CLEAR CELL CHONDROSARCOMA - A REPORT OF 2 CASES

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ABSTRACT

Clear cell chondrosarcoma is a form of chondrosarcoma that was first described by Unni in 1976. It is essentially a low-grade chondrosarcoma with many similar clinical, radiological and histological features as the more common chondrosarcomas. However, the distinguishing feature of this variant is in the presence of the characteristic clear cells histologically.

We relate two such cases of clear cell chondrosarcoma in Singapore. A short discussion covering the incidence/prevalence of this tumour, its common presenting clinical, radiological and histological features follows. We also review the available world literature, highlight the salient and differentiating aspects of this particular tumour, and touch on its management and eventual prognosis.

Keywords: Clear cell chondrosarcoma, management, prognosis

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INTRODUCTION

In 1976, Unni et al described 16 cases of a rare form of chondrosarcoma[1]. They called it 'clear cell chondrosarcoma' because of the characteristic appearance of its constituent cell. Since then, many more cases have been reported in the English language literature[2-7]. Isolated cases have also appeared in French, Czechoslovakian, Russian and Japanese reports. Recent articles have confirmed the specificity of this disease and the supplement of the Armed Forces Institute of Pathology[8] on tumours of the bone and cartilage has acknowledged this entity.

We relate our experience with two cases in Singapore and review up-to-date articles in the English language literature.

METHODS AND MATERIAL

Medical records of the two patients with clear cell chondrosarcoma were reviewed. One patient was seen at the Singapore General Hospital and the other was initially seen at Mount Alvernia Hospital and then referred to Alexandra Hospital. Radiographs and CT scans were examined. Pertinent clinical, radiological and pathological information was obtained. Both patients underwent 'en bloc' resection of the tumour. Both gross and microscopic sections from the lesions showed characteristic pathological features.

CASE REPORTS

Case 1

A 48-year old Chinese male was seen at the Department of Orthopaedic Surgery, Singapore General Hospital in December 1987 with a two year history of intermittent right hip pain spreading to the buttock.

There was a prominent limp on walking. There was no history of trauma, fever or any other joint pains elsewhere. Systemic review was essentially normal and there was no loss of appetite or weight.

On physical examination, the findings were confined to the right hip. Range of movement was full although there was a slight pain on internal rotation. Trendelenburg test was positive for the right hip and the patient walked with an antalgic gait.

Radiographs of the pelvis showed a large osteolytic lesion with speckled areas of calcification in the right superior pubic ramus extending to the symphysis pubis and to the medial acetabular wall laterally. CT scan of the pelvis showed a large mass involving the right pelvic bone extending to and above the acetabulum. Areas of lucency with bone destruction and involvement of the marrow cavity were seen. There was no definite cortical break or lymphatic enlargement. A bone scan done showed increased uptake in the right pelvis, in particular, the right half of the ilium, from the pubic ramus to the anterior superior iliac spine and acetabulum. No additional lesions were found. An intravenous ureterogram done showed indentation of the right lateral wall of the bladder and involvement could not be excluded. A pre-operative diagnosis of chondrosarcoma was made and the biopsy of the lesion showed clear cell chondrosarcoma.

The frozen section report showed a malignant tumour, probably chondroid in nature. The paraffin section showed clear cell chondrosarcoma.

Operation was performed three days later. The tumour was found to be arising from the medial wall of the superior pubic ramus and encroaching upon the medial wall of the acetabulum up to the sciatic notch (Stage IB). A right internal pelvectomy was done. The ilium was divided above the acetabulum and the pubic ramus divided. The head of the femur was osteotomised at the neck of the femur. The shortened femur was then fused to the remaining ilium (Type II Enneking resection)[9]. This resulted in a 6 cm shortening of the right leg.

Gross pathology of the resected specimen showed that the tumour extended from the pubic ramus to above the acetabulum measuring about 10 cm medially to laterally. The tumour had formed a cavity causing thinning and erosion of the pubic bone and articular cartilage of the acetabulum. There was infiltration of the tumour into the soft tissue and muscle. Microscopic sections showed clear cell chondrosarcoma of the pubic bone.

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Post-operatively, the patient was placed on a hip spica that was worn for three months. He was up with non-weight bearing crutches after six weeks. Patient is presently still on follow-up.

Case 2

A 34-year old female Chinese was seen at Mount Alvernia Hospital for a painful left hip of five months' duration. There was no history of trauma, fever or any other complaints. Systemic review was essentially normal. Physical examination of the left hip was normal. X-rays done showed a lytic lesion over the neck of the left femur. Curettage of the lesion followed by bone grafting and pinning of the left femoral neck was done. Histology of the lesions showed a low grade clear cell chondrosarcoma and the decision was made to resect the tumour.

CT scan of the left hip was carried out but unfortunately, the metal pins made it almost impossible to demonstrate the bony abnormalities in any detail.

Bone scan done showed a solitary focus of increased uptake over the left head and neck and trochanteric regions of the femur suggestive of a localised malignant lesion at that site. There was no increased uptake elsewhere. A wide resection of the proximal femur through the previous scar was done. Continuity was restored by using a free vascularised fibular graft arthrodesis. The fibular graft was inserted to fit snugly in the distal femoral canal and proximally in a slot in the acetabulum. An 18 hole broad neutral plate was used to hold the graft. Blood supply was achieved by anastomosing the profunda femoris to the peroneal vessels.

Histology of the resected specimen showed remnant clear cell chondrosarcoma in the head and neck of the femur especially in the medullary zones of the upper shaft and neck with focal erosions of the cortex antero-medially. There was a satellite tumour nodule in the soft tissue on the lateral aspect.

The patient has been followed up for seven months with no signs of tumour recurrence. She is able to weight-bear and the graft is in place.

DISCUSSION

Clear cell chondrosarcoma is a rare tumour[1,3]. It represents only 2-4% of all chondrosarcomas[10] and has only been recently recognised. About 60 odd cases have been reported in the world so far. Enough experience has been accumulated with this disease to outline precisely its clinicopathological profile. By definition, it is a malignancy arising from cartiliginous cells that takes on a pattern in which the chondrocytes are swollen and have a clear colourless cytoplasm[1-3,6,10,11]. The histological features are the basis for its name.

It occurs in men twice as often as in women[1,10]. Of 47 cases studied by Bjornsson and Unni in 1984[2], 34 were males, and 13 females. The age distribution is somewhat unusual for primary tumours of the bone in that the incidence spans the entire range from adulthood through middle and old age[1]. The youngest patient reported so far is 14 years old and the oldest is 84 years old[2]. The third and fourth decades are the commonest age groups at presentation[1,6,10].

The symptoms most often are non-specific[1]. As in these 2 cases, the symptoms that bring the patient to seek medical attention is vague local pain - usually of long duration[1,2,6] and some limitation in the range of motion in the adjacent joint. Most patients (50%) will have symptoms between 1 - 5 years and 15-18% for longer than 5 years[1,2]. Occasionally, the patient may present following trauma, at which time a pathological fracture may be seen. In Unni's paper, 29 cases presented initially with a pathological fracture. In one of his patients, vertebral involvement caused cord compression with resultant neurological deficit[1]. When the lesion occurs in a flat bone, it may cause local expansion and disfigurement.

One of the most common findings was the propensity for the tumour to involve the end of a long bone. The majority of tumours involve the epiphysis[1,2,6]. Extension to the metaphysis is frequent with larger lesions. Only 5% of such tumours arise from the diaphysis or metaphysis. This is in contradistinction to the conventional chondrosarcoma which is usually a metaphyseal-diaphyseal lesion when it occurs in long bones. The preference of clear cell chondrosarcoma for the epiphysis makes it difficult to distinguish it from chondroblastoma, giant cell tumour, epiphyseal osteosarcoma and epiphyseal enchondroma[6,11].

Among the long bones, the proximal end of the femur is the most commonly involved[1,2,10]. This is followed by the proximal end of the humerus and tibia. Other rare sites of presentation include the skull, ischium, maxilla, ulna and the phalanx[1,2]. Multiple tumour sites are not uncommon - the lesion may appear simultaneously in multiple sites in the skeleton or an interval may lapse between the initial lesion and the new ones.

Of 32 long bone tumours available for roentgenographic evaluation in the Bjornsson and Unni study of 1984[2], 30 involved the epiphysis and metaphysis. One tumour involved the metaphysis and diaphysis respectively. Three tumours involved the epiphysis, diaphysis and metaphysis.

The most commonly roentgenographic pattern is that of a purely lucent lesion. Thirteen tumours were lucent but contained areas of calcification within the tumour. The character of calcification is soft and fluffy like that seen in chondroblastoma. Expansion of bone is usually present, although the degree of expansion is variable. The lesion is usually well-defined but larger lesions have ill-defined margins. Endosteal irregularity is not infrequent but periosteal reaction does not occur. In 7 of these cases, the lesion was complicated by a pathological fracture.

The role of the CT scan in bone tumours is mainly for imaging and staging purposes[12]. The CT scan picture of chondroblastoma and chondrosarcoma has been studied by various authors - Hudson & Hawkins (1981), Keney & Gilule (1981), Mayes & Wallance (1981).

However, the CT features of clear cell chondrosarcoma has not been worked out. There is only one report by Kumar et al in Radiology 1985[4], who found that the CT demonstrated the lesion more distinctly than common radiography. Here, 3 separate cases of clear cell chondrosarcoma were studied. He found that it provided more information about the tumour matrix and delineated the lobulated margins of the lesion. In the rare case where there is adjoining soft tissue extension, the CT provides useful additional information. It has not been ascertained whether the CT scan can pick up calcifications not shown on plain radiography; thereby revealing the cartiliginous nature of the neoplasm. Further studies are needed to obtain more information.

Histologically, the clear cell chondrosarcoma has distinctive pictures as reported by Unni et al in 1976[1]. Macroscopically, the glassy and translucent appearance of the typical chondrosarcoma was not usually present. Instead, the lesion tends to be soft and solid although a few cysts may occasionally be seen[1-3,5,6,11,12]. The main tumour cell has a central vesicular nucleus with a strikingly clear cytoplasm and well-defined borders. The nuclei are monomorphic with a few mitotic figures. The clear cells exhibit a lobular pattern seen in most cartiliginous tumours. Benign giant cells, either singly or in small clusters are seen invariably at the periphery of the lobules. These cells are not usually seen in conventional chondrosarcomas. Whether these cells are an integral part of

the tumour or a reactive component is not known. Small or larger areas of conventional chondrosarcoma, typically Broders' grade II are found in 50% of the cases[2]. Their presence confirms that the lesion is malignant and precludes the diagnosis of benign chondroblastoma. Their presence also suggests that they are basically chondrosarcomas with a peculiar tendency to form clear cells. Other secondary structures in microscopic areas mimicking those of other primary lesions of the bone are common and are a frequent source of confusion and misdiagnosis[2], for eg: aneurysmal bone cyst-like, osteosarcoma-like, osteoblastoma-like, chondroblastoma-like and giant cell tumour-like changes.

Trabeculae of bone and osteoid may be present but they do not have features of malignant bone or osteoid.

Faraggiana and Sender[3] have recently done ultrastructural studies of these clear cells using electron microscopy. They found that most of the clear cells show very irregularly shaped nuclei with deep indentation, large dilated rough endoplasmic reticulum, bundles of actin filaments and adundant glycogen. All of these characteristics even if non-specific point to the chondroid nature of these cells. The cells are pleomorphic covering general stages of differentiation. Some cells resemble the early chondroblast, others the mature chondrocytes. The clear cells are the more differentiated chondrocytes with large amounts of glycogen giving the appearance of a clear cytoplasm which is strongly PAS positive. The ultrastructure of the multinucleate giant cell is also of interest. They appear very similar to osteoclasts but because of the rare association with osteoid trabeculae, it is believed they probably represent reactive macrophages. The distinction may be purely academic, as macrophages have been shown by fusion to give rise to osteoclasts.

The differential diagnosis of this tumour on radiography include chondroblastoma, aneurysmal bone-cyst, osteoblastoma, giant cell tumour, epiphyseal osteosarcoma, plasmacytomas and renal cell metastasis[4]. Of these, the most difficult to distinguish is the chondroblastoma because of its identical radiographic appearance[1,2,5,6]. However, the clear cell chondrosarcoma tends to occur in relatively older patients (3rd and 4th decades), compared with the 2nd decade for chondroblastoma. Periosteal erosion is rare and metaphyseal involvement is invariably seen. The ultimate differentiation is only made histologically[2,6]. The clear cells typical of clear cell chondrosarcoma are never seen in chondroblastoma.

The dominant cells in chondroblastoma vary from spindle to oval cells and have a slightly acidophilic cytoplasm. Rarely, malignant transformation of chondroblastoma has been reported (Kalm & Fredwood). In such cases, the cells show features of conventional chondrosarcomas but no clear cells are seen.

Rarely, when the lesion is cystic, it may resemble an aneurysmal bone cyst. However, in such cases, careful search for the cells clinches the diagnosis[2]. Epiphyseal osteosarcomas can also mimic clear cell chondrosarcomas and again, the differentiation is made at histology by the presence of anaplastic cells similar to conventional osteosarcomas[11]. Clear cells may also be seen in metastases from renal cell carcinoma. Clear cells in such lesions are rich in glycogen and fat, in contradistinction to clear cell chondrosarcoma which contain only glycogen. The lesion may mimic giant cell tumour; however, in the latter, the giant cells are multinucleated and do not resemble the benign-appearing giant cells of clear cell chondrosarcoma. Occasionally, the brown tumour of hyperparathyroidism requires differentiation by review of the clinical and laboratory data.

It is important to recognise that the clear cell chondrosarcoma is a unique low-grade chondroid malignant tumour with clinical, therapeutic and prognostic features distinct from those of chondroblastoma and chondrosarcoma[2]. Of the 47 cases in Bjornsson & Unni's series, 7 (15%) died of their tumours. It is not possible on histological grounds to predict which tumours would metastasise.

According to the surgical staging system advocated by Enneking et al[2,9], the low-grade biologic behaviour of clear cell chondrosarcoma makes it a Stage I or low-grade lesion. Moreover, because the cortex, although fully expanded, usually remains intact, most of these lesions are Stage IA (intracompartmental), rather than Stage IB (extraoseous and extracompartmental). Following the nomenclature of standardisation of the surgical procedure by Enneking et al, and adopted by the Musculoskeletal Tumour Society, the aggressiveness of the surgical procedure should be tailored to the surgical stage of the lesion - hence, 'en bloc' resection with a wide margin of normal bone and soft tissue surrounding the lesion is the procedure of choice[1]. Excision alone with curettage has an unacceptable recurrence rate (80%)[2]. In addition, its use alone as primary treatment is only for patients who refuse more extensive surgery. In two cases treated with irradiation, disease-free intervals were obtained for ten to twenty years. Radiotherapy can provide some symptomatic relief but is of no curative value[1].

Since the lesions tend to occur usually at the end of a long bone, especially the proximal femur or humerus, this necessitates adequate resection of the end of the long bone, thus compromising the function in the adjacent joint. Hemiendoprosthesis, allografts and arthrodesis have been used with varying degrees of success[12]. Lesions occurring in the pelvis require internal pelvectomy and has yielded high success rate with maintenance of acceptable function[9,14,15]. Arthrodesis of the proximal femur to the pelvis is not necessary to achieve adequate function in most cases and although many of the patients have significant shortening, they can usually walk with a single cane or appropriate lift. However, if the central acetabulum has been resected, arthrodesis is required. Recently, reconstruction of the pelvic defect with an allograft or ceramics has been tried experimentally[9,12,14,15]. The complication rate for allograft is high in the early series. Allografts are usually deep frozen bone or cartilage protected with 10% glycerol or PMSA. They yield about 20 - 70% viable chondrocytes[12]. Allografts require immunosuppression for two years and there is a high infection rate with serous drainage. Other serious complications include delayed union (14%) and fracture (7%).

CONCLUSION

Clear cell chondrosarcoma is a low-grade malignancy which is usually curable, provided the lesion is resected with a cuff of normal tissue. Recurrence occurs usually in those cases where surgery is conservative, with only curettage of the lesion. It should not be treated lightly as distant metastases to the long bone and brain have been reported.

REFERENCES

1. Unni KK, Dahlin DC, Beabout JW, Sim FH. Chondrosarcoma - Clear Cell Variant. J Bone Joint Surg 1976; 58(A) : 676-83.
2. Bjornsson J, Unni KK, Dahlin DC. Clear Cell Chondrosarcoma of Bone - Observation in 47 Cases. Am J Surg Pathol 1984; 8 : 223-30.
3. Faraggiana T, Sender B, Glicksman P. Light and Electron Microscopic Study of Clear Cell Chondrosarcoma. Am J Clin Pathol 1981; 75 : 117-21.
4. Kumar R, David R, Cierney G. Clear Cell Chondrosarcoma. Radiology 1985; 154(1) : 45-8.
5. Kahn LB, Wood FM, Ackerman LV. Malignant Chondroblastoma - Report of 2 Cases and Review of Literature. Arch Pathol 1969; 88 : 371-6.
6. Charpentier YL, Forest M, Postel M, Tomeno B, Abelanet R. Clear Cell Chondrosarcoma - Report of 5 Cases including Ultrastructural Study. Cancer 1979; 44 : 622-9.
7. Marrore RC, Mike V, Huffer R, et al. Chondrosarcoma of the Pelvis and Upper End of Femur - Analysis of Factors Influencing Survival Time in

116 Cases. J Bone Joint Surg 1972; 54(A) : 561-72.
8. Spjut HJ, Feahner RF, Ackerman LV. Tumours of Bone and Cartilage in Atlas of Tumour Pathology. 2nd Series. S Armed Forces Institute of Pathology, Washington DC Suppl. 1981.
9. Enneking WF, Dunham WK. Resection and Reconstruction for Primary Neoplasm Involving Luminate Bone. J Bone Joint Surg 1978; 60(A) : 731-46.
10. Greenspan A. Tumours of Cartilage Origin. Orthop Clin North Am 1987; 20(3) : 347-66.
11. Tsuneyoshi M, Dorfman HD. Epiphyseal Osteosarcoma - Distinguishing Features from Clear Cell Chondrosarcoma, Chondroblastoma and Epiphyseal Enchondroma. Hum Pathol 1987; 18 : 644-51.
12. Healey JH, Lane JM. Chondrosarcoma - A Review of Literature. Clin Orthop and Related Research No. 204 March 1986; 119-29.
13. Huvos AG, Marcove RC, Erlandson RA. Chondrosarcoma of Bone - A Clinocopathological and Electron Microscopic Study. Cancer 1972; 29 : 760-71.
14. Johnson JTH. Reconstruction of the Pelvic Ring Following Tumour Resection. J Bone Joint Surg 1978; 60(A) : 747-51.
15. Steel HH. Partial or Complete Resection of the Hemipelvis. J Bone Joint Surg 1978; 60(A) : 719-30.