A prospective study for diagnosing joint diseases by synovial fluid analysis and percutaneous needle biopsy of synovium

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ABSTRACT

Background: Arthritis is an important cause of morbidity, presenting as monoarticular or polyarticular lesion. Percutaneous synovial aspiration and biopsy can help in identifying specific aetiological diagnosis. The study was conducted with the objective to evaluate the efficacy of percutaneous synovial biopsy as a diagnostic aid and study the characteristics of synovial fluid in various joint diseases.

Methods: Percutaneous synovial biopsy along with synovial fluid analysis was studied in all the 100 enrolled cases of arthritis. The fluid was subjected to physical, biochemical, and cytological analysis.

Results: Of the 100 cases, monoarticular joint involvement predominated over polyarticular (n=80; 80%), knee joint (60%) was most commonly affected in monoarticular and polyarticular arthritis. Rheumatoid arthritis (RA) (n=33; 33%) is the most common aetiology followed by tuberculosis (n=22). Males predominated over females in this study (n=61; 61%).

Conclusions: The evaluation of synovial fluid and synovial biopsy in joint diseases will stimulate its use as routine investigative procedure in the diagnosis of various puzzling joint disorders. Both these procedures can be done simultaneously through the same site of aspiration by the same needle.

Keywords: Joint diseases, Synovial fluid, Synovial biopsy

INTRODUCTION

Rheumatoid arthritis (RA) is an inflammatory arthritis that affects nearly 1% of the world’s adults. It is characterized by symmetric polyarticular inflammation of the synovium, typically of the small joints of the hands (MCP and PIP), wrists and feet. This inflammation results in pain and stiffness, and can lead to progressive joint damage resulting in deformities and loss of function.\(^1\) The clinical examination can disclose synovial thickening and swelling, indicators of joint inflammation. At the time of presentation, nearly 70% of radiographs can be normal, but MRI and ultrasound with power Doppler have higher sensitivity to detect smaller erosions and synovial inflammation, and may reveal changes even when X-rays are normal.\(^2\)

Arthritis 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.\(^3,6\) The relatively frequent occurrence of this problem has led to the indiscriminate use of NSAIDs by medical practitioners, without arriving at a specific etiological diagnosis. The latter can be easily arrived at by using a fairly simple technique of percutaneous synovial aspiration and biopsy and specific treatment be instituted in cases like tuberculosis.
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.7

METHODS

Patients presenting with complaints of Joint pathologies visiting Outpatient department of Narayana medical college & Hospital, Nellore, of which 100 of them willing to undergo procedure were participated in the study, with proper informed written consent. The period of study was from August 2013 to September 2016. Detailed history taking and meticulous clinical examination was done in all cases with reference to various symptoms.

Close attention was paid to location, nature and course of joint involvement. In cases of polyarthritis the location of joint first involved and the pattern of progression to other joints was noted. Morning stiffness, frequency and periodicity of the episode with characteristic waxing and waning, barometer relationship were the other important considerations noted. Fever, fatigue, anorexia, asthenia, cough were important constitutional enquiries made in cases where systemic diseases were suspected. Complaints of ‘red eye’, dysentery, urethritis were other important points in history taking. A special effort was made to probe and find out any history suggestive of noninflammatory osteoarthritis, chronic infection and inflammation like tuberculosis, rheumatoid lesion and gout and severe inflammation like septic arthritis.

In conventional laboratory aid a special note was made for the level of erythrocyte sedimentation rate (ESR). Rheumatoid arthritis (RA) factor, serum uric acid level estimation, C – reactive protein (CRP) were done in suspicion of rheumatoid lesion and gouty arthritis. In suspected case of tuberculosis, sputum and 24 hour urine for AFB by concentration methods and Mantoux test were carried out. In suspected pyogenic arthritis, culture of throat swab, urine and blood were done. Beside routine Roentgenographic examination of affected joint in different planes AP, lateral and oblique, X-ray chest was done in suspected cases of tuberculosis.

All these patients after through clinical evaluation were subjected to synovial fluid study and synovial needle biopsy. Synovial fluid was aspirated before arthroscopy. Analysis was started as soon as the fluid was aspirated. The fluid was subjected to physical, biochemical, and cytological analysis. The parameters studied in physical examination included color, clarity, viscosity, mucin clot test, and wet preparation. The biochemical analysis included difference in fasting blood and 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). RA factor was estimated in synovial fluid. Bacteriological analysis includes Gram’s staining, acid fast (AFB) staining, culture and sensitivity and PCR to detect Mycobacterium tuberculosis DNA.

Procedure of arthrocentesis of knee joint

The patient was admitted or detained in the ward for the needle biopsy and aspiration. The patient was kept starving for at least 6 hours prior to the procedure so that the fasting level of glucose could be determined. Arthrocentesis and synovial biopsy was carried out in operation theater as a minor surgical procedure.
The needle A was taken out leaving the cannula (B) in position. Now the notched needle C which had been previously fitted with a 20 ml syringe was inserted through the lumen of the cannula so that its blunt end saw tooth entered the synovial space. Strong suction was then applied to the barrel of the syringe and the toothed needle was slightly withdrawn after the aspiration of few ml of synovial fluid, when the notched orifice become occluded by synovial membrane and further aspiration become impossible. The suction was maintained to hold the synovial specimen within the notch. The syringe and the inner needle were held motionless in the right hand where left hand slowly advanced the outer cannula using a slight twisting and rotating motion for about 1 cm to ensure that specimen has been severed and held in the notch. The outer cannula was then left in situ and the inner needle with the attached syringe was removed. The piece of synovial tissue was removed from the notch with a needle point and the same process repeated several times in different direction and region of the joint. The specimens were collected in a vial containing formalin (10%) solution and sent for histopathological examination.

After the procedure, one dose of intravenous Cefuroxime (as per weight and age) is given and compression bandage was applied over the joint and if needed the patient was observed in the ward for 48-72 hours for any evidence of post aspiration infection like throbbing pain, high fever or any untoward effect otherwise patient is left to go home and advised for follow-up with reports.

RESULTS

Evaluation of synovial fluid and synovial biopsy studies of 100 cases of joint disease during the study has been made and following are observations.

Mono articular pathologies were 68% and poly were 32% as shown in Figure 4. Various joints involved in poly and mono arthropathies are enumerated in Table 1. Knee joint was found to be affected more than other joints in both mono and poly arthritis.

 Variety of joint pathologies diagnosed by synovial fluid analysis and biopsy are illustrated in Table 2.

![Figure 3: Sites of tissue taken.](image)

Figure 4: Affection of joint disease.

![Figure 5: Incidence of trauma in various joint diseases.](image)

Table 3 presents the age pattern in different joint diseases. Rheumatoid arthritis was found between age group of 31-50 and above 50 dominantly and tubercular arthritis was found mainly in the younger age group between 11-30 years in most of the cases. Males predominated over females in this study (n =61, 61%) as given in Figure 6. In osteoarthritis of course it was observed that above 45 years, both sexes were almost equally affected.
Table 4 presents the ESR in synovial fluid. It was observed that rise of ESR above 30 was found in total 66 cases (66%). The raised ESR level found in patients of tuberculous arthritis, rheumatoid lesion and pyogenic arthritis. In chronic nonspecific synovitis, osteoarthrosis and traumatic arthritis ESR was found at normal range.

Rheumatoid factor was found to be present in synovial fluid in all cases of rheumatoid arthritis, where as it found to be positive in 10 serum samples of the same patients as shown in Table 5.

**Table 1: Showing number of monoarticular/polyarticular affection of different joints.**

| S. No. | Joints | Monoarticular involvement (no. of cases and % involvement among mono articular) | Polyarticular involvement (no. of cases and % involvement among poly articular) |
|--------|--------|-----------------------------------------------------------------|-----------------------------------------------------------------|
| 1.     | Knee   | 43 (63.23%)                                                      | 17 (53.12%)                                                     |
| 2.     | Hip    | 11 (16.17%)                                                      | 2 (6.25%)                                                       |
| 3.     | Wrist  | 7 (10.29%)                                                       | 3 (9.38%)                                                       |
| 4.     | Hand   | -                                                               | 5 (15.63% )                                                    |
| 5.     | Elbow  | -                                                               | 3 (9.38%)                                                       |
| 6.     | Foot   | 3 (4.41%)                                                       | -                                                               |
| 7.     | Ankle  | 2 (2.94%)                                                       | 1 (3.12%)                                                       |
| 8.     | Shoulder | -                                                           | 1 (3.12%)                                                       |
| 9.     | S.I. joints | 2 (2.94%)                                           | -                                                               |

**Table 2: Showing variety of joint diseases.**

| S. No. | Name of disease      | No. of cases | Monoarticular (A) | Polyarticular (B) | Total (A+B) |
|--------|----------------------|--------------|-------------------|-------------------|-------------|
| 1.     | Rheumatoid arthritis | 33           | 5 (5%)            | 28 (28%)          | 33 (33%)    |
| 2.     | Tubercular arthritis | 22           | 21 (21%)          | 1 (1%)            | 22 (22%)    |
| 3.     | Chr. nonspecific synovitis | 18 + 2     | 16 + 2           | 1 (1%)            | 18 (18%)    |
| 4.     | Osteoarthrosis       | 11           | 11 (11%)          | -                 | 11 (11%)    |
| 5.     | Traumatic arthritis  | 6            | 6 (6%)            | -                 | 6 (6%)      |
| 6.     | Gouty arthritis      | 3            | 3 (3%)            | -                 | 3 (3%)      |
| 7.     | Septic arthritis     | 4            | 4 (4%)            | -                 | 4 (4%)      |
|        | **Total**            | **100**      | **100 (100%)**    | **100 (100%)**    | **100 (100%)** |

**Table 3: Showing age distribution pattern in different joint diseases.**

| S. No. | Joint disease       | No. of cases | Age in years range | 0 – 10 | 11 – 30 | 31 – 50 | Above 50 |
|--------|---------------------|--------------|--------------------|--------|---------|---------|----------|
| 1.     | Rheumatoid arthritis| 33           | -                  | 5      | 17      | 11      |
| 2.     | Tubercular arthritis| 22           | 1                  | 15     | 6       | -       |
| 3.     | Chr. Nonspecific synovitis | 18     | 1                  | 12     | 5       | -       |
| 4.     | Septic arthritis    | 4            | 2                  | 2      | -       | -       |
| 5.     | Traumatic arthritis | 6            | -                  | 3      | 3       | -       |
| 6.     | Osteoarthrosis      | 11           | -                  | -      | 1       | 10      |
| 7.     | Gouty arthritis     | 6            | -                  | -      | 6       | -       |

**Table 4: Level of erythrocyte sedimentation rate (ESR).**

| Mm in 1st hr (Wintrobe) | No. of cases | Percentage |
|-------------------------|--------------|------------|
| 0 – 10                  | 20           | 20         |
| 11 – 20                 | 6            | 6          |
| 21 – 30                 | 8            | 8          |
| 31 – 49                 | 36           | 36         |
| 50 and above            | 30           | 30         |
Table 5: RA factor in 33 cases of rheumatoid arthritis.

| Specimen     | Positive | Negative |
|--------------|----------|----------|
| Serum        | 26       | 7        |
| Synovial fluid | 33       | 0        |

The findings of Table 6-8 determines the type of joint disease in the study participants as tabulated in Table 9 and they were graded as given below.

Figure 5: Incidence of trauma in various joint diseases.

In all 100 cases with joint diseases, arthrocentesis and closed synovial biopsy using Parker Pearson needle was done commonly in knee joint (n =60; 60%).

Physical properties, biochemical nature (specific gravity, synovial fluid protein in gm% and blood – synovial fluid sugar difference in mg/100 ml) and cytological picture (total WBC/mm³ and predominant cells) of synovial fluid in joint diseases of different pathology have been shown in Table 6, 7 and 8 respectively. On bacteriological examination of synovial fluid, pyogenic arthritis was observed in two cases in which staphylococcus had shown its presence in the culture medium.

Figure 6: Sex distribution of the disease.

Histopathology

With Parker-Pearson needle technique adequate representative synovial tissue for histopathology was obtained in 90 cases (90%) out of 100 and their break down in different joint disease was given in Table 10 and number of failure cases was given in Table 11.

The clinical findings of synovial fluid were matched with the histopathological studies in 74 out of 100 cases. In rest of 13 cases (26%) the histopathological diagnosis differs from the clinical diagnosis as given in Table 12.

Table 6: Showing physical properties of synovial fluid in normal and diseased joints.

| No. | Disease                  | Volume in ml | Appearance color/clarity | Viscosity | Mucin clot test | Fibrin clot | Specific gravity |
|-----|--------------------------|--------------|--------------------------|-----------|----------------|-------------|-----------------|
| 1   | Normal                   | 3.5 ml       | Straw/ clear             | High      | Good           | -           | 1014-1020       |
| 2   | Rheumatoid arthritis     | Variable     | Yellowish to greenish/ cloudy | Low       | Fair to Poor    | +           | 1019-1025       |
| 3   | Tubercular               | Moderate Increase | Yellow/ turbid        | Low       | Poor           | +           | 1020-1026       |
| 4   | Chronic nonspecific      | Moderate Increase | Yellowish/ clear     | Low       | Fair to Good   | +/-         | 1014-1018       |
| 5   | Septic arthritis         | Abundant     | Yellow, grey/ turbid    | Low       | Very Poor      | +           | 1025-1028       |
| 6   | Osteoarthritis           | Scanty       | Pale/ clear             | High      | Good           | -           | 1014-1016       |
| 7   | Traumatic arthritis      | Variable     | Hemorrhagic or xanthochromic | High     | Good           | -           | 1015-1018       |
| 8   | Gouty arthritis          | Variable     | Yellowish/ cloudy       | Low       | Fair           | +           | 1018-1022       |
| 9   | Alkaptonuria             | Variable     | Turns to black on standing |       |                |             |                 |
| 10  | Pseudogout               | Variable     | Yellow, milky           | Firm-friable |                |             |                 |
Table 7: Showing cytological appearance of normal and diseased joints.

| No. | Condition                      | Total WBC count/mm | Predominant cell%                                                                 |
|-----|--------------------------------|--------------------|----------------------------------------------------------------------------------|
| 1.  | Normal synovial fluid          | <200               | Mixed cell with poly, Lympho mono poly less 12 (25%)                              |
| 2.  | Rheumatoid arthritis           | 7000 – 15000       | Polymorphs 65 to 80%                                                              |
| 3.  | Tubercular arthritis           | 4000 – 11500       | Lymphocytes 60 to 80% with monocytes                                             |
| 4.  | Chronic nonspecific arthritis  | 400 – 10000        | Variable from polymorphs to lymphocytes                                          |
| 5.  | Osteoarthrosis                 | 200 – 500          | Variable from polymorphs to lymphocytes                                          |
| 6.  | Gouty arthritis                | 7000 – 13500       | Polymorphs 60 to 80%                                                              |
| 7.  | Septic arthritis               | >10000             | Polymorphs 80 to 95%                                                              |

Table 8: Showing protein content of synovial fluid and blood – synovial fluid glucose difference in various joint diseases

| S. No. | Condition                      | No. | Protein gm% | Blood – synovial fluid glucose level difference mg% |
|--------|--------------------------------|-----|-------------|-----------------------------------------------------|
| 1.     | Normal synovial fluid          | 1.5 – 2.5 | <10         |
| 2.     | Rheumatoid arthritis           | 33  | 3.5 – 6.4   | >20 - <30                                           |
| 3.     | Tuberculous arthritis          | 22  | 4 – 6.8     | >20 - <35                                           |
| 4.     | Chronic nonspecific synovitis  | 18  | 2 – 3       | >10 - <16                                           |
| 5.     | Osteoarthrosis                 | 11  | 1.5 – 2     | <20                                                 |
| 6.     | Traumatic arthritis            | 6   | 1.5 – 2     | <20                                                 |
| 7.     | Gouty arthritis                | 6   | 3           | <25                                                 |
| 8.     | Septic arthritis               | 4   | 5 – 7       | >50                                                 |

Table 9: Gradings of joint diseases as per clinical findings.

| Grade | Disease                                      |
|-------|----------------------------------------------|
| Grade I: Non inflammatory e.g.              | Traumatic arthritis (6 cases)                |
|       | Osteoarthrosis (11 cases)                    |
|       | Synovial chondromatosis (1 case)             |
|       | Osteochondritis dissecans (1 case)           |
| Grade II: inflammatory (mild to moderate)   | Chronic nonspecific synovitis (16 cases)     |
|       | Rheumatoid arthritis (33 cases)              |
|       | Gouty arthritis (6 cases)                    |
|       | Tubercular arthritis (22 cases)              |
| Grade III: Sever inflammation               | Septic arthritis (4 cases)                   |

Table 10: Showing breakdown of 90 successful closed needle synovial biopsy in joint diseases.

| S. No. | Joint diseases    | Total no. of cases | Percentage (%) |
|--------|-------------------|--------------------|----------------|
| 1.     | Rheumatoid arthritis | 31                | 27.9           |
| 2.     | Tuberculous arthritis      | 21                | 18.9           |
| 3.     | Chronic nonspecific synovitis | 15            | 16.66          |
| 4.     | Osteoarthrosis          | 9                 | 10             |
| 5.     | Traumatic arthritis     | 5                 | 5.55           |
| 6.     | Gouty arthritis         | 5                 | 5.55           |
| 7.     | Septic arthritis        | 4                 | 4.44           |

Table 11: Showing location of 5 cases of failure.

| Location        | Number cases |
|-----------------|--------------|
| Hip joint diseases | 6            |
| Foot            | 2            |
| Knee joint      | 2            |
Table 12: Showing the cases where histological diagnosis differed from clinical diagnosis.

| S. No. | Clinical diagnosis                  | Histopathological diagnosis   |
|--------|------------------------------------|-------------------------------|
| 1.     | Tuberculous arthritis, left hip (case 7) | Chronic nonspecific synovitis |
| 2.     | Tuberculous arthritis, right hip (case 12) | Chronic nonspecific synovitis |
| 3.     | Nonspecific synovitis, right knee (case 13) | Tuberculous arthritis |
| 4.     | Osteoarthritis both knee (case 16) | Rheumatoid arthritis |
| 5.     | Tuberculous arthritis, left ankle (case 20) | Rheumatoid arthritis |
| 6.     | Tuberculous arthritis, right knee (case 21) | Chronic nonspecific synovitis |
| 7.     | Rheumatoid arthritis, right knee (case 27) | Chronic nonspecific synovitis |
| 8.     | Tuberculous arthritis, right hip (case 74) | Rheumatoid arthritis |
| 9.     | Rheumatoid arthritis, right knee (case 34) | Tuberculous arthritis |
| 10.    | Tuberculous arthritis, right wrist (case 62) | Rheumatoid arthritis |
| 11.    | Tuberculous arthritis, right hip (case 31) | Rheumatoid arthritis |
| 12.    | Rheumatoid arthritis, right knee (case 5) | Chronic nonspecific synovitis |
| 13.    | Rheumatoid arthritis, right knee (case 92) | Tuberculous arthritis |

Figure 7: Characteristic features of rheumatoid arthritis (a = showing deformities of hand and feet in a patient of rheumatoid arthritis; b = X-ray hand and wrist demonstrating metacarpophalangeal joints demonstrate marked narrowing, subluxation, and ulnar deviation and arthroscopic view of the knee joint showing edematous hypertrophied synovial villi; c = histology of RA synovitis).

Figure 8: Characteristic features of tuberculous arthritis (a = X-ray hand and wrist demonstrating soft-tissue swelling and severe osteopenia of the carpal bones; b = histology of tuberculous synovitis).

Figure 9: a = Histology of chronic nonspecific synovitis revealing collagenous tissue with acute and chronic inflammatory cells; b = histology of septic arthritis revealing large number of neutrophils in fibrin background.
On the basis of synovial fluid evaluation (physical, biochemical and cytological examination) and according to severity of inflammation, the various types of arthritis are grouped. The results of all categories are in accordance with the findings of Venkataraman et al and Singhal et al.14,15

From the present study comparing with that of previous workers, it is proposed that a fairly reasonable interpretation can be made after synovial fluid evaluation as outlined earlier, correlating with clinical and radiological findings in rheumatoid arthritis, septic arthritis, gouty arthritis, traumatic arthritis, osteoarthritis and also tuberculosis arthritis.16 In some cases clinical, radiological and synovial findings are equivocal or inconclusive. In these cases, it is only the synovial biopsy that solves the diagnostic dispute.

Comparing the present study with that of Naib and Broderick et al, it is evident that both Naib and Broderick et al have shown good correlation.17,18 It may be due to better facility like viscometry for measuring viscosity, large number of cases included in their series and they have got more experience in the subject.

From the present study comparing with previous study synovial biopsy has been found to be of important diagnostic value in correlating the diagnosis after clinico-radiological and synovial fluid evaluation. Closed needle synovial biopsy as merited against open synovial biopsy through arthrotomy has been found quite satisfactory (90%) in obtaining the adequate synovial tissue for histologic examination both in the present study as well as in the study of previous workers and their success rate was 100%.8

The difficulty in negotiating the needle into the joint, particularly hip, being deeper with accompanying contracture were principal causes of failure in getting the adequate synovial tissue for histologic examination, as experienced in the present study and also in the series of Schumaker.16

In the present study of 100 cases of arthritis, histologic examination of closed needle synovial biopsy proved to be of diagnostic value in correlating and confirming the diagnosis of definite pathology after clinic radiological and synovial fluid evaluation in 68 (68%). Out of the rest 32 (32%) cases, in 16 (16%) cases no histopathologic diagnosis of any definite disease could be obtained and were labeled as chronic nonspecific synovitis. In 16 cases (16%) where the clinico-radiological and synovial analyses were equivocal and inconclusive, synovial biopsy only gave conclusive diagnosis of definite pathology. In another 16 cases (16%) the clinical radiological, synovial fluid findings and even the histologic study by closed needle biopsy were inconclusive for any definite disease and were labeled as chronic nonspecific synovitis. These cases were proved chronic nonspecific synovitis also by open biopsy.

DISCUSSION

Affection of the joints, monoarticular or polyarticular by various diseases is a common orthopedic problem. On the basis of clinical examination with conventional radiological and laboratory aids, the diagnosis often can be reasonably made. These findings are sometimes equivocal and therefore necessity of tissue diagnosis arises. Closed needle biopsy is a simple outpatient procedure without complications that aids in establishing the diagnosis after clinical and radiological correlation. Careful review of literature would reveal that the importance of this simple procedure as an aid to diagnosis of joint diseases has been stressed by various authors from time to time.8-11 Further, it has been mentioned in the literature that the macroscopic features of inflammation seen at arthroscopy do not predict the microscopic features. Thus, the use of closed needle biopsy technique is justified.12

Involvement of knee has been found commonest in joint disease both by present study and also by previous workers.13-15 Monoarticular involvement of knee has been found more common than polyarticular affection both in present study 60 (65.78%) and by previous workers Bhatia et al (68%).9

Tubercular and rheumatoid were seen in maximum numbers and next common group chronic nonspecific synovitis. Septic arthritis, osteoarthritis and traumatic arthritis formed the third common group. Rheumatoid lesion and osteoarthrosis were seen largely a polyarticular affection, while tubercular arthritis, chronic nonspecific synovitis, septic arthritis, gout and traumatic arthritis were predominantly single joint involvement. This observation noticed by present study almost tallied with study of previous workers.14,15

Figure 10: a =X-ray shows soft-tissue swelling medial to the first metatarsophalangeal joint and bilateral erosions of the head of the proximal phalanx; b =polarised microscopy showing negatively birefringent needle-shaped urate crystals.

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CONCLUSION

The evaluation of synovial fluid and synovial biopsy should be an important part of investigative procedure in patients presenting with joint effusion. The nature of underlying synovial tissue reaction is often reflected in synovial fluid and synovial tissue histologic study which may give conclusive diagnosis where clinical diagnosis is equivocal.

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