Cytologic differential diagnosis of giant cell lesions of bone
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Key words: Giant cell lesions—Bone—Cytology—Morphology—Differential diagnosis

diagnosis of open biopsy materials as well as needle aspiration cytology appears to be useful in both primary and metastatic bone lesions.9,5,7. Cytologic characteristics of giant cell lesions can be interpreted on many occasions with reference to clinical and radiological evaluation.

On the other hand, immunohistochemistry (either by the peroxidase antiperoxidase [PAP] technique or avidin-biotin complex [ABC] method) can be applied even to smear preparations and often gives rise to valuable information for differential diagnosis.

In this study, the numbers of nuclei in multinucleated giant cells in different giant cells lesions were examined and histograms were compared.

Materials and Methods

Materials were composed of smear preparations obtained by open biopsy or needle aspiration of bone
A giant cell with approximately 50 nuclei is seen. Note uniform round nuclei with prominent nucleoli. ×900

lesions which histologically exhibited varying degrees of osteoclast-like multinucleated giant cells. The lesions included conventional giant cell tumor (2 cases), chondroblastoma (3), osteoblastoma (1), non-ossifying fibroma (2) and giant cell rich osteosarcoma (2).

Most smears were stained with Pap. stain and some with Giemsa or PAS stains. For immunohistochemical studies, the avidin-biotin-complex method by Hsu, et al.3) was carried out after fixation by 70% ethanol. The antisera used were those of S-100 protein (Jimro, Takasaki, Japan), factor XIIIa (Behring, Marburg, W. Germany) and alkaline phosphatase (Merk, Darmstadt, W. Germany).

The numbers of the nuclei and the frequency were measured by microscopy and histograms made for each tumor.

Results

1. Giant cell tumor

Many cells were obtained. In addition to multinucleated giant cells (Fig. 1), mononucleated, occasionally binucleated spindle cells consistent with "stromal cells" were seen (Fig. 2). The cell and nuclear sizes varied to some extent. Cells with mitotic figures were occasionally observed. These cells showed a somewhat greenish cytoplasm and contained prominent nucleoli. These cells appeared larger than those of non-ossifying fibroma. Hemosiderin-laden cells were occasionally seen.

Fig. 1 Multinucleated giant cell in giant cell tumor

Fig. 2 "Stromal cells" in giant cell tumor

Fig. 3 Non-ossifying fibroma

S-100 protein was not demonstrated in any cells, while factor XIIIa was positive in the spindle cells.

2. Non-ossifying fibroma

Although abundant cells were obtained, they were not as many as in giant cell tumor. Besides the osteoclast-like giant cells, spindle cells resembling fibroblasts were predominant (Fig. 3). The nuclei were small and uniform and showed rather indistinct nucleoli. Spindle cells with relatively plump cytoplasms were sometimes observed. Hemosiderin-laden spindle cells were also recognized. No xanthoma cells were found in the present series of cases.

3. Chondroblastoma

Many cells were obtained. Besides multinucleated giant cells, round to polygonal in shape were
Fig. 4 Chondroblastoma

Besides two multinucleated giant cells, round tumor cells with distinct cell borders and nuclear indentation are seen. A chondroid matrix is occasionally seen (inset). ×900

Fig. 5 S-100 protein in chondroblastoma cells

Chondroblastoma cells are intensely positive for this protein. ×900

seen. The cytoplasmic border was distinct. The centrally located nucleus often exhibited indentations (Fig. 4). Binucleated cells were occasionally observed. The cytoplasm was somewhat greenish. In one case, round uniform cells intimately associated with deeply alcian-blue stained chondroid matrix were observed (Fig. 4, inset).

S-100 protein staining was intense in these cells (Fig. 5).

4. Osteoblastoma

Limited numbers of cells were obtained. Besides the osteoclast-like giant cells, round or oval shaped single cells were seen, and showed often eccentrically located nucleus and rather deeply stained homogeneous cytoplasm (Fig. 6). A prominent nucleolus was often observed. The unclei varied in size to some extent, but nuclear pleomorphism was absent. Alkaline phosphatase was demonstrated in these cells. Material suggesting osteoid matrix was seen in the case.

5. Giant cell-rich osteosarcoma

Numerous cells were obtained. Besides osteoclast-like giant cells, spindle, oval or polygonal cells with prominent variations in the nuclear and cell shape and size were observed (Fig. 7). Tumor giant cells with bizarre nuclei were also noted. Relatively well-differentiated osteoblasts with oval cell shape and eccentric atypical nuclei were seen (Fig. 7, inset). Alkaline phosphatase was strongly demonstrated in these cells (Fig. 7, inset). No osteoid-like material was present.
6. Diagrammatic patterns of the frequency of nuclear numbers in osteoclast-like giant cells

As shown in Fig. 8, the patterns among the giant cell lesions studied in the present study differed to some extent.

Multinucleated giant cells in giant cell tumor showed wide variations in the nuclear numbers. Cells with less than 10 nuclei were much more frequent in non-ossifying fibroma.

In chondroblastoma, 1-9 and 10-19 nuclei were relatively frequent in comparison to giant cell tumor. The pattern in osteoblastoma and chondroblastoma was rather similar. In giant cell-rich osteosarcoma, the numbers of nuclei showed rather wide distributions.

Discussion

Osteoclast-like giant cells are often seen not only in many neoplastic (either benign or malignant) but also in non-neoplastic bone lesions. Therefore, differential diagnosis among these is always necessary in both histological and cytologic examinations. The diagnostic value of aspiration cytology and open biopsy cytology in bone lesions has been reported5,6,7). Since tissue diagnosis by fine needle biopsy of bone lesions appears useful as has been emphasized5,6,8), simultaneously obtained cytologic materials can be expected to give valuable information on many occasions.

Attention should be paid to both osteoclast-like
giant cells and cells other than these. Cells other than multinucleated giant cells in giant cell tumor, non-ossifying fibroma, chondroblastoma and osteoblastoma all show fairly characteristic cytologic features as shown in the present study. However, prior to cytologic interpretation material, clinical data, especially the patient’s age, location and radiological features, should always be reviewed to enhance accuracy. Immunohistochemical examination of smear preparations is also useful when antisera with relative specificity can be obtained. S-100 protein can be constantly demonstrated in cells of a cartilaginous nature, but never in osteoblasts or fibroblastic cells. Staining for alkaline phosphatase is usually positive in osteoblasts, but negative in fibroblasts. Factor XIIIa was strongly demonstrated in stromal cells of giant cell tumor and spindle cells of non-ossifying fibroma.

While the histogram patterns of nuclear numbers of multinucleated giant cells cannot be used for definitive diagnosis of a specific lesion, the different patterns can provide valuable information.

Acknowledgement
The authors wish to thank Mr. J.P. Barron, Associate Professor, St. Marianna University School of Medicine for his review of the English manuscript.

Summary
Cytologic studies of giant cell lesions of the bone containing varying degrees of osteoclast-like giant cells were carried out in order to clarify differential diagnostic characteristics. The lesions included giant cell tumor (2 cases), chondroblastoma (3), non-ossifying fibroma (2), osteoblastoma (1), and giant cell-rich osteosarcoma (2). Needle aspiration materials or smear preparations of open biopsy were stained with Pap. stain, and some with Giemsa and PAS stains. Immunohistochemical stain by the avidin-biotin-peroxidase complex method (ABC method) was also performed with antisera of S-100 protein, blood coagulation factor XIIIa and alkaline phosphatase. Tumor cells other than multinucleated giant cells, such as stromal cells in giant cell tumor, chondroblasts in chondroblastoma, osteoblasts in osteoblastoma were stressed as cytologic characteristics. S-100 protein for cartilage cells, alkaline phosphatase for osteoblasts and factor XIIIa for fibroblastic cells were also helpful. Diagrams of numbers and the frequency of nuclei in multinucleated giant cells revealed some differences among these tumors.

References
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