軟骨形成性骨腫瘍の細胞学的鑑別診断

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Introduction

The histology of chondrogenic tumors of bone can be misinterpreted and it is particularly different to discriminate between enchondroma and chondrosarcoma, chondrosarcoma and chondroblastic osteosarcoma and also between chondroblastoma and giant cell tumor. Needle biopsy tissue diagnosis and the cytology of bone tumors have been reported to be useful for a definitive diagnosis by some investigators1,4-6).

On the other hand, immunohistochemical demonstration of S-100 protein in chondrogenic tumor cells appears to be very useful3,7) and for this smear preparations can be employed.

Average nuclear and cell diameters of tumor cells were measured and the histograms obtained were compared among the different tumors.

Materials and Methods

The chondrogenic tumors cytologically studied are shown in Table 1. Three cases of chondroblastic osteosarcoma were included in order to elucidate characteristics different from conventional chondrosarcoma.
Table 1 Cytologically examined chondrogenic tumors of bone

<table>
<thead>
<tr>
<th>Type of Tumor</th>
<th>Material Source</th>
<th>Cytology Source</th>
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</thead>
<tbody>
<tr>
<td>Enchondroma</td>
<td>Metacarpal, Femur</td>
<td>Open biopsy, Curettage</td>
</tr>
<tr>
<td></td>
<td>Rib, Femur</td>
<td>Resection, Curettage</td>
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<tr>
<td>Osteochondroma</td>
<td>Fibula</td>
<td>Resection</td>
</tr>
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<td></td>
<td>Femur</td>
<td>Needle aspiration</td>
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<tr>
<td>Chondroblastoma</td>
<td>Femur</td>
<td>Curettage</td>
</tr>
<tr>
<td></td>
<td>Patella</td>
<td>Curettage</td>
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<tr>
<td></td>
<td>Humerus</td>
<td>Curettage</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>Rib</td>
<td>Needle aspiration</td>
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<td></td>
<td>Vertebral</td>
<td>Curettage</td>
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<tr>
<td></td>
<td>Femur</td>
<td>Resection</td>
</tr>
<tr>
<td>Chondrosarcoma, dedifferentiated</td>
<td>Femur</td>
<td>Needle aspiration, Disarticulation</td>
</tr>
<tr>
<td>Chondroblastic osteosarcoma as control</td>
<td>Femur</td>
<td>Open biopsy</td>
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<tr>
<td></td>
<td>Tibia</td>
<td>Open biopsy</td>
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<tr>
<td></td>
<td>Ilium</td>
<td>Open biopsy</td>
</tr>
</tbody>
</table>

The sources of material for cytologic evaluation were fine needle aspiration biopsy, curettage tissue, resected specimens or pleural effusion (Table 1). All cases were stained by Pap., Giemsa and PAS.

For the immunohistochemical study smear preparations were fixed in 95 percent ethanol. The avidin-biotin-peroxidase techniques (ABC method) of Hsu, et al.2) was used in the present study. The antiserum of S-100 protein was diluted 2,000 times.

For the average nuclear and cell diameter, the maximum diameter and the minimum diameter of a tumor cell and its nucleus were measured in 100 randomly selected cells using a micrometer. Then the average diameters were calculated and diagramatized (Figs. 8 and 9).

Results

1. **Enchondromas (four cases) and osteochondromas (three cases)**

Limited numbers of relatively uniform and rather small round-to-oval cells were obtained (Fig. 1). Most cells were mononucleated and showed small, uniform and pyknotic nuclei. The nucleoli were indistinct in most cells. Areas of definite chondroid matrix were intimately associated with the tumor cells. Binucleated cells were only occasionally seen.

2. **Chondroblastomas (three cases)**

Many cells, including osteoclast-like multinucleated giant cells, were obtained. Isolated, mononuclear, round-to-polygonal cells (Fig. 2a) consistent with chondroblastoma cells were observed. The cells exhibited a characteristically rather distinct cell border, frequently indented nuclei and homogeneous, usually rather clear cytoplasm. In one case there were areas of cell clusters associated with distinct chondroid matrix which stained deeply with alcian blue and purple red in Giemsa stain (Fig. 2b).
No calcification was present. The giant cells showed uniform round nuclei with distinct eosinophilic nucleoli. S-100 protein was positively stained not only in round chondroblastoma cells but also in some multinucleated giant cells (Fig. 3, arrow).

3. Low grade chondrosarcoma (two cases)

More cells were obtained than in osteochondroma and enchondroma cases. Round or oval tumor cells intimately associated with chondroid matrix were observed (Fig. 4a). Many cells showed uniform, round and pyknotic small nuclei and were mostly mononucleated. However, binucleated cells were also seen and some nuclei were definitely enlarged with evenly distributed chromatins (Fig. 4b). The cytoplasm of most tumor cells was clear.

4. Moderate grade chondrosarcoma (one case)

Many cells were obtained. Round-to-oval cells were predominant, but there was some variation in cell size. Most tumor cells showed definitely enlarged nuclei, though chromatin was rather fine (Fig. 5). Small nucleoli were sometimes observed. Some cells were associated with surrounding chondroid matrices. Degenerated or necrotic cells were also present. No calcification was evident.

5. Dedifferentiated chondrosarcoma (one case)

Numerous cells were obtained. Spindle, round or large pleomorphic cells with relatively pleomorphic nuclei were predominant. Most were single, but cluster formation was occasionally seen. Binucleated or multinucleated giant cells with dense, coarse chromatin were evident (Fig. 6). One or more nucleoli were observed.

In limited areas uniform round tumor cells with clear cytoplasm and round-to-oval nuclei were seen associated with chondroid matrix (Fig. 6).

6. Chondroblastic osteosarcoma (three cases)

One case (femur) showed cytological features suggesting moderate degree chondrosarcoma.

In other two cases (tibia and ilium), spindle, round or oval tumor cells with enlarged, hyperchromatic nuclei were observed in addition to cells intimately associated with chondroid matrix (Fig. 7a). The oval tumor cells with eccentric, hyperchromatic nuclei and rather dense, greenish staining cytoplasm, suggesting characteristic malignant osteo-
Small round cells with chondroid matrix (a) and spindle or oval cells with bizarre nuclei (b) are characteristic. a, b ×400

In addition to chondrosarcoma cells (a), oval cells with eccentric malignant nuclei suggesting osteosarcoma cells (b) can be noted. a, b ×600

Fig. 8 Comparison of nuclear diameters in benign and malignant chondrogenic tumors

The numbers in parentheses indicate average nuclear diameters (μ).

Discussion

The diagnostic usefulness of cytology in bone tumors has been reported4,5,6. For practical purposes, in routine histological examinations of cartilage-forming tumors, the differential diagnosis between enchondroma and low grade chondrosarcoma, and also between chondrosarcoma and chondroblastic osteosarcoma were close to those of benign cartilage tumors.
sarcoma is of prime importance. Cytologic observations appear to be valuable, because cartilage matrix closely associated with tumor cells can often be recognized, even in aspiration or smear preparation materials.

In benign tumors such as enchondroma and osteochondroma limited numbers of tumor cells are obtained. Tumor cells with small, rather uniform pyknotic nuclei are characteristic of a benign lesion. Enlargement of nuclei and frequent binucleated cells are suggestive of malignancy. If many cells with features of cartilage cells are obtained and show nuclear variations, atypical nuclei and frequent binucleation, a cytological interpretation of chondrosarcoma can be established. However, chondromyxoid fibroma may reveal some cellular and nuclear variations. Sanerkin and Jeffree mentioned more scattered osteoclasts, smaller and condensed nuclei in this tumor than in chondrosarcoma.

Chondroblastic osteosarcoma, which is often difficult to distinguish from pure chondrosarcoma, exhibited generally ovoid tumor cells with eccentric, hyperchromatic nuclei and rather dense greenish-stained cytoplasm, in addition to cells with features of a cartilaginous nature. The former cells represent osteosarcoma cells. In a case in which osteosarcoma is suspected based on the clinical features (especially age, location and radiological findings), one has to evaluate the cytology very carefully to detect possible osteosarcoma cells.

Dedifferentiated chondrosarcoma shows characteristic histological features. Furthermore, if tumor cells are obtained from both well-differentiated cartilaginous portions and poorly-differentiated portions, cytologic interpretation of this tumor is possible.

Chondroblastoma shows characteristic cytological features as was shown in the present study. Immunohistochemical demonstration of S-100 protein in such cells is very useful (Fig. 3), since the stromal cells and multinucleated giant cells of giant cell tumor are negative for this protein.

On the other hand, the histograms of cell and nuclear diameters are different between benign and malignant chondrogenic tumors, as shown in Figs. 8 and 9. This method can provide some valuable information, though it is time-consuming.

In conclusion, cytological evaluation of chondrogenic tumors is useful. However, in the diagnostic pathology of bone tumors, the cytologic interpretation should always be conservative, and the necessity of clinical and radiological evaluation prior to final cytologic as well as histological diagnosis is emphasized.

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Summary

An attempt was made to elucidate the cytological characteristics of chondrogenic tumors of bone for the purpose of differential diagnosis. Materials were obtained by needle biopsy aspiration, curettage, resected specimens or pleural effusion of enchondroma (four cases), osteochondroma, chondroblastoma, conventional chondrosarcoma, chondroblastic osteosarcoma (three respectively) and one dedifferentiated chondrosarcoma. Cartilage matrix closely associated with tumor cells was recognized to varying degrees in all cases. Nuclear features such as enlarged nuclei, double or multiple nuclei, bizarre nuclei and high N/C ratio, in addition to the abundance of cells obtained appeared useful for the cytologic interpretation of chondrosarcoma. Chondroblastomas revealed characteristic cytology features different from those of giant cell tumor and the immunohistochemical demonstration of S-100 protein, which is not seen in the latter was especially useful. Measurement of average cell and nuclear diameters exhibited different characteristic histograms between benign and malignant chondrogenic tumors.

References

4) Sanerkin, N.G. and Jeffree, G.M.: Cytology of Bone Tumours, pp. 51-72, John Wright & Sons Ltd., Bristol, 1980.