A 10 year retrospective comparison of the diagnostic usefulness of synovial fluid and synovial biopsy examination

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Abstract

***Background/Aims*—Synovial fluid examination is thought to be the pathological investigation of choice in most joint disorders, with only a few specific conditions necessitating biopsy, although no evidence based studies are available to support this belief. This study sought to investigate the validity of this assumption.**

***Methods*—One hundred and three cases in which synovial fluid aspiration and synovial biopsy had both been performed at arthroscopy were studied. The amount of diagnostically useful information produced by each investigation was assessed.**

***Results*—In most cases, both investigations provided the same amount of information and were generally equally specific or equally non-specific. Overall, the biopsy provided more information than the fluid in 29% of cases and vice versa in 18%. When only those cases in which both tests were adequate were considered, the biopsy provided more specific information than the fluid in a small number (9%) of cases, but these cases could not be predicted.**

***Conclusion*—The diagnostic usefulness of a biopsy approximates and occasionally exceeds that of a fluid. In the arthroscopic situation, the main advantage of performing both tests is that it provides a "failsafe mechanism" for the rare occasions when one of the samples is inadequate.**

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Synovial fluid examination is thought to be the pathological investigation of choice in joint disease, particularly inflammatory monoarthropathy, because it is a simple, rapid, cheap, and relatively non-invasive diagnostic test.[1–5] In contrast, synovial biopsy is considered to be of use in the investigation of some specific conditions such as amyloidosis, pigmented villonodular synovitis, Whipples disease, metastases, and haemochromatosis.[6] There are several studies of the use of synovial biopsy for the investigation of both inflammatory joint disease and joint disease of unknown cause.[7–10] The general consensus seems to reflect the opinion of Bywaters[11] that "synovial biopsy may still have a small role in the eventual diagnosis of difficult undiagnosed monoarticular arthritis, provided that synovial fluid and other examinations have been pertinaceously explored to no avail". However, there are no evidence based studies comparing the amount of diagnostically useful information provided by both synovial fluid aspiration and synovial biopsy to support the above beliefs. Here, we review a large series of cases where both investigations have been performed to determine their relative clinical value, given their differing degrees of patient morbidity and cost.

Methods

We examined 103 cases (1988–98) in which both a synovial fluid examination and a synovial biopsy had been performed. The case mix was selective in that it excluded cases in which there were pre-existing clinical indications for performing either synovial fluid aspiration or biopsy alone.

All the samples were taken for diagnostic purposes. Fluid and tissue samples were taken at the same time during the course of an arthroscopic examination in all but two cases in which the biopsy had been performed one and two years after the fluid aspirate.

All the fluids and all but four of the biopsies had been reported by the same pathologist (AJF), the remaining biopsies being reported by three other pathologists working in the same department. The fluids and biopsies had all been reported with knowledge only of standard demographic data and brief clinical information, such as the involved joint and the nature of the symptoms/signs.

The synovial fluid report contained the following standard data: clarity and colour of the fluid, the nature of any mucin clot formation, the white blood cell count/mm^3, the differential nucleated cell count, and the presence or absence of ragocytes (cells containing immune complexes) and crystals or other solid material. Each report contained a final summary sentence/diagnosis.

The biopsy reports comprised a macroscopic and microscopic description with a final summary sentence/diagnosis. The final sentences/diagnoses were included to aid clinical interpretation of the pathological findings and thus provide a clinically useful result. These summaries were studied by an independent pathologist (JSJ) and allocated a letter from A to D inclusive (see below), according to the diagnostic usefulness of the data produced:

(A) Specific diagnosis or a short list of specific diagnoses given.
(B) Described as inflammatory or non-inflammatory only ("ball park diagnosis").

Table 1 Categorisation of the investigations by diagnostic usefulness

	A	B	C	D
Fluid	44	53	1	5
Biopsy	54	45	2	2

A, specific diagnosis or a short list of specific diagnoses given; B, described as inflammatory or non-inflammatory only ("ball park diagnosis"); C, no diagnosis despite an adequate specimen; D, inadequate specimen.

Table 2 Number of cases with a particular outcome

Fluid result/biopsy result	Number of cases
A/A	26
A/B	15
A/C	2
A/D	1
B/A	24
B/B	28
B/C	0
B/D	1
C/A	0
C/B	1
C/C	0
C/D	0
D/A	4
D/B	1
D/C	0
D/D	0

A, specific diagnosis or a short list of specific diagnoses given; B, described as inflammatory or non-inflammatory only ("ball park diagnosis"); C, no diagnosis despite an adequate specimen; D, inadequate specimen.

(C) No diagnosis despite adequate specimen.
(D) Inadequate specimen.

The information yield was then compared for each diagnostic procedure in each case to ascertain which test, if any, had the greater diagnostic power. In cases where one or other investigation provided more information than its counterpart, we looked at the underlying diagnosis to determine whether one test was consistently more informative in any particular pathological state.

Finally, in cases where a diagnosis or some clinically useful information (A or B) had been yielded by both tests, the information was examined to determine whether both the synovial fluid and the biopsy produced concordant or discordant diagnoses. If only one of the investigations had yielded useful information the case was labelled "not applicable". The aim of our study was to assess the information yield rather than the accuracy of the two investigations because this last point has already been studied.[4]

Table 3 Pathological diagnoses in cases where the fluid report was more specific than the biopsy report (n = 15)

Fluid diagnosis	Biopsy diagnosis	Concordance
Osteoarthritis	Primary inflammatory arthritis	Discordant
Inflammatory arthritis? Viral	Primary inflammatory arthritis	Concordant
Seronegative	Primary inflammatory arthritis	Concordant
Trauma	Non-inflammatory arthritis	Concordant
Gout	Primary inflammatory arthritis	Concordant
Seronegative	Primary inflammatory arthritis	Concordant
Seronegative	Primary inflammatory arthritis	Concordant
Seronegative	Primary inflammatory arthritis	Concordant
Gout	Inflammatory arthritis, no crystals	Concordant
Seronegative	Inflammatory arthritis	Concordant
Seronegative	Primary inflammatory arthritis	Concordant
Osteoarthritis	Non-inflammatory arthritis	Concordant
Gout	Inflammatory arthritis	Concordant
Gout	Inflammatory arthritis	Concordant
Seronegative	Primary inflammatory arthritis	Concordant

Results

Tables 1 and 2 show the results of the categorisation process.

One or other or both of the investigations in all 103 cases studied produced clinically useful information. In 93 of the cases both investigations produced some clinically useful information (AA + AB + BA + BB).

Of the 10 cases in which one of the two investigations was non-contributory (C or D), six were fluids and four were biopsies.

Of the non-contributory fluids, five were inadequate because of insufficient sample volume or delayed arrival at the laboratory, and one showed an inexplicable pattern despite being an adequate sample. In four of the five cases in which the fluid was inadequate, the biopsy yielded a specific diagnosis (A) and in the remaining case the biopsy yielded a ball park diagnosis (B). In the case with the inexplicable fluid pattern, examination of the biopsy resulted only in discrimination between an inflammatory and a non-inflammatory process, but the biopsy was performed one year later than the fluid, so it cannot be compared directly with the other cases in our study. The other case with non-synchronous investigations yielded concordant diagnoses with a different degree of specificity (A/B).

Of the non-contributory biopsies, two were deemed inadequate for diagnosis because they comprised adipose tissue or were very superficial in nature, and two could be described but not further interpreted by the reporting pathologist. In three of these four cases the fluid provided a specific diagnosis (A), and in the remaining case the fluid could distinguish that it was a non- inflammatory rather than an inflammatory process (B).

In 54 of the 103 cases (52%) both tests yielded the same amount of diagnostically useful information (AA + BB), the most common situation being that both were equally nonspecific (B/B = 28 cases). The next most common outcomes were for both investigations to give a specific diagnosis (A/A = 26), for the biopsy to yield a specific diagnosis when the fluid could only indicate whether it was inflammatory or not (B/A = 24), and finally for the fluid to give a specific diagnosis when the biopsy could only indicate whether it was an inflammatory process or not (A/B = 15).

Category A (specific diagnosis or short list of specific diagnoses) represents a more clinically useful level of diagnosis than category B (inflammatory versus non-inflammatory). Category A was achieved in 41 (AA + AB) of the fluids and 50 of the biopsies (AA + BA); thus, in nine cases an adequate synovial biopsy provided more specific information than did an adequate synovial fluid.

In 19 cases (18%) the fluid provided more information than the biopsy (AB + AC + AD + BC + BD). Table 3 shows the diagnoses given in the 15 cases in which a specific versus a ball park diagnosis was provided (A/B).

In 30 cases (29%) the biopsy provided more information than the fluid (BA + CA + CB + DA + DB). Table 4 shows the diagnoses given

Table 4 Pathological diagnoses in cases where the biopsy report was more specific than the fluid report (n=24)

Fluid diagnosis	*Biopsy diagnosis*	*Concordance*
Non-inflammatory arthritis	Loose body	Concordant
Primary inflammatory arthritis	Reactive arthritis/RA	Concordant
Non-inflammatory arthritis	Normal	Concordant
Primary inflammatory arthritis	Inflammatory arthritis? Reactive arthritis	Concordant
Primary inflammatory arthritis	Inflammatory arthritis? Seronegative	Concordant
Inflammatory arthritis	JCA/dermato-arthritis	Concordant
Non-inflammatory arthritis	Synovial chondromatosis	Concordant
Non-inflammatory arthritis	Primary inflammatory arthritis/JCA	Discordant
Primary inflammatory arthritis	Psoriatic arthritis	Concordant
Primary inflammatory arthritis	Seronegative	Concordant
Primary inflammatory arthritis	Seronegative	Concordant
Primary inflammatory arthritis	Primary inflammatory arthritis/fb reaction	Concordant
Non-inflammatory arthritis	Haemangioma	Concordant
Primary inflammatory arthritis	Primary inflammatory arthritis? Reactive arthritis	Concordant
Primary inflammatory arthritis	Vasculitis	Concordant
Non-inflammatory arthritis	Synovial chondromatosis	Concordant
Primary inflammatory arthritis	Primary inflammatory arthritis. Probable reactive arthritis. RA/Bechets?	Concordant
Primary inflammatory arthritis	Primary inflammatory arthritis? RA	Concordant
Inflammatory arthritis	Primary inflammatory arthritis	Concordant
Primary inflammatory arthritis	Seronegative	Concordant
Non-inflammatory arthritis	Osteoarthritis	Concordant
Primary inflammatory arthritis	Seronegative	Concordant
Non-inflammatory arthritis	Post trauma	Concordant
Non-inflammatory arthritis	Fb reaction	Concordant

Fb, foreign body; JCA, juvenile chronic arthritis; RA, rheumatoid arthritis.

Table 5 Discrepant cases and the diagnoses given in each report (n = 9)

Fluid diagnosis	*Biopsy diagnosis*
Haemorrhage	Reactive arthritis
Osteoarthritis	Primary inflammatory arthritis
Non-inflammatory	Inflammatory arthritis
Non-inflammatory	Inflammatory arthritis
Non-inflammatory	Primary inflammatory arthritis
Non-inflammatory	Primary inflammatory/juvenile chronic arthritis
Haemarthrosis and seronegative arthritis	Osteoarthritis
Non-inflammatory	Primary inflammatory arthritis
Non-inflammatory	Primary inflammatory arthritis

in the 24 cases in which a specific versus a ball park diagnosis was provided (B/A).

When useful diagnostic information (A or B) was yielded by both tests, it was concordant in 83 cases but discrepant in nine (table 5). In the concordant tests, 55 (66%) were inflammatory and 28 (34%) were non-inflammatory. The discrepancies did not appear to reflect inexperience because they did not lessen over time (one each in 1990, 1991, 1993, 1995, and 1996 and two each in 1988 and 1998) and did not include the four cases reported by different pathologists.

Discussion

There are certain clinical situations in which either biopsy or synovial fluid analysis is the most appropriate investigation. For example, joint aspiration is preferable to obtain material for rapid crystallographic and bacteriological examination and biopsy for the investigation of neoplastic or granulomatous disease, or when there is insufficient fluid to aspirate (< 0.5 ml). Because synovial fluid aspiration is relatively non-invasive and is applicable in a wide spectrum of joint disorders[1] (with even amyloidosis being diagnosed from synovial fluid[12]) it is usually seen as the investigation of choice.

Our results suggest that, where there is no clinical indication for performing one test in preference to the other, both synovial biopsy and synovial fluid aspiration provide the same amount of information in most cases (52%).

Naturally, the morbidity incurred by a test is an important consideration in its selection, but if an invasive test such as an arthroscopy is already being undertaken, the test with the highest yield of diagnostically useful information should be used, particularly in situations where cost is a consideration.

In our study, biopsy examination provided more specific information than fluid examination in 29% of cases and vice versa in 18.4% of cases.

Although biopsy yields more specific diagnoses in some cases, the fluid tends to be more specific when the underlying pathological condition is an inflammatory one; of the concordant cases in which the biopsy was more specific, 65% were inflammatory and 35% were non-inflammatory, but of the concordant cases in which the fluid was more specific, 86% were inflammatory and 14% were non-inflammatory. Unfortunately, this observation is unhelpful in the practical question of which test to perform when there is no indication of the underlying pathology.

In conclusion we have found that, without prior knowledge of the diagnosis, both tests provide the same information in most cases. Although the biopsy provided some information when a synchronous synovial fluid could provide none at all, mainly as a result of its inadequacy, there were nine cases in which an adequate synovial biopsy provided more information than an adequate synovial fluid aspirate. By comparison, an adequate synovial fluid aspirate provided more information than an adequate synovial biopsy in only four cases. Our study challenges the commonly held perception of the synovial biopsy in non-specific joint disease as a "last resort" when the fluid is unhelpful. Our findings indicate that the diagnostic usefulness of a biopsy approximates and occasionally exceeds that of a fluid, implying that it does have a small but important role in diagnosis as well as providing a failsafe mechanism for the rare occasions on which the aspirate is non-contributory.

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