



# Clear Cell Chondrosarcoma Diagnosed by Fine Needle Aspiration: A Case Report with Brief Review of the Literature

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## Abstract

Clear cell chondrosarcoma (CCC) is a rare neoplasm. Reported here, is a case of a female patient with a history of marginal zone lymphoma of the thyroid presented with right hip pain. Magnetic resonance imaging (MRI) of the right hip revealed an abnormal signal, which subsequently was biopsied via fine-needle aspiration (FNA). The cellblock preparation from the cytology sample was further analyzed which revealed atypical chondroid cells with vacuolated cytoplasm, eccentric nuclei, and prominent nucleoli. The cellblock material showed fragments of nonmalignant bone and malignant chondroid cells with enlarged nuclei and prominent nucleoli in a background of multinucleated giant cells. Immunohistochemistry studies performed on cellblock cytology material ruled out other differentials such as malignant melanoma or metastatic epithelial tumor. These findings were consistent with the diagnosis of malignant cartilaginous tumor with features of CCC. Eventually the patient underwent surgical resection revealing a 5.0 x 4.0 – cm, white, cartilaginous mass with scattered fleshy areas involving the greater trochanter and extending into the intertrochanteric area. Histomorphologic features, together with immunohistochemistry (IHC) studies, confirmed the initial diagnosis of CCC made via cytology sample. Our case highlights how cytology material alone can be sufficient to provide a definitive diagnosis of CCC.

**Keywords:** Clear cell; Chondrosarcoma; Cytology; Immunohistochemistry; Fine-needle aspiration

## Abbreviations

CCC: Clear Cell Chondrosarcoma; MRI: Magnetic Resonance Imaging; FNA: Fine Needle Aspiration; IHC: Immunohistochemistry

## Introduction

Cytopathology focuses on the ability to make a diagnosis by looking at a smear of cells on slides. Diagnosis of tumors utilizing cytology sampling was first recognized in the 18<sup>th</sup> century and further progressed and became a standardized subspecialty of pathology in the late 20<sup>th</sup> century. It is important to distinguish between tissue biopsy and cytological studies, which may include; exfoliative cytology such as body fluids, cytology smears such as Pap testing studies, and FNA among others. FNA is performed to obtain cellular material in the needle tract. FNA studies cells instead of tissues with minimal equipment, with minimal or no risk for the patient, and is more cost effective than tissue biopsy.

However, until recently, cytological studies were not as widely used as tissue biopsy studies [1].

Chondrosarcomas are the third most common malignant bone tumor after the osteosarcoma and Ewing sarcoma [2]. Clear cell chondrosarcoma (CCC) is a rare subtype of chondrosarcomas usually involving the epiphysis of long bones in young and middle-aged adults.

Clear cell chondrosarcoma (CCC) is a rare neoplasm usually involving the epiphysis of long bones in young and middle-aged adults [3]. The humerus and femur are the most common sites of CCC, which presents with a low-grade clinical course with late metastatic characteristic to the lungs and skeletal system. [4]. It comprises 2% of all chondroid lesions and is predominantly found in males at a frequency of 3:1 male to female ratio and most patients are between the ages of 25 to 50. The literature shows that marginal excision or curettage is associated with a recurrence rate of 70% of higher [5]. Our case focuses on the idea of cytology alone being sufficient for diagnosis of CCC. FNA of the right femur revealed numerous atypical chondroid cells with vacuolated cytoplasm, eccentric nuclei, and prominent nucleoli. The cellblock material prepared from the FNA sampling showed abundant fragments of bone, along with numerous areas of malignant chondroid cells with enlarged nuclei, and prominent nucleoli, in a background of multinucleated giant cells. The scarcity of CCC makes it diagnostically challenging, and even more challenging in cytology sampling.

## Case Presentation

We report a case of a 47-year-old woman with a history of marginal zone lymphoma of the thyroid, who presented with right hip pain. The patient had no other significant medical history or known risk factors for malignancy. Magnetic resonance imaging

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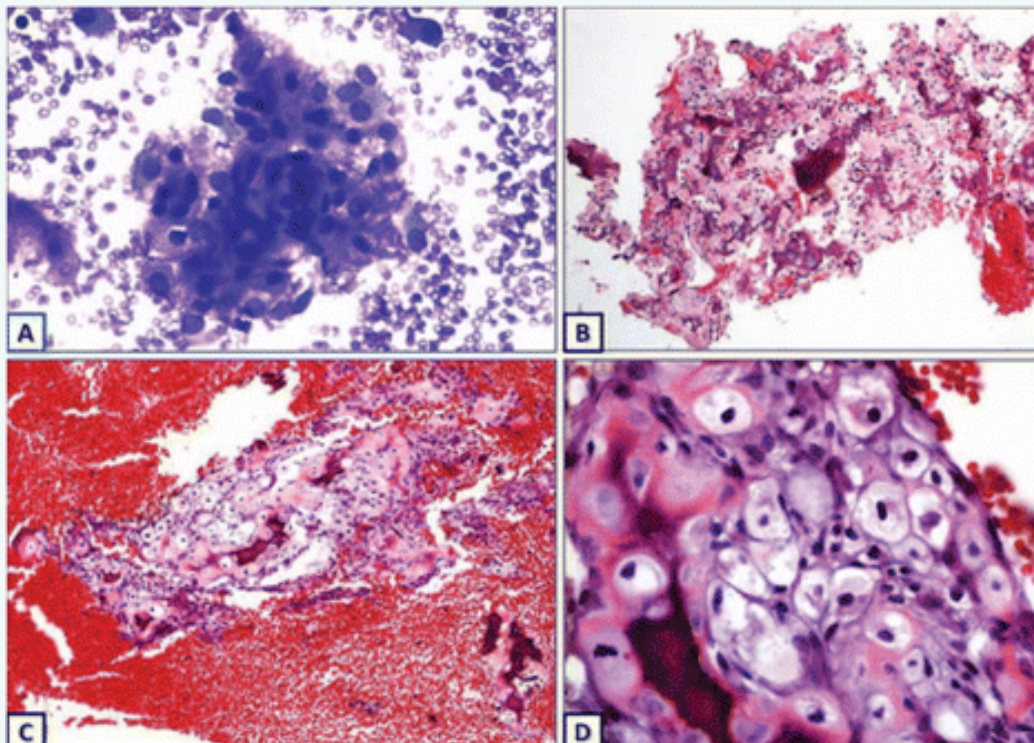


of the right hip showed an abnormal signal within the greater trochanter and intertrochanteric area of right femur. The patient subsequently underwent a fine-needle aspiration biopsy of the right femur, and the obtained sample was sufficient to produce a good cellblock for further diagnostic studies. Cytology slides revealed numerous atypical chondroid cells with vacuolated cytoplasm, eccentric nuclei, and prominent nucleoli (Figure 1, A). The cellblock material showed abundant fragments of bone, along with numerous areas of malignant chondroid cells with enlarged nuclei, and prominent nucleoli, in a background of multinucleated giant cells. No malignant bone was identified in the cytology sample. All identified osteoid material was reactive bone formation ruling out osteosarcoma (Figure 1, B through D). Minimal or no mitosis were identified, and no myxoid cellular stroma were identified. The chondrosarcoma was diagnosed as low-grade, grade 1 of 3. Immunohistochemistry studies showed that the malignant cells were positive only for S-100, but negative for all other melanocytic markers (HMB-45 and Melan-A), ruling out other possible malignant melanoma. Possible metastatic epithelial tumor was also ruled out as the tumor cells were negative for Pan Cytokeratin (CAM5.2, AE1/AE3, CK7, CK8, CK18, CK20, and epithelial membrane antigen were all negative). Leukocyte common antigen (LCA) was also negative in support of non-lymphoid origin of the tumor.

These cytomorphologic features, together with the pattern of immunocytochemistry studied were consistent with the diagnosis of malignant cartilaginous tumor with features of CCC. No evidence of metastatic lesions were found in any part of the body. Subsequently, the patient underwent surgical resection of the lesion, revealing a 5.0 × 4.0-cm, white tan cartilaginous mass with scattered fleshy areas involving the greater trochanter and intertrochanteric area of right femur. Histologically, the lesion consisted of sheets of large epithelioid-like cells with abundant clear cytoplasm, large round nuclei, and prominent nucleoli, admixed with osteoclast-like giant cells in background of cartilaginous matrix. The background also showed scattered areas of conventional low-grade chondrosarcoma as well as areas of reactive non-malignant osseous formation. The surgical margins were free of chondrosarcoma and surgical resection was not followed with any other therapeutic modality such as chemotherapy, radiation, or cryosurgery. The surgical excision histomorphologic findings confirmed the initial diagnosis of low-grade CCC made on cytology sample preoperatively. The patient was free of recurrence or metastasis for five years, after which she was lost to follow up as she moved to her home country.

## Discussion

Clear cell chondrosarcoma is known to be a low-grade



**Figure 1** Cytologic analysis of Clear Cell Chondrosarcoma.

(A) - Large atypical cells with clear cytoplasm eccentric nuclei, and prominent nucleoli in background of chondroid matrix (DQ stain X100)

(B) & (C) The background also contain fragmented spicules of reactive bone formation and reactive osseous material (H&E stain X40 and X20 respectively)

(D) - Sheets of low-grade chondroid cells, many with clear cytoplasm in background of chondroid matrix and reactive osseous material (H&E stain X100)



malignant tumour. Recent reports indicate that only about 200 cases with clinical data have been reported in the literature. Only rare reports described the diagnosis of CCC by cytology sampling [6]. The case presented here highlights that cytology material alone can be sufficient to provide a diagnosis of CCC. Our report, to our knowledge, adds to the limited existing literature on cytologic diagnosis of CCC. Until recently, diagnoses via cytology were not as well practiced as tissue biopsies, however as proven in our case, cytology sampling is sufficient to provide a definitive diagnosis of CCC. Besides the cytologic features of clear cell chondrosarcoma described in our case, other reports described additional cytology features such as uniform spindle-epithelioid and histiocytoid cells with rare giant cells [3]. Jiang et al., also described plasmacytoid cells with foamy cytoplasm and chondroid type extracellular matrix [6]. Cytology sampling proved to be diagnostic for other tumors with clear cell features, such as ovarian clear cell carcinoma. The clear cell cytomorphology of these tumors can be challenging with the main differential diagnosis of metastatic malignant melanoma and other metastatic malignancy such as carcinoma or lymphoma. Immunohistochemistry studies are essential in ruling out such possibilities. The immunohistochemical expression profiles of cytokeratins (CAM5.2, AE1/AE3, CK7, CK8, CK18, and CK20), and epithelial membrane antigen were utilized, and were all-negative in our case. Suguru Matsuura et al. [7], reported epithelial marker studies in five cases of clear cell chondrosarcoma. Of the 5 cases of clear cell chondrosarcoma, 3 demonstrated positive staining for AE1/AE3 and some form of cytokeratin in the clear cell component. Although our case was positive for S-100, which is known to be positive in cartilaginous tumors, the negative reaction to other melanocytic markers HMB-45 and Melan-A ruled out possible malignant melanoma. In addition, the negative lymphoid marker LCA was useful in ruling out possible lymphoma.

Clear cell chondrosarcoma comprises 2% of all chondroid lesions, initially with minimal clinical symptoms, but can later presents with unusually very late metastasis. Based on available data, if symptoms are present, CCC most commonly presents with pain for months to years at the site of the lesion. Rarely, pathological fractures may be seen in this type of tumors. Histologically, and cytologically, CCC may also resemble chondroblastoma, thus multiple FNA passes to sample a heterogenous areas within the lesion is very critical to avoid misdiagnosis, especially since CCC is malignant in nature, whereas chondroblastoma is benign. The classical histomorphologic and cytomorphologic features of Chondroblastoma are well described and the distinction between the two entities is not challenging as long as the representative sections are fully representative of the tumor. A definitive diagnosis may be made by recognizing the characteristic "clear cell" appearance of the clear cell chondrosarcoma on cell block. CCC tends to affect males more than females and tends to arise at the epimetaphyseal region of long bones, especially the femur and humeral head [6,8].

Although our patient was free of recurrence or metastasis for five years, low-grade chondrosarcoma should undergo close follow up to watch for possible late metastasis. Minna Laitinen

et al reported an unusual case of clear cell chondrosarcoma with very late recurrence and lung metastases, 29 years after the primary surgery [4].

It is important to closely follow clear cell chondrosarcoma patients for decades or possibly for life, as the malignancy tends to metastasize or recur after an extended period of time. The course of metastasized disease may be unusually slow, thus relatively aggressive treatment in metastasized and recurring cases is justified [4].

Cytology sampling alone can provide a definitive diagnosis of clear cell chondrosarcoma. There are very few reports of FNAC diagnosis of clear cell chondrosarcoma and other variants such as mesenchymal, and de-differentiated types as they are very rarely found [9]. The marriage of cytology and radiology has allowed for minimally invasive, safe, accurate, and cost-effective diagnosis of suspicious masses, previously accessible only by surgical biopsy techniques. As a result, cytologists are increasingly called upon to diagnose disease in specimens procured under image guidance for different organs. Rather than causing delay, cytology facilitates timely diagnosis and management and is an integral part of a multimodal approach to various tumor diagnoses [10]. On-site cytology interpretation increases the diagnostic yield of the procedure by allowing for additional needle passes as necessary [11]. The process culminates in a multidisciplinary conference such as tumor board where the results of clinical, radiologic, cytologic, and laboratory evaluations are discussed, and a treatment is planned [12,13]. In our case, the definitive diagnosis of CCC was solely established utilizing cytology sampling including cellblock preparations. It is our hope that reporting this case will add to the growing knowledge of the cytologic criteria for diagnosis of clear cell chondrosarcoma and avoid diagnostic errors, and that continued investigation drives further development of efficacious diagnostic criteria for improving patient outcomes by providing the optimal management of the tumor.

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