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Cytomorphological Analysis of Synovial Fluid in a Tertiary Care Hospital

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Abstract
Synovial fluid helps to distinguish between various inflammatory, non-inflammatory, traumatic, septic and crystal induced arthritis, to the extent that it is called as the liquid biopsy of the joints. Analysis of synovial fluid is a minimal invasive technique and is vital in diagnosis and management. Inconclusive cytology reports may result from inadequate sampling to lack of ancillary studies. 72 synovial fluid samples from November 2015 to May 2017 in cytology section of Pathology Department was included in tertiary care hospital the study. Along with the routine cytological study, biochemical parameters and crystal examination with clinical correlation was done. Total of 72 cases taken in which 48 and 16 cases were acute and chronic synovitis respectively .6 cases of gout and 2 cases of rheumatoid arthritis. All cases of gout in the study showed high ESR level, thick consistency, whitish appearance and needle shape crystals. The cases with acute synovitis showed aspirates of high cellularity. Gout shows high glucose level. Proteins level were high for acute synovitis and rheumatoid arthritis Synovial fluid cytology with other biochemical , microbiological and polarized microscopy for needle examination with clinical correlation is important for detail study of synovial fluid analysis and management.

Keywords: *FNAC, Synovial fluid, Macroscopic examination, Biochemical analysis, Crystal examination.*

Introduction

Synovial fluid [SF] is semi liquid avascular hypocellular connective tissue rather than true body fluid surrounded by incomplete layer of cells. It consists of a transudate of plasma supplemented with high molecular weight saccharide rich molecules notably hyaluronans. There are two main cell types in synovial fluid. Type A synoviocytes, are phagocytes and remove debris from the synovial fluid. Type B cells produce hyaluronans Synovial fluid [SF] is semi liquid a vascular hypo cellular connective tissue rather than true body fluid surrounded by incomplete layer of cells.[1]

Qazi et al study quoted that biochemical analysis for protein and glucose in synovial fluid helps in diagnosing the different types of arthritis; with the help of basic synovial analysis including volume, general appearance, viscosity, cell count and crystal examination.

Synovial fluid helps to distinguish between various inflammatory, non-inflammatory,

traumatic, septic and crystal induced arthritis, to the extent that it is called as the liquid biopsy of the joints[2].

Analysis of synovial fluid is minimal invasive technique and is vital in diagnosis and management. Inconclusive cytology reports may result from inadequate sampling to lack of ancillary studies.

Ropes and Bauer were first to point out that there is difference in the cell count and appearance of abnormal SF. Hollandes et al implemented the use of synovial fluid analysis in different forms of arthritis and introduced the term 'synovianalysis'. They evaluated the gross appearance of SF along with cell count, microbiology and biochemical tests. Hollandes and Mc Carty found definitive way of diagnosing psedo gout from gout using urate monosodium monohydrate (MSUM) and pyrophosphate dehydrate [CPPD] under polarizing microscope.[3]

A Indian study observed eosinophils in cases of rheumatoid arthritis and tuberculous synovitis.[4]

Suprun and Mansoor, Liu et al and Nicol and Naib reported crystals of uric acid in synovial fluid of gouty arthritis but in pseudogout calcium salt crystals were identified.[5]

The presence of cholesterol crystals in joint fluid is considered as indicator of chronicity of the the effusion or cell necrosis.[6]

The distinction between inflammatory and non inflammatory joint disease is very crucial since intra articular corticosteroid injection can result in rapid resolution of joint inflammation.[7]

There is a need for further ancillary investigations in analyzing synovial fluid cytology like cell count, crystal identification, biochemical analysis and microbiological studies.

Without such data, we will remain ignorant as to the value of SF analysis.

Aims and Objective

1. To analyze cytomorphological features of synovial fluid.
2. To correlate the cytological parameters with other laboratory parameters to obtain relevant diagnostic criteria.

Material and Methods

It is a descriptive study done for a period of 18 months including 72 synovial fluid samples after obtaining ethical committee clearance. The samples of cases with haemarthrosis were excluded in the study.

Sampling

Synovial fluid samples from November 2015 to May 2017 sent to cytology section of Pathology Department, tertiary care hospital was included in the study.

The fluid was analysed for macroscopic appearance for its volume, clarity and viscosity.

Cytology smear was made and Pap, MGG and toulidine blue was done for all cases and Giemsa and AFS was done for selective cases.

One part of the fluid was taken for biochemical analysis for glucose and protein and for few cases C reactive protein and ESR was done.

One more wet preparation was taken for study under polarizing microscope to view the crystals if any.

Statistical Analysis

The data was entered in Microsoft Excel and analysed using Epi Data analysis V2.2.2.186 and Stata 12 software. The continuous variables like age, biochemical parameters (Glucose, protein values, C reative proteins, ESR at half and one hour), duration of illness, percentage of synovial cells, number of cells and volume of synovial fluid were expressed as Mean (standard deviation) or median (Inter quartile range) based on distribution of data. The categorical variables like age category, gender, number of joints involved, type of joint, past history, pain, viscosity of synovial fluid, colour of synovial fluid, presence of crystals, cellularity of synovial fluid, presence of inflammatory cells, mast cells, back ground properties, Rheumatoid factor, AFS staining and

gram staining results were expressed in percentages. The association between age, duration of complaints, volume, percentage and number of cells in synovial fluid, biochemical parameters (Glucose, protein values, C reative proteins, ESR at half and one hour) and final diagnosis were identified using Kruskal Wallis test. The association between sex, site of lesion, number of joints, pain in the joint, viscosity, colour, crystals, cellularity, inflammatory cells, mast cells, back ground characteristics and final diagnosis was identified using Fishers exact test. The p value of less than 0.05 was considered for statistical significance.

Results

Table: 1. Comparison of Macroscopic Examination, Cellularity and Crystal Examination of Each Diagnosis

Parameter	Acute synovitis (n=48)	Chronic synovitis (n=16)	Gout (n=6)	Rheumatoid arthritis (n=9)	p value
Viscosity					
Thin	48(100.0)	16 (100.0)	4 (66.7)	2 (100.0)	
Thick	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	0.011#
Colour					
Clear	3 (6.3)	0 (0.0)	1 (16.7)	0 (0.0)	
Yellow	45 (93.8)	16 (100.0)	4 (66.7)	2 (100.0)	0.089
White	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	
Crystals					
No crystas	48 (100.0)	16(100.0)	0 (0.0)	2 (100.0)	
Needle	0 (0.0)	0 (0.0)	6 (100.0)	0 (0.0)	<0.001#
Cellularity					
High	8 (16.7)	0 (0.0)	1 (16.7)	0 (0.0)	
Moderate	36 (75.0)	9 (56.3)	5 (83.3)	2 (100.0)	0.027#
Scanty	4 (8.3)	7 (43.8)	0 (0.0)	0 (0.0)	

Significant p value *Fischer exact test

Table: 2 Association Between Inflammatory Cells And Diagnosis

Parameter	Acute synovitis (n=48)	Chronic synovitis (n=16)	Gout (n=6)	Rheumatoid arthritis (n=9)	p value *
Inflammatory cells					
Absent	0	0	1 (16.7)	0 (0.0)	
Present	48 (100.0)	16 (100.0)	5 (83.3)	2 (100.0)	0.111
Neutrophils					
Absent	0 (0.0)	5 (31.3)	1 (16.7)	0 (0.0)	
Present	48 (100.0)	11 (68.8)	5 (83.3)	2 (100.00)	0.001#
Monocytes					
Absent	31 (64.6)	10 (62.5)	6 (100.0)	1 (50.0)	
Present	17 (35.4)	6 (37.5)	0 (0.0)	1 (50.0)	0.309
Lymphocytes					
Absent	21 (43.8)	0 (0.0)	2 (33.3)	2 (100.00	
Present	27 (56.3)	16 (100.0)	4 (66.7)	1 (0.0)	0.001#
Histiocytes					
Absent	45 (93.8)	16 (100.0)	6 (100.0)	1 (50.0)	
Present	3 (6.3)	0 (0.0)	0 (0.0)	1 (50.0)	0.169
Phagocytes					
Absent	46(95.8)	15 (93.8)	6 (100.0)	2 (100.00	
Present	2(4.2)	1 (6.3)	0 (0.0)	0 (0.0)	1.000
Eosinophils					
Absent	48 (100.0)	16 (100.0)	6 (100.0)	2 (100.0)	
Present	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Degenerating cells					
Absent	48 (100.0)	16 (100.0)	6 (100.0)	2 (100.0)	
Present	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA

Significant P value,* Fischer exact test

Table 3 Correlation between Biochemical Values and Diagnosis

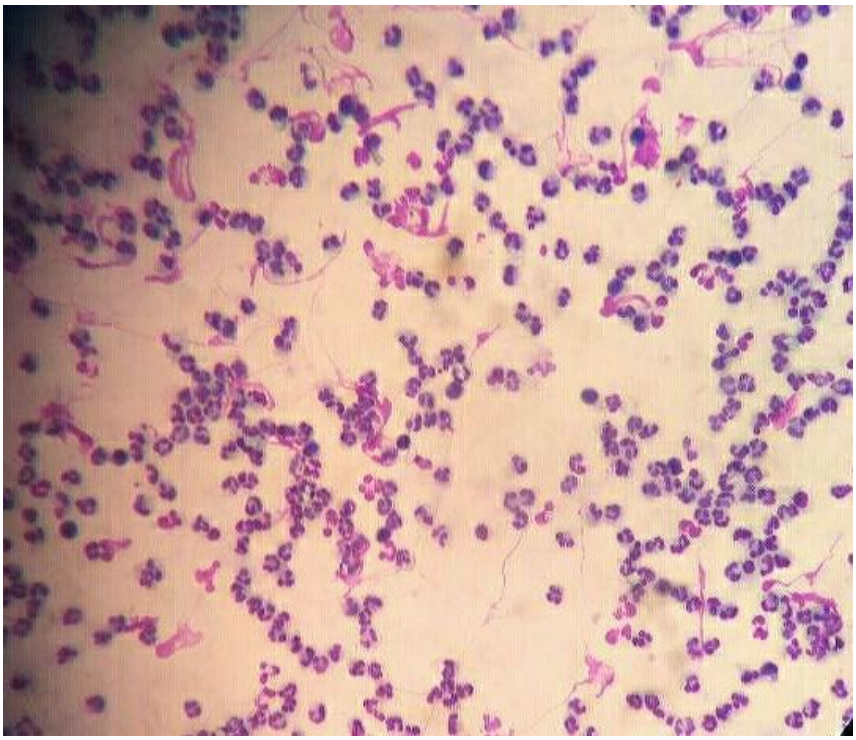
Diagnosis	Median glucose values	Median protein values	Median C Reactive protein values
Acute synovitis	78.5	5.05	1.2
Chronic synovitis	76	3.9	0.6
Gout	92.5	2.95	2.4
Rheumatoid arthritis	63	4.15	2.4

Table 4: Comparison of Diagnosis with ESR Values

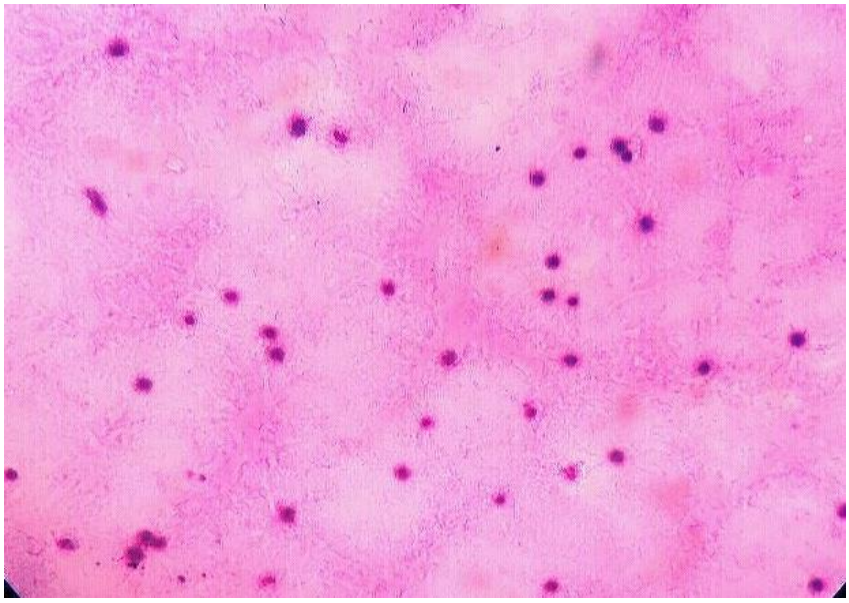
Diagnosis	Median values of ESR at 1 hour
Acute synovitis	71
Chronic synovitis	30
Gout	135
Rheumatoid arthritis	70

Table: 5. Final Diagnosis

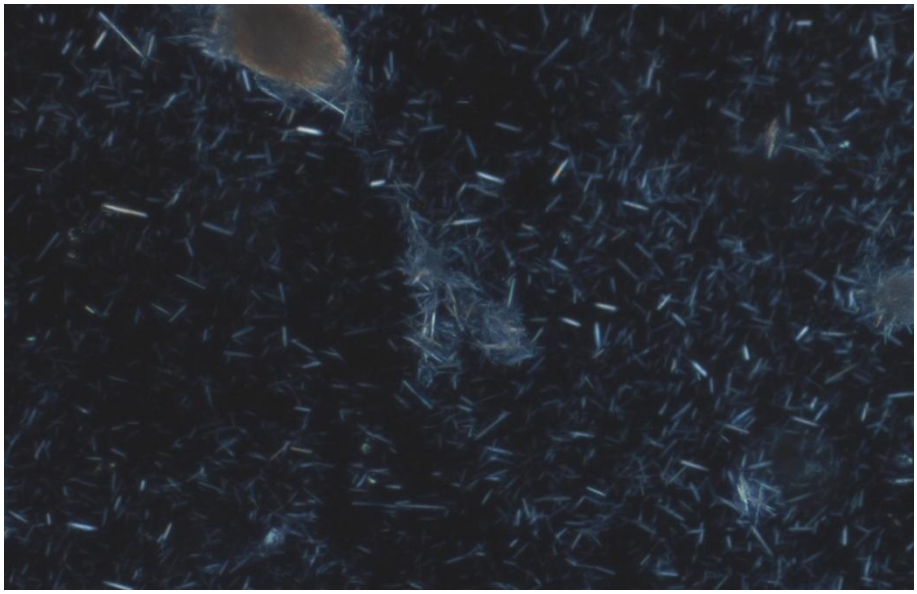
Final diagnosis	Number
Acute synovitis	48
Chronic synovitis	16
Gout	6
Rheumatoid arthritis	2
Total	72



Picture: 1 Acute Synovitis- Smear Showing Predominantly Neutrophils (MGG Stain under 40x)



Picture 2: Smear of Chronic Synovitis Showing Lymphocytes (MGG stain under 40



Picture: 3 Needle Shaped Crystals of Gout (Polarising Microscopy)

Discussion

Cases of acute synovitis showed high cellularity with high neutrophilic preponderance with normal amount of glucose level and high amount of protein levels. Those cases had increased C reactive protein with mild increase in ESR levels. These cases of acute synovitis had increased mast cells. Cases of chronic synovitis had moderate to low cellularity with normal glucose level and protein level were moderate in level. C reactive protein was within normal limits and ESR was also within normal limits. These cases showed presence of few mast cells. Cases of Gout showed mild to moderate cellularity with mild increase in glucose levels and protein level within normal limits. These cases had high C reactive protein and very high levels of ESR. Cases of Rheumatoid arthritis showed very high cellularity with normal glucose levels and high protein levels. These cases had mild raised C Reactive protein and mild raised ESR levels. These cases had high RA factor, hence diagnosed as Rheumatoid arthriris. They contains few mast cells in their smear. In all the suspicious cases AFS and Giemsa was done and no significant result had came.

Table: 6. Correlation of Present Study with Other Studies

Qazi et al mentioned [8]	Glucose Gout- 90mg/dl	Protein Reumatoid arthritis (4.1-6.5gm/dl) Traumatic arthritis(4.2-6.4gm/dl)
Present study	Glucose (median) Gout -92.5mg/dl	Protein (median) Rheumatoid arthritis – (4.15gm/dl)
Sangeeta et al mentioned	Normal to decrease glucose[9] All inflammatory condition	No significant correlation
Present study	Normal to low glucose in other inflammatory conditions	

Table: 7 Correlation of Present Study with Other Studies

Qazi et al showed increase in C Reactive protein	C Reactive protein is increased in Rheumatoid arthritis
Present study	C Reactive protein is increased in Rheumatoid arthritis
M.N.Saptarini et al mentioned increase in ESR [10]	Rheumatoid arthritis
Present study shows increased ESR	Gout

Conclusion

The study of synovial fluid with cytological study as well as its clinical and biochemical correlation was important for the correct diagnosis. Examination under polarized microscope for crystal was very important to confirm cases of Gout and pseudogout.

In this study we have correlated few data to reach a better diagnosis. Many entities were correlating with the previous studies done on the synovial fluid and few of the entities are mildly different in compared to other studies.

In the present study we have correlated different entity for better evaluation and to help clinician for better diagnosis and treatment.

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