Review Article

INTERNATIONAL JOURNAL OF SURGERY ONCOLOGY

OPEN

Aneurysmal bone cyst of the pelvis and extremities: Contemporary management

Shahryar Noordin, MBBS, FCPS[a], Tashfeen Ahmad, MBBS, FCPS, PhD[a,b,*], Masood Umer, MBBS, FCPS[a], Salim Allana, MBBS, MPH[c], Kiran Hilal, MBBS, FCPS[d], Nasir Uddin, MBBS, FCPS[e], Pervaiz Hashmi, MBBS, FCPS[a]

Abstract

Aneurysmal bone cysts are tumors of bone occurring predominantly in the metaphyses of long bones and posterior elements of spine in adolescents and young adults. Radiographically, on x-rays they appear as eccentric metaphyseal expansile lytic lesions containing "fluid-fluid" levels. Computed tomographic scan and magnetic resonance imaging clearly define the cysts and fluid-fluid levels; the former delineates cortical expansion and the latter the fibrovascular component clearly. Magnetic resonance imaging is particularly useful in differentiating aneurysmal bone cysts from malignant lesions. Histologically, these cysts are characterized by fibrovascular tissue, multinucleated giant cells, inflammatory cells, fiber-osteoid, "blue bone," and blood filled lacunae. Chromosomal translocation has been found, implying a neoplastic basis for the development of aneurysmal bone cysts. Malignant transformation has been reported where radiation therapy was used, and in cysts associated with sarcomas. A high ratio of cellular component as compared with osteoid, and a high mitotic index have been reported to be associated with higher recurrence after treatment. Management is aimed at addressing patients' symptoms and preventing/treating fracture, and can broadly be divided into non-operative management (drug and radiation therapy), minimally invasive strategies (angiographic embolization, percutaneous injections), and operative management (curettage and bone grafting, en bloc excision). To reduce chances of recurrence, adjuvants such as electrocautery, high speed burr, phenol, cryotherapy, and argon beam laser have been used with variable degrees of success. With contemporary management, a cure rate of 70%–90% is expected.

Keywords: Aneurysmal bone cyst, Aneurysmatic bone cyst, Benign bone tumor, Upper limb, Lower limb, Pelvis, Management, Medical, Percutaneous, Surgical

Aneurysmal bone cysts (ABCs) are benign, rapidly growing cystic tumors in the bone that were first described by Jaffe and Lichtenstein in 1942[1]. These cysts usually appear as expansile lytic bone lesions that have a tendency to be locally aggressive. These cysts appear as primary lesions in ~70% cases with remaining 30% being secondary with preexisting osseous lesions[2,3]. ABCs represent about 1%–2% of all primary bone tumors[4]. Primary ABCs are seen at 0.14 per 100,000 of the population per year with a slightly female preponderance. ABCs are seen at all ages, but most patients have been reported to be in their second decade of life with 75%–90% cases occurring before the age of 20 years[5].

Topography

ABCs can appear in the entire skeleton but commonly appear in the metaphysis of long bones including femur, tibia, fibula, humerus, skull, and posterior elements of the spine. Usually these appear as a solitary lesion but can also occur as secondary lesions adjacent to osteoblastomas, chondroblastomas, giant cell tumors (GCTs), chondromyxoid fibroma, fibrous dysplasia or nonossifying fibroma[5–8]. There are many reports of ABCs affecting the skull and craniofacial bones, which can be associated with fibrous dysplasia alone[9–11] or as part of a syndrome such as McCune Albright syndrome[12] and cementoosseous syndrome[13]. Axial (vertebral and craniofacial) involvement has been reported in association with focal dermal hypoplasia, also known as Goltz syndrome[14].

Apart from the usual metaphyseal location, literature reports rare cases of ABCs located in atypical sites such as cortical regions[15] within the sternum[16], vertebral body[17], ribs[18], and patella[19,20].

Clinical presentation

Patients usually present with pain and swelling in the vicinity of the affected bone. Constitutional symptoms are uncommon due to its benign nature. When the lesion continues to expand, it progresses to form an expansile mass which may be visible or

Departments of [a]Surgery, [b]Biological & Biomedical Sciences, Aga Khan University, Karachi, Pakistan, [c]Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, Departments of [d]Radiology and [e]Pathology and Microbiology, Aga Khan University, Karachi, Pakistan

**Corresponding author. Address: Department of Surgery, Aga Khan University, Stadium Road, Karachi 74800, Pakistan. Tel: +00922134864350; fax: +00922134932095. E-mail address: tashfeen.ahmad@aku.edu (T. Ahmad).*

This manuscript has been peer reviewed.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

International Journal of Surgery Oncology (2019) 4:e71

Received 4 June 2018; Accepted 10 November 2018

Published online 2 July 2019

http://dx.doi.org/10.1097/IJ9.0000000000000071

palpable if superficial. Sometimes the symptoms may appear or worsen during pregnancy[21].

Depending on the topography of the ABC, symptoms from pressure on adjacent structures can occur. If the vertebral column is involved, the patient may have neurological deficits due to the mass effect on the cord or nerve roots as well as torticollis and stiff and painful scoliosis[6,21]. In facial lesions located in orbital bones, swelling and diminishing vision have been reported[10]. Involvement of cortical regions can lead to pathological fracture[15]. In skeletally immature patients when the ABC is adjacent to the growth plate, children can develop limb length discrepancies in addition to coronal/sagittal deformities[22].

Classification

A number of classifications have been described. Enneking[23] described 3 stages. Stage 1 is a latent cyst that remains static or heals spontaneously. The cyst has minimal inflammation or periosteal reaction. Stage 2 is the active cyst with progressive growth but no cortical destruction is seen. Patients will have mild symptoms and cortical thinning on roentgenograms with a layer of reactive bone separating the lesion from normal bone. Stage 3 cysts are locally aggressive cysts that rapidly expand with significant cortical destruction. These patients present with the most symptoms.

Capanna et al[24] described 5 morphologic subgroups. Type 1 are central, well contained lesions with no or slightly expanded outline. In type 2 lesions the entire bony segment is involved with marked expansion and cortical thinning. Type 3 lesions involve only one metaphyseal cortex eccentrically. Type 4 lesions are subperiosteal lesions that expand away from bone and are least common. Type 5 lesions are periosteal and expand peripherally with cortical erosion.

Pathogenesis

The exact pathogenesis of ABC is debatable. Although the presumed role of blood vessels in the pathogenesis of "aneurysmal" bone cysts has been challenged[25] currently the most favored mechanism proposed is injury to the precursor lesion having numerous meshwork of capillaries. The capillary pressure thus increased by extravasated blood leads to destruction[26–28]. These cystic spaces are actively connected with the host capillary network. This has been demonstrated by various studies including blood pressure measurements in the cysts, lack of venular blood clotting, and venographic studies[27,28].

Recently, cytogenetic and molecular studies suggested neoplastic nature of ABC by identifying the presence of t(16;17) in ABC, including solid variant. The most common translocation is t(16;17)(q22;p13) which leads to fusion of the cadherin 11 gene (CDH11) with USP 6 (ubiquitin specific peptidase 6/Tre-2)[29]. This fusion gene inhibits maturation of osteoblasts and dysregulate bone morphogenetic protein signaling pathway. USP6 gene rearrangements are seen in ~70% cases of primary ABCs employing fluorescent in situ hybridization, a figure increased to 100% when next generation sequencing is employed[30], and are lacking in secondary ABC cases[31]. Interestingly, translocation occurs in stromal spindle cells and not seen in other components of ABC[31]. USP6 fusion genes are also found in nodular fasciitis[32]. This may be the basis for nodular fasciitis like areas seen in ABC. Moreover, USP6 fusion gene is present in other conditions such as myositis ossificans[33], giant cell reparative granuloma (GCRG) in extremities[34] and fibro-osseous pseudotumor of digits[35]. The frequency of USP6 gene rearrangements in these conditions ranges from 70% to 90% (**Table 1**).

Table 1

Frequency of USP6 gene rearrangements in different lesions.

Type of Lesion	Type of Translocation	Fusion Gene(s)	Positivity (%)
Aneurysmal bone cyst[31]	t(16;17)(q22;p13)	CDH11-USP6	70
Nodular fasciitis[32]	t(17;22)(p13;q13)	MYH9-USP6	90
Myositis ossificans[33]	Not known	COL1A1-USP6*	89
Giant cell reparative granuloma[34]	t(16;17)(q22;p13)	CDH11-USP6	89
Fibro-osseous pseudotumor of digits[35]	Not Known	USP†	80

*Reported in 1 case.

†Partner gene not known.

Gross features

ABC appears as a circumscribed spongy or multiloculated cystic lesion. The cystic spaces are of variable size ranging from few millimeters to several centimeters, and are filled with blood (**Fig. 1**). These spaces are separated by thin white septae. More solid areas are often present peripherally within the intramedullary component of the lesion. The extramedullary soft tissue component is demarcated by thin shell of reactive bone.

The more solid peripheral part may represent either solid portion of ABC wall or component of a tumor in which secondary ABC has developed. These areas need to be extensively sampled to rule out possibility of an underlying primary tumor[36].

Microscopic features

Multiple variable sized cystic spaces filled with blood are seen on low power examination (**Fig. 2A**). The cystic spaces do not have endothelial lining and are surrounded by variably thick fibrous septae. The septae contain uniform bland spindle cells, scattered osteoclast-like multinucleated giant cells, capillaries and varying amounts of matrix (**Fig. 2B**). Increased mitotic figures are sometimes seen within the stroma, however no atypical mitoses noted. Necrosis is not seen unless complicated by a fracture. The giant cells tend to cluster near the membrane surface. Osteoid is usually found as a thin layer (so-called fiber osteoid) along the long axis of the septae. Reactive woven bone with osteoblastic rimming also follows the contours of fibrous septae (**Fig. 2C**, arrow). Approximately half of cases demonstrate basophilic woven bone known as "blue bone" (**Fig. 2D**). A peculiar calcification called chondroid aura is sometimes seen. Other bony lesions do not exhibit this peculiar feature[2]. The septae and more solid areas are composed of loose, fibrous tissue rich in capillaries, inflammatory cells, multinucleated giant cells and extravasated red blood cells. These foci resemble and mimic nodular fasciitis or young granulation tissue[36].

Apart from these histologic findings, immunohistochemical studies have been conducted on ABCs to identify possible association of specific markers with diagnosis and prognosis. P63 has been studied in giant-cell rich lesions, and shown to be present in only 22% of ABCs compared to 96% of GCTs[15]. CD68 is a

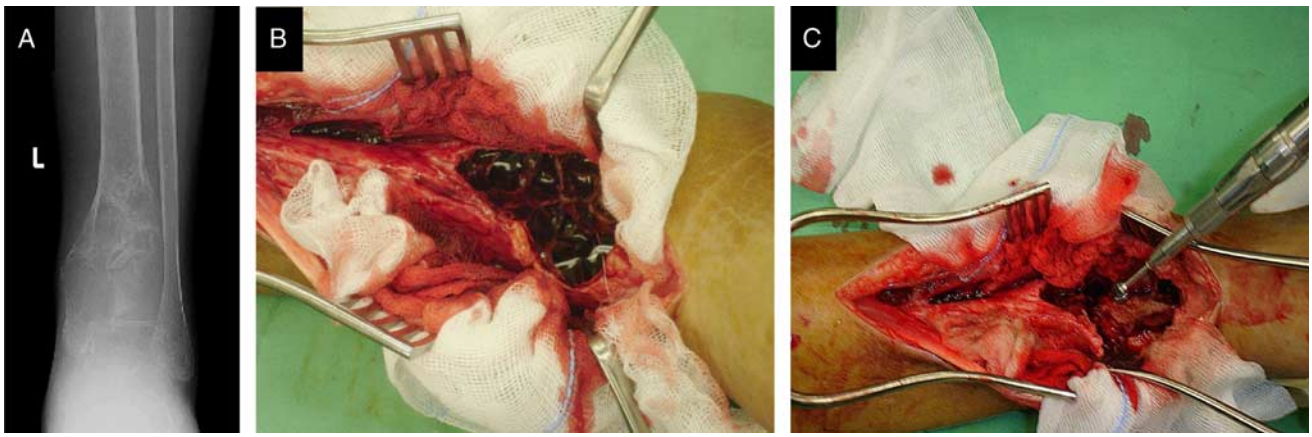

Figure 1. X-ray showing an aneurysmal bone cyst of the distal tibia, appearing as a cystic expansile lesion (A). Intraoperative images showing a cavity filled with hemorrhagic cysts (B). After excision of visible lesion, curettage of the cyst walls using high-speed burr is being performed as an adjuvant (C).

macrophage lineage marker which is present in 93% of giant cells in ABC, but it is also highly present in other osteoclastic/giant cell lesions[37]. Thus CD68, P63 and no other immunohistochemical marker to our knowledge has been shown to be specific for the diagnosis of ABC. However, Docquier[38] showed that if the ratio of CD68 negative/CD68 positive cells is ≥ 4.1, there is 100% positive predictive value for healing of the ABC and negative predictive value for recurrence, suggesting the potential role of this ratio in prognostication of ABC. USP6 is another promising marker as discussed above, and its specificity for the giant cells in ABCs can differentiate it, especially the solid variant, from other intraosseous giant cell-rich lesions such as GCRGs in the axial skeleton, GCT of bone and brown tumor[30,39,40].

Histologic variants

Secondary ABC

Primary ABC accounts for approximately 30% of all cases. ABC-like areas develop in the background of various secondary tumors including GCT of bone, chondroblastoma, chondromyxoid fibroma, fibrous dysplasia, ossifying fibroma, osteoblastoma and osteosarcoma[8,27,41–45]. The behavior and prognosis of these "secondary" ABCs" mirror those of the underlying tumor. Molecular studies employing fluorescent in situ hybridization have shown that gene rearrangements of USP6 are present in 70% of primary ABCs, and are highly specific because these are absent in secondary ABC associated with other lesions[29,31,34,39].

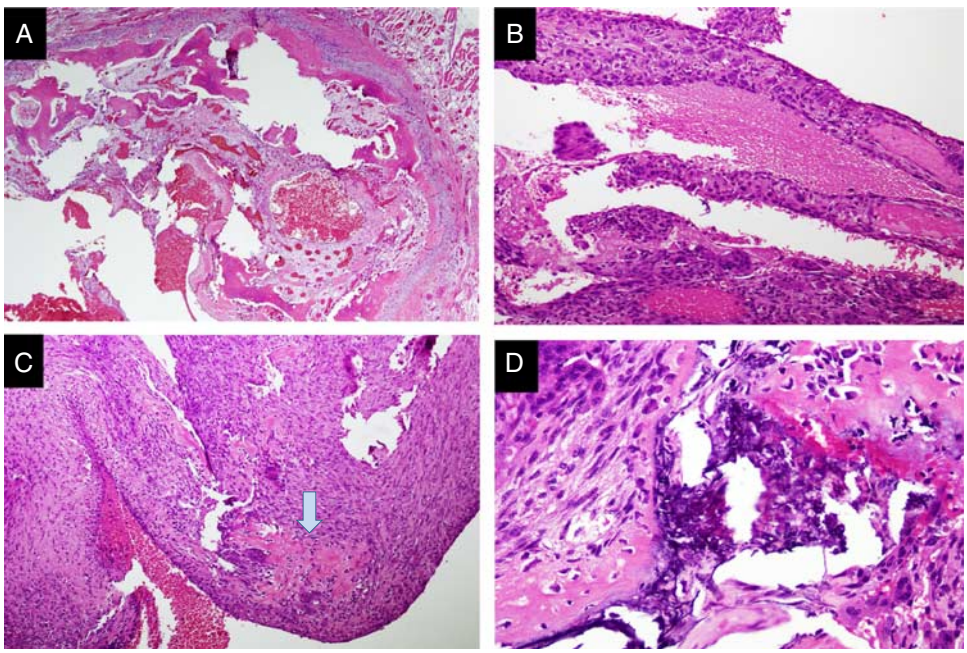

Figure 2. A, Low power examination shows multiple cystic cavities filled with blood. The lesion is surrounded by rim of reactive bone at periphery. B, The fibrous septate focally show flattened spindle lining and exhibit scattered osteoclast-type giant cells in the wall. C, Wall of cyst containing reactive woven bone (arrow) admixed with plump osteoblasts. D, The so-called blue bone with basophilic staining.

Solid ABC

Solid ABC shares the same components as those of fibrous septa of conventional ABC. There is florid fibroblastic and fibrohistiocytic proliferation with scattered osteoclast-type giant cells. Blue bone and small spaces filled with blood are helpful features in identifying solid ABC. Abundant woven bone with prominent osteoblasts and foci of degenerative calcifying fibromyxoid tissue is present. Focal small dilated blood filled spaces seen and clue to diagnosis[46].

Differential diagnosis

Differential diagnosis of ABC includes benign lesions, such as unicameral bone cysts, or tumorous lesions such as chondromyxoid fibroma, chondroblastoma, GCT or osteoblastoma[2]. Two findings differentiate ABC from unicameral bone cyst, septa and fluid-fluid levels, and magnetic resonance imaging (MRI) is an excellent modality to demonstrate these[47]. GCT is almost never seen before closure of the growth cartilage, and tends to involve the epiphyseal-metaphyseal region of long bones[5]. Histologically, solid foci of tumor show osteoclast type giant cells distributed homogenously among mononuclear cells in GCT in contrast to scattered distribution in ABC. The giant cells have usually fewer nuclei as compared with numerous nuclei in osteoclast cells of GCT. GCRG is another lesion which appears similar radiologically to ABC. Clinically, however, GCRGs typically arise in small bones of hand and jaw. Both GCRG and solid ABC show identical histologic features and may be difficult to differentiate, though blue bone and blood-filled spaces would be more suggestive of solid ABC. Distinction of ABC from telangiectatic osteosarcoma is of crucial importance especially in small biopsies. ABC grossly resembles telangiectatic osteosarcoma. Histologically, atypical cells and atypical mitoses are found in fibrous septae in telangiectatic osteosarcoma, these are not seen in ABC. The pathologist needs to examine the biopsy material carefully to rule out the presence of atypical cells and atypical mitoses. Osteoid may or may not be seen in telangiectatic osteosarcomas.

It is important to correlate with radiologic features and biopsy tissue should be thoroughly sampled especially from solid areas to exclude any underlying lesion. ABC-like areas can be seen secondary to a variety of lesions (as described above). The behavior of such a "secondary ABC" is determined by the primary lesion.

Diagnosis

Clinical and radiologic features may be sufficient for a presumptive diagnosis of ABC, but establishing the diagnosis is essential before committing to definitive treatment. Percutaneous needle biopsy, with or without image guidance [fluoroscopy/ultrasound/computed tomography (CT)] depending upon location, is the preferred method for definitive diagnosis. The expected findings on the biopsy have been described in the previous sections. A presumptive diagnosis of ABC, however, is usually based on the appearance of the lesion on imaging.

Plain radiography

Plain radiography has high diagnostic accuracy for cysts involving the appendicular skeleton especially long bone. The characteristic features in long bones on plain film eccentric metaphyseal lytic lesion comprised almost entirely of fluid-like radio-opacity. The growth plate grows away from lesion; hence long-standing lesions are located in the metadiaphyseal region of long bones. However, it has also been reported as a purely diaphyseal lesion in few cases[27,48]. A combination of plain film with MRI and CT is required on body part which are difficult to evaluate on plain film, for example, pelvis, chest wall, spine or temporo-mandibular joint.

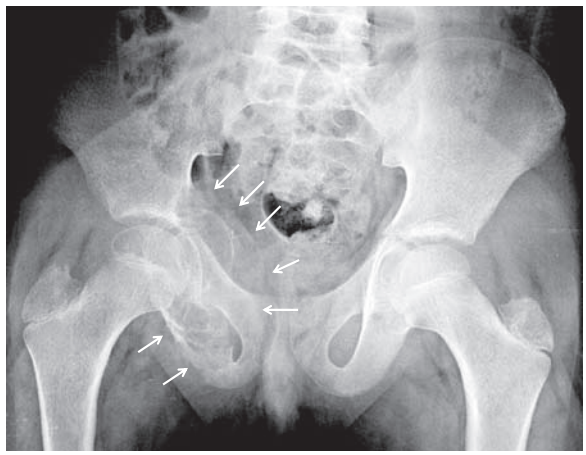

Figure 3. Anteroposterior radiograph of the pelvis of a 16 year-old boy with an aneurysmal bone cyst of ischium. Arrows point to margins of an expansile lesion of ischium. The cortex is thinned out but but intact. Internal matrix shows soap-bubble appearance.

The size of this lesion can be 2–20 cm. It appears as lytic expanded lesion which may have trabeculation which give soap-bubble appearance. The cyst is eccentric and expands into soft tissues. Erosion and thinning of cortices can be seen in big lesions (**Fig. 3**). These are geographic lesion with a narrow zone of transition. The margin of the lesion is sclerotic and thin can be complete or in complete. A periosteal reaction is usually absent; however, it is not uncommon to see it in case of the rare entity of surface type of ABC. The expansion or ballooning of cortex can result in loss of distinct margins. In this case lesion should be carefully evaluated and should be reported as aggressive lesion rather than neoplastic lesion.

ABCs are sometime hard to differentiate from aggressive neoplastic process such as sarcoma, especially in ribs, scapula, or sternum, when associated with a large soft tissue component[27,49,50].

CT

On CT, the visualization of depressions, defects, and protrusions in bone cortex is better seen than any other imaging modality including MRI. This finding helps surgeon for better surgical planning and to evaluate the exact extension of lesion. CT is also helpful to distinguish between intra and extra osseous component of cyst and its extension.

Thin cortical rim is better visualized on CT than on radiograph. The cortex appears as thinned, "eggshell" with focal cortical destruction and absent calcified tumor matrix (**Figs. 4A–C**). The zone of transition is narrow, and nonsclerotic. The lesion shows rounded "cysts" that show fluid-fluid levels which is caused by hemorrhage followed by blood component sedimentation. The septa and fluid-fluid levels are also visualized but better

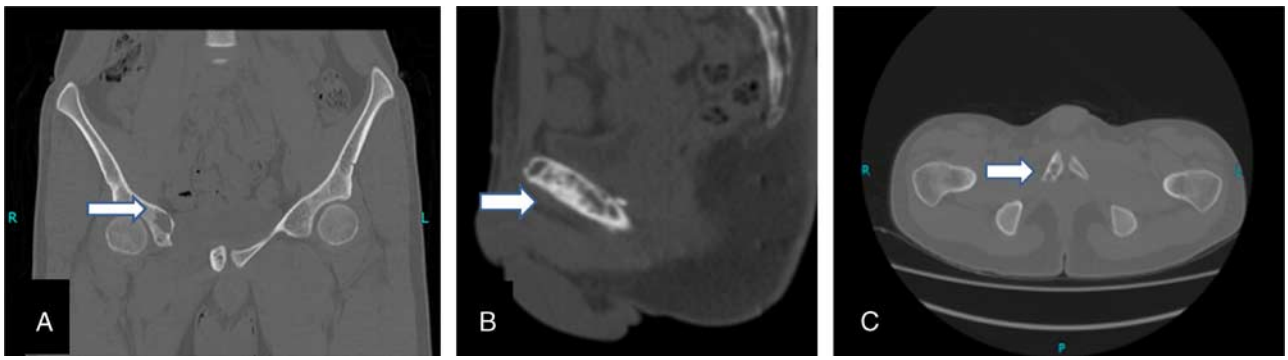

Figure 4. Coronal (A), sagittal (B), and axial (C) computed tomographic images of an 18-year-old boy with an aneurysmal bone cyst of the pubic bone, showing a lytic expanded mass with a thin rim of cortex peripherally but extensive destruction of cortex around (arrow).

seen on MRI. Fluid-fluid levels are not specific for ABC and can be seen in other conditions like GCT or telangiectatic osteosarcoma.

Fluid levels may not be identified by CT because body movement can mix the fluids. Patient has to remain motionless for some time to allow the fluid in cyst to settle and allow fluid levels to be seen on CT[50]. On unenhanced CT balloon-like expansile mass centered on posterior elements in spinal aneurysmal cyst which usually extends into epidural space and may cause spinal canal narrowing. On enhanced CT, enchantment of tumor margin and septae is seen. In cases of solid ABC diffuse enhancement is noted[49–51].

MRI

On MRI, ABCs appear as geographical lesions with thin, low signal sclerotic margins. These cystic lesions are isointense to skeletal muscle on T1 and hyperintense on fluid-sensitive sequences[22,50,52–55] (**Fig. 5A**). Cysts are separated by septae of varying thicknesses (**Figs. 5A, B**). On postcontrast sequence, enhancement of septa is seen but not of the cystic component. A well-defined rim of low signal intensity around the lesion reflects periosteum or pseudocapsule. The surrounding edema, both in bone and soft tissue appears hyper intense on T2 and STIR sequences.

Fluid-fluid levels are excellently demonstrated by MRI on fluid-sensitive sequences, and are seen in 20%–100% cases of aneurysmal bone cysts[41,52,56]. These levels are produced by layering of the breakdown products of hemorrhage within the cyst. Signal of superior layer in cyst typically follows fluid and dependent portion shows decreased signal on T2WI relative to T1WI (**Figs. 5A, B**). Cysts of different signal intensity are seen on all sequences depending on different stages of blood components. O'Donnell and Saifuddin[57] examined relation between fluid-fluid levels and malignancy and found that malignant neoplasms most commonly showed fluid-fluid level in less than third of the lesion. With increase in the total volume of fluid-fluid level, the chance of malignancy is very less likely; there was no malignancy in lesions with 100% fluid-fluid.

On MRI it is very important to evaluate permeativeness of lesion to differentiate it from telangiectatic osteosarcoma. Aggressive lesion like telangiectatic osteosarcoma can show 2/3 of lesion with fluid-fluid levels because of high grade predominantly necrotic bone tumors. These tumors show small solid component but differentiation with ABC's can be difficult solely on MRI. In these cases plain radiography and clinical features should be used to differentiate between telangiectatic osteosarcoma and ABC[57].

Ultrasound

High resolution ultrasound can be used for initial assessment of uncertain soft tissue lesions and for ultrasound guided biopsy. But ultrasound has limited role in intramedullary bone lesions as sound waves cannot penetrate the normal cortex. Ultrasound can be used in evaluation of postoperative sites for tumor recurrence particularly if there is significant artifact on MRI or CT due to orthopedic metallic prosthesis.

Ultrasound features of ABC include, cystic mass with a thin echogenic shell and multiple intra osseous fluid levels. The cortices of the affected bones are markedly thinned allowing sound waves to be transmitted for further characterization of the inner structure of the lesions. Fluid-fluid levels move with change in patient position[58].

Natural history of ABCs

The fate of ABCs depends on the location and biological activity at the time of diagnosis. On the basis of x-rays, biological activity of ABCs can be classified as latent (or quiescent), active, and aggressive[23]. Latent lesions having an intact rim of cortical bone may not lead to a fracture. Spontaneous healing of these cysts has been reported[59], and some lesions resolve after biopsy[60]. Active lesions pose a risk of fracture due to cortical thinning, may present with a fracture, or signs and symptoms of nerve compression due to bone expansion. Involvement of joints may lead to instability, especially in facet joints of the spine. In children, proximity to growth plate may lead to growth abnormalities resulting in limb length discrepancy or angular deformities over time. Aggressive lesions may manifest as bone destruction, erosion of articular bone, progressive neurological impairment, and appear similar to malignant tumors. True malignant transformation is rare; it has been reported in cases previously operated and irradiated for ABC[60–62].

Thus, ABCs may result in fracture and joint involvement, lead to deformity and restricted range of motion, compromise neurological function, affect epiphyseal growth in children and rarely transform into a malignant lesion.

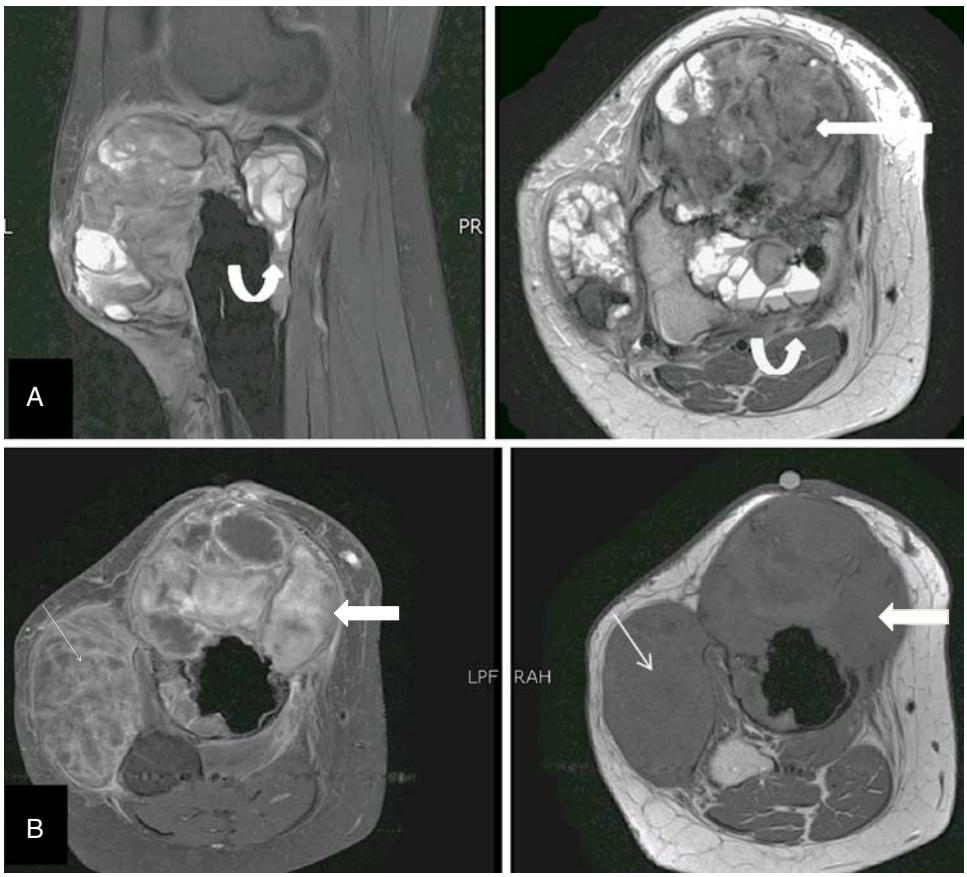

Figure 5. Magnetic resonance images from a 27-year-old female with an aneurysmal bone cyst of the proximal tibia. A, Sagittal STIR and axial T2WI image show multicystic expansile lesion showing multiple fluid/fluid levels in the proximal condyle of right tibia extending up to the articular surface. Signal intensities of the various components of lesion. Solid component is hypointense to marrow (long arrow). Superior cyst layer is isointense and dependent portion of the cyst is slightly hyperintense (curved arrow). B, Axial T1WI without contrast and T1W C + magnetic resonance imaging reveal avid enhancement of the septa (thin arrow) and soft tissue (thick arrow) between the dilated, blood-filled cystic spaces.

Management of ABCs

General principles

Management of ABCs entails addressing the patients' symptoms and prevention/treatment of fracture. Symptoms may be due to pain from elevated intracystic pressure, bone expansion, and compression of adjacent structures. Nerve compression is common in spinal lesions, leading to neuropathic or myelopathic symptoms. The main stay of management remains the same as that described by Jaffe and Lichtenstein[63], that is curettage of the cyst cavity and reconstruction of the defect with bone graft. This results in decompression of the cyst which relieves pain, and permits healing of the cavity. However, some lesions may resolve spontaneously without surgery, or with percutaneous treatment. Thus, broadly speaking management options can be divided into nonoperative management, minimally invasive strategies, and operative management, and decision-making requires assessment of patient, imaging and consideration of natural history.

Management choice depends on whether the lesion is latent, active or aggressive, and aims at preventing complications from the activity of the lesion.

Nonoperative management

Considering the benign nature of the lesion, nonoperative management may be considered in selected cases. Options for nonoperative management include wait-and-watch, splinting of extremity lesions, drug treatment and radiation therapy.

Wait-and-watch

For latent lesions causing pain alone, without neurovascular symptoms, and without impending fracture on x-ray it may be reasonable to just observe the lesion with serial x-rays, on 3–6 monthly follow-ups. Spontaneous healing of these cysts has been reported[59]. Analgesics and modification in activity level appropriate to the level of pain may be sufficient to control symptoms. Postbiopsy the lesions often show healing, thus it is prudent to wait for 4–6 weeks after the biopsy before deciding about further interventions as involution of the cyst may occur postbiopsy[60]. A percutaneous biopsy technique has been described as a "Curopsy" which includes use of core needle biopsy and pituitary rongeur/curette to obtain lining membrane from different parts of lesion, resulting in healing in majority of cases[42]. Pathogenetically, increased intracystic pressure due to

hemodynamic abnormalities has been suggested[64], hence it is likely that biopsy results in relief of pressure in the cyst and compartments within the cyst, leading to cyst healing. In case of active lesions in the upper extremity and lesions in the leg/foot, pain control may be achieved by splinting or casting, with or without restricting loading depending on cortical involvement on x-ray suggesting impending fracture.

Drug treatment

Bisphosphonates have been used[65] for their role in inhibiting osteoclasts on the pretext that cyst lining shows multinucleated giant cells and cyst formation in bone requires osteoclastic activity. Denosumab, an intravenously administered monoclonal antibody against RANK ligand approved for use in osteoporosis, has been used in a few cases to treat spinal and appendicular ABCs[66–68] resulting in response within 2 months and subsequent healing and remodeling of the lesions. As for teriparatide, a parathyroid hormone analogue used in osteoporosis and fracture nonunions, we are not aware of any reports on its use in ABCs.

Radiation therapy

Although this is effective for cyst resolution, it carries a risk of malignant transformation in the otherwise benign disease, as well as risk of ischemia to the viscera or spinal cord. Situations such as recurrence in spinal lesions not amenable to other methods may be an indication for radiotherapy[62].

Minimally invasive strategies

Angiographic embolization

The effect of angiographic treatment such as selective arterial embolization has been positive in spinal lesions[69,70], but inconclusive as an independent treatment in the appendicular skeleton[71]. However, this may be used to reduce intraoperative hemorrhage in spinopelvic lesion surgery (discussed in the Operative management section).

Percutaneous intralesional injections

Several agents have been reported to have been used to treat ABCs through percutaneous injections. These include methylprednisolone, calcitonin, bisphosphonate, alcoholic zein, bone marrow aspirate, bone substitute and doxycycline, but the experience is either limited to case reports or short series, results have been variable and contradictory, or multiple injections are required[60,61,72–78]. Methylprednisolone acetate injection alone has been reported to exacerbate the lesion, hence it is not recommended[60,61]. Two agents used for sclerotherapy, however, may be promising. Three percent polidocanol (hydroxypolyaethoxydodecan) or absolute alcohol appears to be effective in resolving the cyst in majority of cases[75,79]. Two to 3 injections may be required, but these are otherwise safe[75,79–82].

Radionuclide ablation

This entails intralesional injection of radioisotope emitting ionizing radiation which ablates adjacent tissue. For ABCs, CT-guided injection of chromic phosphate P^{32} into the cyst has been shown to result in cyst resolution in a series of 5 patients with spinopelvic lesions[81].

Cryoablation

Using image guided percutaneous probe, cryoablation has been used successfully in cases of spinal ABC[83]. Radiofrequency ablation, which generates heat, is not recommended due to risk of damage to surrounding neural structures.

Stem cell injection

Studies on percutaneous injection of concentrated stem cells from bone marrow[84] and injection of whole bone marrow have shown to be effective in resulting in cyst resolution[85,86], presumably through bone marrow derived stem cell differentiation into osteoblastic lineage.

Operative management

In preoperative planning, strategy to avoid potential intraoperative hemorrhage from the cysts needs to be incorporated. Lesions of the spine, sacrum and pelvis may bleed excessively, hence preoperative angiographic embolization may be justified[60,61,87], with due consideration to the risk of ischemia to vital structures supplied by the same feeding vessels.

The mainstay of operative management has been intralesional curettage and bone grafting. This approach, however, is fraught with a substantial risk of recurrence. Thus, literature shows a recurrence rate of up to 20% by the use of curettage alone[88]. Wide margin (en bloc) excision is therefore sometimes preferred in aggressive lesions as it has the lowest risk of recurrence[41,89], but carries a higher morbidity in the form of pain, limb length discrepancy, muscular weakness and restriction of joint motion. In periarticular lesions, excision of the articular segment may be required, necessitating arthrodesis or joint replacement. Moreover, en bloc resection may not be technically feasible in certain locations[90]. Hence, conservative surgery with intralesional curettage with or without bone grafting is now generally considered as the standard of operative care used in conjunction with adjuvants such as electrocautery, high speed burr, phenol (carbolic acid), cryotherapy (with liquid nitrogen) and argon beam laser. These adjuvant methods have been shown to result in reduction of recurrence rates to 5%[91], but argon beam has been reported to increase risk of fracture[92] presumably from osteonecrosis due to the laser. The cyst cavity can be managed with bone graft or polymethyl methacrylate "bone cement." Moreover, β tri-calcium phosphate and atelocollagen combined with autologous bone marrow mononuclear cells has been reported to resolve the cyst in 1 case[93]. In children, 5% recurrence has been reported following surgical treatment (intralesional extended curettage/en bloc resection with or without bone grafting and internal fixation). Main factor associated with recurrence was proximity to the growth plate[22,94].

Some of the treatment options are illustrated form our cases in the figures. **Figure 6** shows images from a patient with ischial tuberosity ABC treated with excision of the lesion, intralesional curettage with high speed burr and obliteration of the cavity with bone graft and tricalcium phosphate bone substitute. **Figure 7** shows images from a patient with an ABC of the lateral femoral condyle managed with intralesional curettage and use of structural bone grafting with tricortical iliac graft to buttress the buttressing subchondral bone and fibular strut grafts for structural support. Both these patients had successful healing without recurrence on 4-year follow-up.

A summary of the treatment options is provided in **Table 2**.

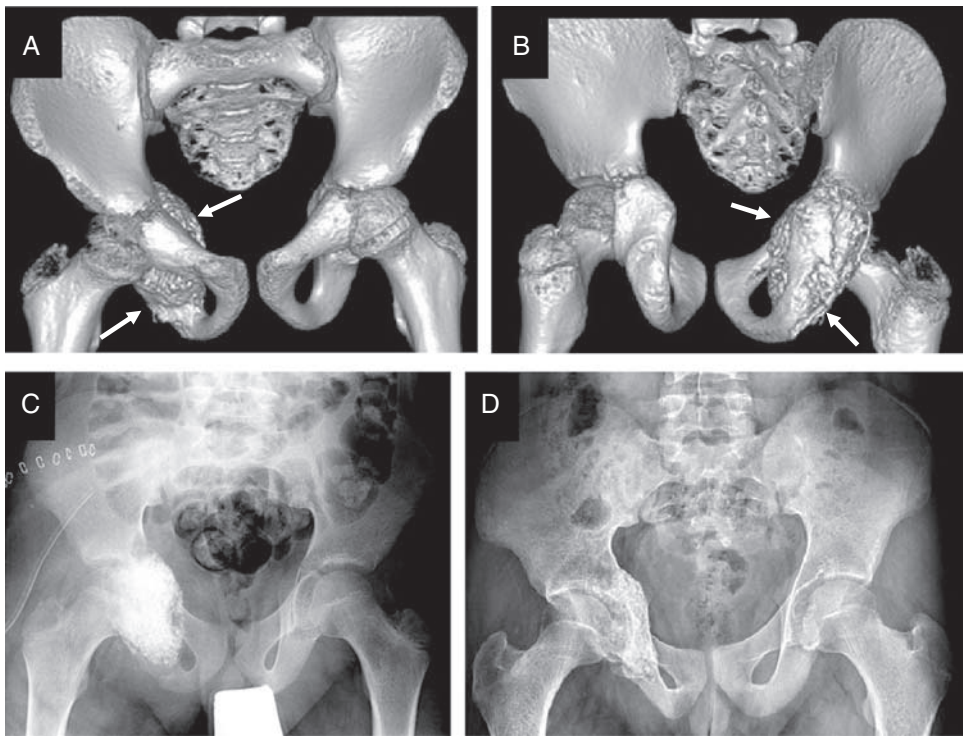

Figure 6. Anterior (A) and posterior (B) view of preoperative 3D computed tomography reconstruction of pelvis showing expansile lesion of left ischium (arrows). C, Postoperative x-ray following intralesional curettage and obliteration of cyst cavity with bone graft and substitute (tricalcium phosphate). D, Four-year follow-up x-rays showing healed cyst with incorporation of graft and remodeling.

Prognosis and outcome

Being a nonmalignant condition, the prognosis is generally good. For spinal lesions, pretreatment neurological impairment may recover to a variable degree, depending on severity and duration of neural compression. Fracture healing is generally successful using bony stabilization and bone grafts, and the above described methods generally result in resolution of the cyst. Surgical resection with intralesional curettage and adjuvants has been shown to result in recurrence-free outcome in 80%–90% of cases[95,96]. Considering the risk of recurrence, ABCs require long-term follow-up. There is no general protocol for follow-up; depending on the apparent biological activity of the lesion, more or less frequent follow-up visits may be required. Thus for quiescent lesions a yearly follow-up may be adequate, while for active and aggressive lesions follow-up visits may be warranted every 2–4 months.

Recurrence

With contemporary management the risk of recurrence is in the range of 5%–30%[60]. A number of risk factors have been postulated in the recurrence of ABCs. Mankin et al[88] in a 20-year follow-up study of 150 ABC tumors, published a local recurrence of almost 20%. In some reports age younger than 12 years has been associated with an increased risk of recurrence[2,22,96,97]. Contrary to that Dormans et al[95] did not report a significant difference in children older or younger than 10 years of age. Gibbs et al[96] reported an increased rate of recurrence in skeletally immature patients undergoing curettage with a high speed burr. Histologic characteristics have also been evaluated as potential indicators of recurrence. In 2010[38], it was shown that a higher ratio of cellular component as compared with osteoid was associated with recurrence. Ruiter et al[98] reported a higher recurrence rate with a mitotic index of ≥ 7 per 50 fields. De Silva et al[99] postulated immature lace pattern and fibromyxoid nodular fasciitis like area to be associated with higher recurrence. Recurrent lesions generally require a more aggressive approach to management. With joint involvement and segmental instability, en bloc excision with prosthetic replacement or instrumentation may be required.

Malignant transformation

Literature reports with malignant transformations of ABCs have been published[60–62,100]. Brindley and colleagues reported recurrence in cases where adjuvant radiation was used in addition to primary treatment. They also reported recurrence in secondary ABCs associated with telangiectatic osteosarcoma and fibroblastic osteosarcoma.

Summary

ABC is a benign locally aggressive bone tumor that usually appears in the first 2 decades of life with a slight female preponderance. Decision-making in ABCs entails consideration of the location, for example, diaphyseal, periarticular, spinal, the lesion activity, that is latent, active or aggressive, the cortical thinning with likelihood of fracture, and the effect on surrounding tissues/organs, for example neural elements. In general, nonoperative measures can be applied in latent and active lesions including wait and watch,

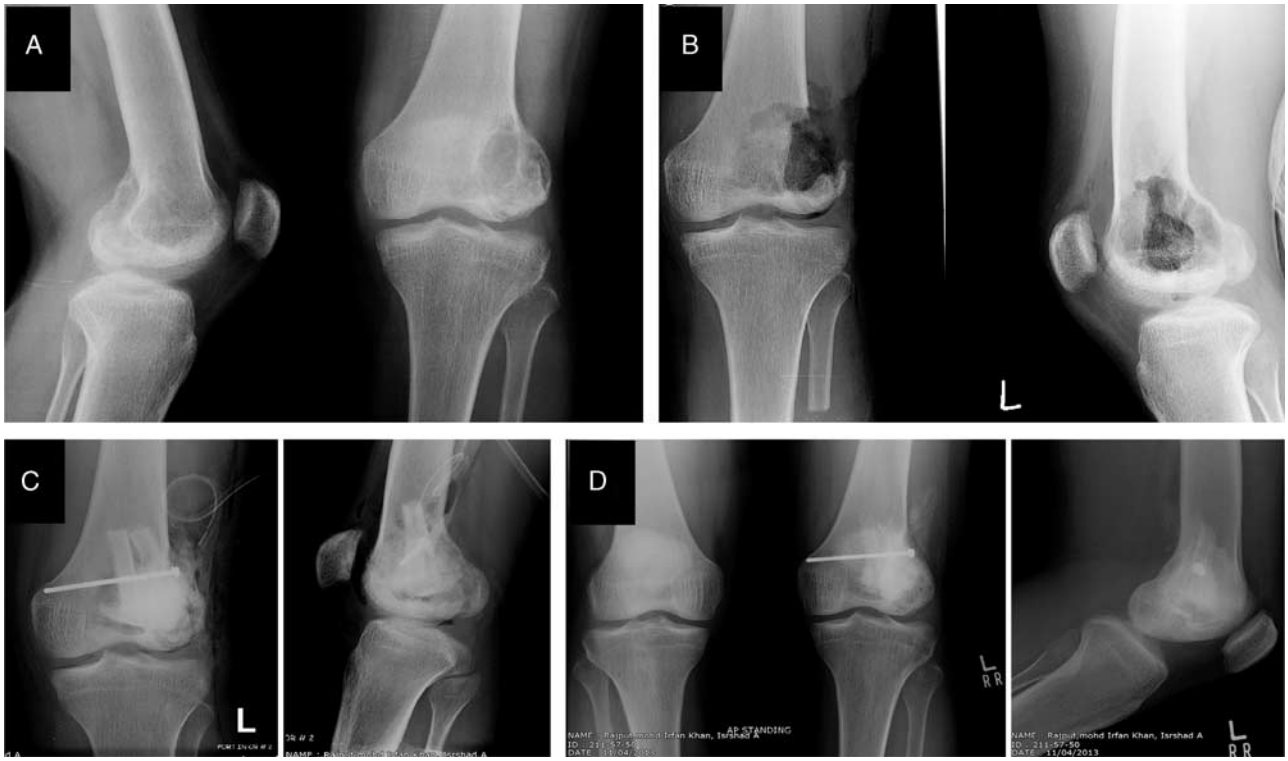

Figure 7. A, Anteroposterior and lateral radiographs of an adult patient with aneurysmal bone cyst of the lateral femoral condyle. Intraoperative radiographs showing (B) appearance after intralesional curettage, and (C) after bone grafting using tricortical iliac graft for buttressing subchondral bone, fibular strut grafts for structural support, cortico-cancellous chips to fill the defect and a screw for stabilization. D, outcome after 4 years; no recurrence of cyst, incorporation of bone graft and absence of degenerative arthritis.

Table 2

Treatment strategies for aneurysmal bone cysts.

Intervention	Method	Indications	Setting	Effect	Limitations
Denosumab	IV	All ABCs	Outpatient	Osteoclast inhibition	Infection, eczema, and hypocalcemia, osteonecrosis
Bisphosphonates	Oral/IV	All ABCs	Outpatient	Apoptosis, inhibition of angiogenesis, bone formation	Jaw osteonecrosis
Radiation therapy	Extracorporeal	ABCs in bones near vital organs	Outpatient	Necrosis of tumor cells	Radiation induced sarcoma
Biopsy/"Curopsy"	Percutaneous	ABCs in accessible locations	Outpatient	Breakage of cyst lining and compartments	—
Radionuclide ablation	Percutaneous	ABCs in bones near vital organs	Outpatient	Necrosis of proliferating cells	Radiation induced sarcoma
Sclerotherapy: Polidocanol, alcohol	Percutaneous	All ABCs	Outpatient	Fibrosis and ossification	Multiple sessions needed
Stem cell therapy	Percutaneous	All ABCs	Outpatient	Osteogenesis	Case reports
Bone marrow injection	Percutaneous	All ABCs	Outpatient	Osteogenesis	Case reports
Steroid injection	Percutaneous	—	Outpatient	Exacerbates lesion	Should be avoided
Embolization	Trans-arterial	ABCs in difficult to access regions	Outpatient	Necrosis of tumor and other cells	Risk of ischemia to organs supplied by same artery
En bloc excision	Surgical	ABCs in expendable/ reconstructible bones	Inpatient	Complete resection	May need bone reconstruction
Intralesional excision	Surgical	All ABCs	Inpatient	Gross clearance	Risk of recurrence
High speed burr	Adjunct to surgery	All ABCs	Inpatient	Margin clearance	—
Phenol	Adjunct to surgery	All ABCs	Inpatient	Margin clearance	—
Cryotherapy	Adjunct to surgery	All ABCs	Inpatient	Margin clearance	Fracture, skin necrosis/wound infection
Argon gas laser	Adjunct to surgery	All ABCs	Inpatient	Margin clearance	Fracture risk
Bone grafting	Adjunct to surgery	All ABCs	Inpatient	Osteoconduction and osteoinduction	Donor site morbidity

ABC indicates aneurysmal bone cysts.

"curopsy," percutaneous intralesional alcohol or polidocanol, and radionuclide ablation in resistant cases. For aggressive lesions intralesional curettage is the treatment of choice along with use of intraoperative adjuvants on the cyst wall such as electrocautery, high speed burr, phenol, and cryotherapy. Large cavities require bony reconstruction with bone graft or cement. En bloc resection may be required in aggressive lesions with major destruction of bone and joint. Preoperative angioembolization should be considered in spinal and pelvic lesions. The chances of local recurrence are increased in young children and those with stage 3 aggressive tumors. Surgical resection with intralesional curettage and adjuvants is the mainstay of treatment with successful outcome in the range of 70%–90%[95,96].

Ethical approval

As this is a review article and not a primary study, ERC approval was not sought. No patient identifying elements are included in any of the images.

Sources of funding

No funding was obtained for this work.

Author contribution

S.N.: Lead author, literature search, manuscript write-up. T.A.: Lead co-author, literature search, manuscript write-up. M.U.: Co-author, case details, imaging, final manuscript review. K.H.: Co-author, radiology images, Literature search, manuscript write-up. N.U.: Co-author, pathology images, Literature search, manuscript write-up. S.A.: Literature search, manuscript write-up. P.H.: Manuscript write-up and review.

Conflict of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Shahryar Noordin.

References

[1] Jaffe HL, Lichtenstein L. Solitary unicameral bone cyst with emphasis on the roentgen picture, the pathologic appearance and the pathogenesis. Arch Surg 1942;44:1004–25.
[2] Rapp TB, Ward JP, Alaia MJ. Aneurysmal bone cyst. J Am Acad Orthop Surg 2012;20:233–41.
[3] Cottalorda J, Kohler R, Sales de Gauzy J, *et al*. Epidemiology of aneurysmal bone cyst in children: a multicenter study and literature review. J Pediatr Orthop B 2004;13:389–94.
[4] Leithner A, Lang S, Windhager R, *et al*. Expression of insulin-like growth factor-I (IGF-I) in aneurysmal bone cyst. Mod Pathol 2001; 14:1100–4.
[5] Mascard E, Gomez-Brouchet A, Lambot K. Bone cysts: unicameral and aneurysmal bone cyst. Orthop Traumatol Surg Res 2015;101(suppl): S119–27.
[6] Park HY, Yang SK, Sheppard WL, *et al*. Current management of aneurysmal bone cysts. Curr Rev Musculoskelet Med 2016;9:435–4.
[7] Bonakdarpour A, Levy WM, Aegerter E. Primary and secondary aneurysmal bone cyst: a radiological study of 75 cases. Radiology 1978;126:75–83.
[8] Martinez V, Sissons HA. Aneurysmal bone cyst. A review of 123 cases including primary lesions and those secondary to other bone pathology. Cancer 1988;61:2291–304.
[9] Kaloostian PE, Gokaslan ZL. Surgical management of primary tumors of the cervical spine: surgical considerations and avoidance of complications. Neurol Res 2014;36:557–65.
[10] Lucarelli MJ, Bilyk JR, Shore JW, *et al*. Aneurysmal bone cyst of the orbit associated with fibrous dysplasia. Plast Reconstr Surg 1995;96: 440–5.
[11] Wang K, Allen L, Fung E, *et al*. Bone scintigraphy in common tumors with osteolytic components. Clin Nucl Med 2005;30:655–71.
[12] Tournis S, Balanika A, Megaloikonomos PD, *et al*. Secondary aneurysmal bone cyst in McCune-Albright syndrome. Clin Cases Miner Bone Metab 2017;14:332–5.
[13] Jacomacci WP, Veloso Perdigao JP, Veltrini VC, *et al*. Associated aneurysmal bone cyst and cemento-osseous dysplasia: a case report and review of the literature. Gen Dent 2017;65:28–32.
[14] D'Alise MD, Timmons CF, Swift DM. Focal dermal hypoplasia (Goltz syndrome) with vertebral solid aneurysmal bone cyst variant. A case report. Pediatr Neurosurg 1996;24:151–4.
[15] Shooshtarizadeh T, Movahedinia S, Mostafavi H, *et al*. Aneurysmal bone cyst: an analysis of 38 cases and report of four unusual surface ones. Arch Bone Jt Surg 2016;4:166–72.
[16] Cosio-Lima L, Cosio Pascal M, Monges-Nicolau A. Aneurysmatic cyst of the manubrium sterni: case report and literature review. Acta Ortop Mex 2009;23:306–10.
[17] Gajdos M, Sulla I, Vyrostko J. Aneurysmal bone cyst. Acta Chir Orthop Traumatol Cech 1995;62:251–3.
[18] Mazanec K, Habanec B. Aneurysmal bone cyst of a rib. Cesk Patol 1986;22:15–9.
[19] Traore A, Doukoure B, Sie Essoh JB, *et al*. Primary aneurysmal bone cyst of the patella: a case report. Orthop Traumatol Surg Research 2011;97:221–4.
[20] Oh JH, Kim HH, Gong HS, *et al*. Primary aneurysmal bone cyst of the patella: a case report. J Orthop Surg (Hong Kong) 2007;15:234–7.
[21] Li L, Tan LA, Wewel JT, *et al*. Spinal aneurysmal bone cyst presenting as acute paraparesis during pregnancy. J Clin Neurosci 2016;28:167–9.
[22] Lin PP, Brown C, Raymond AK, *et al*. Aneurysmal bone cysts recur at juxtaphyseal locations in skeletally immature patients. Clin Orthop Relat Res 2008;466:722–8.
[23] Enneking WF. A system of staging musculoskeletal neoplasms. Clin Orthop Relat Res 1986;204:9–24.
[24] Capanna R, Bettelli G, Biagini R, *et al*. Aneurysmal cysts of long bones. Ital J Orthop Traumatol 1985;11:409–17.
[25] Vollmer E, Roessner A, Lipecki KH, *et al*. Biologic characterization of human bone tumors. VI. The aneurysmal bone cyst: an enzyme histochemical, electron microscopical, and immunohistological study. Virchows Arch B Cell Pathol Incl Mol Pathol 1987;53:58–65.
[26] Clough JR, Price CH. Aneurysmal bone cyst: pathogenesis and long term results of treatment. Clin Orthop Relat Res 1973;97:52–63.
[27] Kransdorf MJ, Sweet DE. Aneurysmal bone cyst: concept, controversy, clinical presentation, and imaging. AJR Am J Roentgenol 1995;164:573–80.
[28] Lichtenstein L. Aneurysmal bone cyst; observations on fifty cases. J Bone Joint Surg Am 1957;39-A:873–2.
[29] Oliveira AM, Hsi BL, Weremowicz S, *et al*. USP6 (Tre2) fusion oncogenes in aneurysmal bone cyst. Cancer Res 2004;64:1920–3.
[30] Guseva NV, Jaber O, Tanas MR, *et al*. Anchored multiplex PCR for targeted next-generation sequencing reveals recurrent and novel USP6 fusions and upregulation of USP6 expression in aneurysmal bone cyst. Genes Chromosomes Cancer 2017;56:266–77.
[31] Oliveira AM, Perez-Atayde AR, Inwards CY, *et al*. USP6 and CDH11 oncogenes identify the neoplastic cell in primary aneurysmal bone cysts and are absent in so-called secondary aneurysmal bone cysts. Am J Pathol 2004;165:1773–80.
[32] Erickson-Johnson MR, Chou MM, Evers BR, *et al*. Nodular fasciitis: a novel model of transient neoplasia induced by MYH9-USP6 gene fusion. Lab Invest 2011;91:1427–33.
[33] Bekers EM, Eijkelenboom A, Grunberg K, *et al*. Myositis ossificans—another condition with USP6 rearrangement, providing evidence of a

relationship with nodular fasciitis and aneurysmal bone cyst. Ann Diagn Pathol 2018;34:56–9.
[34] Agaram NP, LeLoarer FV, Zhang L, *et al*. USP6 gene rearrangements occur preferentially in giant cell reparative granulomas of the hands and feet but not in gnathic location. Hum Pathol 2014;45:1147–52.
[35] Flucke U, Shepard SJ, Bekers EM, *et al*. Fibro-osseous pseudotumor of digits—expanding the spectrum of clonal transient neoplasms harboring USP6 rearrangement. Ann Diagn Pathol 2018;35:53–5.
[36] Czerniak B. Dorfman and Czerniak's Bone Tumors. 2nd ed. Philadelphia: Elsevier Health Sciences; 2015.
[37] Liu B, Yu SF, Li TJ. Multinucleated giant cells in various forms of giant cell containing lesions of the jaws express features of osteoclasts. J Oral Pathol Med 2003;32:367–75.
[38] Docquier PL, Delloye C, Galant C. Histology can be predictive of the clinical course of a primary aneurysmal bone cyst. Arch Orthop Trauma Surg 2010;130:481–7.
[39] Matcuk GR Jr, Chopra S, Menendez LR. Solid aneurysmal bone cyst of the humerus mimics metastasis or brown tumor. Clin Imaging 2018;52: 117–22.
[40] Li HR, Tai CF, Huang HY, *et al*. USP6 gene rearrangement differentiates primary paranasal sinus solid aneurysmal bone cyst from other giant cell-rich lesions: report of a rare case. Hum Pathol 2018;76: 117–21.
[41] Vergel De Dios AM, Bond JR, Shives TC, *et al*. Aneurysmal bone cyst. A clinicopathologic study of 238 cases. Cancer 1992;69:2921–31.
[42] Reddy KI, Sinnaeve F, Gaston CL, *et al*. Aneurysmal bone cysts: do simple treatments work. Clin Orthop Relat Res 2014;472:1901–10.
[43] Nasser MJ. Psammomatoid ossifying fibroma with secondary aneurysmal bone cyst of frontal sinus. Childs Nerv Syst 2009;25:1513–6.
[44] Gotmare SS, Tamgadge A, Tamgadge S, *et al*. Recurrent psammomatoid juvenile ossifying fibroma with aneurysmal bone cyst: an unusual case presentation. Iran J Med Sci 2017;42:603–6.
[45] Reddy AV, Reddy KR, Prakash AR, *et al*. Juvenile ossifying fibroma with aneurysamal bone cyst: a case report. J Clin Diagn Res 2014;8: ZD01–2.
[46] Sanerkin NG, Mott MG, Roylance J. An unusual intraosseous lesion with fibroblastic, osteoclastic, osteoblastic, aneurysmal and fibromyxoid elements. "Solid" variant of aneurysmal bone cyst. Cancer 1983; 51:2278–86.
[47] Chung JW, Lee HS. Secondary aneurysmal bone cystic change of the chondroblastoma, mistaken for a primary aneurysmal bone cyst in the patella. Knee Surg Relat Res 2014;26:48–51.
[48] Fletcher CD, Unni KK, Mertens F. Pathology and Genetics of Tumours of Soft Tissue and Bone. Lyon: IARC Press; 2002.
[49] Boriani S, Lo SF, Puvanesarajah V, *et al*. Aneurysmal bone cysts of the spine: treatment options and considerations. J Neurooncol 2014;120: 171–8.
[50] Yalcinkaya M, Lapcin O, Arikan Y, *et al*. Surface aneurysmal bone cyst: clinical and imaging features in 10 new cases. Orthopedics 2016;39: e897–903.
[51] Doyle A, Field A, Graydon A. Recurrent aneurysmal bone cyst of the cervical spine in childhood treated with doxycycline injection. Skeletal Radiol 2015;44:609–12.
[52] Van Dyck P, Vanhoenacker FM, Vogel J, *et al*. Prevalence, extension and characteristics of fluid-fluid levels in bone and soft tissue tumors. Eur Radiol 2006;16:2644–51.
[53] Ilaslan H, Sundaram M, Unni KK. Solid variant of aneurysmal bone cysts in long tubular bones: giant cell reparative granuloma. AJR Am J Roentgenol 2003;180:1681–7.
[54] Molina CA, Gokaslan ZL, Sciubba DM. Spinal tumors. In: Norden AD, Reardon DA, Wen PCY, editors. Primary Central Nervous System Tumors: Pathogenesis and Therapy. New York: Springer; 2011: 529–47.
[55] Rodallec MH, Feydy A, Larousserie F, *et al*. Diagnostic imaging of solitary tumors of the spine: what to do and say. Radiographics 2008;28:1019–41.
[56] Sandomenico F, Cappabianca S, Iovino M, *et al*. Aneurysmal bone cyst: diagnostic role of computerized tomography and magnetic resonance. Radiol Med 1996;92:525–9.
[57] O'Donnell P, Saifuddin A. The prevalence and diagnostic significance of fluid-fluid levels in focal lesions of bone. Skeletal Radiol 2004;33:330–6.
[58] Glazebrook KN, Keeney GL, Rock MG. Ultrasound of primary aneurysmal bone cyst. Case Rep Radiol 2014;2014:101069.
[59] McQueen MM, Chalmers J, Smith GD. Spontaneous healing of aneurysmal bone cysts. A report of two cases. J Bone Joint Surg Br 1985;67:310–2.
[60] Cottalorda J, Bourelle S. Modern concepts of primary aneurysmal bone cyst. Arch Orthop Trauma Surg 2007;127:105–4.
[61] Docquier P-L, Glorion C, Delloye C. Kyste osseux anévrismal. EMC - Appareil locomoteur. 2011. DOI: 10.1016/S0246-0521(11)55890-5.
[62] Campanacci M. Aneurysmal bone cyst. In: Campanacci M, Enneking WF, editors. Bone and Soft Tissues Tumors. Padova: Piccin; 1999:815–32; S127.
[63] Jaffe HL, Lichtenstein L. Non-osteogenic fibroma of bone. Am J Pathol 1942;18:205–1.
[64] Biesecker JL, Marcove RC, Huvos AG, *et al*. Aneurysmal bone cysts. A clinicopathologic study of 66 cases. Cancer 1970;26:615–25.
[65] Cornelis F, Truchetet ME, Amoretti N, *et al*. Bisphosphonate therapy for unresectable symptomatic benign bone tumors: a long-term prospective study of tolerance and efficacy. Bone 2014; 58:11–6.
[66] Lange T, Stehling C, Frohlich B, *et al*. Denosumab: a potential new and innovative treatment option for aneurysmal bone cysts. Eur Spine J 2013;22:1417–22.
[67] Pauli C, Fuchs B, Pfirrmann C, *et al*. Response of an aggressive periosteal aneurysmal bone cyst (ABC) of the radius to denosumab therapy. World J Surg Oncol 2014;12:17.
[68] Skubitz KM, Peltola JC, Santos ER, *et al*. Response of aneurysmal bone cyst to denosumab. Spine (Phila Pa 1976) 2015;40:E1201–4.
[69] Amendola L, Simonetti L, Simoes CE, *et al*. Aneurysmal bone cyst of the mobile spine: the therapeutic role of embolization. Eur Spine J 2013;22: 533–41.
[70] Rossi G, Mavrogenis AF, Facchini G, *et al*. How effective is embolization with N-2-butyl-cyanoacrylate for aneurysmal bone cysts. Int Orthop 2017;41:1685–92.
[71] Cottalorda J, Bourelle S. Current treatments of primary aneurysmal bone cysts. J Pediatr Orthop B 2006;15:155–67.
[72] Shiels WE II, Mayerson JL. Percutaneous doxycycline treatment of aneurysmal bone cysts with low recurrence rate: a preliminary report. Clin Orthop Relat Res 2013;471:2675–83.
[73] Simm PJ, O'Sullivan M, Zacharin MR. Successful treatment of a sacral aneurysmal bone cyst with zoledronic acid. J Pediatr Orthop 2013;33: e61–4.
[74] Topouchian V, Mazda K, Hamze B, *et al*. Aneurysmal bone cysts in children: complications of fibrosing agent injection. Radiology 2004;232: 522–6.
[75] Varshney MK, Rastogi S, Khan SA, *et al*. Is sclerotherapy better than intralesional excision for treating aneurysmal bone cysts. Clin Orthop Relat Res 2010;468:1649–59.
[76] Shiels WE II, Beebe AC, Mayerson JL. Percutaneous doxycycline treatment of juxtaphyseal aneurysmal bone cysts. J Pediatr Orthop 2016;36:205–12.
[77] Peraud A, Drake JM, Armstrong D, *et al*. Fatal ethibloc embolization of vertebrobasilar system following percutaneous injection into aneurysmal bone cyst of the second cervical vertebra. AJNR Am J Neuroradiol 2004;25:1116–20.
[78] Szendroi M, Antal I, Liszka G, *et al*. Calcitonin therapy of aneurysmal bone cysts. J Cancer Res Clin Oncol 1992;119:61–5.
[79] Lambot-Juhan K, Pannier S, Grevent D, *et al*. Primary aneurysmal bone cysts in children: percutaneous sclerotherapy with absolute alcohol and proposal of a vascular classification. Pediatr Radiol 2012;42: 599–605.
[80] Batisse F, Schmitt A, Vendeuvre T, *et al*. Aneurysmal bone cyst: a 19-case series managed by percutaneous sclerotherapy. Orthop Traumatol Surg Res 2016;102:213–6.
[81] Bush CH, Adler Z, Drane WE, *et al*. Percutaneous radionuclide ablation of axial aneurysmal bone cysts. AJR Am J Roentgenol 2010;194: W84–90.
[82] Rastogi S, Varshney MK, Trikha V, *et al*. Treatment of aneurysmal bone cysts with percutaneous sclerotherapy using polidocanol. A review of 72 cases with long-term follow-up. J Bone Joint Surg Br 2006;88:1212–6.
[83] Griauzde J, Gemmete JJ, Farley F. Successful treatment of a Musculoskeletal Tumor Society grade 3 aneurysmal bone cyst with N-butyl cyanoacrylate embolization and percutaneous cryoablation. J Vasc Interv Radiol 2015;26:905–9.

[84] Barbanti-Brodano G, Girolami M, Ghermandi R, *et al*. Aneurysmal bone cyst of the spine treated by concentrated bone marrow: clinical cases and review of the literature. Eur Spine J 2017;26(suppl 1):158–66.
[85] Docquier PL, Delloye C. Treatment of aneurysmal bone cysts by introduction of demineralized bone and autogenous bone marrow. J Bone Joint Surg Am 2005;87:2253–8.
[86] Hemmadi SS, Cole WG. Treatment of aneurysmal bone cysts with saucerization and bone marrow injection in children. J Pediatr Orthop 1999;19:540–2.
[87] Boriani S, De Iure F, Campanacci L, *et al*. Aneurysmal bone cyst of the mobile spine: report on 41 cases. Spine (Phila Pa 1976) 2001;26:27–35.
[88] Mankin HJ, Hornicek FJ, Ortiz-Cruz E, *et al*. Aneurysmal bone cyst: a review of 150 patients. J Clin Oncol 2005;23:6756–2.
[89] Campanacci M, Capanna R, Picci P. Unicameral and aneurysmal bone cysts. Clin Orthop Relat Res 1986;204:25–36.
[90] Flont P, Kolacinska-Flont M, Niedzielski K. A comparison of cyst wall curettage and en bloc excision in the treatment of aneurysmal bone cysts. World J Surg Oncol 2013;11:109.
[91] Peeters SP, Van der Geest IC, de Rooy JW, *et al*. Aneurysmal bone cyst: the role of cryosurgery as local adjuvant treatment. J Surg Oncol 2009;100:719–24.
[92] Steffner RJ, Liao C, Stacy G, *et al*. Factors associated with recurrence of primary aneurysmal bone cysts: is argon beam coagulation an effective adjuvant treatment. J Bone Joint Surg Am 2011;93:e1221–9.
[93] Bulgin D, Irha E, Hodzic E, *et al*. Autologous bone marrow derived mononuclear cells combined with beta-tricalcium phosphate and absorbable atelocollagen for a treatment of aneurysmal bone cyst of the humerus in child. J Biomater Appl 2013;28:343–53.
[94] Erol B, Topkar MO, Caliskan E, *et al*. Surgical treatment of active or aggressive aneurysmal bone cysts in children. J Pediatr Orthop B 2015;24:461–8.
[95] Dormans JP, Hanna BG, Johnston DR, *et al*. Surgical treatment and recurrence rate of aneurysmal bone cysts in children. Clin Orthop Relat Res 2004;421:205–11.
[96] Gibbs CP Jr, Hefele MC, Peabody TD, *et al*. Aneurysmal bone cyst of the extremities. Factors related to local recurrence after curettage with a high-speed burr. J Bone Joint Surg Am 1999;81:1671–8.
[97] Basarir K, Piskin A, Guclu B, *et al*. Aneurysmal bone cyst recurrence in children: a review of 56 patients. J Pediatr Orthop 2007;27:938–43.
[98] Ruiter DJ, van Rijssel TG, van der Velde EA. Aneurysmal bone cysts: a clinicopathological study of 105 cases. Cancer 1977;39:2231–9.
[99] de Silva MV, Raby N, Reid R. Fibromyxoid areas and immature osteoid are associated with recurrence of primary aneurysmal bone cysts. Histopathology 2003;43:180–8.
[100] Brindley GW, Greene JF Jr, Frankel LS. Case reports: malignant transformation of aneurysmal bone cysts. Clin Orthop Relat Res 2005;438:282–7.