



Research Paper

Chondroblastoma in pelvis and extremities- a single centre study of 177 cases

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ABSTRACT

Introduction: Chondroblastoma is a rare benign bone tumour that usually occurs in children and young adults. They are cartilaginous tumours arising in the epiphysis or apophysis of a long bone. The tumour is classified as benign, although rare cases of pulmonary metastases have been reported. The aims of this study were to describe clinical, radiographic characteristics of chondroblastoma; to analyse the local recurrence rate and complications associated with surgery.

Material and methods: This retrospective study included 177 patients, who had been diagnosed with a chondroblastoma in extremity between 1990 and 2015.

Results: The most common site was proximal tibia 20%, followed by proximal humerus 19%, proximal femur 18%, distal femur 16% and foot 15%. One patient has died of the disease and one patient is alive after being operated for lung metastases. There was local recurrence in 25/177 (14%) patients. The median time to local recurrence was 10 months (range 3–158 months). The most common site for local recurrence was proximal tibia (22.2%). The proximal femur was the location in 32/178 (18%) of the cases. 18/32 (56%) were in the greater trochanter and 14/32 (44%) in the femoral head. The mean age was lower in tumours located in femoral head when compared to the greater trochanter; 19.5 years and 13.9 years respectively ($p = 0.004$). Tumours located in greater trochanter were all curetted without further complications. Local recurrence was seen more often in femoral head tumours, though without statistical significance; 3/14 (21%) and none, respectively ($p = 0.073$).

Conclusions: Chondroblastoma is a rare benign to intermediate grade bone tumour with a potential to metastasise. Femoral head chondroblastoma is rare, presenting 4.5% of all chondroblastoma cases. Around 50% of the chondroblastoma in femoral head, occur in patients with open growth plates.

Introduction

Chondroblastoma is a rare benign bone tumour that typically arising in children and young adults. These cartilaginous tumours are classically found in the epiphysis or apophysis of long bones, most commonly the proximal tibia followed by proximal femur and proximal humerus. [1] Chondroblastomas are usually symptomatic and rarely discovered incidentally on plain radiographs. The tumour is classified as benign, although some extremely rare cases of pulmonary metastases have been reported. [2] While straightforward cases with classical features may lead to a quick diagnosis, there are few other tumours like giant cell tumour (GCT) and aneurysmal bone cyst (ABC) that might give an overlap in clinical presentation, radiological feature, and the presence

of giant cells and hemosiderin on microscopic examination. However, recent studies by Behjati et al. and Presneau et al. have identified a K36M mutation in either H3F3A or H3F3B gene. This gene mutation 70%–95% specific for chondroblastoma. In GCT a separate specific mutation of G34M in H3F3A gene has been found. Surgery has remained the mainstay of treatment, usually meticulous curettage of the lesion followed by filling the osseous defect with bone auto/allograft, bone substitute or cement. Recently radiofrequency ablation has also been introduced in the treatment of chondroblastoma [3,4].

Local recurrence after treatment varies considerably, ranging from 10% to 35%; predisposing factors for local recurrence are not clear, but location, young age and epiphyseal location at the time of diagnosis may increase the risk [5–7] though this is not clear from the available

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evidence Sailhan [1].

The aim of this study was to perform a retrospective analysis of all patients undergoing treatment for chondroblastomas. The objectives of this study were to describe the clinical and radiological characteristics of chondroblastoma, and to analyse the recurrence rate and complications associated with surgery giving specific attention to lesions arising in the proximal femur.

Material and methods

This retrospective study included 177 patients, identified from a prospectively maintained database, who had been diagnosed with a chondroblastoma of the extremity between 1990 and 2015 at a single tertiary referral centre. All patients were diagnosed and treated at this single centre. Those who were primarily treated elsewhere and referred for the management of a recurrence were excluded. The multidisciplinary team (MDT) diagnosis was based on clinical, radiological and histological criteria. Details of the clinical data collected, at the time of presentation and local recurrence, included the site (appendicular, extremity or pelvis), primary tumour size (cm), type of operation at the time of primary or local recurrence, presenting symptoms and their duration, gender, age, pathological features and functional and oncological outcomes including local recurrence free survival (LRFS). Resection and LR specimens were examined by specialised bone sarcoma pathologists. The histopathology was studied with special emphasis as to whether there was evidence of an associated aneurysmal bone cyst. We retrospectively reviewed the cases with pulmonary metastases; immunohistochemical studies of mutant H3 (H3K36M) were performed in one case, but the other disseminated case was so old that histological blocks were not available.

The radiographs at presentation were reviewed for the site and size of the lesion. The status of the adjacent physis was also determined and recorded as either open or closed.

Statistical analysis

Descriptive statistics were used to display demographic data. The Kaplan-Meier method was used to determine LRFS. Survival rates were calculated from the date of operation to the date of LR. Kruskal-Wallis test was used for statistical analysis means between the groups. Univariable analysis was performed by comparing groups with log-rank test with subsequent multivariable Cox proportional hazard analysis of significant variables to identify predictors of LRFS. A p value < 0.05 was considered significant. All statistical analysis was completed using SPSS Statistics 24.0 (IBM, New York, USA).

Results

The most commonly affected site was the proximal tibia (20.2%) (Fig. 1a and b), followed by proximal humerus (19.1%), proximal femur (18.0%) (Fig. 2a and b), distal femur (15.7%) and foot (14.6%). In the foot, 7/26 (27%) originated in calcaneus, 18/26 (69%) in talus and one (4%) in the navicular. In the proximal femur, 18/32 (56%) were located in the greater trochanter and 14/32 (44%) in the femoral head. The location of tumours is summarized in Fig. 3.

Two patients presented with a pathological fracture, one in the proximal femur and one in the olecranon. Delays in diagnosis were common. The median duration of symptoms was 36 weeks, but the range was wide, ranging from no symptoms prior to pathologic fracture to 10 years of pain.

Two patients developed metastatic disease, which was confirmed by histological analysis of the metastases to be chondroblastoma. After metastatectomy one patient subsequently died of disease, the other is alive post pulmonary metastatectomy and chemotherapy. In both cases the histology was later carefully re-reviewed without change in the diagnosis and the case with available blocks showed nuclear positivity

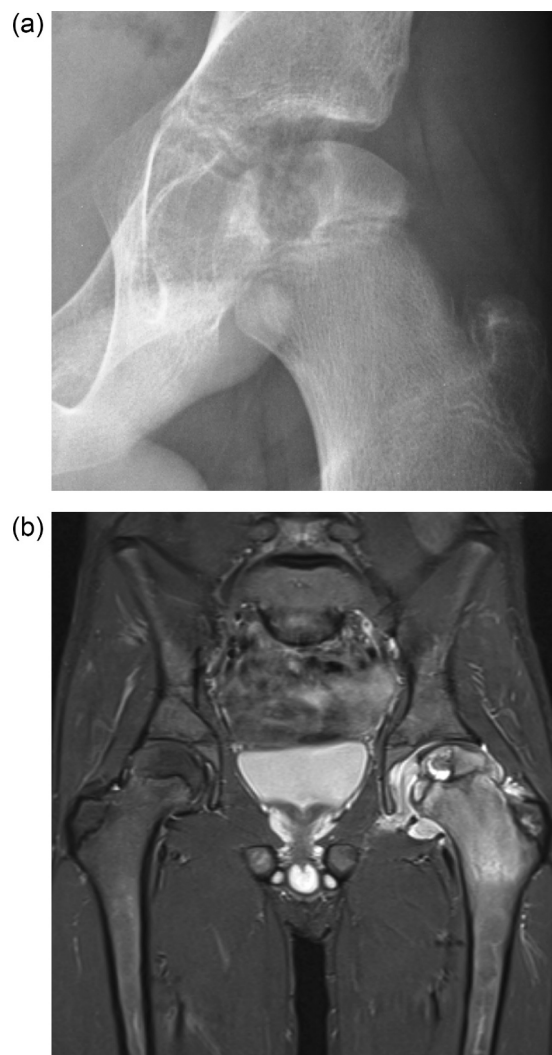


Fig. 1. (a) Radiograph showing a chondroblastoma located in the epiphysis of the proximal part of the femur. (b) T2-weighted MRI showing the bone lesion in proximal part of the femur. Note the marrow oedema of the epiphysis and metaphysis surrounding the chondroblastoma.

for H3K36M antibody.

Local recurrence (LR) was seen in 25/177 (14%) patients. The mean time to LR was 18 months (range 3–158 months) following initial treatment. The median time to LR was, however, 10 months as in all but one case, LR occurred within 24 months. In this one outlying case, a 24 year-old male, who presented with a chondroblastoma in the proximal tibia initially treated by curettage, developed minor symptoms 10 years after initial treatment. Imaging and histology confirmed recurrent chondroblastoma which was treated with repeat curettage and augmentation with cement 13 years after the primary operation. Of the 25 cases of LR, 7 patients had two LRs and 18 had only 1 episode of LR. LR was most common for tumours of the proximal tibia (22.2%).

In 26% of cases, a secondary aneurysmal bone cyst (ABC) component was seen on histology. This feature was most common for chondroblastoma of the foot, where 46% of the cases were reported to have a significant ABC component. (Fig. 4a and b) The results are summarized in Table 1.

Surgical treatment

116/177 (65%) cases were treated by curettage alone, without augmentation or packing of the defect. In 33 cases (18.6%), the post

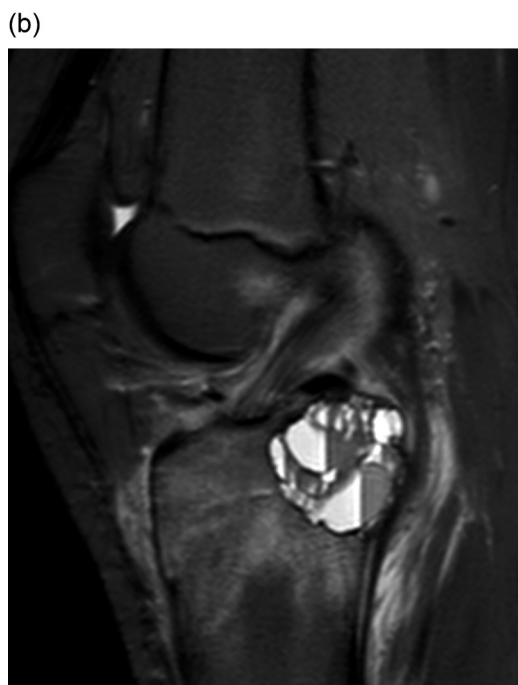


Fig. 2. (a) Radiograph showing a chondroblastoma located in the proximal part of the tibia. (b) T2-weighted MRI showing significant aneurysmal bone cyst component in the chondroblastoma in proximal tibia.

curettage defect was packed with autologous bone graft whilst only 3 cases (1.7%) were augmented by cement. Radiofrequency ablation (RFA) was used in 22 (12.4%). The decision to use RFA was determined on a case by case basis following discussion at a multidisciplinary team meeting. In general, RFA was considered for smaller lesions (< 2 cm) away from critical structures (including subchondral lesions when RFA risked damage to the overlying cartilage), without a soft tissue component. Endoprosthetic replacement was required in two cases and

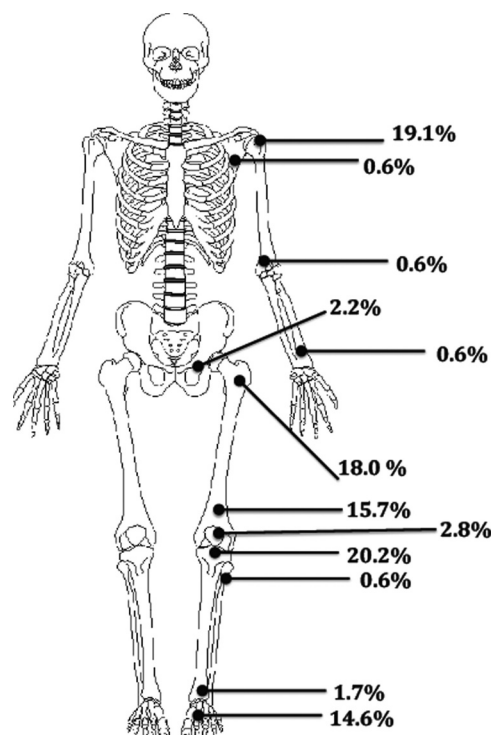


Fig. 3. Illustration showing the site distribution of the 177 lesions.

osteoarticular allograft was used in one patient. Local recurrence developed in 17/116 (14.7%) cases after curettage, 3/22 (13.6%) after RFA, 4/33 (12.1%) after curettage with bone grafting and none after endoprosthetic replacement, curettage with cementation or osteoarticular allograft.

Local recurrence free survival

Local recurrence free survival (LRFS) at 1-year was 90.3% and 84.7% at 2-years. Advanced age was a significant risk factor for greater local recurrence (HR 0.856, 95% CI 0.768–0.955, $p = 0.005$).

Proximal femur

32/177 (18%) lesions arose in the proximal femur. 18/32 (56%) were located in the greater trochanter and 14/32 (44%) in the femoral head. The mean age was statistically lower in tumours located in femoral head when compared to the greater trochanter (19.5 years compared to 13.9 years ($p = 0.004$)), as was the mean size of tumour (53 mm for greater trochanter tumours compared to 26 mm in femoral head lesions ($p = 0.001$)). Among femoral head tumours, the physis was open in 7/14 patients (50%). (Fig. 5) Tumours located in the greater trochanter were all curetted without further complications or LR. Tumours located in the femoral head were treated in a number of different ways, largely dependent on the location of the lesion. Curettage via a lateral, subtrochanteric entry drill hole, was used in 6/14 cases. An open approach to the femoral neck, raising a trapdoor in the femoral neck was used in 2/14 cases. In 2 cases, an open approach to the femoral head was used to allow a chondral flap to be elevated and curettage of the underlying lesion. The remaining 5 cases underwent RFA.

Local recurrence was seen more frequently in femoral head tumours when compared to tumours located in the greater trochanter, though the numbers were too small to give statistical significance; 3/14 (21%) and none, respectively ($p = 0.073$). All LRs in femoral head tumours occurred in patients treated by a minimally invasive approach via a drill along the femoral neck. One patient eventually developed femoral head

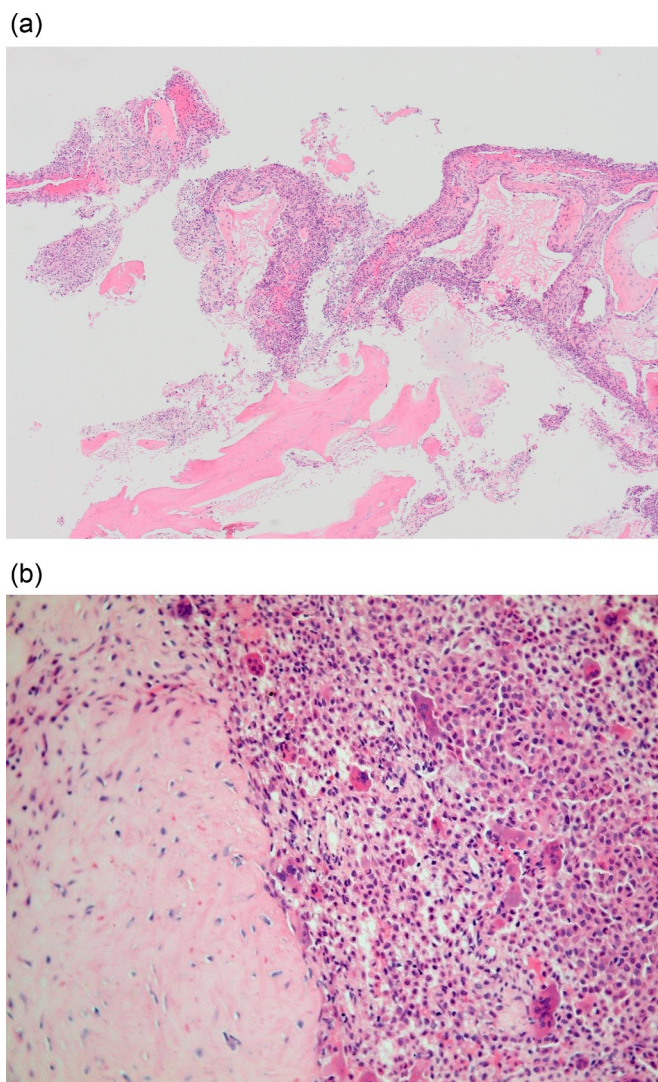


Fig. 4. (a) Curettage sample of a chondroblastoma with prominent secondary ABC like features. Small tumour fragments consisting of solid sheets of mononuclear cells with irregular nuclear outline are noted. Scattered giant cells are seen. (b) Pale eosinophilic chondroid deposits are also noted.

collapse and one had a growth plate fusion ending in slight limb length discrepancy without further treatment. Results of proximal femur tumours are summarised in Table 2.

Discussion

Chondroblastoma is a rare benign to intermediate grade bone tumour. There are few larger studies published in the literature [1,5,7–10], but to our knowledge this is the largest single centre study looking at the radiological, surgical and clinical aspects of the disease, and recurrence following treatment.

There was a strong male preference, with a male:female ratio of 2.3 to 1. Our results are in accordance with the literature, where male:female ratio has been varying between 1.56 and 3.48 to 1. [1,9,10] The mean age of 18 years is in accordance with other publications and thereby our study resembles a very typical cohort of patients with chondroblastoma.

A cystic (aneurysmal bone cyst, ABC) component is seen often in chondroblastomas. The role of the ABC component is interesting and has been discussed in previous publications. Some authors have suggested that the cystic component is seen more often in cases with local

Table 1
Patient characteristics

Characteristics	Number
Eligible patients	177
Location	
Proximal tibia	36 (20.3%)
Proximal humerus	34 (19.2%)
Proximal femur	32 (18.1%)
Distal femur	28 (15.8%)
Foot	26 (14.7%)
Talus	18/26 (69%)
Calcaneus	7/26 (27%)
Navicular	1/26 (4%)
Patella	5 (2.8%)
Pelvis	4 (2.3%)
Distal fibula	3 (1.7%)
Proximal ulna	2 (1.1%)
Proximal fibula	1 (0.6%)
Scapula	1 (0.6%)
Distal humerus	1 (0.6%)
Hand	1 (0.6%)
Gender	
Male	124 (70.1%)
Female	53 (9.9%)
Special histological features	
Significant secondary ABC component	47 (26.6%)
Patella	5 (100%)
Foot	12 (46.2%)
Proximal femur	10 (31.3%)
Proximal tibia	8 (22.2%)
Distal femur	6 (21.4%)
Atypical chondroblastoma	10 (5.6%)
Giant cell rich	4 (2.3%)
Local recurrence	24 (13.6%)
Proximal tibia	8/36 (22.2%)
Proximal femur	3/32 (9.4%)
Proximal humerus	4/34 (11.8%)
Distal femur	4/28 (9.4%)
Metastasizing disease	2 (1.1%)
Mean time to local recurrence in months (range)	17.6 (3–158)
Mean age in years (range)	18.3 (8–48)
Mean size of the tumour in mm (range)	36 (10–100)
Mean duration of symptoms in weeks (range)	49 (0–208)

recurrences [7,11,12] however, other series have not confirmed this [1,7,13]. In our results, we did not see any correlation between ABC rich chondroblastomas and the incidence of local recurrence. The overall rate of ABC rich chondroblastoma was 26% in our study, which is in accordance with the previous literature where the overall rate of ABC rich chondroblastomas has varied between 23%–25%. [5,14] If secondary ABC formation included microcystic degeneration with haemorrhage, the rate of ABC formation has been reported to increase as high as 83%. [10] The definition of ABC rich chondroblastoma is vague, and in this study a significant amount, more than 50% of the surface, was required to present with ABC component, before the tumour was labelled as an ABC rich chondroblastoma. In our study, we observed that a significant ABC rich component was most often located in chondroblastomas in small bones like the patella and the bones of the foot. This may be of clinical significance where a solitary ABC is diagnosed and further nonsurgical sclerotherapy is considered as a treatment option.

The proximal femur was the third most common location after the proximal tibia and proximal humerus which is in accordance with the current literature. [1,5] Tumours in the proximal femur are located more often in the greater trochanter than in the femoral head. Several differences were noted when femoral head tumours were compared to those of the greater trochanter. Tumours in the greater trochanter were significantly larger and occurred in older patients, when compared to those of the femoral head. The mean age was 19.5 years in comparison to 13.9 years in patients with femoral head tumours. In patients with femoral head tumours, the growth plate was open in half of the patients.

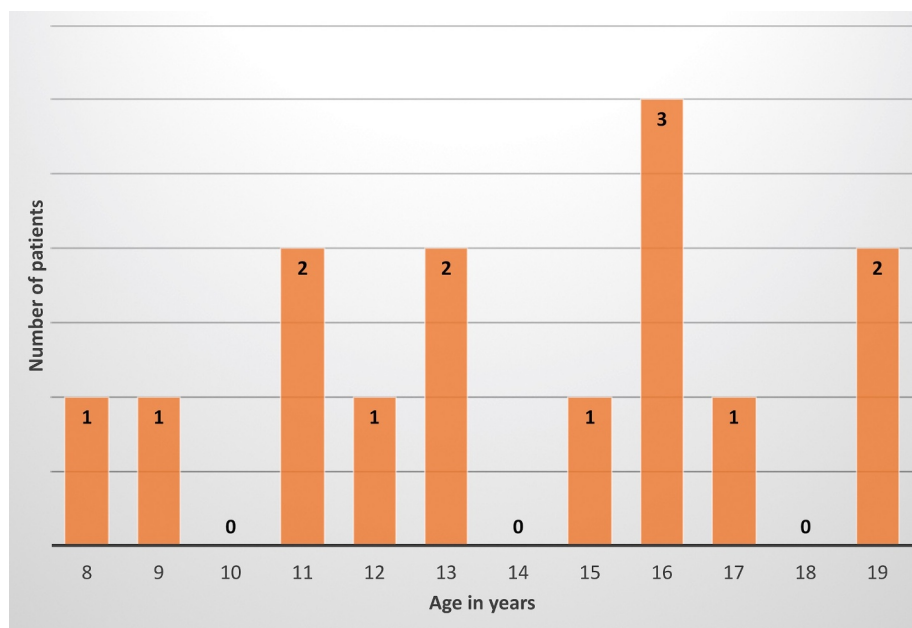


Fig. 5. The incidence of femoral head tumours according to age.

Table 2

Characteristics of 32 patients with chondroblastoma either in greater trochanter or femoral head.

	Greater trochanter	Femoral head	p-value
Number	18	14	
Mean age in years	19.5	13.9	0.004
Duration of symptoms in weeks	64	50	0.659
Size in mm	53	26	0.001
Local recurrence	0/18	3/14	0.073
Male gender	13/18	11/14	0.504
Secondary ABC component	2/18	2/14	0.597
Giant cell rich component	1/18	1/14	0.691

Surgical treatment of greater trochanteric lesions was associated with no local recurrences. This may well be due to the ease of access to this location allowing a more detailed curettage. Treatment of femoral head tumours can be extremely challenging, particularly in children with open physes, or for tumours abutting the subchondral plate where curettage or RFA risks the overlying cartilage. In the past, the traditional approach to the femoral head has been via subtrochanteric drill hole in the lateral femur. Gaining surgical access through the femoral neck to the femoral head results in a higher incidence of LR, presumably due to the poor access afforded to allow a detailed curettage of the lesion. In our experience, the rate of local recurrence was three out of six treated by a transcervical approach, and none in those treated by a direct approach. A direct hip joint approach provided good access and exposure of the lesion. Interestingly, secondary femoral head collapse, either due to an unstable cartilage defect or due to avascular necrosis, was not seen in any of the patients treated by this approach.

Previous series, and our results show, RFA to be an attractive option for treatment of chondroblastoma. [3,4,15–18] In the femoral head, we observed no local recurrences after RFA, and when including all anatomical locations treated with RFA, the rate of local recurrence was comparable to curettage. There was a learning curve to RFA as demonstrated by the higher incidence of LR seen in cases treated by RFA in the early phase of the study population. However, it should be noted that when first adopted as a treatment option, it was largely reserved for challenging tumour locations such as the posterior aspect of the proximal tibia and femoral head, making direct comparison with more

traditional surgical treatments difficult. Having demonstrated its efficacy, of course, RFA is now employed for far more lesions dependant largely on the size and location of the tumour. We did, however, observe more LR following RFA in the early part of the study mostly likely representative of the learning curve of the procedure. In addition, at the early stages, RFA was selected as the treatment option for cases of chondroblastoma in challenging locations, including the posterior tibia plateau and femoral head. However, following initial successes with the approach, this has now been expanded to all locations that fulfil the criteria for its use.

The overall rate of local recurrence was 13.6%, which is in accordance with the literature. The only factor identified as a significant risk for LR was young age, known to be a risk factor for local recurrence. [7] Whilst the posterior part of proximal tibia had the highest rates of local recurrence, there was no significant difference in comparison to other locations in terms in relation to LR.

Chondroblastoma is often regarded as a benign condition, despite the recent reclassification of the tumour as an intermediate grade lesion with local aggressiveness and a small risk of metastasis [19]. The incidence of metastases is rare with only a few individual reports in literature [20,21]. A few larger series have reported the incidence to be between 2.7% and 3.3% [5,8] though this was not the finding in this study. In some other large published studies, the rate of metastasis was not been reported or did not exist, [1,5,7,9,10] raising questions about the histological classification of the primary tumour in those series that report a higher incidence. The incidence of metastasis of 1.1% in our study is, we believe, is more reliable, as our series presents the largest available in the literature, and all cases of both primary lesions and metastatic lesions, were reviewed by experience musculoskeletal pathologists. K36M mutation identified with immunohistochemical staining is a useful ancillary study with which to establish the diagnosis of chondroblastoma. The diagnosis of metastatic chondroblastoma is rare and consequently questions of accuracy of the primary histological diagnoses. In addition to any histological review, K36M immunohistochemical staining positivity confirmed the original chondroblastoma diagnosis in one case of metastasis. As previously reported, K36M immunostaining has been shown to be highly specific for chondroblastoma diagnosis [22]. K36M staining has been a useful tool in the diagnosis of metastasised chondroblastoma but does not determine the aggressive behaviour of chondroblastoma itself [4,22].

Conclusions

In conclusion, although usually categorized as benign, chondroblastoma has metastatic potential. Whilst rare, occurring in only 4.5% of cases, the femoral head location for chondroblastoma raises distinct challenges for treatment as they often occur in young patients with open growth plates. Where tumours of the femoral head occur, the preferred treatment should be by RFA where lesions are amenable, or by formal open procedures due to the high incidence of LR seen with less invasive approaches.

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