosed histopathologically as tuberculous synovitis.

3.4.Septic Arthritis:

Synovial fluid analysis was done in one clinically suspected patient which was confirmed histopathologically and was turbid in appearence which showed total leukocyte count of 65,200 cells/cu.mm, polymorphs - 91%, lymphocytes - 9%, ragocyte count 90%, sugar - 35mg% and protein level of 5g%

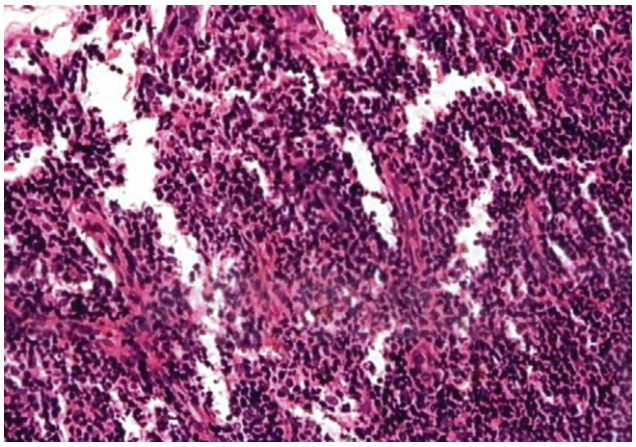
3.5.Morphology

Grossly the synovial biopsy specimen appeared grey white in 3 patients, grey white to grey brown in 1 patient and pearly white in the remaining one patient, size ranged from 0.5-2cm.

The microscopic features are as shown in microphotographs [Fig.7].

In 5 histopathologically diagnosed cases two were clinically diagnosed as septic arthritis, other two as nonspecific and the remaining one was diagnosed as osteoarthritis.

Fig -7. Septic arthritis:Dense polymorphonuclear leukocytic infiltration (H&E.40X)



3.6.Rheumatoid arthritis:

ESR value was raised from 40-49 mm/hr and rosewaaler was seropositive in 3 patients and ASLO titer was raised in one patient.

Synovial fluid analysis was done in all patients, on gross examination all were pale yellow and translucent, two patients showed fair mucin clot. Predominant cells were polymorphs followed by lymphocytes and macrophages. However synoviocytes were absent. Total leukocytic count ranged from 6,000 to 10,000. In 2 patients we could able to demonstrate ragocytes in geimsa stain.

3.7.Morphology:

Gross: 3 specimens were pearly white in colour and the remaining one was grey white in colour and measured 1.5 - 3 cm in diameter.

Microscopically all the 4 patients (100%) showed dense infiltration of lymphocytes, plasma cells, villous hypertrophy, and 3 patients showed hyperplasia of synoviocytes. The other features like fibrin with entrapped acute inflammatory infiltrates were seen in 2 patients, lymphocytic aggregates and lymphoid follicles in 1 patient and focal collagen degeneration in 1 patient [Fig.8-10].

Fig -8. Rheumatoid arthritis:Villous hypertrophy with hyperplasia of synoviocytes (H&E,10X)

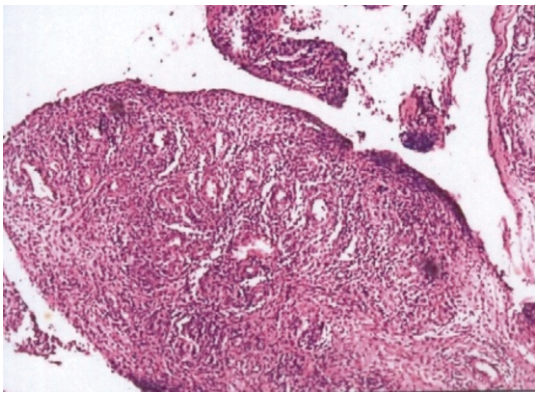


Fig -9. Rheumatoid arthritis:Lymphoid follicles (H&E.10X)

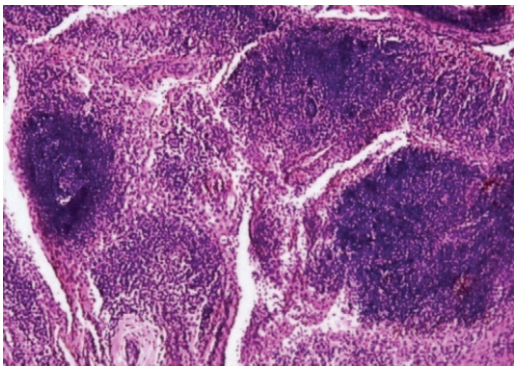
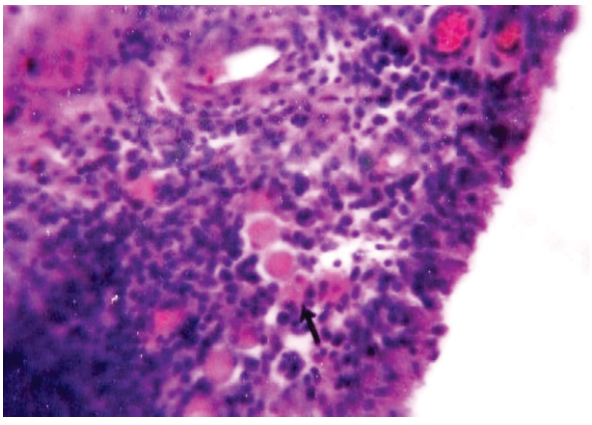


Fig -10. Rheumatoid arthritis:Lymphocytes, plasma cells and russel bodies (arrow) (H&E.40X)



4.Discussion

Surgical corrective procedures in chronic arthritis have made an easy access to synovium for histopathological studies. Exploratory arthrotomy and synovial biopsy are recognized procedures for early diagnosis of joint diseases particularly when clinical and radiological findings are inconclusive. Synovial membrane biopsy in chronic synovitis of the knee has been claimed to give more accurate information about the disease. [10, 11]

Chronic non specific synovitis was the common inflammatory synovial lesion comprising 59 patients (71%) from 83 inflammatory synovial lesions. Followed by tuberculous synovitis in 15 patients (18.07%) where as in Abhyankar et al, study tuberculous arthritis was the common lesion followed by rheumatoid arthritis and degenerative joint disease. [12]

In the present study majority of the inflammatory lesions occured in 11-50 years age group, with peak incidence between 41-50 years. Similarly in a study by M.S.Sant [13] majority of the patients were between 11-30 years indicating growing age and early adulthood is the commonest age group requiring synovial biopsy studies for early diagnosis of synovial lesions.

Males were most commonly affected than females in this study with M: F ratio of 1:0.6. Similarly in study of M.S.Sant males were more commonly affected than females with a M: F ratio of 1:0.58, probably indicating more stress on male joints than female joints. However female prepondarance was seen in rheumatoid arthritis which agrees with the incidence observed by many authors. [9,14,15]

In the present study knee joint was the common joint involved by inflammatory synovial lesions in 56 patients (67.4%) out of 83 clinically suspected inflammatory synovial biopsies and it was most commonly affected by chronic non specific synovitis in 44 patients (78.57%) followed by tuberculous synovitis in 6 patients (10.7%). Similarly knee joint was involved in 138 patients (55%) out of 251 synovial biopsies in the study done by M.S.Sant in 1994 and the author encountered chronic non specific synovitis in 65 patients (47.10%) as the common lesion affecting the knee joint followed by tuberculous synovitis in 40 patients (28.98%).[13]

4.1.Chronic non specific synovitis

Chronic non specific synovitis formed the commonest type of inflammatory arthritis occuring in 59 patients (71%). In the present study the term chronic non specific synovitis was concluded in absence of specific inflammatory etiological agent or related features and in absence of diagnostic features related to rheumatoid arthritis.

This high incidence of chronic non specific synovitis in the present study may represent an early stage of rheumatoid arthritis, in which the disease is still in the stage of evolution without a full fledged picture of rheumatoid arthritis, some patients may be due to early osteoarthritis not satisfying histopathological and radiological features for its diagnosis. If these patients are closely followed up and repeat biopsies are carried out in due course, they may present with specific diagnostic features or patients may have self limited disease or may undergo complete therapeutic remissions.

In the present study 59 patients (71%) of chronic non specific synovitis were encountered, the most common age group affected was 11-50 years with male dominance. M.S. Sant in their study in 1994 had similar incidence of chronic non specific synovitis in 65 patients (47.1%). [13]

Abhyankar et al, in the study of 200 synovial biopsies, 80 patients diagnosed as chronic non specific synovitis were reexamined and classified into various disease entities. Following reclassification only 6 patients (3%) remained as non specific synovitis indicating the necessity of follow up or reexamination of the said lesions for further categorization. [12, 16]

4.2.Tuberculous synovitis

Among 83 clinically suspected inflammatory synovial biopsies, tuberculous synovitis was the second most common lesion in inflammatory synovitis constituting 18.07%.

Histopathological features like caseating granulomas were seen in 7 cases (46.6%) & non caseating granulomas were seen in 8 (53.3%) cases in the present study where as in Steven Berney et al (1972) study [17] Caseating granulomas were seen in 11 (57.89%) & non caseating granulomas in 8 (42.11%) indicating higher incidence of non caseating granulomas in the present study. Other features like caseation (46.6%) , Epithelioid cell reaction (100%) , No giant cells (6.7%) were seen in the present study whereas in Lal K.B. & Gupta (1972) study [18] these features were seen in 66.6%, 87.5%, 18.7% respectively indicating that epithelioid cell reaction as the predominant feature. [19, 20, 21]

Composition of synovial fluid reflects pathological phenomena occuring within the joint. Because of the unusual relationship between the tissues within the joint, chemically mediated events such as inflammation or enzyme mediated degradation occuring within the synovium and cartilage are reflected in changes within the synovial fluid. [22]

In the present study synovial fluid analysis was done in two clinically suspected patients of TB synovitis which showed features attributable to tuberculosis and our findings were comparable to the other studies by Freemont A.J., and Denton in 1995 where neutrophils were predominant cells [22] where as Sakhuja et al, encountered biochemically high protein content with mononuclear cells as a predominant component instead. [23]

4.3.Septic arthritis

Septic arthritis may be caused by haematogenous infection or direct inoculation of joint following trauma or surgery. Septic arthritis is common in neonates and infants. [24] In the present study the diagnosis of septic arthritis was mainly based on the morphology. A total of 5 patients (6.02%) of septic arthritis were encountered in this study. The most common age group was 0-10 years and all patients were males and majority presented with pain and swelling. Laboratory findings were not informative except raised ESR in all patients and increased leukocyte count in synovial fluid analysis in one patient only. Sakhuja A.C. et al in their study in 1981 encountered 7 patients (20%) of septic arthritis in the age group between 1-55 years with a male dominance. In the same study apart from histomorphological features, they showed similar morphological and biochemical findings in synovial fluid analysis. [23]

4.4.Rheumatoid arthritis

It is predominantly a disease of peripheral joints frequently involving the small joints of hands and feet. [1] The peak age incidence is in 20-40 years. However the age group involved in present study was between 31-40 and 71-80 years indicating no age is immune.

In the present study female preponderance was seen with a male to female ratio of 1:3. Similar observations were made by many authors in the literature which states that rheumatoid arthritis is 2-3 times more common in females than males. [1, 9, 14] Knee, ankle, elbow and multiple joints were affected in one patient each in the present study, where as in Abhyankar et al study, knee and wrist joints were involved in majority of the patients. Polyarticular involvement was seen in only 1 patient (25%) which is less when compared to the study of Garg et al (1973) [25] where in polyarticular involvement was seen in 13 (56.52%) of the total 23 patients of rheumatoid arthritis.

Of the total 4 patients, serological test for rheumatoid factor was positive in 3 (75%) and sero negative in one (25%). Many authors have also observed seronegativity in 10-30% of rheumatoid arthritis patients [9, 14, 26]. Higher incidence of seropositivity (75%) was seen in the present study compared to studies by Grimley & Sokoloff [27], Garg et al [25], where the seropositivity was quite less. However Graciela et al [26], showed similar observations like the present study. [28, 29]

Although these histopathological changes are highly characteristic of rheumatoid arthritis, it must be understood that they are not pathognomonic. Qualitatively similar changes may be seen in patients with psoriatic arthritis, systemic lupus erythematosis and even rarley with osteoarthritis in which large quantities of cartilage and bone are shed and incorporated into the synovium, elliciting an immune and foreign body inflammatory response. But the synovitis in these conditions is less severe than seen in a great majority of patients with rheumatoid disease [30, 31]. Along with these important histological criteria serology was also taken as an important factor for establishing a diagnosis of rhematoid arthritis.

In Rheumatoid arthritis patients, the histopathological features may be non specific suggesting the diagnosis of chronic non specific synovitis. However when there is diffuse infiltration of plasma cells with variable number of lymphocytes, with or without focal or occasional lymphocytic aggregates it is worthwhile to do serological test for rheumatoid factor and to conclude rheumatoid arthritis. It is more advisable and especially when there is clinical suspicion. [32]

The entire spectrum of typical histological findings may not be seen in synovial biopsies of all patients of rheumatoid arthritis. The histological picture may be even non specific and the only consistent finding may be infiltration of plasma cells and lymphocytes as observed by Garg et al (1973). [25]

5.Conclusion

• Majority of the inflammatory synovial lesions could be classified into various subgroups by histopathological study.

• High incidence of chronic non specific synovitis may represent smouldering infection where the causative agent was not demonstrable or represented an inflammatory response to local microtrauma or as an articular manifestation of a systemic disease. If these patients are closely followed up and repeat biopsies are performed, transition to definitive arthritis may occur.

• The classical histological picture of rheumatoid arthritis may not be seen in all synovial biopsies of rheumatoid arthritis patients. The histopathological features may be non specific suggesting the diagnosis of chronic non specific synovitis. However in many early rheumatoid arthritis patients with strong clinical or histopathological features suggestive of rheumatoid arthritis; it is worthwhile to do serological test for rheumatoid factor to exclude rheumatoid arthritis.

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