

Overview of Benign Bone Cyst Management by Bone Marrow and Bone Substitute Composite

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Abstract

Bone cysts are tumor-like structures that resembled cavities and have variable fluid contents. It occurs most often in children whose skeletons are still growing and people up to age 30. Bone cyst is often asymptomatic in flat bones unless detected incidentally on imaging. Bone marrow contains two types of stem cells: mesenchymal and hematopoietic. Red bone marrow consists of a delicate, highly vascular fibrous tissue containing hematopoietic stem cells. Yellow bone marrow contains mesenchymal stem cells or marrow stromal cells. Several reports recommended the use of calcium sulfate (CaSO₄) based bone graft substitutes. Therefore, this study aimed to review the assessment and management of benign bone cyst management using bone marrow and bone substitute composite.

Keywords: Benign Bone Cyst; Bone Marrow; Bone Substitute Composite; Management

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1. Introduction

Bone cysts are often asymptomatic and found incidentally on radiographs. Sometimes, they may present with pain due to repeated hemorrhages or pathological fracture [1]. Benign bone cysts are often strongly affected by the hormones that cause growth. This usually is between the ages 14 to 16 in girls and 16 to 19 in boys [2]. Benign cystic lesion seen in metaphyseal-diaphyseal region of long bones in growing children. Pathological fracture is a one of the presentation of patient. X-ray and MRI are diagnostic in all types of benign bone cysts but biopsy is needed to confirm the diagnosis as in aneurysmal bone cyst, enchondroma, osteoblastoma [3]. The indication to treat bone cyst is to prevent a pathological fracture and to manage symptoms, especially pain. Historically, surgical curettage and cyst excision with bone graft were the optimal choices to treat bone cysts. Based on meta-analysis bone cyst healing rate after surgical curettage was comparable 90% whether auto graft/allograf [1-3]. Pathological features differentiate according to type of cyst as cystic lesion filled with fluid in simple bone cyst, or blood cavernous with septa as in aneurysmal bone cyst, or hyaline cartilage formation as in enchondroma, or dense fibrous tissue formation as in fibrous dysplasia [4]. The four main categories of benign bone tumor are: bone-forming (osteoid osteoma, osteoblastoma, fibrous dysplasia), cartilage-forming (osteochondroma, enchondroma), connective tissue, and vascular; the latter two are rare. A fifth category

is idiopathic (eg, aneurysmal bone cyst, simple bone cyst) [5].

Management varies with tumor type, location, symptoms, and risk of recurrence. Some (eg, enchondroma, osteochondroma, fibrous dysplasia) typically are asymptomatic, and generally require no intervention. Others (eg, osteoid osteoma, aneurysmal bone cyst, simple bone cyst) can cause symptoms and require percutaneous ablation or surgery. Still others (eg, osteoblastoma) can be aggressive and require surgery and other therapies. Malignant transformation is rare for all benign bone tumors, but patients with these tumors should be monitored with serial imaging [6].

2. Unicameral Bone cyst

Unicameral (or simple) bone cyst a common, benign, fluid-filled lesion found almost exclusively in children. Unicameral bone cysts or simple/solitary bone cysts were initially reported by Virchow in 1891 as "cystic structures", thought to be at that time due to anomalies in the local circulation. These cysts can also be multi-loculated. These benign fluid filled cavities enlarge over time, resulting in thinning of the bone. Usually these cysts are reported in the metaphyseal areas of long bones with open physes. Efforts to classify these lesions in a manner that predicts their natural history have not been met with success [7].

Most patients with a bone cysts present to the orthopedic surgeon after sustaining a pathologic fracture, most commonly involving either the proximal humerus or the proximal femur. Others may present to emergency department (ED) physicians, their primary care physicians, or orthopedic surgeons for other reasons, and radiographs obtained in the workup of other complaints may identify asymptomatic bone cysts [8]. A bone cyst probably represents the third or fourth most common benign bone tumor that the orthopedic surgeon confronts (osteochondromas are commonly considered to be the most frequently encountered benign bone tumors in children, followed by fibromas and/or fibrous cortical defects). The lesion may occur in conjunction with other benign bone tumors, such as a nonossifying fibroma. The most common location for the lesion is the proximal humerus, followed by the proximal femur. The proximal humerus and femur together account for nearly 90% of all bone cyst sites. However, virtually any bone may be affected, with the calcaneus being one of these notable alternative locations [9]. The overall outcome and prognosis of bone cysts are good. The lesion is believed to resolve spontaneously in most cases if given enough time [10]. In general, treatment may be summarized as doing nothing more than trying to promote natural healing. Internal fixation may do nothing more than mechanically support the bone while the natural healing process occurs. Most bone cysts will heal by the time of physal closure. Dormans et al. consider patient age as an important factor. Patients older than 10 years heal at a higher rate (90%) than younger patients (60%), irrespective of the treatment modality [11]. On the other hand, Haidar and colleagues consider a lesion located < 2 cm from the physis as a risk factor for recurrence. The risk of recurrence can also be related to the type of treatment rather than the location of the lesion [12]. The diagnosis of a unicameral (simple) bone cyst is strongly suspected on the basis of the lesion's typical radiographic appearance and is confirmed when an appropriate cyst fluid is demonstrated. Specific laboratory tests are not a routine part of the workup of a bone cyst [13]. Plain x-ray is modality of choice and has a high diagnostic accuracy. Cyst is not eccentric and arises centrally in medullary cavity with long axis parallel to length of bone. Because of its central location, the cortical break and soft tissue component are rare. These are metaphyseal and juxtaphyseal in location and geographic in appearance with thin sclerotic margin. The cortical break and periosteal reaction are usually absent nevertheless present in cases of associated fractures [14].

The role of CT is to evaluate cyst present in areas such as pelvis and spine, areas difficult to assess on plain x-ray. CT demonstrates more accurate extent of cyst in complex areas e.g. Spine and pelvis as well as reveal complication such as fracture which are sometime subtle on plain X ray. The CT mainly evaluates cyst wall thickness and risk fracture. CT also helps to differential cyst from a lipoma which is difficult to assess on plain x-ray [15]. The "fallen fragment" of bone is seen as floating bone in intracystic fluid in cases of fracture (Fig.1). The bubble gas sign, a pathognomic features to suggest presence of pathological fracture also known as "rising Bubble sign" is also seen on CT [16]. Some investigators have combined mechanical techniques with biologic agents to enhance outcomes. Dormans et al. used percutaneous intramedullary

decompression, curettage and grafting with calcium sulphate pellets. After a mean follow up of 22 months complete healing was reported in 92% patients [17].

The most common complication is recurrence after treatment and developing a subsequent pathological fracture. Injury to the growth plate may occur secondary to direct cyst expansion, pathologic fracture, or unintended mechanical disturbance during surgical intervention [18].

3. Aneurysmal Bone cyst (ABC)

Aneurysmal bone cysts are non-malignant, tumor-like, vascular lesions comprised of blood-filled channels. Although they can occur in any bone, they are most common in the femur, tibia, and vertebrae. Their expansile nature may result in pain and inflammation, and disruption of joints and growth plates (Fig.2). They can grow locally destructive, and weaken bones to the point of pathologic fracture [19]. Aneurysmal bone cysts occur as a result of a separate primary bone tumor; this may be due to the relatively high rate (1 in 3) of an accompanying bone lesion. These lesions are frequently chondromyxoid, fibromas, chondrosarcomas, fibrous dysplasia, giant cell tumors of the bone, osteblastomas, osteosarcomas, among others [20]. Aneurysmal bone cysts are a rare osseous tumor, comprising 1% to 6% of primary osseous tumors. The majority of aneurysmal bone cysts present in the metaphysis of long bones (67%). They also occur in the spine (15%), particularly the posterior elements, pelvis (9%), and less frequently, they can appear in the craniofacial bones and epiphyses [21]. Patients will typically present with an insidious onset of pain over several weeks to months, with possible swelling or palpable mass. A minority of patients present with a sudden onset of pain as the result of a pathological fracture. Occasionally neurological symptoms may be present if the aneurysmal bone cysts impinging a nerve or if there is spinal involvement [22]. Radiographic findings usually consist of an eccentric or, less commonly, a central or subperiosteal lesion that appears cystic or lytic. Images may show expansion of the surrounding bone with a blown-out, ballooned, or soap-bubble appearance. Some views may show an eggshell-appearing bony rim surrounding the lesion (Fig. 3). One may see the cystic spaces and, rarely, partially ossified septa. Unlike unicameral bone cysts, ABCs tend to expand the bone wider than the adjacent physis [23].

The same characteristics are demonstrated on computed tomography (CT) as on plain radiography; however, CT scans also show internal septation (ie, calcified rim, eggshell appearance), which may be completely or partially intact. Findings from magnetic resonance imaging (MRI) are similar to those from CT, but MRI can more specifically reveal blood within the lesion, as well as expansion into the soft tissues (Fig. 4) [24]. Surgical intervention is typically the treatment of choice to prevent pathological fracture. Based on the lesion size and the region of bone involved, either intralesional curettage, intralesional excision, or en bloc (complete) excision may be an option. Intralesional curettage involves evacuating the cavity of its contents and filling the remaining space with bone graft or cement to strengthen the bone [25]. Intralesional excision is the preferred treatment of choice, which is similar to curettage: the surgeon makes a broad opening through the osseous wall of the lesion and removes the contents. This process allows

a greater amount of the bone to remain intact to reduce patient morbidity when compared to en bloc excision [26]. Surgical excision of aneurysmal bone cysts is usually curative; however, historically, a spontaneous recurrence rate of 19% has been seen. Recurrences tend to happen within the first year of excision, but patients should be regularly evaluated for recurrence up to 5 years after surgery. In patients that have not yet reached skeletal maturity, recurrence could affect future bone growth and cause deformities [27].

4. Enchondroma

Enchondromas are cartilaginous tumors of the benign bone tumor family. Enchondromas are medullary cavity tumors classified in an overarching category of chondromas: benign tumors of hyaline cartilage occurring in bones of endochondral origin. These tumors are usually solitary, central, metaphyseal lesions of tubular bones, favoring the small bones of the hand and feet, followed by the femur and humerus [28]. These are also the most common primary bone tumors of the hand. In the hands, they most commonly involve the proximal phalanges, followed by the middle phalanges, metacarpals, and then distal phalanges [29]. Enchondromas are the most prevalent intraosseous cartilage tumors, accounting for approximately 3% of bone tumors and 13% of benign bone tumors. Most enchondromas begin in the medullary portion of the diaphysis, arising from ectopic cartilaginous nests in the metaphyseal region, and expand outward towards the cortex. Enlarging lesions may cause a pathologic fracture. Enchondromas and osteochondromas can transform into chondrosarcoma [30]. A thorough examination of the hand and wrist is necessary for patients with hand enchondromas. Passive movements of the interphalangeal and metacarpophalangeal joints need to be evaluated. Specifically, the functions of the flexor and the extensor tendons need to be assessed, as the distal phalangeal tumors can cause avulsion of the flexor tendons [29]. Radiographically, enchondromas have varied appearances based on location and extent of calcification, and they may resemble medullary bone infarcts. Enchondromas typically appear as well-defined solitary defects in the metaphyseal region of bones, especially in the long bones. Their appearance depends heavily on the location and extent of the calcification of the tumor. Centrally located lesions usually appear as well-circumscribed areas of rarefaction, most frequently diaphyseal, with an expanded cortex around it. Juxtacortical lesions are eccentric and beneath the periosteum in well-defined cortical defects. Small, flocculent foci of calcification are visible within the tumor [30]. Magnetic resonance imaging (MRI) adds insight into the aggressive and destructive features of the tumor. Indicators of potential malignancy include large size, a large unmineralized component (Fig. 5), significant thinning of the adjacent cortex [31]. Management of symptomatic enchondroma lesions typically involves surgical management in the form of simple curettage with bone grafting. The bone graft used may be allogeneic bone, autogenous, or synthetic bone

substitutes. However, the timing of surgical intervention has also not been shown to have significant benefits. Early and delayed surgical intervention was shown to have similar functional outcomes [30].

5. Chondroblastoma

Chondroblastomas are rare, benign chondrogenic lesions that are most commonly found in the epiphysis of the proximal tibia and distal femur. Patients typically present between the ages of 10 and 20 years with regional pain. Diagnosis showing chondroblasts arranged in "cobblestone" or "chickenwire" pattern with focal areas of chondroid matrix. Treatment is usually extended intralesional curettage and bone grafting [32]. It arises from cartilaginous epiphyseal plate, categorized as cartilage tumor due to its areas of chondroid matrix, but type II collagen is not expressed by tumor cells. May have genetic abnormalities on chromosome 5, 8, 11, 17 [33]. Clinical complaints are often nonspecific. Symptoms are typically present for many months before the patient seeks medical attention. Several imaging modalities are available for establishing the diagnosis of chondroblastoma. Plain radiographs show a fuzzy, round-to-oval, well-delineated lesion with a sclerotic rim (Fig. 6). CT can demonstrate calcifications that are not detectable on plain radiographs. It can depict cortical erosion, matrix mineralization, and soft tissue extension. MRI demonstrates extensive edema surrounding the lesion [34]. The treatment of choice of chondroblastoma is surgical. It consists of complete surgical curettage with or without bone grafting, en bloc resection, or rarely, amputation. Surgical resection alleviates pain, avoids propagation into the joint and adjacent soft tissues, diminishes the likelihood of recurrence, and accurately establishes the diagnosis of chondroblastomas [32].

6. Fibrous Dysplasia

Fibrous Dysplasia is a developmental abnormality caused by a GS alpha protein mutation that leads to failure of the production of normal lamellar bone. The condition usually presents in patients who are less than 30 years of age with an asymptomatic lesion that is found incidentally on radiographs. The proximal femur is most common site, followed by rib, maxilla, and tibia [35]. Central lytic lesions in medullary canal (diaphysis or metaphysis), may have cortical thinning with expansile lesion, highly lytic lesions or a ground glass appearance. "punched-out" lesion with well-defined margin of sclerotic bone is common. CT and MRI is useful for assessing regions with complex anatomy of skeletal structure e.g. face, pelvis, spine, and for detecting subtle un-displaced fractures [36]. The presence of a stress fracture should trigger consideration for correction of alignment, and/or consideration for the necessity of a surgical procedure, possibly involving the use of an intramedullary titanium nail or of a custom-made titanium angled blade plate, to stabilize the bone to prevent an uncontrolled fracture [35].

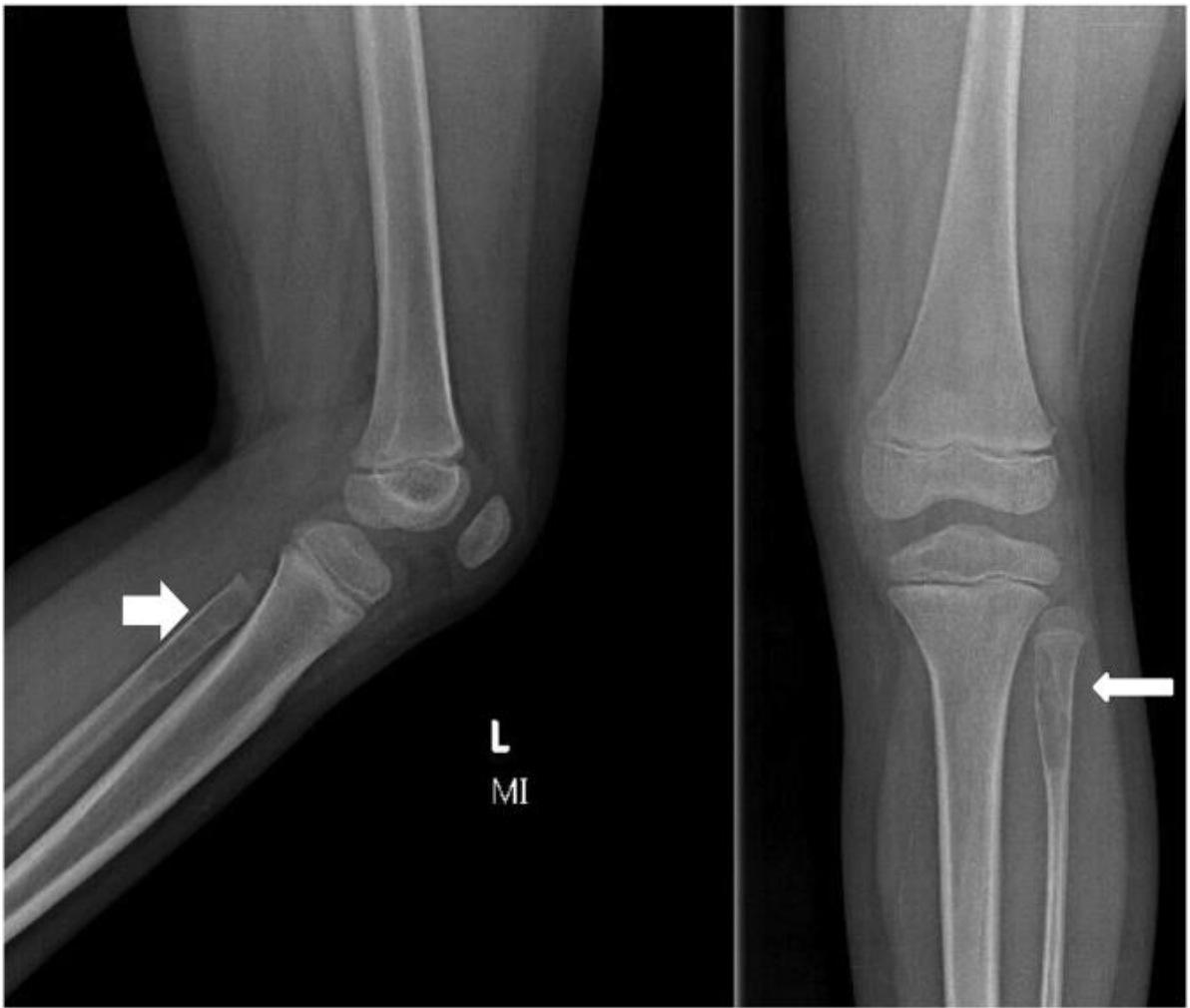


Figure 1: 7 years old boy with left fibula unicameral bone cyst. AP & lateral radiograph shows a central cystic cavitation, well demarcated, with cortical thinning and mild expansion [18].



Figure 2: Aneurysmal bone cyst of the upper arm. Courtesy of Johannes Stahl, the Virtual Radiological Case Collection [26]

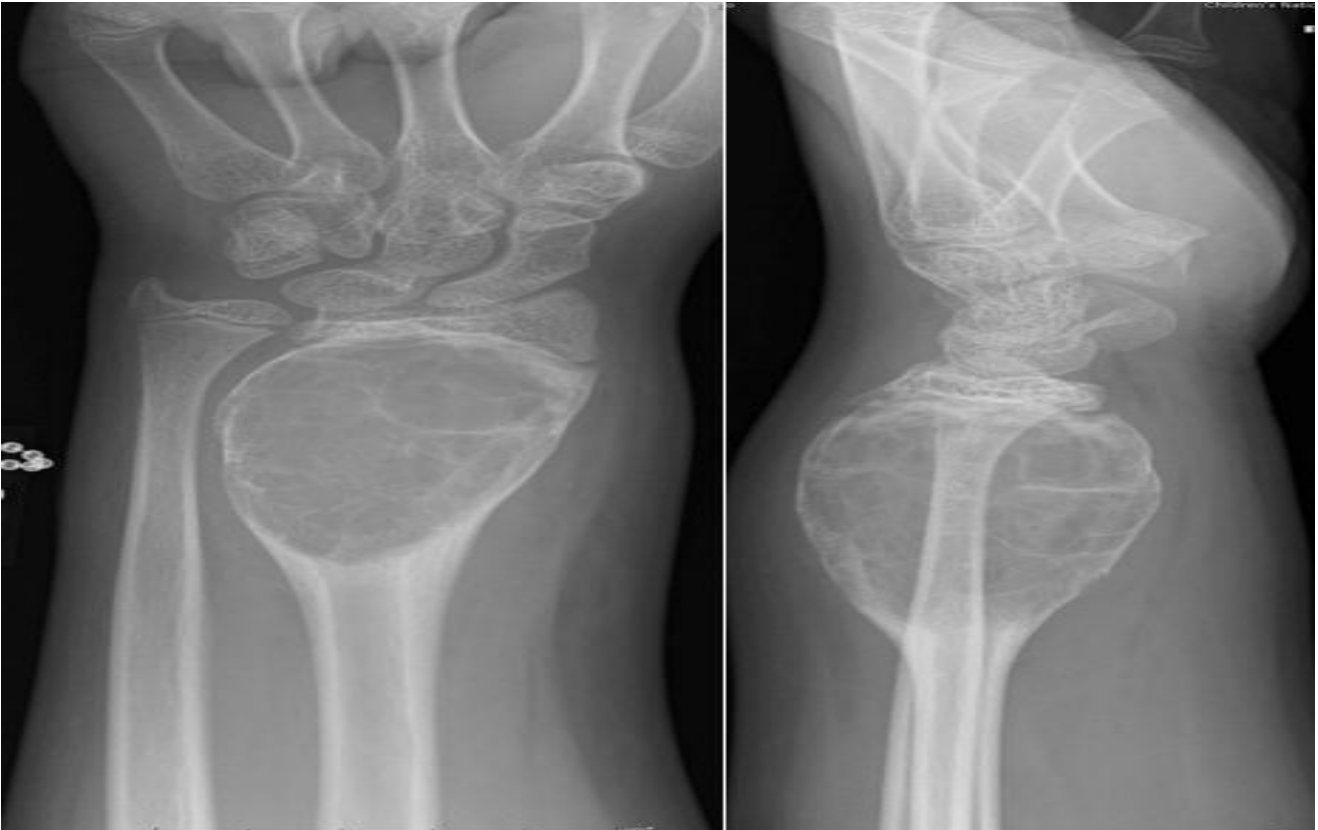


Figure 3: Aneurysmal bone cyst of distal radius. Note multiple septations, lytic cyst cavity, and extensive cortical thinning and expansion [34]

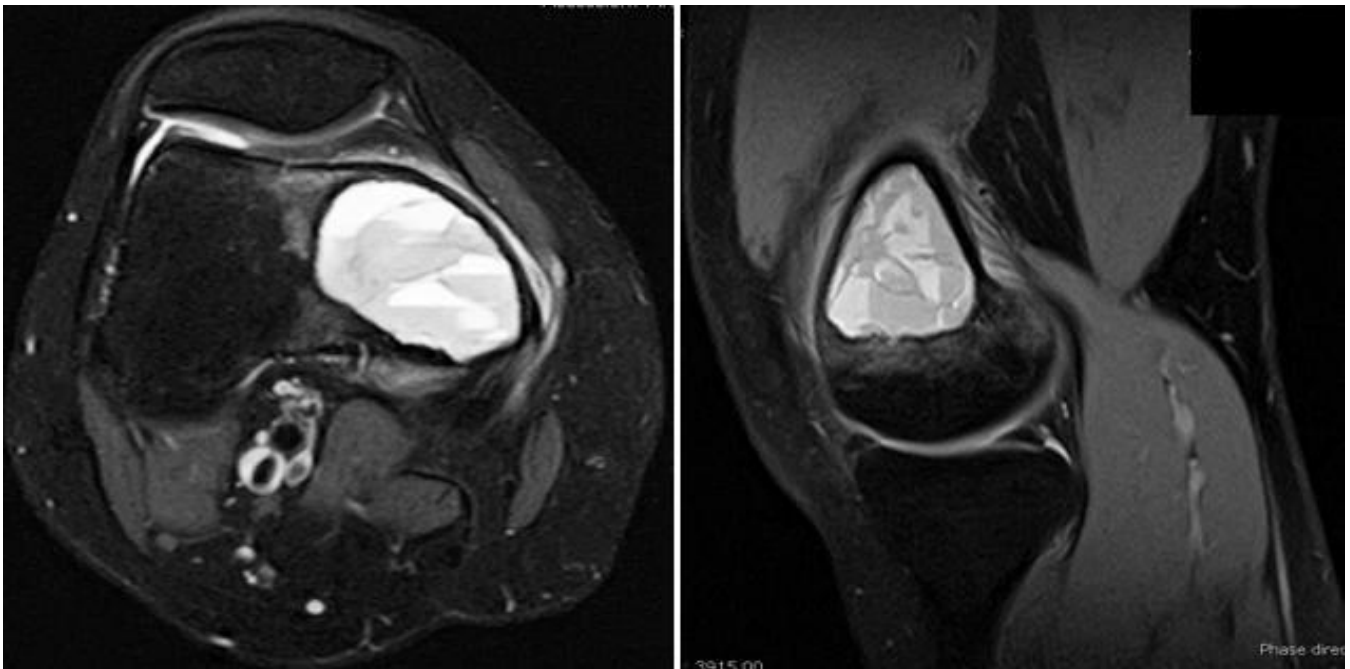


Figure 4: Axial and sagittal T2-weighted MRI of distal femoral aneurysmal bone cyst. Note multiple fluid-fluid levels with multiple blood-filled cavities separated by small septa [36]



Figure 5: An X-ray (left) and MRI scan (right) showing a large enchondroma of the fifth metacarpal of the hand [31]

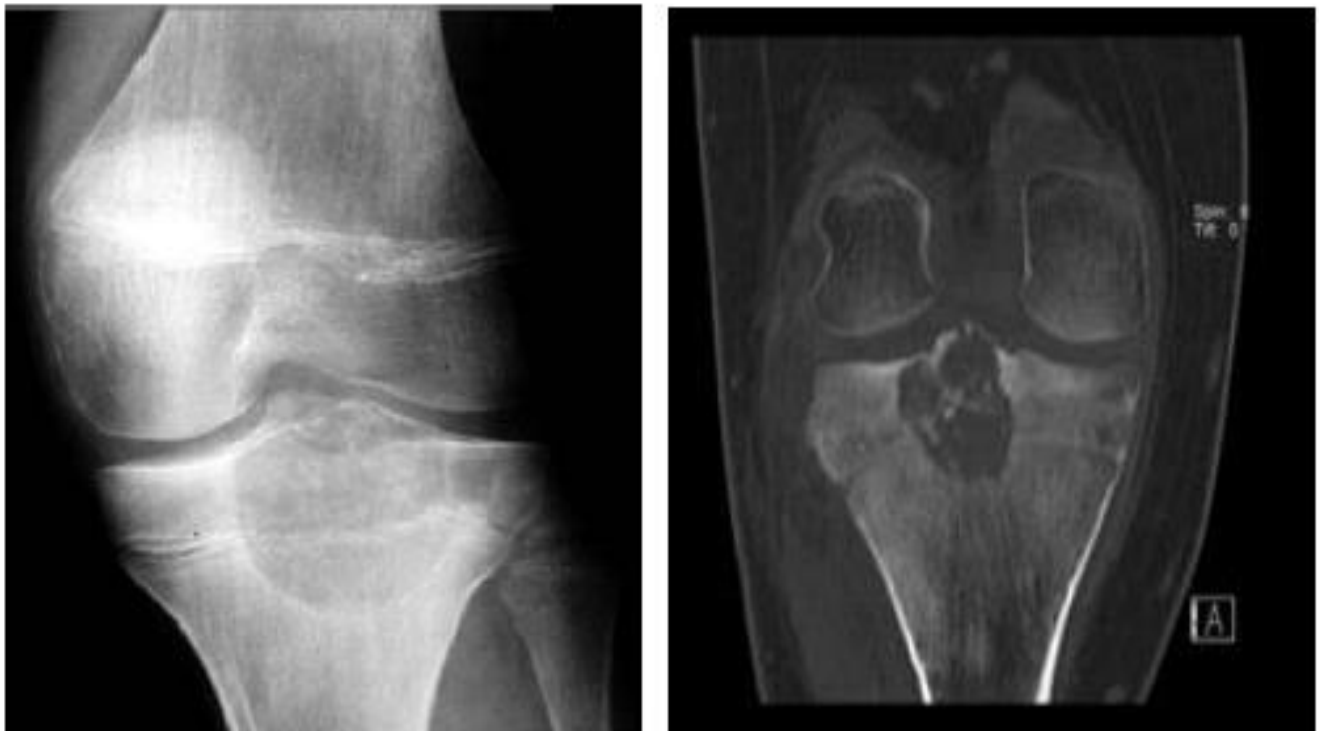


Figure 6: X-ray and CT show chondroblastoma lesion in proximal tibia [36]

7. Treatment by Bone Marrow and Bone Substitute Composite

The purpose of treatment is to restore bone strength, cortical thickness and obliteration of the cyst. Complete filling of the cyst with restoration of cortical thickness was described as healed cyst [37]. Several reports recommended the use of calcium sulfate (CaSO₄) based bone graft substitutes both with or without demineralized bone matrix in benign bone tumors. Although there is another types of bone substitutes as: Hydroxyapatite and tricalcium phosphate {Ca₁₀(PO₄)(OH)₂}(HA) is crystalline form of tricalcium phosphate (TCP) is the primary mineral component of teeth and bone [38]. All treatment modalities were included (conservative and surgical intervention). Studies that utilized injection as a method of treatment were categorized in one treatment group and subgroups were identified based on the material utilized for injection, including; methylprednisolone acetate (MPA) injection, bone marrow injection, combined MPA with bone marrow, combined bone marrow with demineralized bone matrix (DBM), and combined bone marrow with MPA and DBM [39]. Studies on surgical treatment were examined and subgroups were identified, including: curettage only, curettage with bone graft (autograft versus allograft), curettage with bone substitution (calcium sulphate pellets, calcium phosphate pellets, Hydroxyapatite, ceramic substitute), curettage with myoplasty, cyst excision, flexible intramedullary nailing (IM nail) and continuous decompression with cannulated screws [40]. The indication to treat bone cyst is to prevent a pathological fracture and to manage symptoms, especially pain. Historically, surgical curettage and cyst excision with bone graft were the optimal choices to treat bone cysts. Based on meta-analysis bone cyst healing rate after surgical curettage was comparable 90% whether autograft or allograft was utilized [41].

8. Conclusions

The use of bone marrow and bone substitution compound in the treatment of bone cysts is a useful technique that offers numerous benefits in terms of reconstructive and reparative therapy.

Conflict of interest

The authors declare no conflict of interest.

Author contribution

Authors contributed equally in the study.

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