Clear-Cell Chondrosarcoma

— A Case Report —

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Clear-cell chondrosarcoma, a recently specified entity, is a low-grade malignant tumor and has characteristic clinical, roentgenographic and pathologic findings which separate it from conventional chondrosarcoma and other benign tumors. Therefore, correct diagnosis is important from the viewpoint of both prognosis and therapeutic approach.

We report a case of typical recurrent clear-cell chondrosarcoma. Typical round cells with clear cytoplasm, large nuclei, and small nucleoli were well noted. The clear cytoplasm was faintly positive in PAS staining. Electronmicroscopic study showed that these cells were of chondroid origin, showing indented nuclei, large dilated endoplasmic reticulum cisternae, bundles of actin-like filaments and a few glycogen particles.

Key Words: Chondrosarcoma, Clear cell, Bone tumor

INTRODUCTION

Clear-cell chondrosarcoma of the bone, a low-grade malignant tumor, frequently presents diagnostic difficulties. Its clinical, roentgenographic and pathologic characteristics separate it from conventional chondrosarcoma and, more importantly, from several benign bone tumors with which it is often confused. Several recent articles have confirmed the specificity of this disease (Bjornsson et al., 1984; Unni et al., 1976).

We recently had the opportunity to examine one case of typical recurrent clear-cell chondrosarcoma at both light and electron-microscopic levels. We report it here in view of the paucity of available morphologic and fine structural information about this tumor and the considerable clinical importance of correct diagnosis in view points of both prognosis and therapeutic approach.

CASE REPORT

One 47-year-old woman developed left hip pain after she fell on the floor. She also had a history of sustaining a subcapital fracture 6 years before, for which no treatment was given. Physical examination revealed a swelling in left hip with tenderness. X-rays showed an intertrochanteric fracture with nonunion of subcapital fracture. No definite lesion suggesting tumor was noted. At that time, total hip replacement arthroplasty was performed. Diagnosis of clear cell chondrosarcoma was made by histology. However, no further treatment was given. Five years later, November, 1987, swelling around the left hip joint re-developed. It aggravated hip pain, and limping was also associated. X-rays taken on April 20, 1988, revealed an expansile osteolytic lesion in left proximal femur. To confirm tumor recurrence, an open biopsy and subsequent wide resection of tumor and prosthesis insertion were performed. Her postoperative course was uneventful, but she dropped-out from our follow-up.

PATHOLOGIC EXAMINATION

The resected femur head showed a solid yellowish-

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Fig. 1. Cut surface of tumor (left: previous femur head, right: recurrent tumor) revealing solid yellow-white tumor replacing the normal marrow. Multiple cystic areas containing serosanguineous fluid with typical cartilaginous portions are noted.

white tumor completely replacing the normal marrow (Fig. 1, left). Multiple cystic areas contained serosanguineous fluid. Articular cartilage showed irregular pitting and thinning, but definite cortical destruction was not noted. Focal areas of typical cartilaginous portion were scattered throughout the lesion.

The nature of the recurrent tumor was basically the same as that of the previous one (Fig. 1, right). But invasion of tumor into the surrounding soft tissue was seen, and cystic change was more prominent. Focal calcification was also noted. Little necrosis was noted in both tumors.

Fig. 2. Specimen X-ray showing ballooned osteolytic bony lesion without definite calcification.

MICROSCOPIC EXAMINATION

The findings of the first and recurrent tumor were basically the same in nature. Most areas appeared quite cellular, the most common elements being round cells with clear cytoplasm and large nuclei with

Fig. 3. Microscopic finding of round cells with clear cytoplasm and large nuclei with little matrix interposition. Focal areas of calcification are also noted.

Fig. 4. High-power view of a clear cell.

loosely arranged chromatin and small nucleoli. Little matrix was interposed between these cells (Fig.3,4). In some areas, cells were placed in a typical

Fig. 5. Microscopic finding of cystic space mimicking that of aneurysmal bone cyst.

Fig. 6. Electronmicrograph of a clear cell. The cytoplasm is irregularly outlined and contains well-developed Golgi apparatus and endoplasmic reticulum. Multiple glycogen particles are also noted (Lead citrate-Uranyl acetate $\times 5600$).

Fig. 7. Electronmicrograph of the tumor showing bundles of filaments around the nuclei (Lead citrate-Uranyl acetate $\times 28000$).

Fig. 8. Electronmicrograph showing matrix calcification (Lead citrate-Uranyl acetate $\times 22400$).

chondroid-like matrix. They were mostly mononucleate and showed little or no atypia. Focal calcification was noted, and some areas of osteoid-like material deposit were also found. Multinucleate giant cells were scattered throughout the tumor. Mitoses were extremely rare. The clear cells were faintly positive in some areas with PAS staining. The cystic spaces were outlined by some tumor cells and a small amount of fibrinous tissue mimicking an aneurysmal bone cyst (Fig. 5).

ELECTRONMICROSCOPIC EXAMINATION

The characteristic clear cells, when examined by electron microscopy, had an ample irregularly-outlined cytoplasm in which multiple glycogen particles were noted. A few ballooned mitochondria and well developed Golgi apparatus, along with endoplasmic reticuli were noted. The nuclei in these cells had frequent indentations, and the chromatin was finely dispersed. The nucleoli were prominent (Fig. 6). Another frequent finding was the presence of bundles of filaments, measuring 20 to 30 nm thick which were usually around the nuclei (Fig. 7). Other cells had more indented nuclei and more prominent nucleoli. Intracytoplasmic organelles varied in amount. Cells in various stages between these two cell populations were noted. Patchy areas containing dense aggregates of mineral crystals were visible. Some of this calcified material appeared to be related to large, round, electron-dense structures (Fig. 8).

DISCUSSION

Clear-cell chondrosarcoma is a little-studied tumor, having been recognized only recently as a pathologic

entity (Bjornsson *et al.*, 1984; Unni *et al.*, 1976). Correct diagnosis is very important because these tumors have a more malignant behavior than the conventional chondroblastoma, with which they share several histologic characteristics. Therefore they require more aggressive therapy. Clear-cell chondrosarcoma has several obvious similarities to chondroblastoma, such as the presence of well-differentiated cartilage tissue and multinucleate giant cells. Their location in the secondary centers of ossification and their benign roentgenographic appearance are also characteristics of both lesions. The rarity of atypias and of mitoses explains why in the past these tumors have frequently been misdiagnosed as chondroblastoma. However, the characteristic findings of clear-cell, which are thought to represent areas of well-differentiated chondrosarcoma, separate it from chondroblastoma as a different entity (Unni *et al.*, 1976). Electron-microscopy was useful in understanding the nature of clear cells in this tumor (Erlandson *et al.*, 1974; Faraggiana *et al.*, 1981). Most of these cells showed very irregularly-shaped nuclei with indentations, large dilated endoplasmic reticulum cisternae, bundles of actin-like filaments, and a few glycogen particles. In fact, dilated rough endoplasmic cisternae, the presence of filaments and glycogen, and irregular nuclear outlines have been described as very common or typical of cartilage cells in various phases of development and aging and in different chondroid tumors (Johannessen, 1981).

In our case, the cell population covered the whole spectrum of the different stages of chondrocyte development. This suggests that several stages of differentiation are expressed in this tumor. This is in keeping with the well-known pleomorphism of many of the cartilage tumors. However, some fully-differentiated cells can be identified as typical chondrocytes, while embedded in a matrix that is most similar to the matrix of mature cartilage. Such cells are PAS-positive. These findings are never observed in

chondroblastoma and help to rule out it.

Secondary structures, such as aneurysmal bone cyst-like changes and heavy osteoid deposits are common in clear-cell chondrosarcoma and are frequent sources of confusion and misdiagnosis (Bjornsson *et al.*, 1984).

Multinucleated giant cells were invariably present. In our experience, benign giant cells were not seen in association with conventional chondrosarcomas. Whether these giant cells are an integral part of the tumor or whether they are reactive is not clear. But the latter possibility seems more likely, because the nuclei of the giant cells do not resemble those of the clear cells (Unni *et al.*, 1976).

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