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Unicameral bone cysts of the proximal femur in skeletally immature patients: Do radiological parameters, pathological fracture, treatment method and recurrence affect the outcomes?

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Abstract

Unicameral bone cysts (UBC) are reported to be the underlying lesion in 40% of pathological femoral neck fractures in skeletally immature patients. They are typically asymptomatic and incidentally found on imaging. However, when symptomatic, it commonly may present with pathologic fracture that causes pain, swelling, or deformity. The purpose of this study was to assess the natural history of the pediatric proximal femoral unicameral bone cyst, risk factors for pathological fracture and recurrence. Medical records were retrospectively reviewed of patients with pediatric proximal femoral UBC's who underwent surgery between 2004 and 2018. We included 51 consecutive patients with pediatric proximal femoral UBC (36 impending fractures/15 pathological fractures). The patients were evaluated regarding the localization of the UBC and the activity of the cyst. The cyst parameters were measured, and the patients were further assessed regarding the presence of pathological fracture and applied treatment. The pathological fracture group was compared to the impending fracture group using radiological cyst parameters, management options, healing, recurrences, and other related complications. The most commonly affected localizations were combined involvement of femoral neck and intertrochanteric (n=21) The number of latent lesions was 27 and active lesions were 24. The mean cyst index in our series was 3.8±1.2 (1.2-7.2). The cyst index in our series was correlated with pathological fractures. (p=0.048) There were significantly higher cyst index values in recurrent cases. (p=0.016) The cyst extension below the trochanter minor level was found as a risk factor for pathological fractures. (p=0.021) The most common treatment in our series was curettage, graft packing, and plate fixation with 27 patients. The treatment method showed no correlation with consolidation or recurrence rate. According to the healing criteria for UBC's at final follow-up, 36 cysts were completely consolidated, 13 were evaluated as incomplete healing and two were persistent. The recurrence rate was significantly high in UBC's who were operated on at <10 years of age (p=0.006). Accordingly, the active lesions were also significantly related to earlier recurrence (p=0.03). Although younger age, active cysts, and higher cyst index are shown as risk factors for recurrence, not for fracture in proximal femoral UBC's. However, with age, the cyst relatively migrates to the weight-bearing intertrochanteric area, which may inevitably impose a major risk for pathological fractures. Ensuring stability with a plate even in impending fractures of the proximal femur may aid early mobilization and faster recovery.

Keywords: Unicameral bone cyst, pathological fracture, immature proximal femur, cyst index, recurrence

Introduction

Unicameral bone cysts (UBC) of the proximal femur, which accounts for 27% of all UBC's in the pediatric population, are incidentally diagnosed in most cases [1-4]. UBC is reported to be the underlying lesion in 40% of pathological femoral neck fractures in skeletally immature patients [5]. The cortical destruction by the osteolytic effect of the cyst in this weight-bearing area poses a major risk for spontaneous fractures [4]. Several predictors have been proposed for fracture risk in UBC's, which are; cystic index (>3.5 for proximal femur), percentage of bone occupied by the cyst in the transverse plane (>85%), minimal cortical thickness (<2 mm), and being active cyst [6-10]. Pathological fractures of UBC's are reported to promote spontaneous healing of the cyst particularly for humerus [8,11].

The goal of treatment in UBC's of the proximal femur in skeletally immature patients is to promote consolidation, avoid pathological fractures and recurrence [12]. A wide range of recommended surgical treatments for UBC's of the proximal femur including subtotal resection with or without graft packing, curettage with or without graft packing and plate fixation, intracystic steroid injection, multiple drill holes, and intramedullary flexible nails [3,12-15]. However, the choice of treatment remains controversial using controlling weight-bearing, avoiding resultant complications in skeletally immature patients (avascular necrosis, resultant limb length discrepancy, and deformity) [12].

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We sought to answer the following questions; 1) Is there a radiological predictor for impending fractures or an indicator that affects surgical management? 2) What is the effect of pathological fracture in proximal femoral UBC's? 3) Is there a precipitating factor for recurrence in proximal femoral UBC's?

Material and Methods

The data of 96 skeletally immature patients with confirmed histopathological diagnosis of the unicameral bone cyst (UBC) of the proximal femur who applied surgical treatment in our clinic between February 2004 to June 2018 were evaluated, retrospectively. Amongst the study group 17 patients who were below 5 years and over 15 years of age at the time of surgical intervention and 23 patients lacking a minimum follow-up period of 2 years were excluded. Patients younger than 5 years were excluded due to insufficient follow-up period, immaturity at the femoral neck, and lack of surgical indications. Five patients were previously operated in elsewhere center with the diagnosis of UBC, to overcome treatment bias these patients were also excluded, and the remaining 51 patients were included in the study group.

This study (no. 234) was assessed by the Institutional Review Board of Baltalimanı Bone Diseases Training and Research Hospital in the 57th board meeting held on 16.04.2020. The board approved the research on compliance with the rules of ethics and scientific guidelines.

Apart from the epidemiological data, the patients were evaluated regarding localization of the UBC (femoral neck, intertrochanteric, subtrochanteric or combined), metaphyseal or diaphyseal placement, and the activity of the cyst (latent or active). UBCs were classified as active when they are within 1cm of the physis and latent as they progress to a diaphyseal location. The extension of the cyst regarding trochanter minor level (above or below) was evaluated.

The cyst parameters were measured and confirmed by two orthopedic surgeons on anteroposterior (AP) radiographs with picture archiving and communication system (PACS) software. The distance from the growth plate to the nearest border of the cyst was evaluated. The measurement of cyst index, which was defined as the cyst area (the area of the best-fit trapezoid in the cyst) divided by the diaphyseal diameter, was performed on all patients. The ratio of the widest cyst diameter to the growth plate diameter on the AP radiograph was also measured. The medial cortical thickness at the neighboring cortex was evaluated.

The patients were further assessed regarding the presence of pathological fracture and applied treatment. The pathological fracture group was compared to the impending fracture group using radiological cyst parameters, management options, healing, recurrences, and other related complications. The time between the occurrence of pathological fracture and cyst treatment, which was inevitably delayed due to various reasons, was noted. Time to bone healing and UBC consolidation were evaluated via follow-up x-ray views. Consolidation was determined by the UBC healing criteria proposed by Capanna et al. accordingly [16]. The final evaluation was subclassified as "complete consolidation" of the cyst; "incomplete healing" where the cyst was consolidated with bone, but small areas of osteolysis persisted within the cyst; "recurrence" were initially consolidated with bone but large areas of osteolysis with cortical thinning subsequently returned; "persistent" where the cyst showed no evidence of response to applied treatment. The patients were evaluated for recurrence, management of recurrent cyst, avascular necrosis of the femoral head, refracture, and coxa vara during a minimum of 2 years follow-up. MSTS scores at the last follow-up were noted.

The demographic data, distribution of cyst localization, cyst activity, and cyst index were analyzed and compared using the chi-square test. Final values were compared between the two groups using the Students-test and Mann-Whitney U test. Data were analyzed using SPSS 21 (SPSS Inc, Chicago, IL, USA).

Results

The study consisted of 51 patients (45M/6F), with a mean age of 8.5±3.2 (3-15). The most commonly affected localizations were combined involvement of femoral neck and intertrochanteric (n=21) followed by intertrochanteric involvement (n=12). Diaphyseal (n=22) and metaphysodiaphyseal (n=21) cysts were predominant intramedullary involvement types. The number of latent lesions (n=27) was not significantly different from active lesions (n=24). Most of the cysts extended below the lesser trochanter (n=28) (Table 1).

The mean cyst index in our series was 3.8±1.2 (1.2-7.2). The cyst index in pathological fractures in our series was significantly high (p=0.048). Also, there were significantly higher cyst index values in recurrent cases (p=0.016). The mean distance from the growth plate to the nearest border of the cyst was 18 mm (0-72). Age was not significantly related to the distance from the growth plate to the nearest border of the cyst (p=0.99). However, increased cyst index was highly significant with decreased distance from the growth plate to the nearest border of the cyst (p=0.003). The mean ratio of the widest cyst diameter to the growth plate diameter was 0.9±0.2 (0.45-1.41). The mean medial cortical thickness at the neighboring cortex was 4.2±1.3 mm (2.3-7.6). The mean medial cortical thickness at the neighboring cortex at the presence of pathological fractures 4.6±1.3 mm, whereas the mean value in impending fractures was 4.0±1.4 mm, which showed no difference. However, the age distribution was in a variable age group from 5 to 15 years.

The pathological fracture group consisted of 15 patients. When compared to the impending fracture group no difference using healing time, recurrence, other complications, and cyst parameters except cyst index (Table 2 and 3). Cyst extension below trochanter minor level was found significantly related to pathological fractures (p=0.020). However, pathological fractures with a cortical displacement of more than 2 mm demonstrated longer healing time when compared to nondisplaced fractures (p=0.001) (Table 4). The mean time elapsed from the diagnosis of pathological fracture to surgical treatment was 4.8±3.9 days [1-17].

The management of UBC's at the proximal femur varied. The most common treatment in our series was curettage, graft packing, and plate fixation with 27 patients, followed by curettage and graft packing without fixation with 18 patients (Figure 1). Curettage and steroid injection (n=3), curettage, and hip spica (n=2) and curettage only (n=1) were remaining applied treatment methods in our series. The treatment method showed no relation to consolidation or recurrence rate. According to the healing criteria for UBC's at final follow-up, 36 cysts were completely consolidated, 13 were evaluated as incomplete healing and two were persistent (Figure 2). None of the patients in our series were recurrent at their last follow-up.

Table 1. Demographic data of the patients

		Value
Mean Age (years)		8.5±3.2 (3-15)
Gender (M/F)		42/9
Localization	**FN**	7
	IT	12
	ST	8
	FN+IT	21
	IT+ST	2
	FN+IT+ST	1
Cyst Activity	**Latent**	27
	Active	24
Radiological Parameters	**Cyst-Physis distance (mm)**	18±16 (0-72)
	Cyst Index	3.8±1.2 (1.2-7.2)
	Maximum Cyst Diameter/Physis Diameter	0.9±0.2 (0.5-1.4)
	Medial Cortical Thickness Below The Cyst (mm)	4.2±1.3 (2.3-7.8)
Pathological Fracture	**Yes**	15
	No	36
Applied Surgery	**Curettage only**	1
	Curettage + Hip spica	2
	Curettage + Steroid injection	3
	Curettage + Allograft packing	18
	Curettage + Allograft packing + Plate fixation	27
Capanna Healing Classification	**Complete healing**	36
	Incomplete healing	13
	Persistant	2
	Recurrent (At last follow-up)	0
Recurrence	**Yes**	16
	No	35
Follow-up		64.7±31.6 (24-148)

FN=Femoral Neck, IT=Intertrochanteric, ST=Subtrochanteric

Table 2. Comparison of impending fractures and pathological fractures of proximal femur UBC's

	Impending Fracture	Pathological Fracture	p*
Mean Age	8.3±3.3	9.1±2.7	0.426
Number of Active Cysts	17/36	11/15	0.972
Mean Cyst-Physis Distance (mm)	16.7	19.3	0.372
Mean Cyst Index	3.6±1.3	4.3±1.3	0.048
Maximum Cyst Diameter/Physis Diameter	0.9±0.2	0.9±0.2	0.777
Mean Medial Cortical Thickness Below The Cyst (mm)	4.0±1.3	4.6±1.3	0.161
Cyst Extension Below Lesser Trochanter	16/36	12/15	0.020
Capanna Healing Classification	Complete Healing=27/36 Incomplete Healing=7/36 Persistant=2/36	Complete Healing=9/15 Incomplete Healing=6/15	0.584
Mean Consolidation Time	16.2±2.3	16.4±2.3	0.733
Follow-up (months)	67.2	58.9	0.397

* = Students T test

Table 3. Data of pathological fractures

	Value
Age	9.1±2.7
Time to Surgery (day)	4.8
Time to Fracture Healing (week)	5.9±1.2
Time to Consolidation (week)	16.4±2.3
Capanna Classification	Complete Healing=9/15 Incomplete Healing=6/15

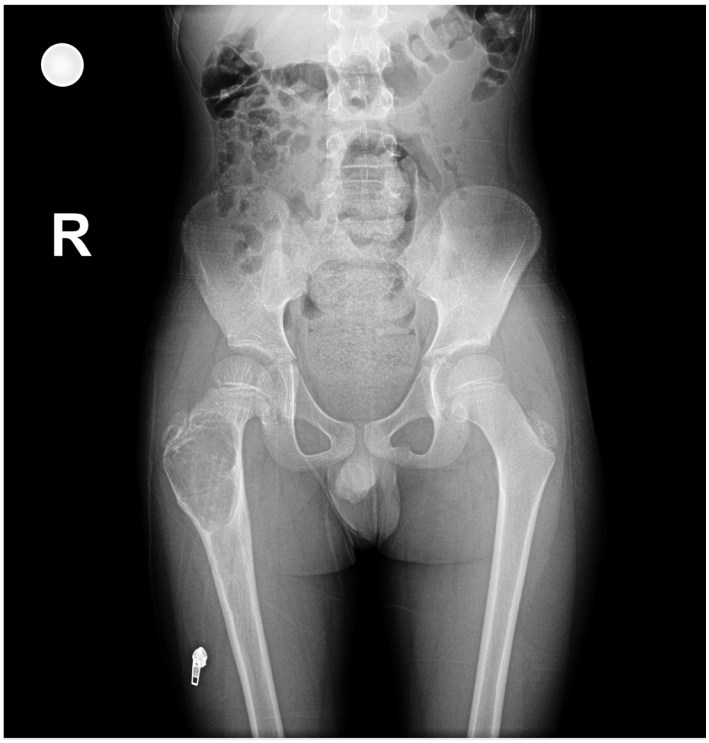

Figure 1a. 10-year-old patient from our series; anteroposterior hip x-ray demonstrates increased cyst index (>4.5), decreased cortical thickness

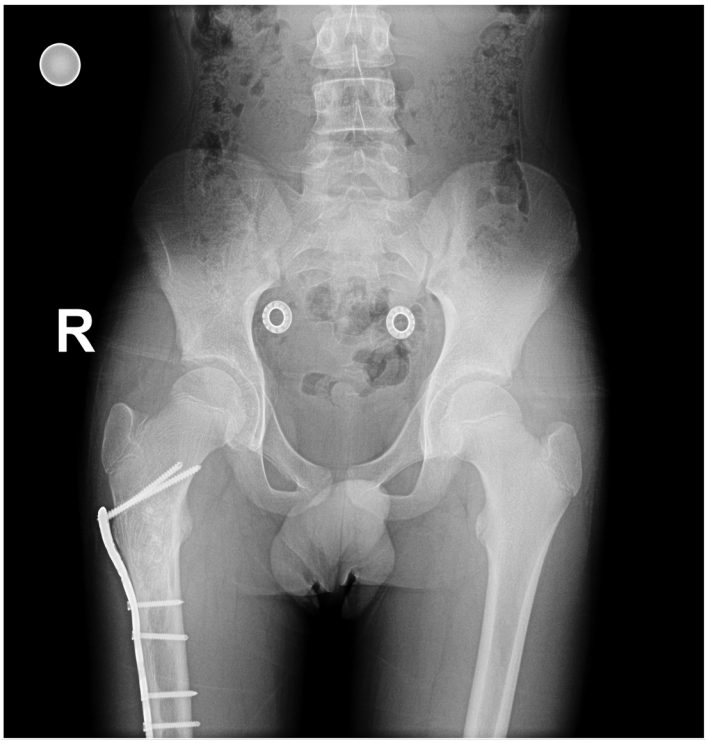

Figure 1c. Complete consolidation of allograft observed at postoperative 24-month follow-up

Figure 1b. The patient underwent curettage + allograft packing + plate fixation

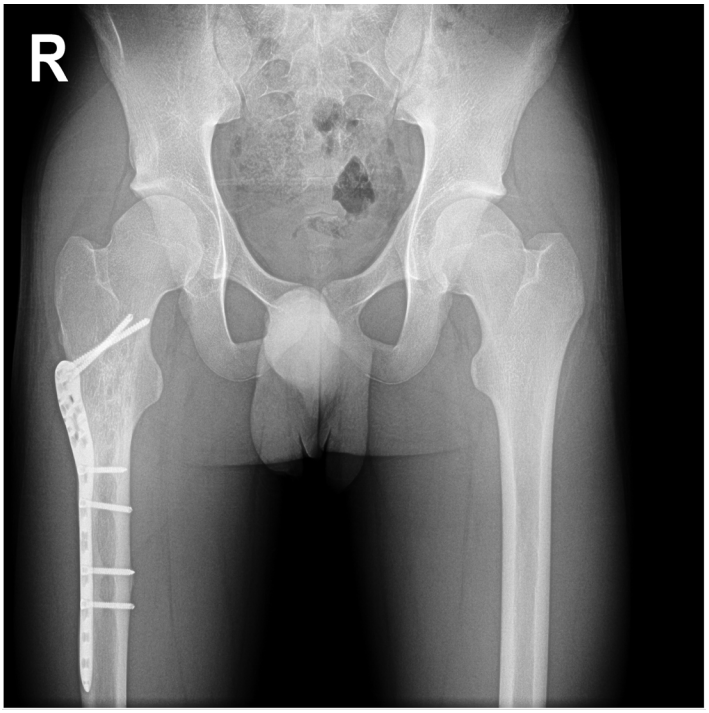

Figure 1d. At postoperative 66-month follow-up, determined as "complete healing" according to the Capanna criteria

Recurrence was encountered in 16 patients with a mean recurrence time of 30.4±14.5 (10-58) months and operated accordingly (Table 5). One patient required surgical management for a secondary recurrence 30 months after the curettage, graft packing, and plate fixation (Figure 3). Curettage, graft packing, and plate fixation was the index method for surgical management of recurrence. The recurrence rate was significantly high in UBC's who were operated on at <10 years of age (p=0.006). Accordingly, the active lesions were also significantly related to earlier recurrence (p=0.03) . Recurrence rate was evident in higher ratios of cyst diameter to the growth plate diameter (p=0.002). There was no evidence of avascular necrosis of the femoral head or refracture in our series however one patient developed coxa vara during follow-up. The mean MSTS score was 96.4% and showed no difference between the evaluated groups. The median follow-up time in our series was 60 months (24-148).

Figure 2a. Anteroposterior hip x-ray of the 11-year-old patient presented with a pathological fracture of more than 2 millimeters displacement

Figure 2b. Early postoperative x-ray shows open reduction + curettage + allograft packing + plate fixation

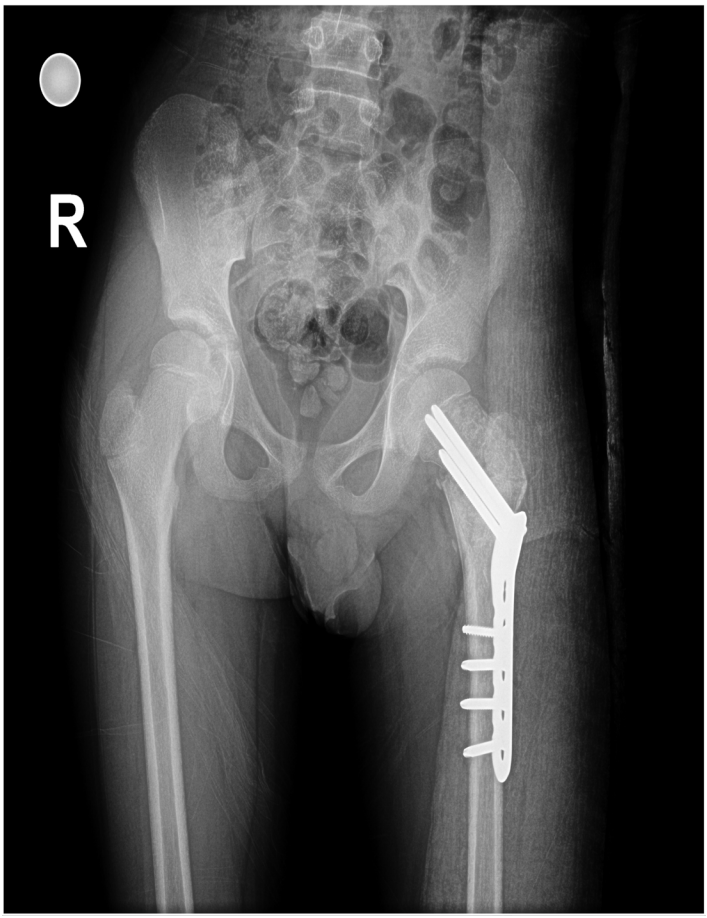

Figure 2c. Fracture healing achieved at postoperative 3-month follow-up

Figure 2d. Minimal graft resorption was seen at postoperative 12-month follow-up

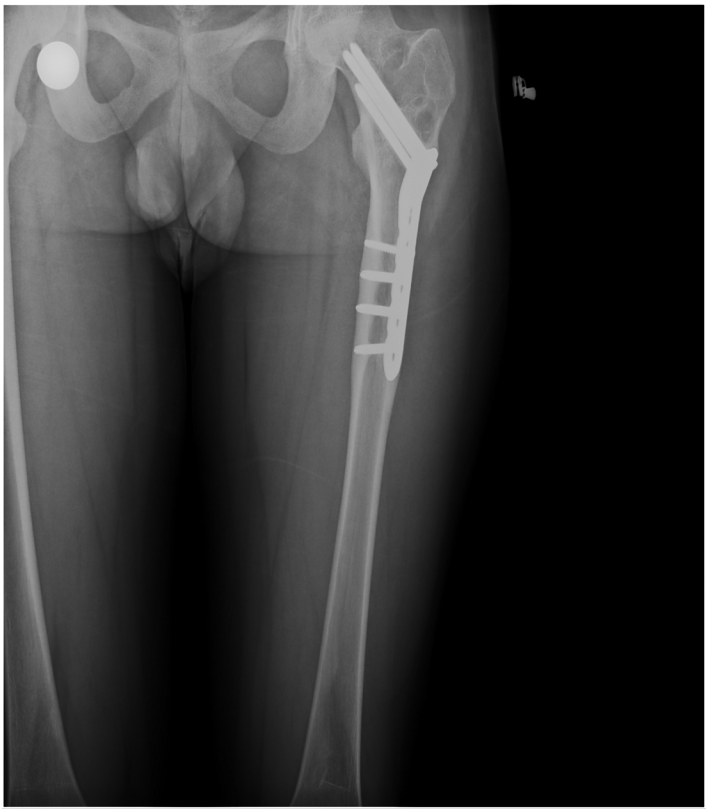

Figure 2e. At 60th-month follow-up the patient determined as "incomplete healing" according to the Capanna criteria

Figure 3a. Anteroposterior hip x-ray of a 7-year-old patient from our series with a cyst index of 4.85 which was evaluated as an impending fracture

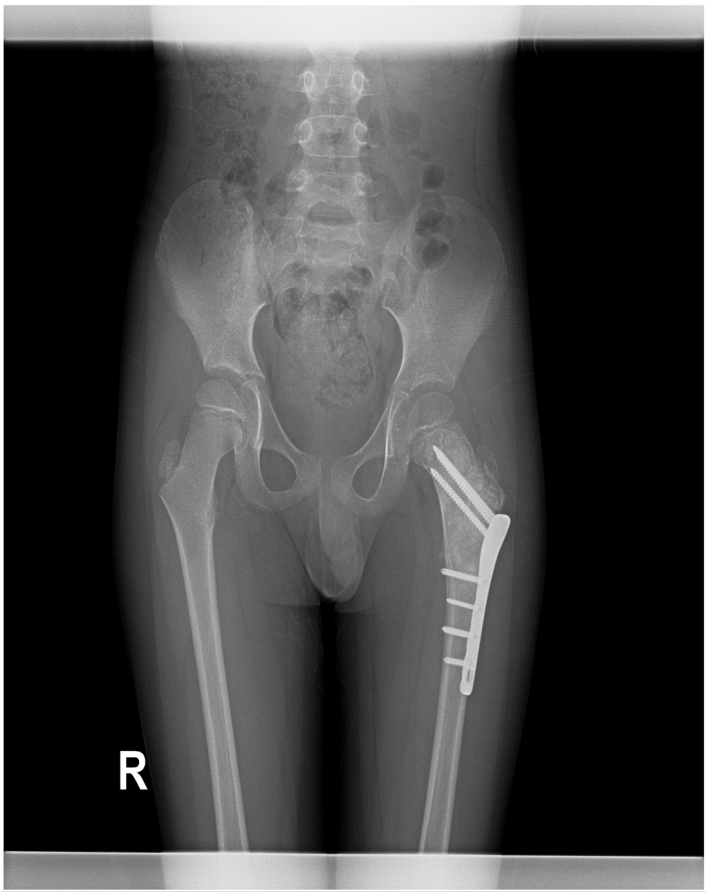

Figure 3b. The patient underwent curettage + allograft packing + plate fixation

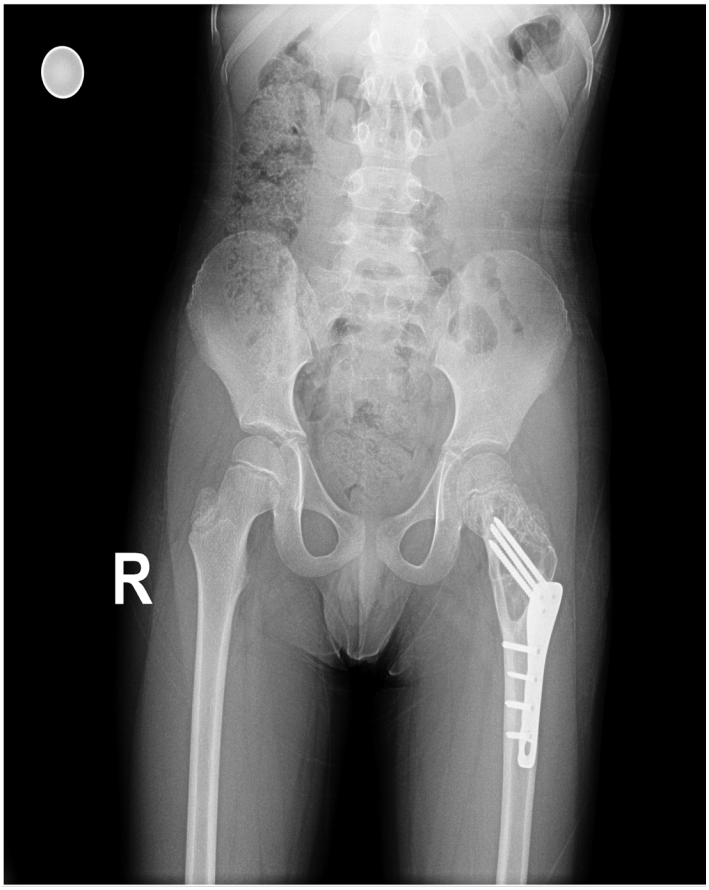

Figure 3c. The cyst recurred at the 9th month postoperatively

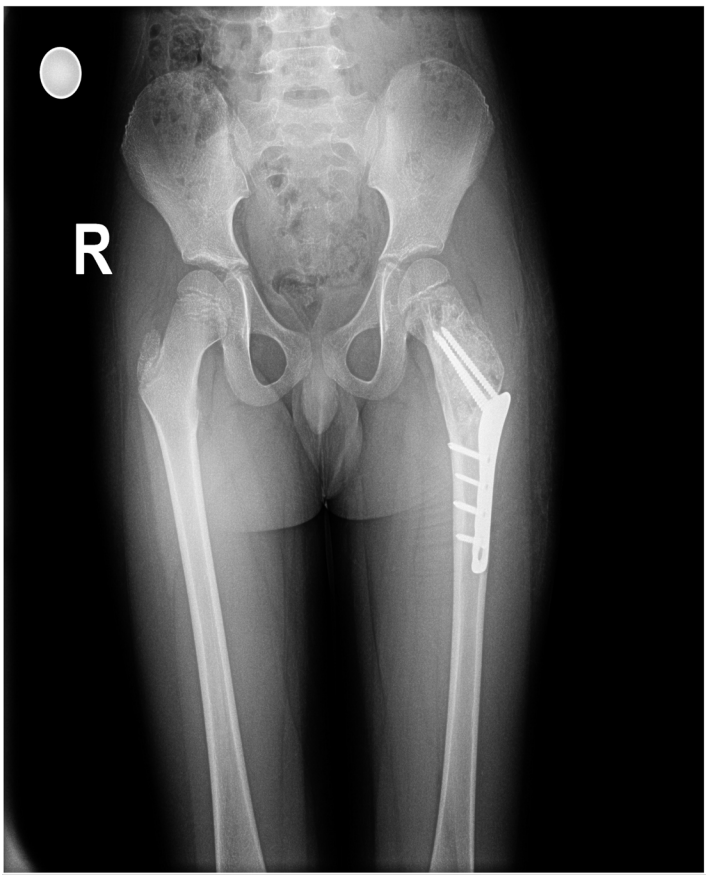

Figure 3d. Curettage + allograft packing + plate fixation is re-applied to recurrent lesion

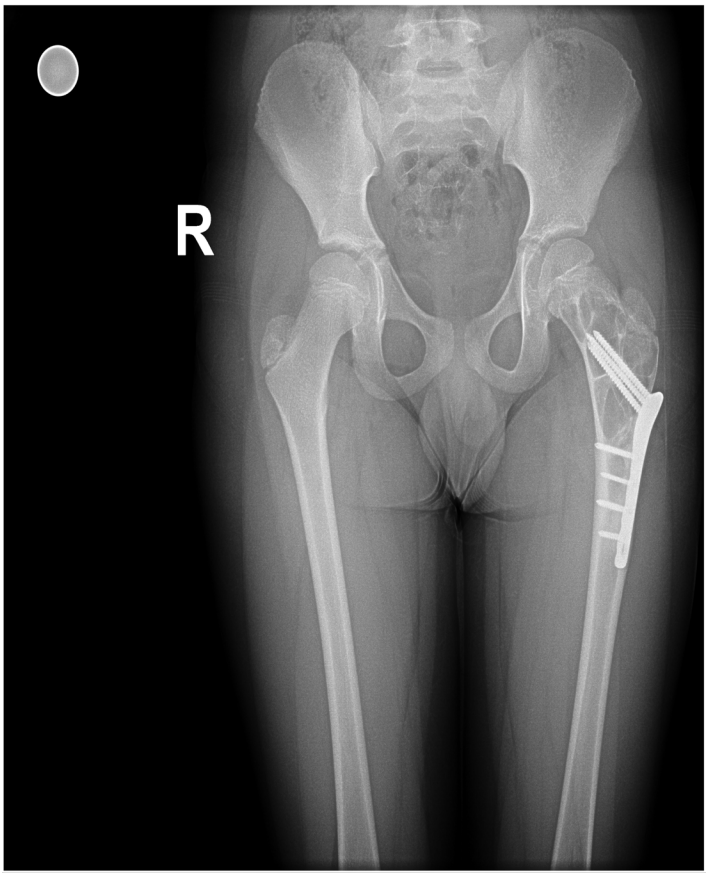

Figure 3e. A secondary recurrence was detected at the 30th month after primary recurrence

Table 4. Comparison of pathological fractures of proximal femur UBC's with a cortical displacement of more than 2 mm and less than 2 mm

	Fracture Displacement <2 mm	Fracture Displacement >2mm	p*
Age	7.6±2.3	10.4±2.4	0.038
Time to Fracture Healing (week)	5.4±0.9	6.3±1.2	0.191
Time to Consolidation (week)	14.1±2.3	18.5±0.9	<0.001
Recurrence	3/7	2/8	0.5

* = Students T test

Table 5. Comparative data of the patients with and without recurrence

	Recurrent	Non-recurrent	p*
Number of patients	16	35	-
Mean Age	6.8±2.6	9.3±3.1	0.006
Active Cysts	9/16	15/35	0.384
Mean Cyst-Physis Distance (mm)	14.6±10.8	19.5±17.8	0.316
Mean Cyst Index	4.4±1.2	3.5±1.2	0.016
Maximum Cyst Diameter/Physis Diameter	1.1±0.2	0.8±1.2	0.004
Applied surgery	Curretage + Hip spica=2 Curettage + Steroid injection=2 Curettage + Allograft packing=6 Curettage + Allograft packing + Plate fixation=6	Curretage only=1 Curettage + Steroid injection=1 Curettage + Allograft packing=12 Curettage + Allograft packing + Plate fixation=21	-
Follow-up (months)	78.7±30.9	58.3±30.3	0.032

* = Students T test

Discussion

Unicameral bone cysts (UBC's) of the proximal femur may inevitably develop pathological fractures in skeletally immature individuals [17]. Although it is known that a meticulous evaluation of fracture risk for UBC's of the proximal femur could lead to the management of the lesion; most lesions are incidental or present with pathological fractures [7]. The goal of treatment is achieving complete consolidation while avoiding pathological fractures and recurrences [12]. In this study we intend to answer the following questions;1) Is there a radiological predictor for impending fractures or an indicator that affects surgical management? 2) What is the effect of pathological fracture in proximal femoral UBC's? 3) Is there a precipitating factor for recurrence in proximal femoral UBC's?

Our study has some limitations. Although the number of patients included in our study is considerably high when compared to related studies in the literature, the number of patients in the fracture group or recurrence group was low to establish a precise comparison. The patients included in our study were all skeletally immature however age was variably distributed, thus age group-specific comparative evaluation was not possible. Furthermore, a median 5 years follow-up may give limited information for long-term complications of UBC's. The choice of treatment methods was determined by the same multidisciplinary board of orthopedic oncology in our institution between 2004 and 2018.

Cyst index is reported to be related to pathological fractures in UBC by numerous studies [4,10,17-19]. Vasconcellos et al. have concluded that applying the cyst index to their patient group did not verify that the test was an accurate predictor of fracture [7]. Accordingly, our series demonstrated that cyst index was significantly correlated to pathological fractures (p=0.048). Apart from fracture risk, some authors stated that a higher cyst index was related to better healing [18]. Although a comparative study reported no relation of cyst index with recurrence; our series demonstrated that higher cyst index values were significantly related to recurrences [17] (p=0.016). From our point of view, further studies are required to establish a predictive factor from radiological parameters for impending fracture.

UBCs in the proximal femur may lead to pathological fractures with serious complications including coxa vara, avascular necrosis, and growth arrest of the proximal femoral physis [20]. However pathological fractures in proximal femur UBC's are reported to result in a better consolidation after primary management of the fracture [4]. Norman-Taylor et al. have managed 20 skeletally immature UBC-related proximal femoral pathological fractures by nonoperative methods and consequently applied steroid injection in persistent cysts. They reported seven refractures, four coxa vara, and two limb length discrepancies [4]. The study has also stated that displaced fractures have demonstrated grade 3 or 4 consolidations after 1 year which was a better result than nondisplaced fractures in their series [4]. In a similar but limited series authors concluded that a longer healing time was needed in patients who did not have a pathologic fracture [3]. In a larger series of 54 patients with proximal femoral UBC's (25/54 were pathological fractures) the authors have reported no difference between the groups using healing time, consolidation, or recurrence [17]. On the other hand in a series with 56 UBC patients, authors compared fractures greater and smaller than 2 mm displacement and stated no difference using healing rates [11]. By the most series in the literature, our study showed no difference between a pathological fracture and impending fracture groups using cyst parameters, healing time, recurrence, or other complications. Pathological fractures with a cortical displacement of >2 mm, demonstrated longer healing time when compared to nondisplaced fractures (p=0.001).

Although some studies support that age is not related to pathological fractures in UBC; most authors concluded that young age (<10 years) is related to recurrence and pathological fractures [8,12,17,21-24]. Young age (<10) was also shown as a predictive factor for recurrence in our series, however, one may presumably think that active lesions were mostly encountered at a younger age. The proximity of the cyst to the growth plate, which is a sign of "active" lesions, eventually becomes distant with age, and with a minimum 2 cm distance from the growth plate, the cyst is accepted as "latent" [25]. With age, the cyst mostly migrates away and separates from the growth plate by a normal area of cancellous bone [10]. As the cyst (relatively) migrates to the weight-bearing intertrochanteric area, it may inevitably impose a major risk for pathological fractures [10]. Particularly the UBC's that extend below trochanter minor level were significantly related to pathological fractures in our series (p=0.021). Regardless of the cyst activity, we recommend against watchful waiting of UBC's in this particular region. Although male gender is reported to be associated with increased incidence of pathological fractures by some authors, whereas the patients in our study were predominantly male, thus a correlation with gender was not established in our study [18].

Proximal femoral UBC's management still remains a controversial [2,3,17,24,26]. The most popular conventional method, curettage and graft packing is renounced by many authors due to complications including epiphyseal arrest, weakened bone, coxa vara, high intraoperative blood loss, and LLD [3,12,27]. Regardless of age, some authors recommended that the use of a pediatric hip screw or side plate in addition to curettage and grafting is essential in patients where the lateral buttress is compromised [28]. Alternative treatment methods in skeletally immature individuals for this particular region including steroid injections, bone marrow injection, cannulated screw insertion, multiple drilling, and intramedullary nail insertion have gained popularity, recently [9,12,17]. In a comprehensive study, where the outcomes of curettage and graft packing were compared to steroid injection in UBC's, 33% and 15% recurrence ratios were found [2]. The authors have also concluded that residual empty spaces might be a source of recurrence in the curettage and graft packing group [2]. The index method in our series was curettage and graft packing supported by a plate. In a minimum follow-up of two years in our series, one coxa vara and one LLD were encountered amongst the aforementioned complications.

Intralesional steroid injection is a common method used for UBC's in the last two decades, however, most of the cysts may require repetitive injections for consolidation [1,2,16]. The response to intralesional steroid injection may differ, up to 76% recurrence with a single steroid injection is reported and even multiple repetitive injections may be insufficient for consolidation [29,30]. Steroid injections in proximal femur UBC's were reported to be associated with high failure rates [31]. Three patients underwent curettage and steroid injection in our series. Two patients, 14 and 5 years old, have developed recurrence at 24th and 58th months respectively.

One patient (3 years old) with a 130th-month follow-up has not developed recurrence yet. The follow-up of restricted daily activities with conservative methods may be challenging for patients and their caregivers [3]. Besides, longer immobilization may lead to muscle atrophy and increases the risk of thrombosis [32]. Two patients (3 and 7 years old) were treated with curettage and hip spica method. The patients were immobilized in hip spica for a mean of 8 weeks and in the course of treatment, patients and their caregivers confirmed having difficulties using compliance to the treatment.

The recurrence rate of UBC's was reported as 30% in the proximal humerus and 17% in the proximal femur in a large study group [22]. Regardless of localization the recurrence after the surgical intervention was as high as 39% within a minimum follow-up of 10 years study [23]. By the literature, the current study, with a minimum follow-up of 2 years, demonstrated a 34.1% recurrence rate. Several factors were identified as predictive factors for recurrences in UBC's, including 5 years of age or older patients, large and multilocular cysts, unimpacted fractures [21]. On the contrary, some authors report no predictive factors for recurrences in proximal femur UBC's [17]. By the most series in the literature, our study showed that earlier than 10 years of age (p=0.006) and cyst diameter to the growth plate diameter ratio (p=0.002) were significantly correlated with recurrence.

Skeletally immature patients with UBC's tend to develop repetitive trauma and pathological fractures eventually. We presumably think that the occurrence of pathological fractures in proximal femur UBC's of skeletally immature individuals is affected by various factors, including cyst activity, cyst localization, and the degree of trauma. The cyst extension below the level of lesser trochanter may be another predictor of pathological fractures in proximal femur UBC's of skeletally immature patients. The choice of treatment method should avoid longer restriction of daily activities and encourage early mobilization in skeletally immature age group. Ensuring stability with a plate even in impending fractures of the proximal femur may aid early mobilization and faster recovery.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Ethical approval
Ethics committee approval was uploaded (2020/405).

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