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Aspiration cytology of soft-tissue tumors

The 10-year experience at an Orthopedic Oncology Center

Since 1972, we have included fine-needle aspiration cytology in the pre-operative evaluation of soft tissue lesions referred to our Orthopedic Oncology Group. In 365 consecutive patients the cytodiagnosis was correctly malignant in 66/74 tumors and correctly benign in 260/271 lesions; cytology was non-diagnostic in four sarcomas and 16 benign lesions. The final pre-operative diagnosis should be based on all pre-operative data to minimize the effect of any misjudgement as regards cytodiagnosis; only two of the 19 false cytodiagnoses were of consequence for the patient.
We conclude that aspiration cytology used in this way is a valuable adjunct to determine the further management of soft tissue tumors.

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The University Hospital of Lund is a treatment center for patients with musculo-skeletal malignancies in the Southern Region of Sweden which has 1.3 million inhabitants. At this Center, the Orthopedic Oncology Group has used aspiration cytology with a fine needle (AC) as an adjunct to the history and clinical examination in the pre-operative evaluation of benign *versus* malignant tumor; the exact histogenetic type of a soft-tissue sarcoma is seldom of importance for surgical planning.

AC has been an accepted method for the evaluation of epithelial tumors for many years (Zajicek 1974, 1979), but not for mesenchymal tumors. We therefore report our experience with AC in a consecutive 10-year series of 365 patients referred to the Center with non-operated soft-tissue lesions suspected of malignancy. Parts of this series have been reported earlier (Åkerman et al. 1981, Rydholm et al. 1982). In this report we further analyse the reliability of AC, the consequences of false cytodiagnoses, and the causes of false and inconclusive cytodiagnoses.

Patients and methods

During 1972–81, 367 patients with soft-tissue lesions were examined using AC at the Center. All patients were referred before any AC or surgery. Two non-operated patients were lost to follow-up, leaving 365 patients for analysis. In 255 patients a histologic diagnosis (surgical specimen or autopsy) was subsequently made. The sarcomas were histologically graded on a four-grade malignancy scale: Grade I-II = low-grade and Grade III-IV = high-grade malignant (Markhede et al. 1982, Rydholm et al. 1983a). The 110 non-operated patients had a clinical follow-up of at least 2 years; in all cases the tumor was unchanged, smaller or had disappeared, and these were considered benign lesions. The histologic diagnosis or the clinical follow-up diagnosis was termed the final diagnosis.

All aspirations were performed by cytopathologists. The technique was the same as for aspiration of epithelial tumors, the outer needle diameter being 0.7–0.8 mm. The site for aspiration was decided by the orthopedic surgeon and the cytopathologist together, usually at the vertex of the palpable mass. The puncture tract could then easily be included in the operative specimen. Multiple aspirations and penetration of the deep tumor border were avoided. The aspirates were stained with hematoxylin and eosin and according to May-Grünwald-Giemsa.

The cytodiagnoses were primarily classified as malignant, suspected of malignancy, benign, or non-diagnostic. In this analysis supected malignancy was classified as malignant. The cytopathologist also tried to differentiate between sarcoma and other malignant tumors such as carcinoma, malignant melanoma or malignant lymphoma; if this was not possible, the diagnosis was classified as "unspecified malignancy". The reliability of AC was evaluated by comparing the primary cytodiagnoses with the final diagnoses.

The consequence of possibly improper surgery because of *false* cytodiagnoses was evaluated. The surgical procedures were:

1. No surgery or marginal excision when the tumor was considered benign.
2. Primary local excision with a wide or radical margin (Enneking 1983) when the preoperative examinations suggested malignancy *and* the operation was possible with little loss of function
3. Incisional biopsy, or in some selected cases, marginal excision when the pre-operative examinations suggested a sarcoma but a wide or radical margin could not be obtained without major loss of function.

The causes of a false or inconclusive cytodiagnosis were analyzed by re-examination of the smears and comparison with the histological slides.

Results

Comparison of final diagnoses and cytodiagnoses, 365 cases (Table 1). The final diagnosis was benign in 110 non-operated lesions, 177 tumors were histologically benign, 62 were sarcomas, 11 were metastatic carcinomas with unknown primaries at the time of aspiration, four were malignant lymphomas and one tumor was histologically classified as an unspecific malignancy.

In 20 cases the aspirates were non-diagnostic, in 19 cases because of insufficient material and in one case because of inconclusive cytodiagnosis. In the other 345 cases the cytodiagnoses were correctly malignant in 66/74 and falsely benign in 8/74 cases, correctly benign in 260/271 and falsely malignant in 11/271 cases. Of 63 cytodiagnostic reports of sarcoma, 51 were histologically verified, and of 62 histopathologic diagnoses of sarcoma the cytodiagnosis was sarcoma in 51, a benign lesion in seven, and in four cases there were non-diagnostic aspirates.

Thus in patients with evaluable aspirates, 96 per cent of the benign lesions and nine-tenths of the sarcomas were correctly diagnosed.

Consequences of falsely malignant cytodiagnoses, 11 cases. In 11 benign tumor cases the cytodiagnosis was sarcoma; one case had no surgery, one case had an incisional biopsy, two cases had marginal excisions and seven cases had surgery with wide or radical margins. In these cases, the history and clinical examination could not exclude a sarcoma.

A subcutaneous, probably inflammatory, lesion had disappeared when the patient was re-examined. The patient died 2 years later with no evidence of tumor.

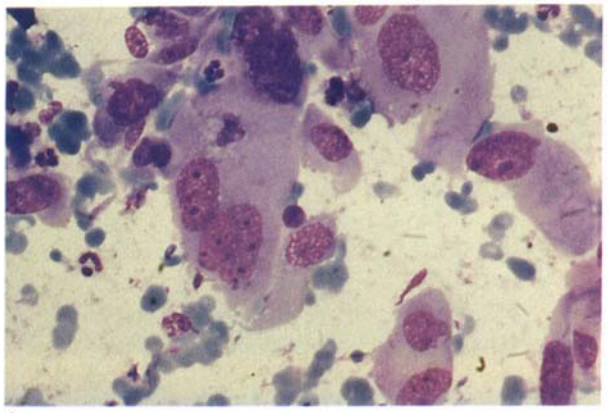
One patient with a deep, firm tumor in the axilla underwent an incisional biopsy with a histologic diagnosis of a probably benign angiomatous tumor. Without further surgery the lesion has remained unchanged for 5 years.

A 15-cm subcutaneous lipoma and a deep lipoma in the axilla were excised marginally.

One subcutaneous lipoma, one subcutaneous

Table 1. Comparison of final diagnosis and cytodiagnosis in 365 patients with soft-tissue tumors

Final diagnosis	Cytodiagnosis				
	Sarcoma	Other malignancy	Benign	Non-diagnostic	Total
Histopathologic diagnosis					
Sarcoma, high grade	39	–	4	4	47
Sarcoma, low grade	12	–	3	–	15
Other malignancy	1	14	1	–	16
Benign lesion	10	–	158	9	177
No histopathology-benign at follow-up	1	–	102	7	110
Total	63	14	268	20	365



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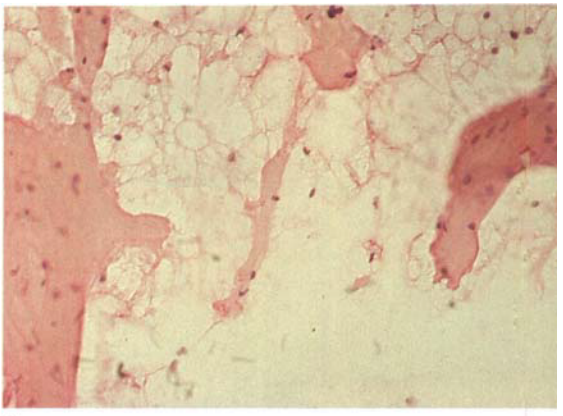

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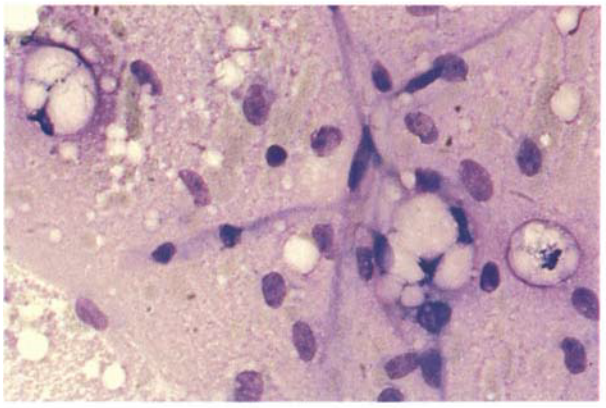

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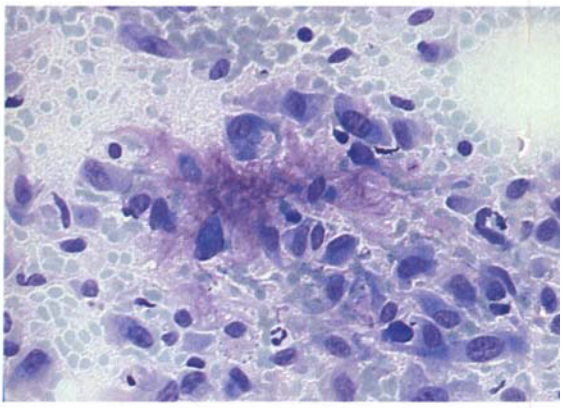

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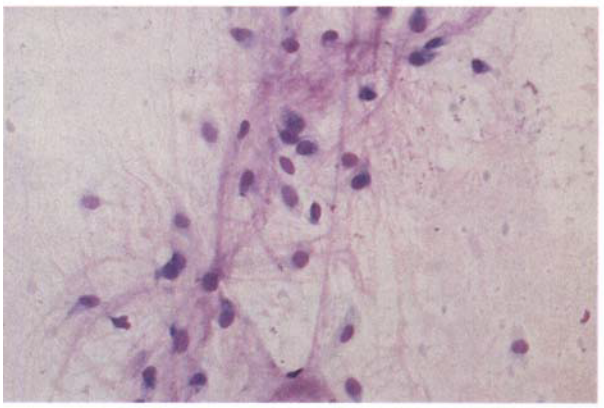

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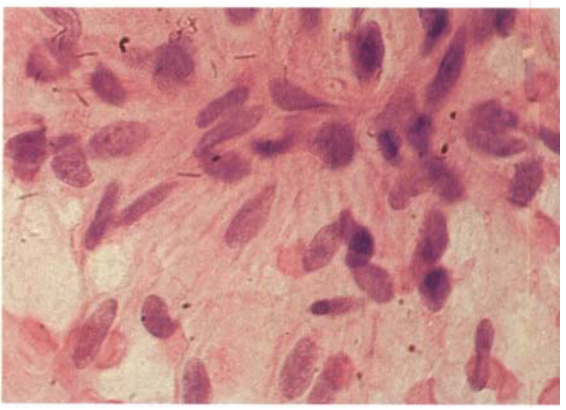

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Figure 1. Aspiration cytology of soft-tissue tumors.

A. High-grade leiomyosarcoma. Dispersed polymorphic cells with very irregular nuclei and multiple nucleoli. (May-Grünwald-Giemsa. ×990.)

B. Typical aspirate from an intramuscular lipoma. Large fragments of benign fatty tissue mixed with fragments of striated muscle. (Hematoxylin-eosin. ×100.)

C. Myxoid liposarcoma. In this field there are three diagnostic features: myxoid background, a branching capillary network and multivacuolated lipoblasts. (May-Grünwald-Giemsa. ×390.)

D. Nodular fasciitis with tufts of fibrillary myxoid material intermingled with fibroblasts of different sizes and shapes. (May-Grünwald-Giemsa. ×390.)

E. Intramuscular myxoma. Scattered benign cells with elongated cytoplasm and ovoid nuclei in a fibrillar myxoid background. (May-Grünwald-Giemsa. ×240.)

F. Part of an aspirate from an unspecified sarcoma, Grade III. The cellular atypia is slight and it is difficult to make an unequivocal cytodiagnosis of sarcoma.
(Hematoxylin-eosin. ×990.)

nodular fasciitis, one intramuscular hemangioma, one intramuscular neurilemmoma and one intramuscular myxoma were primarily excised with wide margins, with no loss of function. One intramuscular desmoid close to the os pubis was primarily treated by a radical excision of the adductor muscle compartment, including the os pubis, a margin indicated for that type of tumor.

One intramuscular hemagioma in the lower part of the triceps muscle had a primary myectomy including the ulnar nerve which was close to the tumor. As a correct pre-operative diagnosis would have saved the nerve, this was the only patient with unnecessary loss of function because of a falsely malignant cytodiagnosis.

Consequences of falsely benign cytodiagnoses, 8 cases. In seven sarcomas and one metastatic carcinoma, the cytodiagnosis was benign. The first surgical procedure was an incisional biopsy in three cases and a marginal excision in five cases.

Three patients had large firm, deep tumors. Clinical examination so strongly suggested malignancy that a marginal excision was considered improper and a wide or radical margin could not be obtained without major loss of function. An incisional diagnostic biopsy was made in these three cases in spite of the benign cytodiagnosis.

Another three patients underwent marginal excisions. One patient was re-operated with a wide margin, whereas the two other patients had no further surgery after diagnosis of a hemangiopericytoma, Grade I, and a neurofibroma with sarcomatous transformation, Grade III, respectively. None of these three patients has had local recurrence or metastases after 4–11 years follow-up.

An intended primary wide local excision was classified as marginal in a myxofibrosarcoma, Grade II. The patient has been followed for 6 years with no recurrence.

In a clinically, cytologically and angiographically benign pretibial subcutaneous tumor, a marginal excision was done and histologic examination showed a myxofibrosarcoma, Grade IV. The second extended local excision was microscopically marginal. After radiotherapy a chronic ulcer developed, and later a wide BK amputation was done. No tumor growth was found on microscopical examination and the patient has no metastases after 8 years. This is the only case where a falsely benign cytodiagnosis may have caused unnecessary invalidity; perhaps tumor spread in the wound hematoma following the marginal excision made the second excision nonradical.

Cytologic re-evaluation of non-diagnostic aspirations, 20 cases. In 12 cases with benign lesions the insufficient material was probably due to faulty aspiration technique. In three sarcomas, all high grade, the aspirates originated from necrotic or cystic areas without any preserved malignant cells. From two desmoids only scattered elongated, fibroblast-like cells could be aspirated and from two benign vascular tumors only blood. In a neurogenic sarcoma, Grade IV, the primary cytologic report was inconclusive: the cytopathologist could not decide whether the tumor was benign or malignant. At re-examination the smear was judged as clearly malignant.

Cytologic re-evaluation of false cytodiagnoses, 19 cases. With our present experience, nine early cases would have been correctly diagnosed as benign or malignant. In one case the aspirated material was insufficient for diagnosis. In four cases with a histologic diagnosis of some type of "spindle-cell" tumor (fibroblastic or vascular) it was difficult to decide whether the tumor was benign or low-grade malignant. In a further case the re-examination also resulted in an inconclusive diagnosis; it was not possible to decide whether the aspirated cells originated from a benign or malignant tumor. In the last four cases, re-evaluation did not change the primary cytodiagnosis; these cases were examples of sampling errors at aspiration.

Discussion

Recent surveys of soft-tissue lesions stated that aspiration cytology (AC) "seldom yields tissue for full pathologic evaluation", "aspira-

tion biopsy has virtually no role in the diagnosis", and "the treatment plan for primary soft tissue sarcomas should not be based on aspiration biopsies in most instances" (Hajdu 1981, Rosenberg & Glatstein 1981, Lawrence et al. 1983). On the other hand, 30 years ago Pack (1954) stated: "The critics of aspiration biopsy are too specific in their demands of the method. The procedure is useful if it permits the differential diagnosis between inflammatory and neoplastic tissues, or , in case of tumor, between the benign and the malignant variety". Our results confirm Pack's statement. However, evaluation of the cytopathologist's report should be made in context with other pre-operative data. The combined information determines, first, if radiographic investigations should be performed, and, second, which surgical procedure is appropriate. This stepwise evaluation means that surgery is based on history, clinical examination, AC and in selected cases, radiographic examinations. This concept requires close co-operation between the surgeon, the cytopathologist and the radiologist to reduce the impact of any false pre-operative data, including AC. Thus, in our series only two of the 19 false cytodiagnoses were of major consequence for the patients.

The primary cytodiagnosis in the evaluable aspirates showed that nine-tenths of both the benign tumors and the sarcomas were correctly diagnosed as such (Figure 1). Thus AC is as reliable for mesenchymal tumors as for epithelial tumors.

In addition to differentiating between a sarcoma and a benign lesion, AC may also identify certain histogenetic types of soft-tissue tumors. Thus we have found that lipoma and myxoid liposarcoma (Figure 1) can be readily diagnosed by AC. Recent experience has shown that neurilemmomas (Dahl et al. 1984), nodular fasciitis (Dahl & Åkerman 1980) and myxomas (Figure 1) (Åkerman & Rydholm 1983) may also be diagnosed by AC. Leiomyosarcoma (Dahl et al. 1981), myxofibrosarcoma (Merck et al. 1980) and alveolar rhabdomyosarcoma (Seidal et al. 1982) have also been the subject of correlative cytologic-histopathologic studies.

Eight of the false cytodiagnoses were made in tumors of fibroblastic or vascular origin, and the diagnostic difficulties were between a benign lesion and a low-grade sarcoma. These tumors need further correlative cytologic and histologic studies. The cytodiagnostic problem of fibromatoses contra low-grade "spindle-cell" sarcomas is still unsolved and an aspirate made up of spindle-shaped cells with such a variation in nuclear size, configuration, chromatin pattern and nucleolar apparatus that the cytopathologist hesitates between a benign cellular proliferation and of a low-grade sarcoma ought to be reported as inconclusive: unspecified spindle-cell tumor.

Only 5 per cent of the aspirates were non-diagnostic in the hands of cytopathologists used to the technique. In order to minimize non-diagnostic aspirates, one aspiration from the periphery of the tumor is advisable when the first attempt yields only cystic fluid or blood.

The risk of distant tumor spread because of AC is negligible and tumor cell growth in the puncture channel is extremely rare (Kline 1981, Frable 1983). Furthermore as an extra precaution, the puncture channel, the site of which was determined by the surgeon, was included in the operative specimen if a sarcoma was diagnosed. To facilitate this we have tattooed the puncture site in cases of suspected malignancy in recent years.

The concept of combining diagnostic and therapeutic surgery for soft-tissue sarcomas was introduced by Stener (1978, 1979) and has been applied at our Center. It is based on two linked assumptions: (1) Since open biopsy is omitted, contamination by tumor cells in the wound hematoma is avoided, and the surgical margin can be kept less extensive than otherwise recommended. (2) This smaller margin justifies primary wide or radical local excisions with minor, predictable loss of function (Markhede & Nistor 1979, Markhede & Stener 1981), which is acceptable should the tumor turn out to be benign. This surgical technique applies especially to intra- or intermuscular tumors (Rydholm et al. 1986). In this series, 45 of the 51 cases with a histologic and cytologic diagnosis of sarcoma had primary surgery with margins intended for a sarcoma.

In a prospective study on part of this series, AC changed the surgical planning in one-third of the patients, and scheduled examinations by computed tomography or angiography were

cancelled following AC in one-third of the patients (Rydholm et al. 1982).

A marginal excision or a misplaced incisional biopsy for a sarcoma may complicate further surgery (Simon 1982). An increased use of AC in the local hospitals in our catchment area has probably saved many sarcoma patients from such complications; in 1980–1981, 35 of the 38 patients with a soft-tissue sarcoma diagnosed in our catchment area were referred to the Center, 10 after a marginal excision, 11 before any biopsy and 14 after a malignant cytodiagnosis but before surgery (Rydholm et al. 1983a).

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