Fine-Needle Aspiration Biopsy in the Diagnosis of Orthopedic Lesions : An Interim Analysis

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ABSTRACT: Fine-needle aspiration biopsy is an old procedure that has found little favor in the diagnosis of musculoskeletal lesions. With the renewed interest in cytologic diagnosis, fine-needle aspiration biopsy is gaining greater usage. Local studies are lacking in this respect. On account of its simplicity, immediate availability of results, economy and safety, the present study was undertaken. Preliminary results show high yield of aspirate suitable for study (81.5%), a great ability to identify tumors (100%) and a strong potential to differentiate between benign and malignant tumors (96%). Accuracy of obtained cytologic diagnosis is good except in metastatic tumors. Comparison of costs showed fine-needle aspiration biopsy to be less expensive than the open biopsy. Abscence of untoward complications and its high patient acceptability further favor its usage. Fine-needle aspiration biopsy is therefore promising as a diagnostic tool for use in orthopaedic lesions.

INTRODUCTION

As early as 1847, Kun reported the use of "an exploring needle, having at its extremity, a small depression with cutting edges. On plunging this into tumor, one can extract a minute portion of tissue; in this way, a microscopic examination can be practised."[1] Six years later, Sir James Paget gave a cytologic description of aspiration biopsy smears similar to present-day interpretations.[1] However, aspiration biopsy had poor acceptance and its use was limited to a few tumor centers in the United States and in Scandinavian countries.[1,2]

The unique combination of clinician, hematologist and pathologist at the Karolinska Institute in Stockholm, Sweden led to the success of needle aspiration biopsy there and its subsequent development in the Scandinavian countries.[3] Authors such as Franzen, Zajicek and Eneroth were actually clinicians with hematologic and cytopathologic training who not only interpreted the material but also examined the patient and performed the biopsy. Current advocates of the clinician-cytopathologist interpretation include Lopes Cardozo, Sodestrom, Lowhagen, Nordenstrom, Dahlgren and Frable.[1,3] Criticism and opposition, nevertheless, obstruct the further acceptance of fine-needle aspiration biopsy and arguments of people like Ochsner and de Bakey are still used today. They are: (1) Fine-needle aspiration biopsy is inherently inaccurate because of the limited amount of material obtained and the difficulty of interpretation of cytologic findings; and (2) There is the danger of seeding and spreading the tumor by piercing it with needles.[1]

The use of fine-needle aspiration biopsy for bone and soft tissue lesions is even less popular.[3-5] Original studies by Martin and Ellis (1930) only had a few soft tissue sarcomas.[1,6] Coley, Sharp and Ellis (1931) first reported a series of 35 consecutive aspirations from bone tumors but it had scanty data.[7] Snyder and Coley[7] expanded their series to 567 aspirations with good results leading them to conclude that: (1) Aspiration biopsy was most valuable in true neoplasms; (2) There was no dissemination of tumor cells this way; and (3) There was no needle tract implantation noted. There are

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even fewer clinicians or pathologists interested in aspiration biopsy of bone tumors, favoring either core needle biopsy or aspiration and preparation of histologic sections with a cell block.[7]

Scant mention of needle aspiration biopsy is made in local literature. A Philippine General Hospital-based study on aspiration biopsy of the thyroid was published in the Philippine Journal of Surgical Specialties. Salgado, et al. reported a sensitivity of 83.3% and specificity of 100% in 37 aspirations.[8]

At the Out-Patient Section of the Department of Orthopedics, University of the Philippines-Philippine General Hospital, as in similar clinics, patients seen for musculoskeletal lesions are evaluated and managed on the basis of clinical presentation and, if necessary, roentgenograms and laboratory data. In some conditions, such as certain tumors, further diagnostic work-up is warranted. An open section or excision biopsy is recommended and the patient is admitted. Histopathologic interpretations are released anywhere between one to four weeks. If, instead of an open biopsy, aspiration biopsy is done, several advantages are noted.[1,5,9,10]

1. Fine-needle aspiration biopsy is a safe and less invasive diagnostic procedure.
2. It is convenient and simple to do in the present set-up.
3. It is time-saving with results available in a day or two.
4. It can accomodate large samples as from an Out-Patient clinic.

In consideration of the merits of fine-needle aspiration biopsy, the present study was undertaken with the following objectives:

1. To assess the diagnostic value of fine-needle aspiration biopsy against the open biopsy for musculoskeletal tumors in terms of:
   (a) ability to obtain sufficient tissue for study;
   (b) differentiation between tumorous and non-tumorous lesions;
   (c) differentiation between benign and malignant lesions, if positive for tumor;
   (d) differentiation between primary and metastatic lesions, if positive for malignancy; and
   (e) ability to give cytologic diagnosis.
2. To compare the results with those of other studies.
3. To compare the costs of fine-needle aspiration biopsy and open biopsy.

This interim analysis is part of a countinuing study.

MATERIALS AND METHODS

Subjects

Sixty-six patients to be admitted for open biopsy to the Department of Orthopedics, UP-PGH starting March 1986 were consecutively chosen and included in the study. Subject pool included 32 males and 34 females.

Basic Equipment

The following materials were used:

1. Gauge 22 to Gauge 19 needles – The external diameter of the needle was within 0.6 to 1.0 mm. The disposable hypodermic needle was sufficient. For deeper lesions, as in the femur and hip area, longer needles of similar caliber were used.
2. 10 to 30 cc glass syringes
3. Alcohol or Betadine antiseptic
4. Sterile gauze pads
5. Microscope slides
6. Fixative jars containing 95% ethyl alcohol
7. Lidocaine 2% – This was used in deeper lesions.

Technique of Aspiration

Prior to surgery, the subjects underwent fine-needle aspiration

1. with the patient in a comfortable position, the lesion was palpated and the site of puncture chosen.
2. The area was prepared with either Betadine antiseptic or alcohol.
3. Syringe and needle were pointed at the site and quickly inserted. Once within the tissue, the plunger was withdrawn to create negative pressure. While maintaining negative pressure, the needle was advanced into the lesion several times in short strokes like a jackhammer or in multiple directions until the syringe hub was positive for some aspirate, bloody or otherwise.
4. After 10 to 12 strokes, there was enough tissue within the needle and the stabs were discontinued.
5. Negative pressure was released slowly. The syringe and needle were then gradually withdrawn. Puncture site was pressed with a sponge.
6. The needle was separated from the syringe. The plunger was withdrawn and with some positive pressure, a drop of specimen was laid, bevel down, onto one end of the slide.
7. The slides were placed into the fixative for at least 15 minutes.
8. Once fixed, the labelled specimen was sent with the appropriate bone Tumor Registry Form

(see Appendix A) to the Pathologist for Papanicolaou staining.

The procedure was repeated as many times as needed. Untoward complications such as hemorrhage and infection were observed. Patient's reactions to the procedure were also noted.

Analysis of Results

Once available, the results of open biopsy were compared with the interpretation of the aspiration biopsy. Testing for the sensitivity and specificity of fineneedle aspiration biopsy was done along several levels, using the open biopsy as the standard.[11] *Sensitivity* is defined as the proportion of cases with diseases detected by open biopsy who have a positive fine-needle aspiration biopsy. *Specificity* is defined as the proportion of cases free of disease according to open biopsy who have a negative fine-needle aspiration biopsy. Additional computations were made for the *positive predictive value* (proportion of cases with positive fine-needle aspiration biopsy who have the disease) and *negative predictive value* (proportion of cases with negative fine-needle aspiration biopsy who are really free of disease).

RESULTS

There were 66 cases available for fine-needle aspiration biopsy. Of these, 56 had confirmatory open section or excision biopsies available for comparison. 10 cases did not return for definitive treatment or further diagnostic work-up. Of the 56 specimens, 44 showed sufficient tissue. A total of 36 tumors were detected.(Table 1).

All cases of Osteosarcoma (7) and Plasmacytoma (2) were diagnosed cytologically. Both cases of Giant Cell Tumor were also read as such; however, in one case, grading was possibile. While there were two cases of Rhabdomyosarcoma, only one was specifically diagnosed. Both Fibrosarcoma and Liposarcoma were accurately diagnosed. Two other malignancies were read as "sarcomatous" The small round cell tumor character of Ewing's sarcoma was noted but definite cytodiagnosis was not possible. Histiocytosis X and Schwannoma were positively identified on fine-needle aspiration biopsy. Of five cases of Metastatic Carcinoma, it was possible to identify only an Adenocarcinoma, a Follicular Carcinoma and a Bronchogenic Carcinoma. Less difficulty in diagnosis of benign tumors was noted, with accurate readings for Ameloblastoma, Osteochondroma, Neurofibroma, Non-ossifying Fibroma, Lipoma, Fibroma and Ganglion Cyst. (See Appendix C.)

TABLE 1
Tumors Detected in 36 Specimens.

Tumor	Number of Cases
Osteosarcoma	7
Sarcoma (unspecified)	3
Metastatic Carcinoma (unspecified)	2
Giant Cell Tumor	2
Plasmacytoma	2
Rhabdomyosarcoma	1
Fibrosarcoma	1
Ewing's Sarcoma	1
Schwannoma	1
Histiocytosis X	1
Liposarcom	1
Metastatic Adenocarcinoma	1
Metastatic Bronchogenic Carcinoma	1
Metastatic Follicular Carcinoma	1
Ameloblastoma	1
Osteochondroma	1
Neurofibroma	1
Non-ossifying Fibroma	1
Ganglion Cyst	1
Fibroma	1
Lipoma	1

When examined according to the site of lesions, several observations were made. (Table 2) For the only inadequate specimen of the "soft tissue group", the histologic section showed a Benign Mesenchymoma, a rare tumor. In the "bone and joint group", there were nine inadequate aspiration specimens broken down as follows: infections (2 Chronic Osteomyelitis and 1 Septic Arthritis), sclerotic tumors (2 cases), deep tumors from greater trochanter (3 cases) and Metastatic Carcinoma from the skull (1 case).

The results were analyzed to compare the efficiency of fine-needle aspiration biopsy against the open biopsy, that is, the procedure was tested on its sensitivity and specificity. Analysis was done using four-fold table along four levels of diagnostic ability of fine-needle aspiration biopsy. (Figure 1). The results of analysis are seen in Table 3.

A comparison of the costs of fine-needle aspiration biopsy and open biopsy was undetaken. (See Appendix B for itemization.)

All the patients tolerated the procedure well. There were no associated morbidities.

TABLE 2
Site of Lesions in 56 Cases.

	Aspiration Specimen		Number of Cases
	Adequate	Inadequate	
Bone/Joint			
Femur	9	1	10
Tibia	3	–	3
Clavicle	3	–	3
Humerus	2	–	2
Elbow Joint	2	–	2
Skull	2	2	4
Femoral Head/Neck	2	1	3
Mandible	1	–	1
Scapula	1	–	1
Shoulder Joint	1	–	1
Ulna	1	–	1
Wrist Joint	1	–	1
Finger Joint	1	–	1
Ilium	1	–	1
Sacrum	1	–	1
Ankle Joint	1	–	1
Greater Trochanter	–	3	3
Rib	–	1	1
Phalanx, finger	–	1	1
SUBTOTAL	32	9	41
Soft Tissue			
Thigh	3	1	4
Subcutaneous	3	–	3
Foot	3	–	3
Hypogastric Area	1	–	1
Inguinal Area	1	–	1
Gluteal Area	1	–	1
Leg	1	–	1
Toe	1	–	1
SUBTOTAL	14	1	15

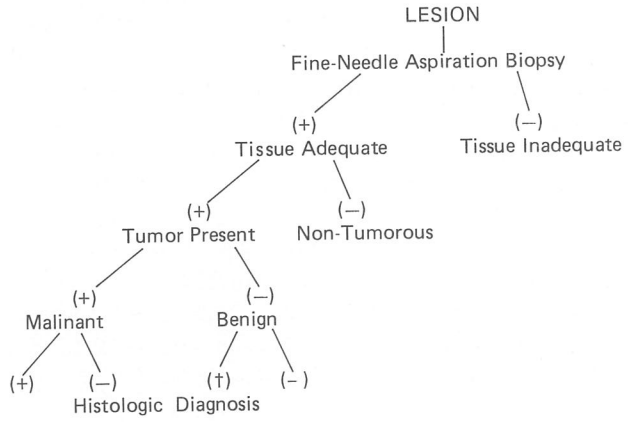

Fig. 1 Algorithm for fine-needle aspiration biopsy.

DISCUSSION

Fine-needle aspiration biopsy is an old procedure that had a long hard climb to respectability, only to fall back into the recesses of medical history, overtaken by methods boasting of greater objectivity. Except for the Scandinavians and a few tumor centers in the United States, its use is avoided in favor of the open biopsy. Recent research is gravitating towards this method, and as the cobwebs are being clearned, its advantages are again being realized. Ottolenghi[9] and Schajowicz and Derqui[5] stated:

1. Fine-needle aspiration biopsy is technically

TABLE 3
Results of Statistical Analysis.

Parameter	Percentages			
	S (%)	f (%)	(+) PV (%)	(–) PV (%)
Adequacy of tissue aspirated	81.5	50	98	10
Presence of tumor tissue	100	82	94	100
Differentiation between benign and malignant tumors	96	64	86	87.5

S = sensitivity
f = specificity
PV = predictive value

simple, except that used for the spine.

2. There is minimal risk of dissemination. No local complications have been noted.

3. The technique can be done in multiple locations and at different levels.

4. It can be used in deep, relatively inaccessible areas like the spine and pelvis.

5. There is a high patient acceptability. Furthermore, it is easy to repeat.

6. Fine-needle aspiration biopsy can be used in an out-patient setting with no special set-up, saving time and money.

7. There are no specialists required. In fact, spcimens can be mailed.

8. The procedure does not prevent early treatment with radiotherapy, that is, there is no need to wait for healing.

9. It does not exclude the subsequent use of open biopsy.

De Santos, et al.[4] compared fine-needle aspiration biopsy directly against open biopsy, favoring the former because:

1. There is adequate specimen obtained which obviates need for surgical intervention.

2. The absence of a surgical scar permits earlier radiotherapy.

3. There is less distortion of host bone; thus, there is a low incidence of post-radiotherapeutic pathologic findings.

4. The technique can rapidly differentiate primary from metastatic lesions, especially if multiple sites are available for biopsy.

5. It is of value in lytic lesions in the pelvis which is relatively inaccessible by surgery.

6. Tissue planes are left undisturbed, making limbsparing possible in the future.[12]

The strongest argument used against the fine-needle aspiration biopsy is the subjectivity of its interpretation.[5] However, its economy, rapidity of results and safety make it a strong alternative especially for underdeveloped countries with large populations.[3] The present trend in fine-needle aspiration biopsy is either to adopt the scandinavian approach as earlier described or to create greater objectivity by several methods such as computerized pattern recognition,[3] and creation of sufficient diagnostic criteria.[4]

With the redisovery of the potentials of fine-needle aspiration biopsy, the authors embarked on this pilot study.

Diagnostic Value

The preliminary results o this study are encouraging, notably in the cytodiagnosis of Osteosarcoma, Giant Cell Tumor and Plasmacytoma. There were two cases of Rhabdomyosarcoma but one could only be read as *"sarcoma"*. This can be explained by the fact that the atypical rhabdomyoblast exhibiting cross-striations must be demonstrated; but somehow, this is not appreciated on aspiration smears. The two other *"sarcomas"* not cytologically diagnosed were found equally difficult to diagnose histologically. A case of Ewing's Sarcoma could only be read as small round cell tumor by cytology, a limitation herein noted. However, it is of interest to note that other sarcomas, that is, Fibrosarcoma and Liposarcoma, as well as other malignancies, that is, Histiocytosis X and Schwannoma, can be cytologically diagnosed. Of equal interest is the observation that of five cases of Metastatic Carcinoma, a primary could be identified in three, which is comparable with histologic interpretation. Benign tumors included in the study were all specifically diagnosed. The ability of fine-needle aspiration biopsy to diagnose nontumorous conditions was demonstrated; but except

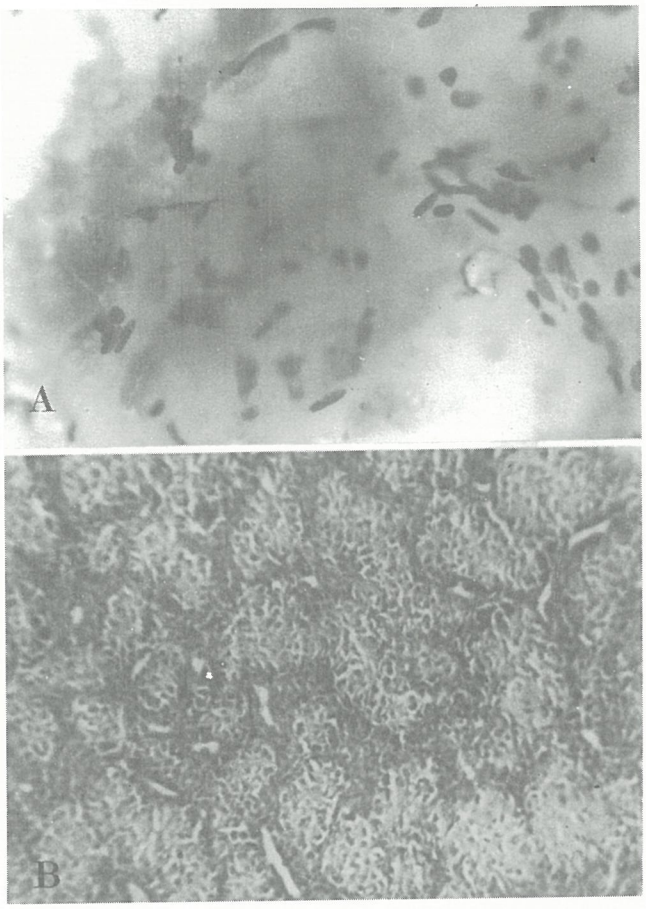

Fig. 2A: Osteogenic Sarcoma (Aspirate, 400x). Acellular hyaline-like grey-violet material

B: Osteogenic Sarcoma (Tissue section, 400x). Histologic section of case in Fig. 2A.

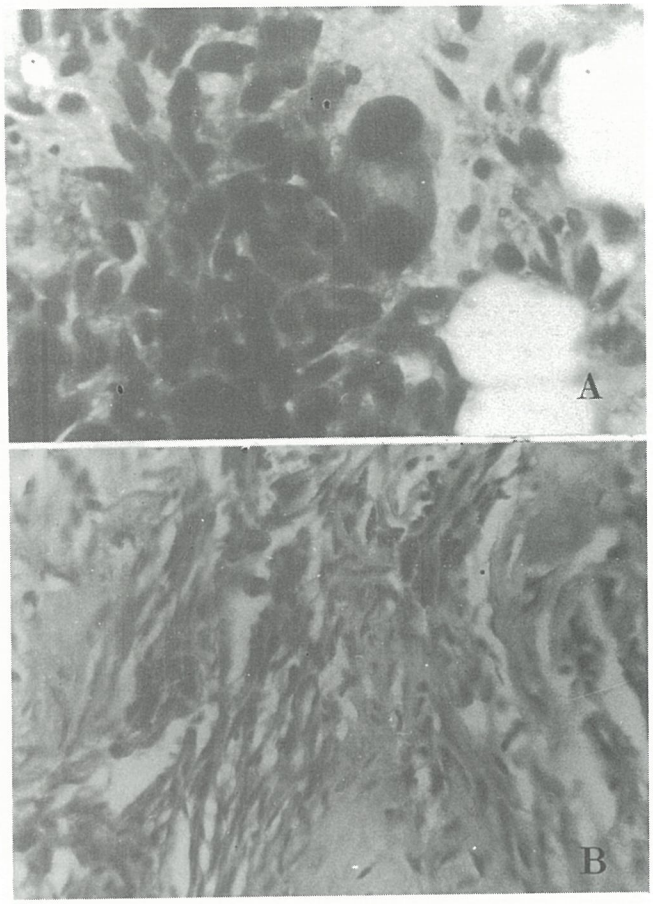

Fig. 3A: Osteogenic Sarcoma, Fibroblastic Type (Aspirate, 400 x). A pleomorphic binucleate giant cell is seen in this area of tumor.

B: Osteogenic Sarcoma, Fibroblastic Type (Tissue section, 400 x). Spindly cells forming new bone are seen.

for one case of degenerative arthropathy and one case of Madura foot, the other smears were read as either *"acute and/or chronic inflammation consistent with osteomyelitis"* or *"synovitis, nonspecific"* (implying Tuberculosis). However, the results showed that if a lesion is tumorous, it will not be missed by fine-needle aspiration biopsy.

For adequacy of specimen obtained, a sensitivity of 81.5% and a specificity of 50% were noted along with positive predictive value of 98% and negative predictive value of 10%. These results, while far from ideal, can be explained on the basis of certain technical aspects. An inadequate specimen was obtained from the thigh but the tumor, a Benign Mesenchymoma, is not always primarily considered. Two other inadequate specimens came from femurs with Chronic Osteomyelitis associated with involucrum formation. Similarly, it is technically difficult to obtain sufficient specimens from an Osteoma or a walled-off Osteoid Osteoma. The depth of aspiration and the frequent plugging of the needle for aspiration of a relatively intact" greater trochanter accounted for poor yield for lesions from that area, and constitutes a specific limitation of fine-needle aspiration biopsy. These problems account for insufficient tissue in most of the *"inadequate specimens"* (7 of 9 cases).

On the following levels of analysis, near ideal proportions were obtained. Preliminary results show a 100% sensitivity and 82% specificity for detecting tumors, along with high positive and negative predictive values of 94% and 100%, respectively. All tumors aspirated can be detected by fine-needle aspiration biopsy. Of the tumors identified, ability to determined which are malignant will be possible in 96% of cases and only 36% may

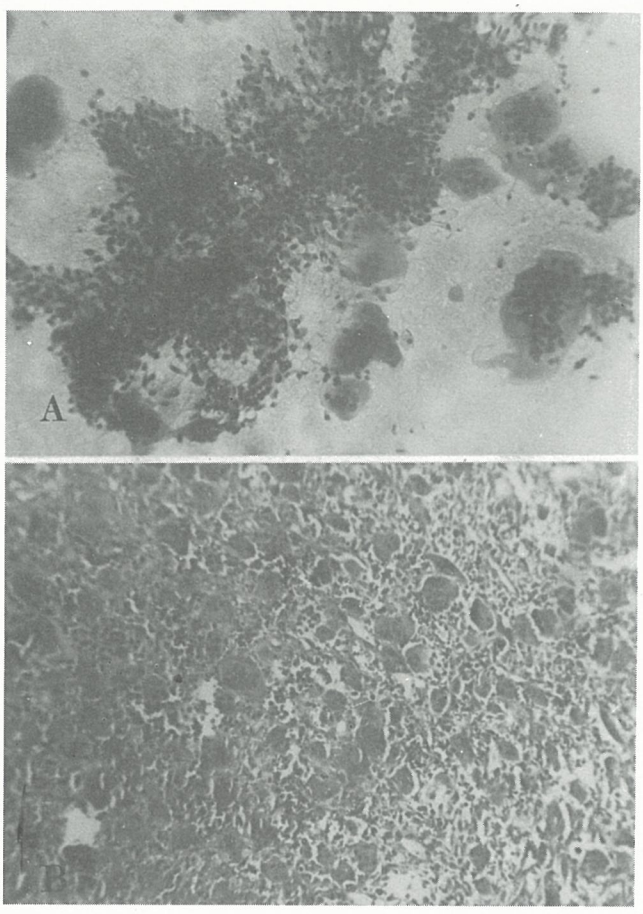

Fig. 4A: Giant Cell Tumor of Bone (Aspirate, 100x). Two cell types are clearly seen.

B: Giant Cell Tumor of Bone (Tissue section, 100 x).

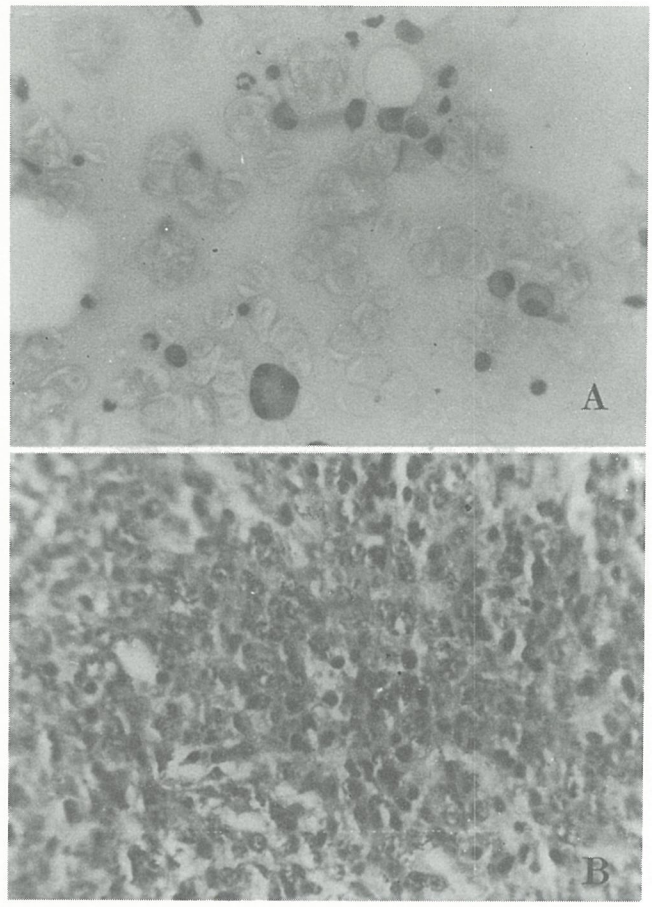

Fig. 5A: Plasmacytoma (Aspirate, 400x). Easily identifiable mature plasma cells are seen. A multinucleated cell is present.

B: Plasmacytoma (Tissue section, 400x). Biopsy of case from Fig. 5A. The histologic diagnosis proved difficult.

be missed. Of the malignant tumors, fine-needle aspiration biopsy may distinguish primary from metastatic tumors in all cases. The extent to which fineneedle aspiration biopsy can give a cytologic diagnosis is acceptable. All the benign tumors were specifically diagnosed. Sixteen of twenty-two malignnat tumors (72.7%) were given complete diagnoses. However, only two of five metastatic leions could be given specific diagnoses. In all, fineneedle aspiration biopsy could give complete cytodiagnosis in 73.5% of all tumors.

Comparison with Other Studies

With the results of this interim analysis, certain similarities with other studies are noted. On the adequacy of tissue aspirated (81.5%), proportions are comparable with those of larger tumor centers such as: (1) Memorial Hospital, New York (82%);[7] (2) M.D. Anderson Hospital (91.2%),[4] and (3) University Hospital, Sweden (82%).[10] However, while Ackerman, et al.[10] of the University Hospital, Sweden, claimed that 90% of their cases can be cytologically diagnosed, such is not the case in the present study. But their 95% ability to differentiate benign from malignant lesions is close to that

TABLE 4
Comparison of Costs – Aspiration Versus Open Biopsy.

Procedure	Cost to Patient	Total Cost*
Aspiration Biopsy	₱17.10+	₱17.10+
Open Biopsy under		
Local Anesthesia	103.74+	453.74+
Regional Anesthesia	257.54+	597.54+
General Anesthesia	549.41+	899.41+

*Includes operating room fees, etcetera

TABLE 5
Comparison of Studies on Aspiration Biopsy.

Study Cited	Sample Size	Diagnostic Accuracy	Needle Size	Remarks
Snyder & Coley[7] Memorial Hospital New York, 1945	567	67.5%	1 mm	– treated as small biopsy – bone tumors only
Ottolenghi[9] Buenos Aires Argentina, 1955	1,061	84.35%	2 mm (special biopsy needles)	– bone lesions only
Schajowicz & Derqui[5] Buenos Aires Argentina, 1968	4,050	76.24%	2 – 4 mm	– both cytologic and histologic diagnosis – bone and soft tissue lesions
Ackerman, et al.[10] University Hospital Lund, Sweden, 1976	150	90.0%	0.8 mm	– cytologic method – bone tumors only
De Santos, et al.[4] MD Anderson Hospital Houston, Texas, 1979	34	85.3%	(special biopsy needles	– treated as core bopsies – used cytologic method also – bone tumors only
THIS STUDY UP-PGH Philippines, 1986	56	73.5%	1 mm or less	– cytologic method only – interim analysis

TABLE 6
Cost Comparison Ratios of Aspiration and Open Biopsies.

Aspiration Biopsy versus Open Biopsy under.	Cost to Patient	Total Cost
Local Anesthesia	6 x	26 x
Regional Anesthesia	15 x	35 x
General Anesthesia	32 x	53 x

obtained in this study (96%). On the level of ability to give an accurate and specific diagnosis, several studies are compared as shown in Table 5. The most striking observation is the lack of any uniformity. Accuracy is anywhere from 67.5% to 90% but the highest proportions belong to a center where cytologic diagnosis is well-developed. The next three are from centers where larger bore needles are used, that is, 2 mm. This study is a close fifth with 73.5%. Memorial Hospital in New York had a 67.5% accuracy, much less than that of this study; however, note that the needle employed is also a 1 mm. outer diameter needle.

Cost-Comparison

Based on the the results of the costcomparison done, the fine-needle aspiration biopsy appears to be a more economical procedure compared to an open biopsy. The latter procedure costs anywhere from 6 to 53 times more than the former. (Table 6). If used as a screening procedure, doing fine-needle aspiration biopsy prior to open biopsy definitely increases the cost per individual. However, once extrapolated to the entire population, costs would be much less because majority of the cases may not need an open biopsy following a needle biopsy.

Complications

Several authros (Jaffe, Dahlin and Lichtenstein) are still skeptical of fine-needle aspiration biopsy.[5]

The following are some misconceptions and corresponding arguments:

1. **"It is a blind method."** The procedure can be done under microscopic guidance. Moreover, with experience, tactile sensitivity can be developed.

2. **"Important organs may be damaged."** With adherence to correct technique and accumulated experience, this is nil.

3. **"Tissues may be altered."** This happens in core biopsies and with the use of trephine needle, but not in *fine*-needle aspiration.

4. **"Hemorrhage may occur."** In the reported studies, this was not a problem.

5. **"Local contamination may take place."** This has been repeatedly proven not to occur.

In this study, the patients tolerated the procedure well except for some mild discomfort not unlike a venipuncture. Moreover, they did not refuse a repeat aspiration. No complications were noted, attesting to the safety of the technique.

LIMITATIONS AND RECOMMENDATIONS

The present study is essentially an interim analysis. The protocol calls for 100 consecutive cases. Statistics done now may not yield the same results upon completion although a trend can be seen.

The study is a non-randomized, uncontrolled one. Thus, the probability of detecting false positives and false negatives is low. The patients were screened clinically, radiologically and by laboratory exams prior to recommandation for biopsy. The ideal situation would be to do fine-needle aspiration biopsy on all out-patient cases with or without lesions; however, this would be unethical and impractical.

The original protocol calls for a second phase which included: (1) Fine-needle aspiration biopsy of deeper lesions which are not as easy to approach surgically; (2) The full application of fine-needle aspiration biopsy as a screening procedure at the out-patient section; and (3) Fineneedle aspiration biopsy to replace open biopsies under certain strict conditions. In connection with the last item, the the indications followed at the M.D. Anderson Hospital may be adopted, and these are as follows:[4]

1. Differentiation of primary from metastatic when no history of primary is known;
2. Evaluation of all small round cell tumors as first step to diagnosis;
3. Suspected infection with aggressive radiographic features simulating malignancy;
4. When open biopsy is not possible;
5. As an alternative to open biopsy in deep, complex areas; and
6. When integrity of overlapping tissues is required for final surgical management.

CONCLUSION

The diagnostic value of fine-needle aspiration biopsy in orthopedic bone and soft tissue lesions was discussed from an interim analysis of 56 cases. A fair sensitivity of 81.5% and poor specificity of 50% was found for adequacy of tissue aspirated, but the technical problems were identified. Sensitivity and specificity for detection of tumor tissue is high, with similarly high proportions for differentiation between benign and malignant tumors. These preliminary results are encouraging, with fine-needle aspiration biopsy showing promise as an adjunctive diagnostic procedure applicable in any out-patient setting. The specific cytologic accuracy of 73.5% is comparable to similar studies. Further conclusions are still to be made as additional results are forthcoming. Studies which cite high accuracy for specific diagnosis make use of larger aspirating needles, trocars and trephines, with the exception of those from Scandinavian countries where fine-needle aspiration biopsy is well-developed. Comparison of costs showed aspiration biopsy to be considerably less expensive than open biopsy. Patient acceptance was high and morbidity was nil.

Aspiration biopsy can be relied upon in the detection of benign and malignant tumors. It is simple, safe and inexpensive. Further use of this revitalized technique especially in underdeveloped nations is recommended.

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