A Case of Osteosarcoma Diagnosed Cytologically

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Introduction

Up to the present, there has been a few work made concerning cytological diagnosis in the field of orthopedics. Recently, we have had a young girl with swelling of the lower thigh; preoperative differential diagnosis as to inflammation or tumor came to the paramount importance because operative procedures would be different depending on its nature. In this regards, we applied cytological technique by aspirating fluid from the local and by analyzing cellular details, and the diagnosis of osteosarcoma was established. We would like to emphasize the usefulness, importance and feasibility of cytological investigations, whenever necessary, on orthopedic patients as daily practice.

Case Presentation

This is a 19-year-old girl complaining of pain at the right thigh. Around February of this year, she started pain especially by bending the right knee joint; pain became particularly severe while sleeping at night and often has woken her up. Soon afterwards gait disturbance appeared with mild fever up to 37.5°C. The patient consulted a local orthopedist and was referred to the Department of Orthopedics, Okayama University Hospital, on the 13th May.

As to the local findings, a distal one third of the right thigh was swollen moderately with slight local heat and tenderness, although movement of the right knee joint was actually not limited. X-ray picture, at the distal metaphysis of the right femur, revealed rather diffuse radiolucency with periosteal thickening, showing a slight tendency to be "onionpeeled" by careful examination (Fig. 1). Neither, however, bone destruction nor fine spiculation and Codman’s triangle was present as we often see in osteosarcoma. Laboratory examinations were not so much contributory except for a few abnormalities: white cell differentials consisted of 10% stab and 61% segmented neutrophils against 27% lymphocytes and 2% monocytes in 7,700 of white blood cell co-

Fig. 1 A radiogram showing diffuse radiolucency with periosteal thickening at the distal metaphysis of the right femur.
Fig. 2 A close-up view of approximately one half of the amputated right femur, showing a cortical thickening (arrow) and replaced bone marrow by tumor growth.

blood sedimentation rate was 22 half an hour, 37 one hour and 77 two hours; and alkaline phosphatase was 4.7 Bessey-Lowry units (normal: 0.8-2.8). Since radiogram did not indicate a definite sign of osteosarcoma in spite of rather elevated alkaline phosphatase, another possibility to be osteomyelitis was highly suspected. Therefore, 3 days prior to operation, aspiration was attempted at the lateral site of a lower one third of the right thigh, about 5-6 cc bloody aspirate was obtained, and the diagnosis to be osteosarcoma was made according to its cytological nature as described below. On 28th May, i.e., the 15th hospital day, a “short-stump and above-knee amputation” was performed by excising 28 cm in length of the distal part of the right femur (Fig. 2).

Cytologically, by May-Grünwald-Giemsa staining, there are small mononuclear and large multinuclear cell clumps seen scattered against the background consisting of red blood cells. Their cell size ranges somewhere between 5-20 times as large as that of neutrophils. Cytoplasm is very basophilic due to rich ribonucleic acid. Numerous mitoses are also present among the cell clumps (Fig. 3). Their cellular details can be much better demonstrated with Papanicolaou staining than with May-Grünwald-Giemsa. In general, nucleus is oval in shape and shows rather thickened nuclear envelope with a coarse chromatin pattern and one to several, irregular-shaped nucleoli. Cytoplasm appears to be somewhat thick and grassy with rather distinct cytoplasmic membrane (Fig. 4). Coarse, PAS-positive granules are also well shown especially along the cell membrane surface (Fig. 5). These cellular details correspond well with histological features in conventional osteosarcoma1). And, these mono- and multi-nucleated cells can be interpreted as malignant osteoblasts. Therefore, these PAS-positive granules might be
believed to represent precursors of the bone matrix\(^2\).

Histologically, a surgically-excised bone tumor shows typical new-osteoid formation along the original bone cortex as well as inside the tumor itself (Fig. 6). The osteoblasts above described are associated closely to the newly-formed osteoid (Fig. 7). Directly-touched smears obtained from postoperative tumor and stained likewise with Panicolaou, May-Grünwald-Giemsa and PAS stainings reveal also very identical characteristics to features out of preoperative, aspirated material.

**Discussion**

In unusual cases, radiograph of osteosarcoma may mimic a benign lesion\(^1\). Likewise, roentgenogram of osteomyelitis may sometimes indicate a possibility of an osteosarcoma, when one sees cortical thickening with reparative new-bone formation in the medullary cavity\(^3\). Although elevated alkaline phosphatase and hot area in \(^99\)Tc-pyrophosphate bone scintiscan can be almost a definite indication to be of a bone tumor rather than inflammation, the most superior preoperative diagnosis could be made either by biopsy or aspiration cytology. Obviously, a careless, preoperative bone biopsy may cause a remote metastasis, if this is a malignant lesion.

In spite of these facts, unfortunately, not so much work has been done up to the present. Kitagawa et al.\(^4\) and Yamada\(^5\) have described some aspects of exfoliative as well as directly-smeared cytologies in osteosarcoma, although these work are apparently not performed for the sake of preoperative diagnosis. Meisels and Berebi-chez\(^6\) have confirmed 3 cases with osteosarcoma by aspirated fluid from the shoulder, knee and, ankle and foot, respectively. Koss\(^7\) states a usefulness of acid and alkaline phosphatase stainings for metastatic prostate cancer or metastatic osteosarcoma. The approach for making diagnosis in various orthopedic diseases can be extended further by performing exfoliative cytology of synovial fluid\(^8\). In the orthopedic field, like in gynecologic, respiratory or urinary systems, we would like to put stress on an importance of cytological studies by staining the materials with various

Fig. 5 Coarse, PAS-positive, intracytoplasmic granules in osteoblasts, seen particularly along the cell membrane surface (arrows). Periodic acid Schiff, × 400.

Fig. 6 Typical newly-formed osteoid along the original bone cortex (OB). Hematoxylin & eosin, ×100.

Fig. 7 A close-up view of the Fig. 6., showing numerous osteoblasts closely associating with new osteoid and one normal-appearing osteoclast (arrow). Hematoxylin & eosin, ×400.
staining methods and also by selecting various possible sites for aspiration.

Summary

We have presented a case of osteosarcoma that was diagnosed preoperatively using cytological technique. This is a 19-year-old girl complaining of pain at the right thigh; a distal one third of the right thigh was swollen with local heat and tenderness. Roentgenogram, at the distal metaphysis of the right femur, revealed diffuse radiolucency with periosteal thickening; this is not particularly pathognomonic for osteosarcoma, and another possibility of osteomyelitis was highly suspected. Therefore, prior to operation, aspiration from the local was attempted. Cytologically, small mononuclear and large multinuclear cell clumps were noticed, their cell size being ranged almost 5-20 times as large as that of neutrophils. Numerous mitoses were also seen. The cellular details corresponded well with histological features in osteosarcoma, and these cells can be interpreted as malignant osteoblasts. According to the diagnosis above established, on the 15th hospital day, the right femoral amputation was made, and our preliminary diagnosis was confirmed postoperatively by histology on the excised tumor. We would like to emphasize the usefulness, importance and feasibility of cytological investigations, whenever necessary, on orthopedic patients as daily practice.

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References