

Understanding Unicameral and Aneurysmal Bone Cysts

Joseph Rosenblatt, DO,* Adrienne Koder, DO*

*St Christopher's Hospital for Children, Philadelphia, PA

Practice Gaps

1. Recognizing benign vs malignant bone cysts on radiographs can be challenging.
2. Clinicians may not always recognize important historical and physical findings associated with bone cysts.
3. It is important for clinicians to know what tests need to be ordered and when to refer to a pediatric orthopedic specialist.

Objectives After completing this article, readers should be able to:

1. Demonstrate a basic understanding of the etiology of unicameral bone cysts and aneurysmal bone cysts.
2. Identify radiographic findings of bone cysts and determine when to order advanced imaging.
3. Implement basic treatment protocols for bone cysts.

Abstract

Bone cysts in the pediatric population are often found incidentally on radiographs or after a cyst has created cortical weakness leading to a pathologic fracture. Most bone cysts are benign, are pain free, and resolve spontaneously. The most common bone cyst is unicameral 1-chamber bone cyst, also known as simple bone cyst. General practice pediatricians may be the first to encounter these lesions, and this article aims to help elucidate their incidence, etiology, clinical findings, radiologic findings, and modern treatment approaches. The other differential diagnoses that should be considered, specifically, aneurysmal bone cyst, are also explored. This summary is not all inclusive, and it is recommended that all patients be referred to a pediatric orthopedist.

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ABBREVIATIONS

ABC aneurysmal bone cyst
MRI magnetic resonance imaging
UBC unicameral bone cyst

SIMPLE BONE CYSTS

Incidence

Simple bone cysts (also known as solitary bone cysts or unicameral bone cysts [UBC]) are benign tumors of childhood and adolescence. They represent approximately 3% of all biopsied primary bone tumors and commonly occur during the first 2 decades of life, most often between 4 and 10 years of age. (1)

Most cysts occur in the metaphyseal region of the proximal humerus or femur (Fig 1). The next most common sites are the proximal tibia and distal tibia. Occasionally, cysts may be found in the calcaneus, fibula, ulna, radius, pelvis, talus, lumbar spine, and other parts of the axial skeleton. Cysts that are pain free are generally benign, and those that have pain may be more likely to be malignant. Because it can be difficult to distinguish pain in the pediatric population, a good history and physical examination is vital to making the diagnosis.

Solitary bone cyst is an accurate term because rarely does more than 1 cyst occur in an individual. The term *unicameral bone cyst* implies that 1 chamber exists. Although 1 large cavity is usually found, a cyst may become multiloculated after a fracture because of the formation of multiple bony septations, thus making the term *unicameral* technically incorrect.

Simple cysts are often categorized as either active or latent according to Jaffe and Lichtenstein based on their distance from the growth plate. In general, patients with active cysts are younger, and active bone cysts have a higher



Figure 1. Radiograph of a 9-year-old boy with right groin pain showing a unicameral bone cyst in the proximal femur.

rate of failure with treatment, regardless of treatment type. (2)(3)(4)(5) A cyst that is less than 0.5 cm from the physis is considered active and possesses greater potential for growth and subsequent fracture. In addition, an active cyst presents with the risk of expanding into and damaging the physis, ultimately causing growth arrest and deformity or limb-length inequality. Epiphyseal involvement is rare but if present it should be considered an aggressive form of an active lesion. (6) A cyst that has grown away from the growth plate is considered latent and theoretically no longer has the capacity for growth (Fig 2). However, latent cysts continue to have the potential for growth, as often seen by their unexpected recurrence after treatment in the young patient. (2) After skeletal maturity, however, it is uncommon for the cysts to recur or progressively worsen. Most commonly, latent cysts grow further from the physis as the bone grows, thus being less of a threat for deformity.

Etiology

The cause of simple bone cysts remains uncertain. To fully explain the etiology of simple bone cysts, a proposed theory should address the following factors: 1) more than 70% are discovered in childhood, 2) more than 95% arise from or involve the metaphysis, 3) most occur in the proximal humerus or femur, 4) a cyst wall and fluid high in protein content are common, and 5) simple bone cysts represent a benign process with a significant recurrence rate after treatment.

There are multiple hypotheses surrounding the formation of simple bone cysts. One proposition is that a synovial cyst with a small amount of synovial tissue becomes entrapped in an intraosseous position after birth trauma or during early development. Over time, increased pressure secondary to secretions leads to expansion of the cystic structure in the bone. (1) Others have postulated that cysts result from a localized failure of ossification in the metaphyseal area during periods of rapid growth. (4) Another popular proposed theory is that the cause of the cyst is blocked circulation (venous obstruction) and drainage of interstitial fluid in rapidly growing bone. (7) The last theory is based on the finding that the chemical constituents of the fluid in simple bone cysts are similar to those of serum. (8)

Furthermore, current literature further substantiates this theory of a blockage or occlusion of the intramedullary circulation. (9)(10)

Clinical Features

Most bone cysts found in the pediatric population will be found incidentally on a radiograph. More often, however, cysts are diagnosed because of pain. The pain may be mild and reflect a microscopic pathologic fracture. More abrupt

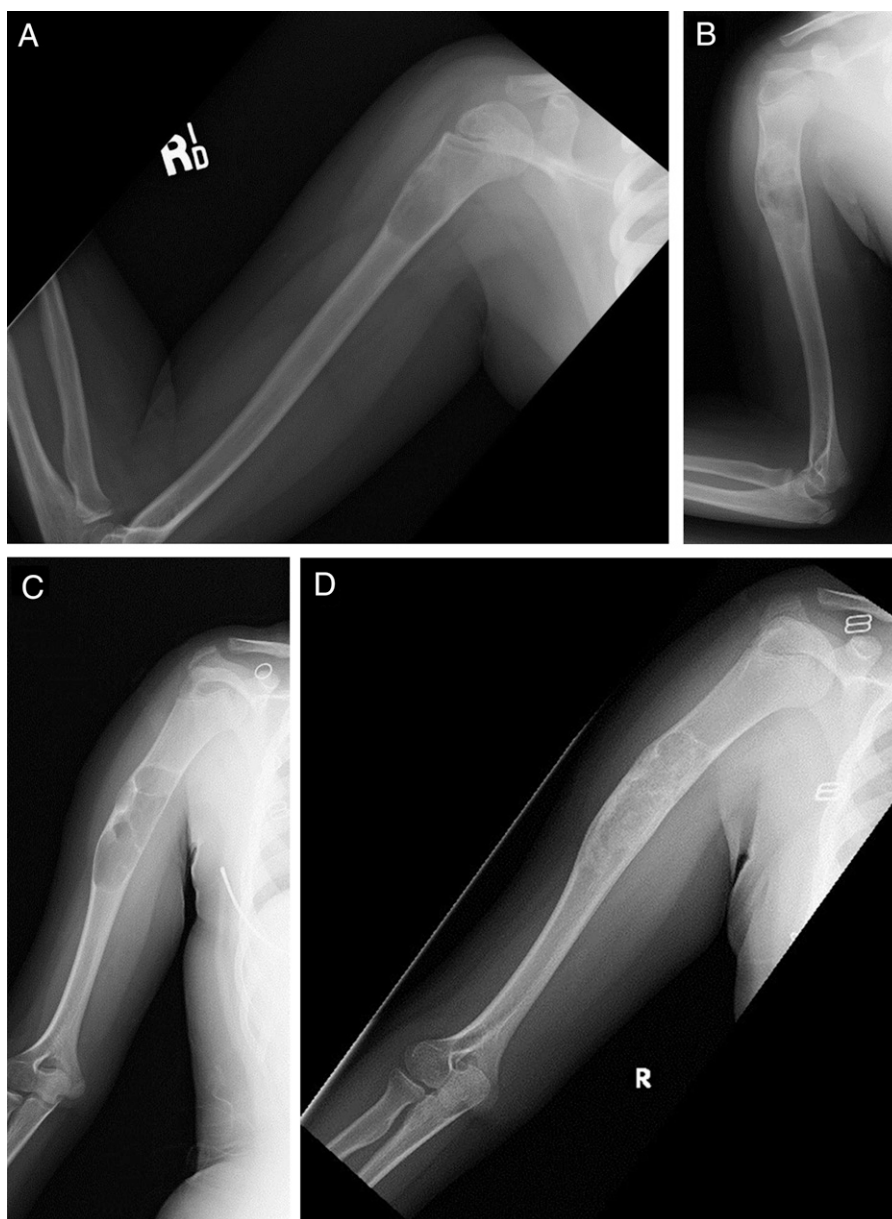


Figure 2. Radiographs showing a solitary cyst evolving from active to latent. A. At 7 years old. B. At 9 years old. C. At 11 years old. D. At 13 years old.

discomfort occurs when a pathologic fracture occurs after relatively minor trauma, such as a fall, throwing a ball, or even closing a car door. In this case a child can present with pain, swelling, erythema, and possibly a deformity. These fractures occur in up to 90% of patients and heal readily, although the cysts do not. (11) After these pathologic fractures, premature physal closure has been reported in nearly 10% of patients. (12)

Physical Examination

The physical examination should include a focused evaluation of the tumor site, including evaluation for the presence

of a mass, swelling, range of motion, effusion, and changes in temperature or color of the involved extremity. In addition, a complete examination of the patient is essential for ruling out secondary lesions, enlarged nodes, or skin changes, such as café-au-lait spots. It is imperative to rule out skin and soft tissue involvement, which would direct the differential diagnosis away from UBC.

Radiographic Findings

Simple bone cysts have several characteristic radiographic features. Their radiographic appearance is so typical that most can be diagnosed without a biopsy.

Approximately 50% occur in the proximal humerus and up to 30% in the proximal femur. The cyst is metaphyseal and usually extends to, but not across, the physis. On rare occasions it can cross the physis into the epiphysis. (13) Typically the cyst is symmetrically expansile and radiolucent, with a thin cortical rim. Over time the physis grows away from the cyst. In many newly diagnosed patients a pathologic fracture occurs with or without displacement. The 1 pathognomonic sign of a simple bone cyst is the “fallen leaf” fragment (Fig 3A) (14) This represents a portion of fractured cortex that settles to the most dependent part of the fluid-filled cyst. However, it is seen in less than 10% of patients, and it should not be expected if the cyst has become multiloculated after a previous pathologic fracture.

Simple bone cysts that have undergone healing after pathologic fracture have a complex appearance on magnetic resonance imaging (MRI) because the previous fracture causes heterogeneous fluid signals and areas of thick peripheral rim enhancement. (11) An MRI may also detect fluid levels, soft tissue changes, and septations not seen on plain film.

Differential Diagnosis

The diagnosis can usually be established based on the presence of typical radiographic findings. Other lesions to be considered in the differential diagnosis include aneurysmal bone cyst (ABC), monostotic fibrous dysplasia, atypical eosinophilic granuloma, endochondroma, and intraosseous ganglia. All these lesions may be radiolucent. Knowing the defining radiologic appearance of these lesions will aid the clinician in differentiating them from simple bone cysts. Both

fibrous dysplasia and ABCs may be in the metaphysis and appear expansile; however, ABCs are more commonly eccentric, where fibrous dysplasia has a “ground glass” appearance and is typically a central lesion.

Enchondromas are well-defined, radiolucent, central medullary lesions that often appear more diaphyseal as a long bone grows. Enchondromas may be associated with cortical thinning and expansion in short tubular bones of the hands and feet, but not in long tubular bones (femur, tibia). Typically found incidentally, intraosseous ganglia are small, well-demarcated radiolucent lesions with a well-defined sclerotic rim in the epiphyses and subchondral region of long bones. (9)

Treatment

Nonsurgical treatment with observation is reasonable for small and asymptomatic UBCs, particularly those in the upper extremity or calcaneus. The main indications for surgical intervention are continued pain, impending/recurrent fracture, and prevention of secondary deformity. (15) A common misconception in the treatment of simple bone cysts in children is that once the pathologic fracture heals, the cyst also has an excellent chance of healing spontaneously. Investigators examining this phenomenon have found that the likelihood of spontaneous healing of the cyst after pathologic fracture is very low, probably less than 5%. (3)(14)(16) Thus, if treatment of the cyst is deemed necessary, it should be undertaken as soon as the fracture has healed. However, overtreatment in skeletally mature persons should be avoided. In these individuals, if the cyst has a sufficiently thick cortex and is located in the upper extremity,

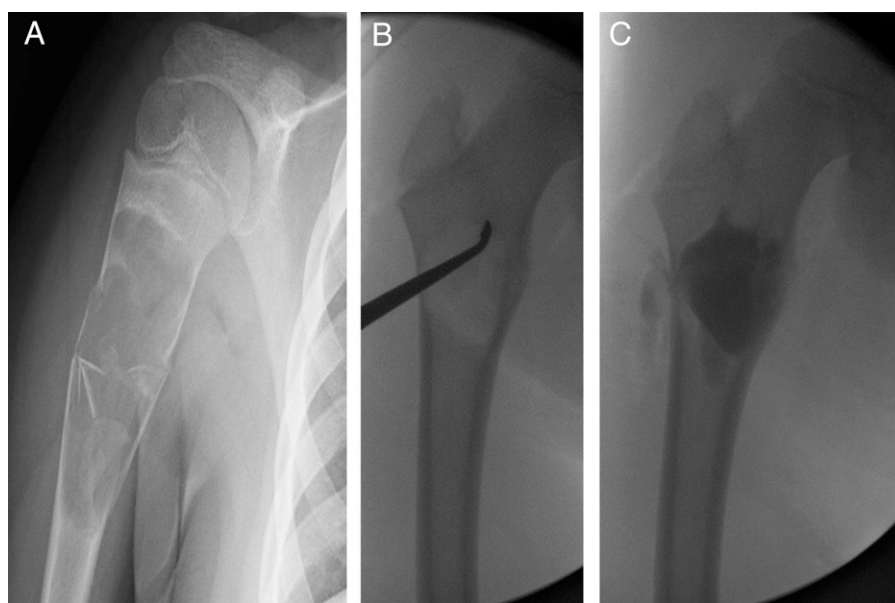


Figure 3. A. “Fallen leaf” sign. B. Percutaneous curettage. C. Grafting with synthetic bone graft substitute.

periodic observation is all that is needed. If the patient is asymptomatic, restriction of activities may not be necessary.

Because of the potential for complications after hip fractures, lesions in this location are usually treated surgically regardless of their size or symptoms.

The preoperative evaluation of patients with simple bone cysts rarely requires more than good-quality radiographs of the lesion. If the diagnosis is equivocal, a bone scan will verify the presence or absence of other abnormal areas. Computed tomography may be helpful in differentiating simple bone cysts from other lesions, such as ABCs or fibrous dysplasia. Findings on MRI of double-density fluid levels and septations associated with low signal on T1-weighted images and high signal on T2-weighted images strongly suggest the presence of an ABC rather than a simple bone cyst. (17)

Several treatment options are available for UBCs. Treatment modalities include injection of corticosteroids into the cyst, injection of autologous bone marrow, multiple drilling and drainage of the cavity, and curettage of the membranous wall followed by bone grafting. A relatively high recurrence rate has been historically associated with all treatment options of simple bone cysts.

Most authors now agree that cyst decompression is essential for adequate healing. A minimally invasive technique with cyst decompression, percutaneous curettage, and use of synthetic bone graft substitutes (injectable calcium sulfate and calcium phosphate) is the preferred treatment at most institutions. (18) (Fig 3B and C)

Medical Therapies

The theoretical use of bisphosphonates and botulinum toxin type A injections for the management of UBCs has been

investigated in some basic science research. (19)(20) However, there are no established or recommended medical noninterventional treatments for this condition. (9)

ANEURYSMAL BONE CYSTS

Incidence

An ABC is a solitary, expansile, radiolucent lesion usually located in the metaphyseal region of the long bones. Fortunately, ABCs are seen much less often than simple bone cysts, and they represent only 1% of all primary bone tumors sampled for biopsy; the annual incidence of primary ABCs approximates 0.1 per 10⁹ individuals. (21)(22) Nearly 70% of affected patients are aged 5 to 20 years, and approximately half of these cysts occur in the second decade of life, although the lesion has been reported in infants. No sex predilection is reported. (21)

Aneurysmal bone cysts can be located throughout the skeleton, and the most common sites are the femur, tibia, spine, humerus, pelvis, and fibula, with approximately half of reported cases occurring in the long bones of the extremities. (21)(23) Although they usually arise in the metaphyseal region of the bone, ABCs may sometimes cross the physis into the epiphysis or extend into the diaphysis. (24)

Approximately 20% of ABCs involve the spine. They may occur anywhere between the axis (25)(26)(27) and the sacrum (28) and can cause spinal cord compression or spinal deformity. (29)(30) In the vertebra itself, the cyst may be found in the body, pedicles, lamina, and spinous process (Fig 4). Involvement of 2 or more adjacent vertebrae is not uncommon. Aneurysmal bone cysts may also occur in the maxilla, frontal sinus, orbit, zygoma, ethmoid, temporal bone, mandible, sternum, clavicle, hands, and feet. (31)

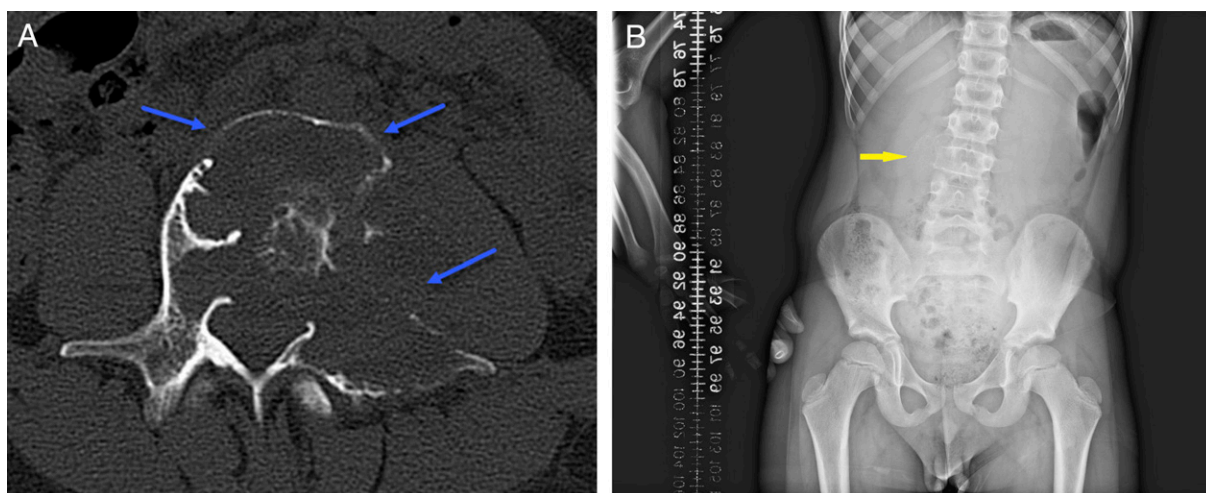


Figure 4. A. Axial computed tomographic scan of a large aneurysmal bone cyst (blue arrows) in the cervical spine. Courtesy of Frank Gaillard (<http://radiopaedia.org/articles/aneurysmal-bone-cyst>). B. Lumbar spine anteroposterior radiograph showing a lytic lesion of right L3 (winking owl sign) (yellow arrow).

Etiology

The etiology of ABCs is not precisely known. The literature suggests that ABCs represent either a primary neoplastic condition or a secondary response (arteriovenous malformation) due to the local destructive effects of an underlying primary tumor. (32)

Recently, genetic research has shed some light on the etiology of ABC, leading some to believe that ABC is a true neoplasm rather than a reactive process. (33) Histopathologic studies have reported that gene rearrangements localized to t(16;17) and involving chromosome segments 7q, 16p, and 17p11-13 confirm a true neoplastic etiology. (31)(34) Others have shown that upregulation of proteases may ultimately lead to tumorigenesis. (28) Immunohistochemical and in situ hybridization studies found insulinlike growth factor I, or messenger RNA coding for this growth factor, primarily localized in multinucleate giant cells in all of the ABCs sampled. (35) Insignificant levels of expression were found in normal human bone tissue. These findings support the theory that genetic factors may play a significant role in the development of primary ABC.

Clinical Features

The clinical presentation of an ABC includes localized pain for several weeks' duration, tenderness, and, if the ABC occurs in an extremity, swelling. As with most benign bony malignancies, secondary symptoms such as fever, weight loss, malaise, nausea, or vomiting are not common. When an ABC involves the spine, progressive enlargement may compress the spinal cord or nerve roots and, similar to any space-occupying lesion, result in neurologic deficits such as motor weakness, sensory disturbance, and loss of bowel or bladder control. Spinal involvement, therefore, mandates urgent intervention.

Radiographic Findings

Aneurysmal bone cysts have a classic appearance of a radiolucent cystic lesion in the metaphyseal portion of the bone. Originally described as a periosteal "blowout" lesion, (36) the lesion is destructive and may expand beyond the surrounding cortical bone. The mass may elevate the periosteum, but it typically remains contained by a thin shell of cortex. Typically, ABCs are eccentric but may also be central or subperiosteal (Fig 5). Lesions in the epiphysis are atypical and should raise suspicion of secondary changes caused by a neoplastic process. (37) Occasionally, computed tomography is used preoperatively to better define the full extent of the lesion, especially with spinal lesions. An MRI with contrast classically demonstrates internal septations that may contain characteristic fluid-fluid levels, caused by layering of blood products in cystic areas of the lesion (Fig 6).



Figure 5. Radiograph of a 14-year-old boy with a large aneurysmal bone cyst in the left humerus (clips seen are from previous vessel ligation).

Differential Diagnosis

The differential diagnosis includes but is not limited to enchondroma, UBC, and lesions from which an ABC may develop; atypical osteosarcoma and telangiectatic osteosarcoma; chondroblastoma; fibrous dysplasia; and giant cell tumor. These lesions may mimic ABCs radiologically or present with fluid levels similar to ABCs on MRI. Most

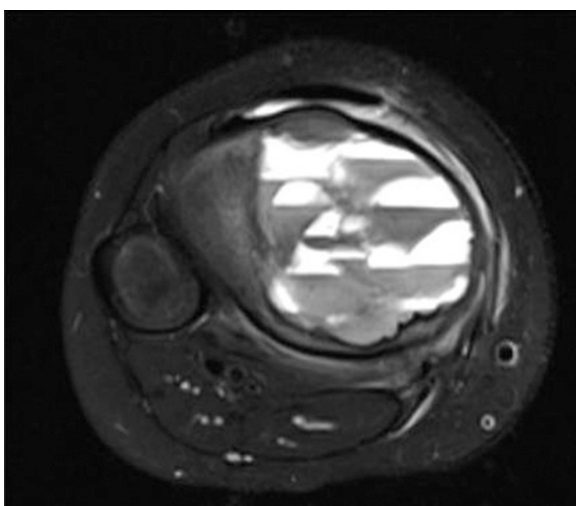


Figure 6. Characteristic fluid-fluid levels seen on this T2-weighted fat-saturated axial magnetic resonance image of an aneurysmal bone cyst. Courtesy of Frank Gaillard (<http://radiopaedia.org/articles/aneurysmal-bone-cyst>).

notably, ABCs are more prominently expansile with a thin cortical shell compared with the other compared lesions.

Treatment

Although spontaneous healing of ABCs has been reported, (38) it is uncommon. Thus, expectant management should be considered only when the diagnosis has been confirmed and the lesion is in a location and currently at a stage that does not pose a risk of fracture or further destruction. Quite often, when the diagnosis of ABC is made, prompt active treatment is recommended.

Presently, curettage and bone grafting, with or without adjuvant therapy, is the accepted method for the management of ABC. Adjuvant therapy may include but is not limited to phenol, liquid nitrogen, peroxide, and argon beam coagulation. Cryotherapy has also been found to reduce the recurrence rate of ABC. A noninvasive management method, sclerotherapy, is based on the theory that ABCs originate as a vascular malformation and can possibly heal if the hemodynamic disturbance were controlled. Recently, radionuclide ablation has been proposed for the management of ABCs. This method has been used successfully to manage other diseases, such as rheumatic synovitis and recurrent hemarthroses associated with hemophilia. (33) Selective arterial embolization is useful for the management of ABCs in areas of limited access, but it is mostly used preoperatively to interrupt blood flow to the lesion. "En bloc resection has been associated with the lowest rate of recurrence after initial treatment compared with other management methods. Unfortunately, this technique is not always feasible due to the location of the lesion and its proximity to other vital structures." (33)

Summary

Unicameral bone cysts (UBCs) and aneurysmal bone cysts (ABCs) have significant differences; however, for the general pediatrician, there are a few key points to ensure proper care and treatment of these bony lesions:

- A UBC is also known as a simple bone cyst and is usually found in patients younger than 20 years, most commonly in the proximal humerus and femur.
- A UBC is a central lytic lesion in the metaphysis and typically resolves with skeletal maturity. However, close follow-up is necessary while the patient is growing due to risk of fracture and growth disturbance.
- Any UBCs that are adjacent to the physis, causing continued pain, or have an associated fracture should be referred to an orthopedic surgeon for monitoring of deformity, surgical intervention or immobilization if fracture is present.

- The ABCs are also found in patients younger than 20 years, most commonly in the metaphysis of long bones.
- An ABC is more expansive than a UBC and may be wider than the width of the physis. On radiographs, ABCs are also eccentric and lytic, with bony septae or a "bubbly" appearance.
- An ABC may have an associated pathologic fracture, and the patient should be referred to an orthopedist. The patient typically will be immobilized until healed, at which time the ABC will be treated operatively.
- It is imperative to always perform a good physical examination because soft tissue swelling may occur in ABCs, but soft tissue edema and local tenderness are more common for the most alarming lesion on the differential diagnosis, the telangiectatic osteosarcoma. Any concerns or increased or continued pain should be referred for biopsy.


For ABCs and UBCs, morbidity is a possibility with any treatment option. There are risks associated with surgical intervention, and there are risks and consequences of pathologic fracture that may occur without intervention. When injection or surgical intervention is warranted, studies that support different management options are lacking evidence quality. There are few to no level A randomized controlled trials. (39) The remaining body of literature on level of evidence remains low. Based on some research evidence as well as consensus, most authors now agree that cyst decompression is essential for adequate healing. A minimally invasive technique with cyst decompression, percutaneous curettage, and use of synthetic bone graft substitutes (injectable calcium sulfate and calcium phosphate) is the preferred treatment at most institutions.

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1. A 5-year-old previously healthy girl is seen in the clinic for a persistent cough for the past 2 weeks. On physical examination she is noted to have a low-grade fever. Pulse oximetry is 95% on room air. Crackles are heard over the right lung base. A chest radiograph shows a right middle lobe pneumonia. In addition, the radiologist reports a small solitary bone cyst in the left upper humerus. The treating physician discusses the findings with the parents and inquires whether the patient has any left upper arm pain. The parents deny that their daughter has any pain. Findings from examination of the left arm are normal. In addition to prescribing oral antibiotics for the pneumonia, which of the following is the most appropriate next step in the management of this patient's bone cyst?
 - A. Bone biopsy from the left upper humerus.
 - B. Bone scan.
 - C. Magnetic resonance imaging (MRI) of the left arm.
 - D. Observation and monitoring for symptoms or pain.
 - E. Skeletal survey.
2. A 7-year-old boy is brought to your office after sustaining a fall while running. He is now limping on the right side. On physical examination there is mild swelling on his right tibia just below the knee joint. The patient is unable to bear weight on his right leg. Radiographs show a right tibial nondisplaced fracture and a bone cyst. The patient was seen by orthopedics, and a posterior splint was placed to his right lower extremity. Which of the following is the most appropriate next step in the management of the bone cyst?
 - A. Cyst curettage after the fracture is healed.
 - B. Observation and reassurance.
 - C. Open pin fixation of the fracture with bone graft of the cyst.
 - D. Removal of the cyst only if no evidence of fracture healing in 6 weeks.
 - E. Weekly corticosteroid injections in the fracture plane around the cyst during the fracture healing phase.
3. You practice in a remote town where you see a 17-year-old young man complaining of occasional left upper arm pain when he lifts heavy objects. On physical examination there is no obvious deformity, swelling, or redness. Radiographs of the extremity reveal a radiolucent cystic structure with a thick cortical rim in the metaphyseal region of the left proximal humerus. The patient is diagnosed as having a solitary left humeral bone cyst. Which of the following is the next best step in the management of this patient?
 - A. Activity restriction.
 - B. Follow-up radiography in 2 months.
 - C. Immobilization of the left arm in a sling for 6 weeks.
 - D. Orthopedic referral for cyst curettage.
 - E. Periodic observation.
4. An 8-year-old boy presents to the clinic with progressively increasing pain in the right thigh area with some swelling. The family denies any trauma, and the patient occasionally limps. There is no history of fevers or weight loss. Bilateral hip and right femur radiographs show a cystic lesion in the metaphysis of the right femur. An MRI of the right femur with contrast shows a cyst with a thin cortical shell with internal septation and fluid levels. Which of the following is the most likely diagnosis in this patient?
 - A. Aneurysmal bone cyst.
 - B. Atypical osteosarcoma.
 - C. Enchondroma.
 - D. Ewing sarcoma.
 - E. Giant cell tumor.

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5. The patient from the vignette in question 4 is referred to orthopedics for further management. The family is worried about the treatment and the potential for recurrence. Which of the following is the most appropriate and effective next step in the management of this patient?
- A. Curettage, bone grafting, and cryotherapy as adjuvant therapy.
 - B. No weight bearing for 3 weeks.
 - C. Observation and reassurance.
 - D. Prescribe nonsteroidal anti-inflammatory drugs and follow up in 2 weeks with repeated MRI to assess involution.
 - E. Weekly corticosteroid injections to the right hip.

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