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Cytogenetic findings in clear cell chondrosarcoma

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Abstract Clear cell chondrosarcoma is a rare cartilaginous tumor of low-grade malignancy that most often arises in the epiphysis of long bones in the third and fourth decades of life. Cytogenetic studies of clear cell chondrosarcoma are few. In this study, the cytogenetic findings of 4 cases of clear cell chondrosarcoma are presented. Clonal chromosomal abnormalities were detected in 3 cases. A tumor specific anomaly was not identified, however, extra copies of chromosome 20 and loss or rearrangements of 9p appear to be recurrent.

1. Introduction

Clear cell chondrosarcoma, first described by Unni et al. in 1976 [1], is a rare cartilaginous tumor of low-grade malignancy with a preference for the epiphysis of long bones. Males are affected 3 times more commonly than females, with a peak incidence in the third and fourth decades of life. Symptoms are nonspecific, usually long standing, and many times referred to the adjacent joint. Radiographically, clear cell chondrosarcoma appears as a well-defined, osteolytic lesion with a distinct sclerotic border.

Clear cell chondrosarcoma may be diagnostically confused with chondroblastoma, giant cell tumor, or even osteosarcoma because of its preference for the epiphysis of long bones and the presence of lace-like or irregular osteoid with osteoblastic and osteoclastic rimming in small biopsy specimens [2–4]. Distinguishing between clear cell chondrosarcoma and other bone tumors is clinically important because treatment and prognosis differ. Recognition of a new diagnostic marker such as a tumor-specific chromosomal anomaly could be beneficial in this regard. Unfortunately, cytogenetic studies of clear cell chondrosarcoma are limited [5–8]. In this study, the cytogenetic findings of 4 clear cell chondrosarcomas and a review of the literature are presented.

2. Materials and methods

The clinicopathologic data of each case is summarized in Table 1. All 4 cases were histologically characterized according to established criteria [9] (Fig. 1).

Cytogenetic analysis was performed on sterile, representative tissue of each case utilizing standard culture and harvest procedures as described previously [10]. In brief, the tissue was disaggregated mechanically and enzymatically and cultured in RPMI 1640 media supplemented with 20% fetal bovine serum for 3 to 7days. Cells were exposed overnight to Colcemid (0.02 μg/mL). After subsequent hypotonic treatment (0.7% sodium citrate for 20 minutes), the preparations were fixed 3 times with methanol and glacial acetic acid (3:1). Metaphase cells were banded with Giemsa trypsin and the karyotypes described according to the International System for Human Cytogenetic Nomenclature (ISCN 1995) [11].

3. Results

Karyotypically abnormal clones were identified in 3 of the 4 clear cell chondrosarcomas examined (Table 1). Two cases exhibited diploid or near-diploid clones. The remaining abnormal case was near triploid. Abnormalities of chromosome 9 (Fig. 2) and gain of chromosome 20 represented shared anomalies.

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Table 1
Clear cell chondrosarcoma; clinicopathologic and cytogenetic data

Case	Age/sex	Location (size in cm)	Source of sample	Surgical procedure	Karyotype	Reference
1	41/M	Distal femur (7.0 × 9.0 × 11.0)	P	Resection	46,XY,der(7)t(7;9)(q11.2;p13),der(9)del(9)(p13)t(7;9)(q11.2;q32)[8]/46,XY[12]	Present
2	47/M	Proximal humerus (6.4)	P	Resection	48,XY,+X,+20[2]/47,XY,+X[1]/37,XY,+X,−5,−6,−7,−8,−9,−10,−10,−15,−16,−18,−19,+20[1]/46,XY[16]	Present
3	30/M	Proximal femur (4.5 × 4.8 × 8.0)	P	Resection	46,XY[31]	Present
4	49/M	Proximal humerus (7.0)	P	Resection	58,XYY,−1,−3,−4,+5,−6,+7,−8,−9,−10,−11,−12,?add(12)(q?),−13,−14,−15,−16,−17,+20[6]	Present
5	25/F	Paravertebral area (5.5 × 6.0 × 6.5)	P	Resection	30,X,+5,+7,+12,+19,+20,+21,+22[18]/58~60,XX,+5,+7,+7,+12,+12,+12,+19,+19,+20,+20,+21,+21,+22,+22[6]/46,XX[13]	[5]
6	45/M	Proximal humerus (8.9)	P	Biopsy	44,XY,i(1)(q10),del(6)(q23q24),−8,der(9)t(8;9)(q13;p21),der(10p),der(12)t(1;12)(p22;p12),add(15p),−18[cp13]/46,XY[2]	[6]
7	51/M	Pelvis (10.0)	R	Curettage	45,X,−Y[4]/46,XY[16]	[7]
8	39/F	Humerus (NA)	NA	NA	46,XX,del(2)(q11~12q21)[8]/46,XX[17]	[8]

Abbreviations: F, female; M, male, NA, not available, P, primary, R, recurrence.

4. Discussion

Clear cell chondrosarcoma is histologically characterized by clear cells with round, large, centrally located nuclei and distinct cytoplasmic boundaries arranged in a lobular growth pattern. Multinucleated osteoclast-like giant cells are often present at the periphery of the lobules. Other types of bone tumors such as chondroblastoma, osteoblastoma, conventional chondrosarcoma, and even osteosarcoma may present differential diagnostic problems with clear cell chondrosarcoma because of overlapping radiographic and/or histopathologic features [1,12]. Due to the rarity of clear cell chondrosarcoma, it has not yet been determined if this entity might be characterized by a specific chromosomal anomaly that could be useful diagnostically.

To date, a total of 8 cases of clear cell chondrosarcoma have been subjected to cytogenetic analysis (including the 4 current cases, Table 1). Seven cases are karyotypically abnormal with most exhibiting a diploid or near-diploid complement (Note, loss of the Y chromosome as the sole

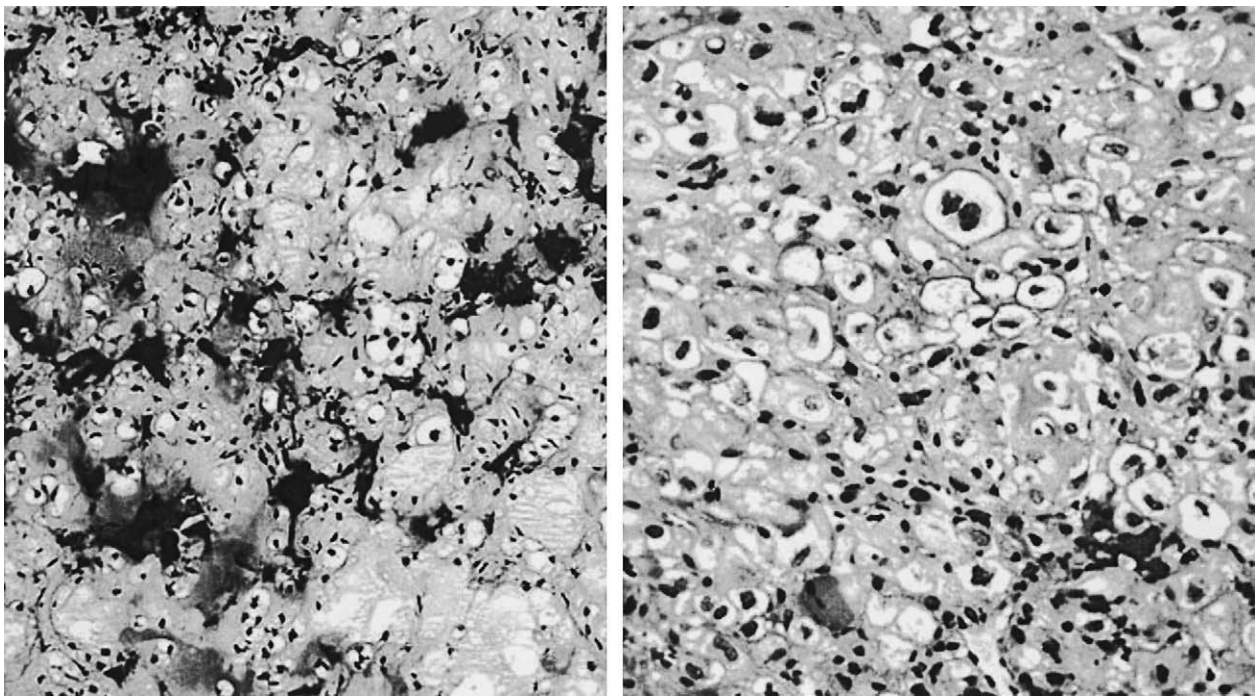

Fig. 1. Representative photomicrographs of cases 1 and 3 (left and right, respectively) illustrate the typical histologic appearance of clear cell chondrosarcoma. Loosely arranged clear cells are embedded among focal woven bone trabeculae (left) and a proliferation of clear cells with relatively uniform, centrally located nuclei are interspersed with occasional osteoclast-like giant cells (right).