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# EVALUATION OF CYSTIC LESIONS OF BONES : A PATHOLOGICAL ANALYSIS

**Orthopaedics**

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## ABSTRACT

**Objective:** Many different neoplastic and non-neoplastic lesions involve the skeletal system. Clinical and radiological tools primarily assess the nature of these lesions. The aim of this study was to analyze the cystic bone lesions in a pathologic point of view.

**Methods:** All bone cysts evaluated under the guidance of clinical information and radiological images. Descriptive data such as age, gender, tumor site, symptoms, and clinical and radiological findings obtained from the hospital's database system.

**Results:** There were 96 cystic bone lesions; 47 were aneurysmal bone cysts (ABCs), 37 were simple bone cysts (SBCs), one was a lesion with features of both ABC and SBC, four were intraosseous ganglia, four were epidermoid cysts, and three were hydatid cysts. The mean ages of the patients with ABCs and SBCs were 18.7 ± 12.8 years (range, 3-75 years) and 23.8 ± 13.3 years (range, 3-62 years), respectively. Most of the lesions located in the long bones.

**Conclusions:** Cystic lesions of the bone rarely encountered in daily pathology routine. As with all conditions affecting the skeletal system, one of the most important steps towards an accurate pathological diagnosis is to perform with clinical and radiological information while evaluating the patients.

## KEYWORDS

Aneurysmal bone cyst, simple bone cyst, intraosseous ganglion, hydatid cyst, epidermoid cyst

## INTRODUCTION

Aneurysmal bone cyst (ABC), simple bone cyst (SBC), and their combinations, usually considered non-neoplastic cystic lesions. Other cystic lesions that may encounter in bone tissue include intraosseous ganglion cysts of undetermined origin, epidermoid cysts, and hydatid cysts of infectious origin. Bone cysts may develop as solitary or multiple lesions. Cystic bone lesions may mimic and behave similarly to a bone tumor.

The aim of this study was to analyze the cystic bone lesions in a pathologic point of view

## MATERIAL AND METHODS

Present study was conducted at Department of Orthopaedics, associated with Department of Pathology, Darbhanga Medical College and Hospital, Laheriasarai, Bihar. The samples sent to the pathology department various surgical methods: bone curettage, excision, and biopsy. Macroscopically, the samples were hemorrhagic, irregular tissues containing areas having the hardness of bone as well. All material routinely fixed in 10% buffered formalin and embedded in paraffin. The pathological evaluation based on routine hematoxylin-eosin stained slides under the guidance of clinical information and radiological images. The age of the patients, gender, localization, symptoms, and clinical and radiological findings obtained from the hospital's database system. The collected information has transferred to the preformed forms to do the statistical analysis.

## STATISTICAL ANALYSIS

The statistical analysiswas performed with SPSS statistical software for Windows, version 20.0 (SPSS Inc, Chicago, IL, USA). Descriptive analysis such as frequency, percentage, mean ± standard deviation, and range (min-max) was used for the patient groups.

## RESULTS

Of the 96 cystic bone lesions in the overview, 47 were ABCs, 37 were SBCs, one was a cystic lesion with features of both aneurysmal and simple bone cyst, four were intraosseous ganglia, four were epidermoid cysts, and three were hydatid cysts.

The mean age of the patients with ABCs was 18.7 ± 12.8 (range, 3-75 years). Of these 47 patients, 23 were female, and 24 were male. The lesions located in the lower extremities in 27 patients, the upper extremities in 6 patients, the sacrum in 5 patients, the vertebrae in 3 patients, the skull in 3 patients, the ribs in 2 patients, and the clavicula in 1 patient. There were concurrent lesions with the ABCs in 6 patients (Table 1). In 2 patients the cystic bone lesions reported as solid ABC. There were five patients with a recurrence, however, none of them underwent malignant transformation in the clinical follow-up time. Microscopic examination revealed blood-filled cavernous spaces without an endothelial lining surrounded by a fibrous wall. The fibrous wall contained multiple multinuclear giant cells, spindle fibroblasts with mitotic figures, and patchy areas of new bone production (Figure 1). No cytologic atypia or atypical mitotic figures observed.

**Table 1 : Characteristics of the aneurismal bone cysts**

| Characteristics | Data (n=47) |
|---|---|
| Age at diagnosis (years) | 18.7±12.8 (range, 3-75 years) |
| Male/Female | 24/23 |
| Localization | |
| Lower extremities | 27 |
| (Femur/Tibia/Fibula/Bone of the feet) | (12/9/3/3) |
| Pelvis | 5 |
| Vertebra | 3 |
| Upper extremities | 6 |
| (Humerus/Radius/Bone of the hands) | 2/2/2 |
| Others | 6 |
| Concurrent lesions | |
| Giant cell tumor | 2 |
| Intraosseous lipoma | 1 |
| Ossifying fibroma | 1 |
| Fibrous dysplasia | 1 |
| Reparative granuloma | 1 |
| Recurrence | 5 |

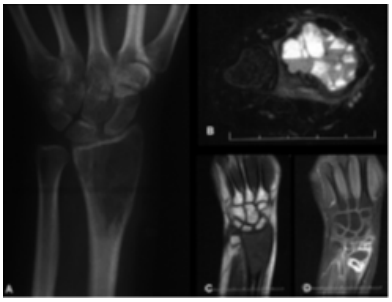

***Figure 1.*** *A. The anteroposterior radiograph showed an osteolytic, moderately expansile lesion in the distal radial metaphysis. B. Axial T2-weighted MR image showed multiple fluid-fluid levels within the lesion. C. Coronal T1-weighted MR image of the lesion. D. On contrast-enhanced coronal T1-weighted MR image, there was an enhancement of the cyst wall and internal septations.*

The majority of cases with an SBC were male (23 males, 14 females). The mean age of these patients was 23.8 ±13.3 years (range, 3-62 years). The lesions located in the lower extremities in 18 patients, the upper extremity in 16 patients, and the pelvis in 3 patients (Table 2). SBCs co-occurred with another lesion in four of these patients. The lesions recurred after excision in 2 patients. There was not any malignant transformation. Microscopically, a thin fibrous cystic wall with interspersed benign giant cells was observed. Patchy areas of hemosiderin-laden macrophages and cell aggregates consisting of mononuclear inflammatory cells were also noted (Figure 2). In cases with accompanying fracture healing and callus formation, proliferating fibroblasts and callus formation were present on the cyst wall and inside the cyst lumen. The patient in whom had a mixed cystic lesion consisting of an ABC, and an SBC was a 12-year-old boy. The lesion located in the distal part of the right tibia.

Comparing the two most common cystic bone lesions, ABCs and SBCs, the male-female distribution was equal in the cases with ABCs, whereas in SBCs there was a male predominance. The mean age of the patients with SBCs was higher than those with ABCs. The recurrence rate was higher in ABCs than for SBCs.

**Table 2 : Characteristics of the simple bone cysts**

| Characteristics | Data (n=37) |
|---|---|
| Age at diagnosis (years) | 23.8±13.3 (range, 6-62 years) |
| Male/Female | 23/14 |
| **Localization** | |
| • Humerus | 13 |
| • Femur | 9 |
| • Tibia | 4 |
| • Pelvis | 3 |
| • Bones of the feet and hands | 5 |
| • Others | 3 |
| **Currents lesions** | |
| • Callus | 1 |
| • Fracture recovery | 3 |
| **Recurrence** | 2 |

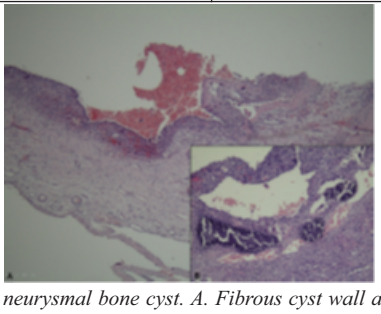

***Figure 2.*** *A neurysmal bone cyst. A. Fibrous cyst wall and a blood-filled cavernous space without endothelial lining were seen. The fibrous wall contained multiple multinuclear giant cells and spindle fibroblasts (Hematoxylin-eosin ×40). B. Patchy areas of the basophilic bone formation called "blue bone" were noted (Hematoxylin-eosin ×100).*

Intraosseous ganglion cysts and epidermoid cysts were also present in our 10-year bone cyst archive. There were four intraosseous ganglion cyst patients. The mean age of the patients was 42 ± 12.1 years (range, 30-58 years). Three of them were female, and one of them was male. The lesions located in the acetabulum in three of these patients and the foot lateral in one patient. Microscopic examination demonstrated a thin fibrous cyst wall with mucinous content. Myxoid changes were present on the cyst wall between areas of loose fibroblastic proliferation (Figure 3). Three of the patients with epidermoid cysts were female, and one was male. Their mean age was 17.7 ± 12.4 years (range, 1-31 years). The location was distal phalanx in three patients and the orbital bone in one patient. The microscopic evaluation showed cystic spaces lined with keratinized squamous epithelium. Our case series included three intraosseous hydatid cysts located in the femur in two patients and the vertebrae in one patient. Two of these patients were male, and one was female; their mean age was 44.6 ± 21.7 years (range, 25-68 years). Microscopically, these lesions characterized by a fibrous cyst wall, a germinative membranous structure on the internal surface, and a few scolices.

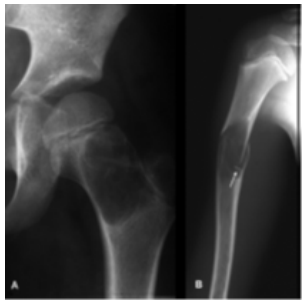

***Figure 3.*** *Simple bone cyst. A. A child with a simple bone cyst in the femoral neck. The anteroposterior radiograph showed a well defined medullary lytic lesion with moderate cortical thinning. B. A child patient with a simple bone cyst in the humerus. The anteroposterior radiograph revealed the cyst complicated by a pathologic fracture. A fragment of the cortex(arrow) was lying medially within the cyst (fallen fragment sign).*

## DISCUSSION

### Aneurysmal bone cysts

ABCs are not considered neoplastic lesions because they may show signs of regression, even after incomplete resection. However, cytogenetic and molecular studies showing karyotypic anomalies on the short arm of chromosome 17 have suggested that the primary ABCs are neoplastic lesions rather than reactive lesions. This cyst may be encountered in all age groups although they have been most commonly reported during the first two decades of life, with a slightly higher prevalence in women compared to men. Pain and swelling are the main symptoms, although compressive symptoms are also sometimes present when the lesions are located in the vertebrae. Our case series also showed that 34 (72.3%) patients were in their first two decades. The female-to-male ratio was 0.95 (23/24). Our case series also revealed that pain and swelling were the most prevalent symptoms.

ABCs, which are composed of blood-filled spaces separated by fibroblasts, osteoclast-type giant cells, and septae consisting of reactive woven bone, may develop either de novo or secondary to hemorrhagic cystic changes due to benign or malignant bone tumors. They may grow in all types of bone although they tend to be located in the metaphysis of long bones, mainly the femur, tibia, and humerus, as well as the posterior portions of the vertebral bodies; 70-80% of all aneurysmal bone cysts are found in these two localizations. In our case series, 29 (61.7%) of the aneurysmal bone cysts were found in the long bones and the vertebrae (Table 1).

Radiological images vary depending on the stage of the lesion and its relationship with the adjacent bone. Eccentric localization is common in long tubular bones, whereas central and parosteal lesions are less common. In earlier stages, lesions appear as small, typically eccentric, and infiltrative masses that do not widen the bone. During the growth phase, they are characterized by marked cortical lysis and destruction. In their stable phase, they may have the classic appearance of an ABC marked by a widened lesion with multiple internal trabeculations and an osseous periphery, which distorts the pattern of host bone. In the healing phase, on the other hand, they appear as irregular, coarsely trabecular, osseous lesions as a result of progressive ossification of the lesion.

ABCs may be primary, or they may co-occur with or develop secondary to another lesion. Most ABCs are labeled primary, although development secondary to a preexisting lesion that described in 20-30% of cases. Many secondary ABCs reported in the literature. It indicated that ABCs accompany, in descending order, giant cell tumors of the bone, chondroblastoma, chondromyxoid fibroma, and fibrous dysplasia. In our case series, six patients had accompanying lesions to ABCs: two of them secondary to giant cell tumors, one of them to ossifying fibroma, one of them to fibrous dysplasia, one of them to intraosseous lipoma, and one of them to giant cell reparative granuloma.

Microscopically, ABCs consist of multiple bloodfilled cavernous spaces without a muscular layer or an endothelial lining. There are also fibrous walls that separate these areas. Fibroblasts, histiocytes, giant cells, inflammatory cell infiltration, osteoid, and chondroid can be found on the fibrous walls. The osteoid usually has a trabecular pattern. It is entirely composed of fibrous septa-like cellular components and contains no or focally distributed widened vascular spaces in its solid variant. It has been reported that solid variant of ABCs usually located in the posterior segments of the vertebral bones.

However, two patients in our series (age; 20 and 22 years) had femoral and calcaneal locations.

Differential diagnosis must include giant cell tumors of the bone, low-grade osteosarcoma, and telangiectatic osteosarcoma. The fibrous septa of ABCs also contain multiple giant cells; however, the age of the patient and the metaphyseal location of the lesion are helpful hints in the differential diagnosis.

Low-grade osteosarcomas contain fewer mitoses and low cellularity compared to a typical ABC.

Many mitotic figures may be observed, especially in the osteoid-containing areas, which creates a challenge in the differential diagnosis from telangiectatic osteosarcoma. Radiologically, a smooth border, an irregular appearance, and a thin calcific line in the cortical bone indicate aneurismal bone cysts. Microscopically, the absence of anaplastic cells and atypical mitotic figures in the fibrous trabeculae, as well as an osteoid pattern that is parallel and linear to the septae, favor the diagnosis.

In approximately 1/3 of the cases, a basophilic bone formation called “blue bone” may be noted, albeit non-diagnostic.

The prognosis of aneurysmal bone cysts is quite favorable. There are case reports in the literature suggesting malignant transformation although this is not an expected finding in general. We detected recurrence in five (10%) cases with age range of 8 to25 years. Recurrent lesions located in the lower extremity and the pelvis in four patients and the maxilla in one patient. In one patient, there was a solid component seen microscopically, which recurred later.

None of the cases in our series had a malignant transformation.

**Simple bone cysts**

SBCs of undetermined origin are considered reactive or developmental lesions. They constitute roughly 3% of cases biopsied from bone tissue. These lesions create an irregularity in the epiphysis plaque.

They are usually observed in the second decade with a prevalence three times higher in men. In our case series, 20 (54%) patients were in their 2nd decade. The number of males and females were 23 and 14, respectively, with a ratio of 1.6. The majority of these lesions is found in the humerus, femur, and tibia. We similarly found that 26 (70.2%) of the SBCs in our case series located in the humerus, femur, and tibia (Table 2). Patients may present with pain. The SBCs could locate adjacent to a pathological fracture or present as an incidental radiological finding.

Likewise, four cases in our case series presented with pathological fractures, whereas the other patients were admitted with pain and swelling. SBCs appear as lesions that may be trabeculated or multiloculated and appear as cystic masses located at the metaphysis in relation with the epiphysis plaque. Cortical thinning, erosion and widening may be present; however, the cortical bone is not destroyed. The growth rate of cystic lesions that are about the epiphysis plaque is slower than that of bone. Therefore, they may appear as metaphyseal cystic lesions in patients of advanced age.

Histologically, there is a cyst wall composed of collagen and thin fibrous tissue, which contains giant cells, hemosiderin-laden macrophages, and lymphocytes. The cyst wall may contain abundant, irregular, and sometimes calcific fibrin deposits.

Because SBCs may have a giant cell component, the differential diagnosis must include giant cell tumors of the bone. The presence of septae in the lesion should raise the suspicion of an ABC. In SBCs, the presence of a fracture is an indication for surgery. Spontaneous regression takes place in 15% of cases; however, the majority of these lesions do not regress, and they even progress.

**Ganglion cysts**

An intraosseous ganglion resembles a 'ganglion' that is located in a tendon sheath, and it is composed of spaces filled with mucoid fluid. Patients are asymptomatic, and these cysts are incidentally detected in radiological studies. Patients may present with pain in the presence of a fracture. In a study of 88 patients, the intraosseous ganglion was most commonly located in the hip and adjacent structures. In our case series, three cases were found in the acetabulum and one in the ankle. Cases with metacarpal and vertebral locations have also reported. These cysts have usually been reported in young and middle-aged adults; the age range in our study was between 30 and 58 years (mean: 42 years). Three of these patients were female, and one was male. In our series, the presenting symptom of all the patients was a pain.

Radiologically, these cysts are lytic masses with well-defined borders which widen the joint cartilage. A sclerotic margin is evident at the periphery of the lesion. Histopathological examination shows a fibrous cyst wall and mucinous material within the cyst. Differential diagnosis must include degenerative joint disease. The absence of any degenerative lesion in the adjacent joint may suggest the diagnosis.

**Epidermoid cysts**

Epidermoid cysts with intraosseous location are rare non-neoplastic lesions in the jaw bone, distal phalanges, or the skull. They are frequently located in the skull and distal phalanges. Location in the skull is thought to occur as a result of developmental defects, whereas distal phalangeal locations are considered secondary to traumatic implantations of squamous epithelium. The most common complaint is swelling of the bone. These cysts have a low growth rate, leading to a marked widening in the host bone. They may also extend to the soft tissues nearby, altering the clinical picture.

Cases in which the lesion is located in the skull and extends intracranially may present with a clinical picture resembling that of a brain tumor. Three patients in our case series had a distal phalangeal location, and one had a maxillary location with extension to the orbital soft tissue. Case series in literature have reported an age range of 21 to 69 years, with the majority of cases being male (87.5%). In our series, three female and one male case were present with an age range of 1 to 31 years (mean: 17.7 years). They presented with pain and swelling.

Radiologic studies have shown that these lesions have a considerably well-defined border with a sclerotic ring. The cortical bone is usually thinned and widened. Histopathological diagnosis is made by noting the cyst wall lined by a squamous epithelium that produces keratin, even if in a focal area.

**Hydatid cysts**

Echinococcosis is a common parasitic infection in countries where livestock farming is practiced. It tends to be localized, in particular, in the liver, lung, and brain. Approximately 3% of all hydatidosis cases are localized in bone, with a predilection for vertebral bones, long bones, and pelvic bones. Patients may present with symptoms of spinal compression when lesions are localized to the vertebral column.

Two of our cases located in the femur, while one located in vertebra. One of the cases in the femur extended to the soft tissue of the thigh. The pain was the primary symptom in both the femoral and vertebral lesions. Two of our patients were male, and one was female; their ages ranged between 25 and 68 years (mean: 44.6 years). Radiologically, the pathognomonic appearance of these lesions is the presence of sister vesicles in the cyst lumen.

## CONCLUSION

Cystic lesions of the bone are not frequently encountered. Differential diagnoses must also include malignant bone tumors. As in all conditions affecting the skeletal system, clinicopathologic meetings where clinical, radiological, and pathological assessments made together, are one of the most important steps towards a correct diagnosis.

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