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FINE NEEDLE ASPIRATION BIOPSY IN THE EVALUATION OF TUMOR-LIKE LESIONS OF BONE

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A consecutive series of bone lesions suspected to be tumors and examined by fine needle aspiration biopsy at the University Hospital Cytology Laboratory in Lund, Sweden, is reported. From 1966 to November 1974, 150 cases were examined. In 123, sufficient cellular material was obtained through aspiration by a needle with an outer diameter of 0.8 mm. The method is described. The reliability of cytology is compared with the results of definite pathology after open biopsy or extirpation of the lesion. In the series of primary benign lesions 28 out of 39 were correctly diagnosed; among primary malignant 27 out of 38 were correct and among metastases 57 out of 73 were correctly diagnosed including those where insufficient cellular material was aspirated. In cases where sufficient material was achieved the reliability of the cytological diagnosis was around 90 per cent. There was one false positive and two false negative reports of malignancy. Fine needle aspiration biopsy with cytology is recommended as a standard step in orthopedic oncological examinations. It has at least the same degree of diagnostic reliability as other diagnostic methods, such as X-ray, for instance; however, it does not replace open biopsy and histology when mutilating surgery is in question.

Key words: biopsy; bone tumor; cytology; differential diagnosis; oncology

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The definite diagnosis of a bone tumor is often a difficult problem and the histologic diagnosis has to be supported by a series of factors such as sex and age of the patient, case history, location of the lesion, the roentgenologic appearance, palpable findings and so on. It is generally accepted that this analysis is a matter of teamwork in which the orthopedic surgeon, the diagnostic and therapeutic radiologist and the pathologist participate. Fine needle aspiration biopsy was tested in this diagnostic work as it has a proven value in tumors in other tissues. With the thin needles used, 0.8 mm outer diameter, local anesthesia was not necessary, and the procedure was quick and almost painless. It could be done ambulatory with very few complications.

The first report of needle biopsies in the diagnosis of bone tumors appeared in

1930 (Martin & Ellis 1930). Since then several important works have been published (Snyder & Coley 1945, Hajdu & Melamed 1971, Schajowics & Derqui 1968).

All these reports have in common the use of rather thick needles, 18 gauge or thicker (at least an external diameter of 1.25 mm) and this necessitated local anesthesia and often a small skin incision to avoid contamination of the aspirate by surface epithelium. With these needles it was often possible to get cellular material both for cytological diagnosis and conventional sectioning and staining, and in Schajowics' analysis of his large material of 4050 cases he stresses the need to combine cytologic and histopathologic examinations.

The reliability of this type of bone biopsy was high in the reports; in Snyder's material of 385 cases of primary bone tumors and metastases 82 per cent showed material sufficient for tumor diagnosis and in 67.5 per cent a definite diagnosis was possible. Only one false positive diagnosis was made.

The fine needle aspiration biopsy, as compared with the above-mentioned biopsy method, is simpler, quicker and kinder to the patient but if this type of needle biopsy is to be of value the cytologist must be able to differentiate primary bone tumors from metastases and to separate the malignant primary bone tumors from the benign tumors and lesions. A preliminary report of cytodiagnosis of bone lesions by means of fine needle biopsy has been published by Stormby & Åkerman (1973).

MATERIAL

The primary histopathological diagnoses were revised by one of us (Berg). The primary cytologic reports were also revised but no change was made in interpretation. The original report was compared with the final report of the histopathological revision.

This material includes all bone tumors or lesions examined by cytology but not every tumor case treated at the Orthopedic Clinic during the period under discussion. Between 1966–1970 the orthopedic surgeon responsible for the case decided if a needle biopsy should be performed but in 1970 a special orthopedic oncology team was established for evaluating the bone tumor cases (orthopedic surgeon, diagnostic and therapeutic radiologist, cytologist, pathologist and in special cases additional specialists). Each week the tumor cases referred to the group were examined and discussed and needle biopsy considered. If angiography was decided upon the needle biopsy was postponed until after the angiography; the other cases were biopsied immediately and the next step in the diagnostic analysis decided upon on the basis of the cytology report. The time interval between the needle biopsy and the subsequent surgical intervention varied between 3 days and 1 week.

The aspirates were examined by all together eight different cytologists during the years and the analysis represents the reliability of the cytodiagnostic method used as a routine procedure.

METHOD

Almost all the biopsies were performed by the cytologist in the same way as for non-osseous lesions.

Thus all the punctures were made with a special holder for disposable plastic syringes. The outer diameter of the needle was 0.7 or 0.8 mm and its length varied between 25 and 80 mm. In cases with a palpable tumor the aspiration was made according to the palpatory findings. In the other cases the sites for the biopsies were chosen on the basis of the roentgenogram and some lesions, especially those in the vertebrae, were punctured during X-ray translumination with TV-amplifier. The aspirates were spread as a conventional blood smear and as a rule fixed in 95 per cent ethanol before staining with hematoxylin-eosin. In a majority of the cases, however, some slides were also air-dried and stained according to May-Grünwald Giemsa. With the eosin stain it was possible to get a stained smear in less than 10 minutes and rapid reports were possible.

RESULTS

With the fine needle it was possible to get sufficient cellular material in 123 of the 150 cases (Table 1).

Table 1. Correlation between cytologic and histologic diagnoses of bone tumors/bone lesions. Lund December 1966–November 1974. 150 cases.

Histologic diagnosis	Cytologic diagnosis						Total
	Primary benign	Suspicion of malignancy	Primary malignant	Metastatic	Suspicion of a metastatic tumor	Insufficient biopsy material	
Primary benign	28	1	1	–	1	8	39
Primary malignant	1	2	27	1	1	6	38
Metastatic	1	–	2	57	–	13	73
							150

Primary malignant bone tumors

The cytologic report on 32 cases with a representative yield showed that two cases were misinterpreted as metastases and one as a benign primary bone tumor. It was, however, possible cytologically to differentiate two main groups of malignant tumors from each other, that is, the osteogenic sarcomas and the round cell sarcomas (Ewing's tumor and malignant lymphomas). Seven of the malignant tumors were chondrosarcomas (Table 2).

Table 2. The cytologic report in seven cases of chondrosarcoma.

Chondrosarcoma	2
Chondromatous tumor-suspicion of malignancy	2
Cystic fluid—no malignant cells	1
Insufficient material	2

It was possible to identify a chondromatous tumor in four cases but the question of malignancy was very difficult to answer from the smears. The aspirates were sometimes highly cellular with

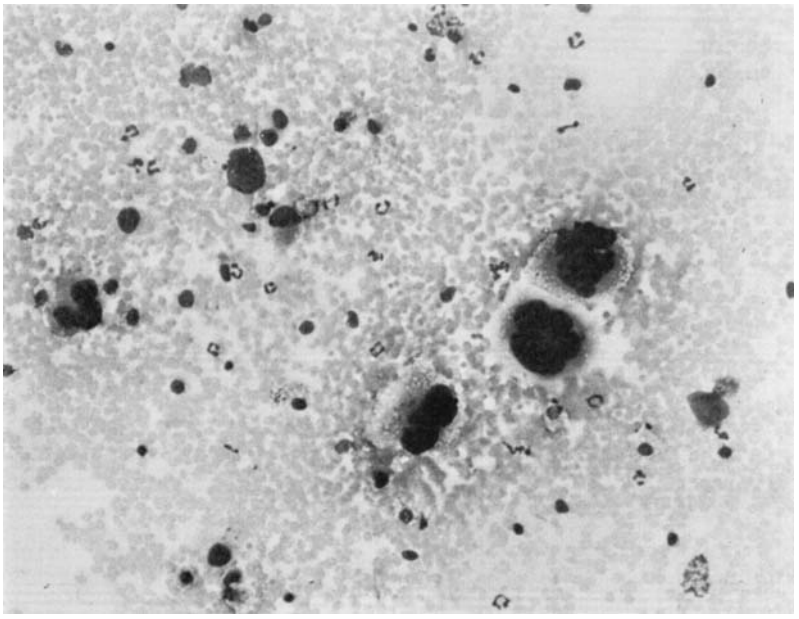

Figure 1 a. Aspiration smear from an osteogenic sarcoma. Dispersed polymorphic often multinucleated tumor cells. × 160.

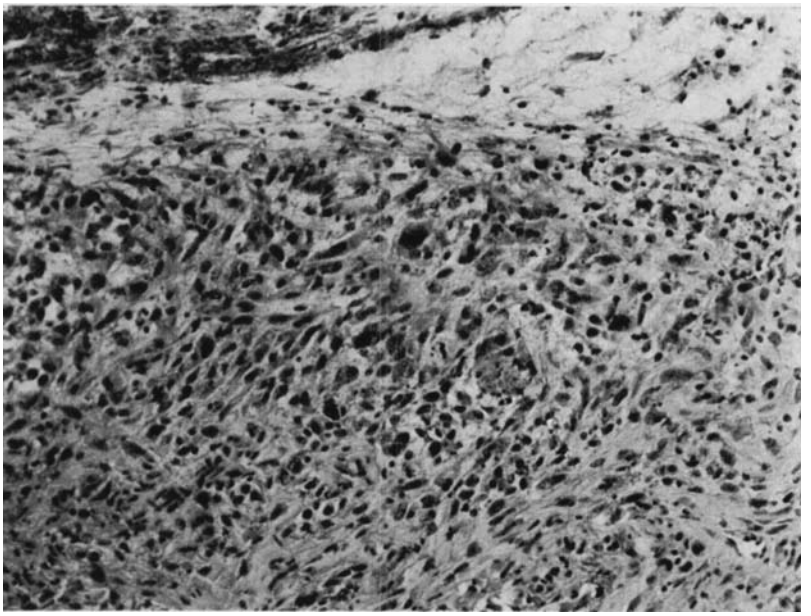

Figure 1 b. Histologic biopsy from the same case of osteogenic sarcoma as in Figure 1 a. × 160.

atypical and multinucleated chondrocytes but in other cases poor in cells and with no apparent atypia.

The aspirates from the osteosarcomas (12 cases) showed a rather uniform picture of pleomorphic tumor cells with multinucleated tumor giant cells, mitosis often atypical and in some cases clumps or strands of a homogenous material surrounding groups of tumor cells. This material was probably osteoid.

In Ewing's sarcomas and malignant lymphomas the cells were more uniform, no giant cells were present and the cytoplasm was rather sparse. The cells showed a strong tendency for dissociation; occasionally small rosette-like cell groups were seen in Ewing's tumor.

Primary benign tumors/lesions

Of the 39 primary benign tumors or lesions it was possible to penetrate the corticalis and to get adequate cellular material in 31 cases.

One case was misinterpreted as a malignant tumor. It was a large chondromyxoidfibroma in the sacrum, later locally resected. This false positive report shows, as in the chondrosarcoma cases, the difficulty involved in differentiating between malignant and benign chondromatous tumors.

Among the benign lesions belonging to "the giant-cell-group" were six giant-cell tumors, two reparative granulomas in the mandible, one osteoblastoma and one case of hyperparathyreoidism. These various types showed similar aspirates: multiple giant cells with several crowded nuclei and between them clusters of mesenchymal cells with rounded or oblong nuclei and indistinct cytoplasm. Without knowledge of the tumor site, roentgenologic findings and the age of the patient it was only possible to report a benign tumor belonging to the "giant-cell-group". The giant cell tumors at the end of the long bones have very characteristic roentgenologic signs, however, and in this location a definite diagnosis of giant cell tumor is possible. No giant cell tumor was considered malignant in the cytologic report.

In the five osteomyelitis cases the aspirates were often pus-like, a few milli-

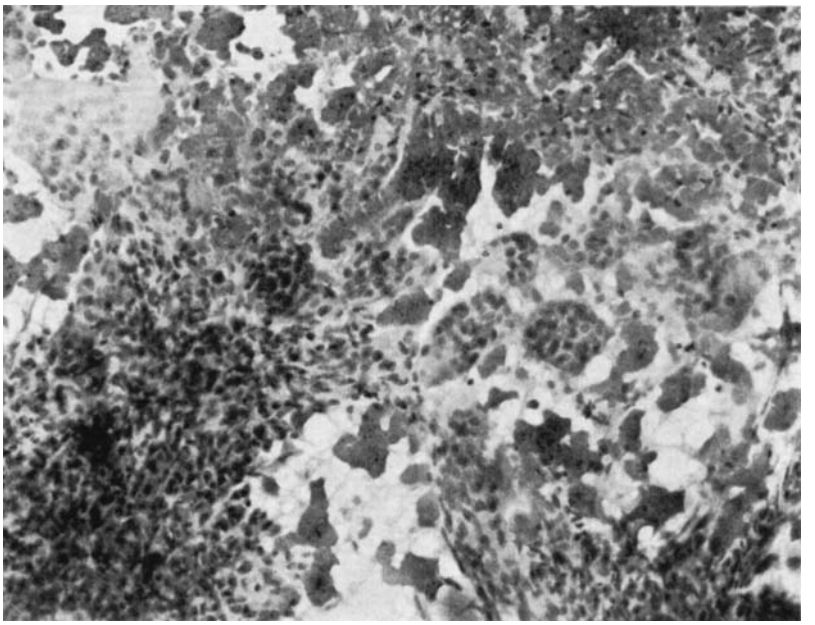

Figure 2 a. The cellular aspirate from a giant-cell tumor. Numerous giant cells and sheets of mesenchymal tissue. × 160.

liters of thick yellow-brown fluid; in the smears thick clusters of cellular debris, polymorphonuclear leukocytes and macrophages were found.

In the cases which proved to be metastatic the fine needle biopsies succeeded in 60 cases out of 73 (Table 1). There was one false negative report. Two cases were considered as primary malignant bone tumors instead of metastatic (cases 3 and 8 in Table 3). In 14 patients the metastatic bone lesion was the first sign

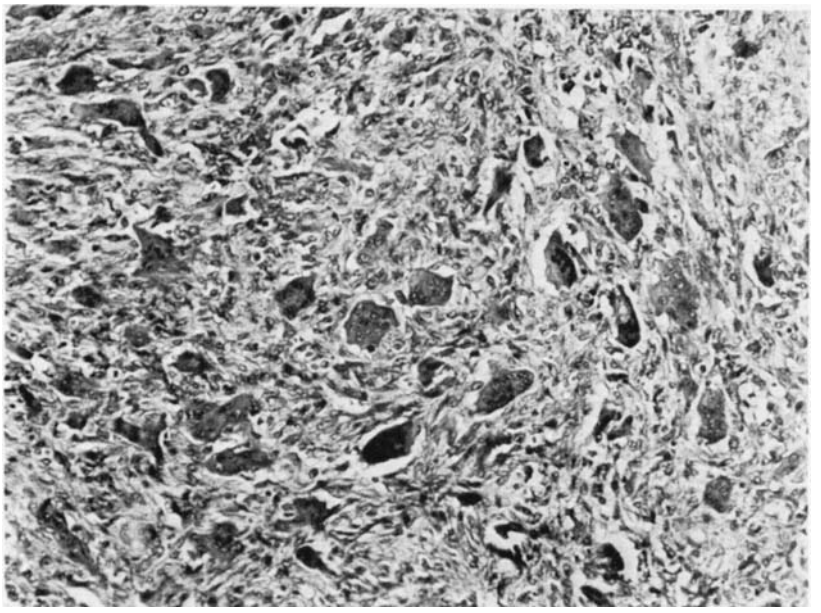

Figure 2 b. Histologic section from the same giant-cell tumor. × 160.

Table 3. Details of eight cases in which cytology was misinterpreted. There were 123/150 cases with sufficient cellular material.

Case	Year	Cytology	Histology
1	1970	Primary benign	Metastasis from renal carcinoma
2	1971	Benign	Sarcoma
3	1971	Suspicion of a metastasis	Fibrous dysplasia
4	1972	Primary malignant	Metastasis from epidermoid carcinoma
5	1972	Metastasis. Renal carcinoma?	Chordoma
6	1973	Primary sarcoma	Metastasis from uterine leiomyosarcoma
7	1973	Chondrosarcoma	Chondromyxoidfibroma
8	1974	Metastasis from adenocarcinoma	Chordoma

of a malignant tumor. The cytology was able to suggest the site of the primary tumor in 6 cases. Vertebral lesions were as reliably diagnosed from cytology as were other lesions (Table 4).

DISCUSSION

Bone lesions in general are not expected to be accessible through a fine needle and a needle biopsy of bone tissue is perhaps expected to yield an insufficient volume of material for a diagnosis, which might be debatable even with conventional sections after fixation and decalcification.

This consecutive series with fine-needle cytology compared with final histology shows that 123 out of 150 bone lesions yielded sufficient material for a diagnosis. This means 82 per cent and compared with Snyder & Cooley's (1945) series with thicker needles this figure is identical. If the accessibility with our fine needles seems therefore to be adequate what about the reliability? In Snyder's series 67.5 per cent gave a correct definite diagnosis and in 82 per cent a definite tumor diagnosis was made. In our series the diagnosis was correct in 72 per cent among the primary benign, 71 per cent in primary malignant and 78 per cent in metastatic lesions. In the lesions with sufficient cellular material it was possible to differentiate primary bone lesions from metastases in 90 per cent and primary benign tumors/lesions from primary malignant tumors in 95 per cent.

Table 4. Details regarding 14 vertebral lesions.

Site	Cytology	Histology
L V	Myeloma	Myeloma
C IV	Myeloma	Myeloma
Th XII	Myeloma	Myeloma
Th XII	Sarcoma	Sarcoma
L II	Chondromatous tumor	Chondrosarcoma
Th XII	Metastasis, adenocarcinoma?	Chordoma
C IV	Primary bone tumor, osteoblastoma?	Giant cell tumor
L IV	Metastasis, adenocarcinoma	Metastasis, adenocarcinoma
Th IV	Metastasis	Metastasis
L III	Primary benign	Metastasis, renal carcinoma
L II	Metastasis	Primary: hepatocellular carcinoma
L III	Metastasis, adenocarcinoma	Primary: carcinoma of the colon
L II	Metastasis, hepatocellular carcinoma?	Primary: hepatocellular carcinoma
L III	Insufficient material	Metastasis from an adenocarcinoma

The cytologic misinterpretations are listed in Table 3. Two cases of chordomas (cases 5 and 8) were supposed to be metastases. When re-analyzing the smears it was possible to identify the mucoid material and the physaliphorous cells in case 8 in the Giemsa-stained smear. In the other case only hematoxylin-eosin-stained smears were available. It is probably impossible to differentiate a leiomyosarcoma metastasis from a primary bone sarcoma (case 6). The primary tumor had not been discovered at the time of the needle biopsy. In cases 1 and 2 the reevaluation of the aspirates showed a very scanty cellular material, and in these cases it would have been better to report that insufficient material was available.

The fine-needle technique described here seems therefore to be as adequate as when a thicker needle is utilized and in addition anesthesia is not needed and the local bleeding is reduced. There were no immediate complications such as pain, hemorrhage or infection after the needle aspirations and no signs of local metastases were ever observed in the puncture canal.

The purpose of using a biopsy method with a total reliability of approximately 70 per cent (including the cases where the aspiration failed to give material) must be compared with the risk, costs and pain involved. In bone lesions, physical findings and X-ray findings, including angiography and scintigraphy, if utilized, all have a limited diagnostic reliability but give important contributions when the question of operability and operative technique arises. Puncture cytology of the type described here is therefore a standard step in our examination of bone lesions at the Center of Orthopedic Oncology. It is used as a guiding influence in some cases leading to unsuspected alternatives but it is only exceptionally used as a basis for radiotherapy without an open biopsy and never for mutilating surgery such as amputation. In locations where a local extirpation is possible without mutilation consequences it may be regarded as giving sufficient information.

The chondromatous group seems to be the most difficult to subspecify by this technique. When a chondromatous tumor is suggested by X-ray and cytology an extirpation of the tumor *en bloc* is curative if benignity is confirmed by histology and adequate as a biopsy if not. In some cases a ganglion-like liquid has induced us to inject X-ray contrast in order to map out the cavity. One of these turned out to be a chondrosarcoma with a large cystic center, however.

Cytology should not be omitted because it is only 70 per cent conclusive as it is more reliable than many other diagnostic measures in these cases and the method as reported here is rapid, pain-free and of little risk and thus appealing. At surgery the canal is removed *en bloc* if possible. The vertebral biopsies are of special interest (Table 4). Here cytology is as reliable as in other locations and open biopsy is often more troublesome. In general metastases are relatively more common in vertebral locations. Cytology is therefore almost indispensable in such cases if there are no signs of medullary compression which would indicate the need for an operative intervention.

The reliability of cytology compared with histology in this series depends on the experience of the cytological laboratory. As with bone pathology in general considerable experience is necessary for safe microscopic diagnoses to be made.

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