Review article

Bone cysts: Unicameral and aneurysmal bone cyst

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A B S T R A C T

Simple and aneurysmal bone cysts are benign lytic bone lesions, usually encountered in children and adolescents. Simple bone cyst is a cystic, fluid-filled lesion, which may be unicameral (UBC) or partially separated. UBC can involve all bones, but usually the long bone metaphysis and otherwise primarily the proximal humerus and proximal femur. The classic aneurysmal bone cyst (ABC) is an expansive and hemorrhagic tumor, usually showing characteristic translocation. About 30% of ABCs are secondary, without translocation; they occur in reaction to another, usually benign, bone lesion. ABCs are metaphyseal, excentric, bulging, fluid-filled and unicameral, and may develop in all bones of the skeleton. On MRI, the fluid level is evocative. It is mandatory to distinguish ABC from UBC, as prognosis and treatment are different. UBCs resolve spontaneously between adolescence and adulthood; the main concern is the risk of pathologic fracture. Treatment in non-threatening forms consists in intracystic injection of methylprednisolone. When there is a risk of fracture, especially of the femoral neck, surgery with curettage, filling with bone substitute or graft and osteosynthesis may be required. ABCs are potentially more aggressive, with a risk of bone destruction. Diagnosis must systematically be confirmed by biopsy, identifying soft-tissue parts, as telanjiastic sarcoma can mimic ABC. Intra-lesional sclerotherapy with alcohol is an effective treatment. In spinal ABC and in aggressive lesions with a risk of fracture, surgical treatment should be preferred, possibly after preoperative embolization. The risk of malignant transformation is very low, except in case of radiation therapy.

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Simple and aneurysmal bone cysts are benign lesions, usually encountered in children and adolescents. Differential diagnosis is essential, as they may in some cases mimic malignant tumor, and their respective treatments are different. The present paper will not deal with subchondral cysts as encountered in osteoarthritides, or with cystic maxillary lesions or soft issue aneurysmal cysts.

1. Simple or unicameral bone cyst

Simple bone cyst is a benign fluid-filled cystic lytic lesion, which may be unicameral (UBC) or partially separated.

1.1. Epidemiology

UBC is a very frequent lesion, with 2 or 3 to 1 male predominance. About 80% of patients are in their second decade [1–4]. UBC is usually solitary.

1.2. Location

UBC mainly involves the long bones, and especially the proximal humerus, followed by the proximal femur; these two locations account for more than 80% of cases [1–4]. Other locations are rarer (proximal or diaphyseal tibia, diaphyseal or distal humerus, diaphyseal or distal femur, fibula, forearm) or exceptional (metacarpus, phalanx, carpal bone, foot bones, scapula, mandible). Iliac bone, rib and radius lesions mainly affect older adolescents and adults [1,2,5].

Calcaneal UBC may be revealed by pain, fissure or true fracture. It is not to be confused with calcaneal pseudocyst, which is triangular and due to rarefaction of cancellous bone trabeculae; imaging
1.5. Complementary examinations

On plain X-ray, UBCs are mainly found (90–95%) on the metaphysis of the long bones, and are juxtaphyseal, radiotransparent, moderately expansive, well-contoured, centered, oblong along the longitudinal axis of the bone, usually unicameral, with fine boney margins and thinning of the facing cortical bone (Fig. 1). Exceptionally, simple bone cysts may be found on the diaphysis, where they are large, multicameral and only slightly expansive [4]. In fractures, there may be a small “fallen fragment” that has migrated via the intracystic fluid (Fig. 2) [3]; this “fallen fragment sign” is considered by some to be pathognomonic [2]. Likewise, an aspect with a gas bubble that has migrated upward (“rising bubble sign”) is also suggestive of UBC [8]. The aspect is often characteristic enough to require no complementary exploration.

Computed tomography (CT) finds a thin-walled lesion, often with pseudo-septum (Fig. 3), and may show a fissure in the cyst. This examination serves mainly to assess cyst wall thickness and fracture risk. It can be used to assess lesion extension in complex regions such as the spine or pelvis [2].

Magnetic resonance imaging (MRI) can confirm the cystic nature of the lesion by showing a liquid signal (Fig. 1B, C). The fluid level is rarely found. The periphery and any septa may show enhancement on gadolinium injection. Fractured UBCs may contain fluid levels and show nodular-like enhancement [2].

Bone scintigraphy [4] and positron emission tomography are non-contributive; there may be normal or hypofixation in non-complicated cysts and hyperfixation in case of fracture.

Cystography is part of the treatment (Fig. 4, particularly B). Contrast enhancement may reveal intracyst walls, any tissular component and the degrees of venous drainage [2,9].

1.6. Differential diagnosis

The main differential diagnosis is with aneurysmal bone cyst (ABC) [4,10]. Other lesions, such as fibrous dysplasia, non-ossifying fibroma, eosinophilic granuloma, enchondroma or chondromyxoid fibroma, may in some forms suggest UBC [2,4].

1.6.1. Anatomopathology

UBC is classified as a benign indeterminate neoplastic tumor. Macroscopically, the cavity may be filled with clear or yellowish fluid, which may be hemorrhagic in case of fracture.

Histologically, the cavity is lined with a thin fibrous membrane, which may contain immature, calcified, flakey cement-like bone matter. In case of fracture, the aspect changes, mimicking an ABC. The fibrous membrane thickens, becoming cellular, with fibroblastic reaction, osteoclastic giant cells, inflammatory cellular elements and hemosiderin and cholesterol deposits [1].

1.6.2. Natural history

UBC develops in the metaphysis of the long bones then, with growth (Fig. 5), migrates toward the diaphysis and usually ends up filled and ossified [4]. UBC is rare in adults, suggesting spontaneous resolution. There is no particular tendency to malign transformation [2,3].

Growth disorder may be induced by the cyst crossing the growth plate and extending toward the epiphysis. Length discrepancy or axial deviation may occur spontaneously or as complications of treatment [3]. Epiphyseal involvement can be analyzed better on MRI than on X-ray [2].

The main complication is fracture, which may lead to resolution in 15% of cases. Clinical factors such as pain, young age or superior humeral location and radiologic factors such as cavity enlargement over time, cavity distance from growth plate, multicameral aspect or early recurrence after primary treatment are signs of cyst activity and fracture risk [2–4,11,12]. This aggressiveness is hard to assess at any given moment in time. Criteria such as the thickness of the remaining cortical bone, cyst/bone diameter ratio or cystic index (cyst area divided by the square of the diameter of the diaphysis)
have been shown to be poorly specific or reproducible; X-ray does not allow reliable 3D assessment, unlike CT [2,13].

1.6.3. Treatment

The main indication for treatment of UBC is fracture risk [3,4,10]. No treatments guarantee cure, except wide resection, which, obviously, is not indicated. All others show failure rates of between 10% and over 30%. It thus seems logical to first try the least aggressive techniques, possibly associated to preventive osteosynthesis. The potential severity of complications in femoral neck fracture (necrosis, residual coxa vara) and the risk of repeat fracture indicate surgery for femoral neck lesions, especially in case of history of fracture [2–4,11,12].

Scaglioni and Bartolozzi suggested treating UBC by methylprednisolone acetate injection [4,14]. The cyst is punctured by two needles, the fluid drawn out, and the cavity opacified with radiologic contrast medium, which, if the fluid is clear (as in some UBCs) and opacification complete, without sepsis, theoretically enables differential diagnosis with respect to ABC (Fig. 4B). Venous drainage found on cystography is claimed to be prognostic, cysts without venous outflow healing better after injection [9]. Wright, in a randomized study, found that corticosteroid injection gave better results than bone marrow injection [15]. Recent publications have revived this “old trick”, with its simplicity, low cost and acceptable success rate. In case of incomplete response to a first injection, treatment is usually repeated once or twice [2,3,12,15,16].

Isolated intracyst injection of demineralized bone powder, bone marrow or bone substitutes has given contradictory results [2,17] and is better seen as an adjuvant to curettage.

Decompression or drainage has been suggested, perforating the cyst wall or creating a communication with the medullary cavity [2,18,19].

Canavese showed that percutaneous intracyst curettage, without filling or injection, gave better results than isolated injection [17]. The cyst walls should be treated systematically and perforated to create a communication with the medullary cavity, the curettage product being aspirated for pathology examination. In some locations, curettage can be performed under endoscopy.

Associating curettage, decompression, filling with bone substitute and bone marrow or demineralized bone powder injection in a single step significantly improves the rate of cure [2,5]. There seem to be no grounds for recommending one filling material over the other. Electrical or chemical cauterization of the cyst walls does not seem to be useful. Autologous iliac graft does not seem to give better results than other methods. Associating drainage by perforated screw or pin is a useful supplement [18,19]. Pinning also provides mechanical protection [2,18]. Bone morphogenetic protein (BMP) is to be avoided, providing no benefit and being liable to cause complications such as inflammation, with a suspected carcinogenic effect [20].

In femoral neck lesions, osteosynthesis should be adapted to the patient’s age, conserving the growth plate and allowing continued growth in children [4,13].

In practice, two distinct situations arise: either diagnosis is prompted by fracture, or the cyst is discovered serendipitously. In both cases, ABC and malignant tumor have to be ruled out.

In fracture, conservative treatment enables fusion and in some cases cyst ossification. The actual cyst is then treated after consolidation of the fracture if no spontaneous filling has begun. In femoral neck lesions, which show a high risk of complication in case of fracture, or iterative fracture of other bones, notably the humerus, treatment comprising curettage, decompression by penetrating the medullary cavity, filling with bone substitute and osteosynthesis seems to give the optimal chances of success.

Non-fractured UBC involving the upper limbs poses little mechanical threat; treatment can be based on aspiration and corticosteroid injection or simple clinical and radiological surveillance up to the end of growth, depending on patient expectations and family context.

2. Aneurysmal bone cyst

Aneurysmal bone cyst (ABC) is a benign, osteolytic, expansive and hemorrhagic lesion. There are various forms of aneurysmal cyst: the usual one is primary or “classical” ABC; others are secondary (associated with another lesion), solid ABC or giant cell reparative granuloma, and soft-tissue aneurysmal cyst.

2.1. Etiology and pathogenesis

The nature and histogenesis of ABC are still unclear; it is classified as an indeterminate tumor, of intermediate malignancy, locally aggressive [21]. It was long thought to be caused by intraosseous or subperiosteal hemorrhage due to abnormal venous circulation, activating osteoclasts and inducing bone resorption and local remodeling. This theory is no longer accepted for primary ABC, which involves rearrangement of USP6 oncogene, on chromosome 17, but remains plausible for secondary ABC, which does not show translocation [21].

2.2. Epidemiology

ABC is rarer than UBC, at 0.14 per 100,000 of the population per year. There may be a slight female predominance. ABC is encountered at all ages, but most patients are in their second decade and 75 to 90% of cases occur before that age of 20; ABC is rarer after the age of 30 and exceptional after 50. It usually occurs singly [10,21,22].

2.3. Location

ABC can involve any part of the skeleton, but especially the long bones (67% of cases), spine (15%) and pelvis (9%). The metaphysis is most often involved, and the bones most frequently involved are the distal femur, tibia, humerus and fibula. In the spine, ABC usually involves the posterior arch, mainly of the lumbar, followed by cervical and then thoracic vertebrae. Pelvic lesions more often
involves the obturator foramen and is peripheral to the triradiate cartilage [23].

2.4. Particular forms

Thirty percent of ABCs are secondary [10,21,23], in reaction to another lesion such as giant cell tumor, chondroblastoma, osteoblastoma, chondromyxoid fibroma, fibrous dysplasia or non-ossifying fibroma. The aspect of ABC may predominate, masking the causal lesion, which has to be explored for. More rarely, secondary ABC is associated a primary malignant tumor (osteosarcoma) or metastatic malignancy, in which case it should not be called “secondary ABC” but rather as such-and-such causal lesion “with aneurysmal remodeling or cystic and hemorrhagic modifications” [21].

Solid aneurysmal cyst or giant cell reparative granuloma accounts for less than 10% of ABCs. On imaging and macroscopically, the aspect is of a full lesion containing crumbly tissue, at some places hemorrhagic; these forms are of good prognosis, with very little recurrence after treatment [23]. Soft-tissue aneurysmal cyst is exceptional. A few apparently fortuitous cases of iterative ABC and of ABC in twins have been reported.

2.5. Clinical symptomatology

ABC is often revealed by pain, sometimes by swelling, and more rarely by fracture [10,22,23]. Symptoms may appear or worsen during pregnancy [10,23]. Spinal lesions may be revealed by pain, torticollis, stiff and painful scoliosis, or more rarely a mass, fracture or neurologic symptoms [10,24].
2.6. Complementary examinations

On plain X-ray, ABC shows as an eccentric, osteolytic, expansive and sometimes trabeculated lesion containing fine-walled cystic cavities (Fig. 6). Internal contours are well defined, with or without an osseous sclerotic ring, and the cortical bone bulges. Loss of cortical contours or extension into soft-tissue may mimic a malignant lesion, indicating an aggressive form (Fig. 7A, B). Central locations are more often found in the short bones of the hands and feet (Fig. 8, particularly A) [10,23].

Vertebral lesions (Fig. 9) involve the posterior arch or both the body and the posterior arch [10,24]. X-ray often fails to establish diagnosis, and complementary imaging is required [10,22].

CT is less sensitive than MRI, and shows fluid levels in only a third of cases. In complex regions such as the spine or pelvis, CT can provide a lesion map, determine fracture risk and assess filling after treatment [10,13].

MRI is the examination of choice to complement X-ray. The typical aspect is an expansive, lesion, lobular or with septa. Multiple fluid levels may be detected on T2-weighted axial sequences at rest; while not specific, they are highly suggestive (Fig. 6B). Gadolinium injection shows enhancement of the cyst walls and internal septa (Fig. 6C). Primary ABC may contain a solid tissular component, also suggesting telangiectatic osteosarcoma or secondary ABC [10,22]. Bone scintigraphy, which is usually non-contributive, shows hyperfixation, and sometimes non-specific central hypofixation. It can help locate a painful lesion, particularly spinal lesions in children.

Cystography may be part of treatment in case of sclerotherapy or if UBC is suspected. Contrast enhancement may reveal intracyst walls, a possible tissular contingent to be biopsied, and the degree of venous drainage. Depending on cyst location and departmental organization, the injection can be made under simple fluoroscopic control (in theater or in the interventional radiology department) or CT.

Arteriography makes no diagnostic contribution, but may be a first step in embolization. It shows a prolonged diffuse blush, with or without a very few afferent vessels, without arteriovenous shunt.

2.6.1. Anatomopathology

Biopsy is essential for diagnosing ABC and may be performed by trocar or, preferably, surgery, or in the form of curettage-biopsy (“curosy”). Firstly, it can rule our telangiectatic osteosarcoma and

Fig. 8. a. Solid ABC of the first metatarsus in a 9 year-old boy. b. Favorable spontaneous evolution after biopsy (droit = right).

Fig. 9. ABC of first thoracic vertebra, revealed by ulnar palsy of the right hand. MRI aspect showing lesion of the posterior arch with vertebral body fracture.

differentiate between UBC and ABC. UBC can be diagnosed with virtual certainty from aspiration of clear fluid and complete opacification of a cavity that is empty on cystography; clear fluid may also, however, be drawn from an ABC, but without showing complete opacity. Hemorrhagic fluid may still indicate a UBC, especially in case of trauma, or even associated UBC and ABC. Biopsy, guided by imaging, focuses on a tissular area. In certain lesions, notably of the spine, the biopsy product may be hemorrhagic, which can be avoided by prior embolization [10,23].

Macroscopically, ABCs comprises multiple anastomotic cavities of between a few millimeters and 2 cm diameter, containing non-coagulated blood and, in longstanding lesions, a serous or serous-hemorrhagic fluid. The cavities are contoured by tissular septa, which progressively ossify in old lesions. Peripherally, the cortical bone is thin or absent, replaced in which case by a thin “egg-shell” of periosteal osteogenic bone [21].

Histologically, the cavities lack endothelial cover and are full of blood. They are contoured by fibrous septa, enclosing fibroblasts, inflammatory lymphohistiocytic elements, siderophages and osteoclastic giant cells. Mitosis may be strong, but not abnormal, in the initial phase. There are no smooth or elastic muscle fibers. There is reactive osteogenesis within the immature septa, comprising a thin network of “woven” or “lacey” osteoids or more mature trabeculae. In more than one-third of cases, there is a strongly calcified basophile fibrochondroid matrix.

In the solid ABC form, hemorrhagic cavities are fewer, while the cellular component is the same as in classical ABC [21].

2.6.2. Differential diagnosis

UBC and ABC affect the same population and locations (proximal humerus, proximal femur), may show similar aspects, and the aspiration fluid is non-specific; diagnosis can therefore be difficult [10,22]. In some cases, the two are associated. ABC is usually more eccentrically located on the metaphysis, with a more aggressive aspect, with walls more bulging and thinner. Trabeculation is greater in ABC. ABC evolves from diaphysis toward epiphysis, unlike UBC. Differential diagnosis between primary ABC and traumatized UBC is difficult. On microscopy, areas of cement-like flakey substance are more characteristic of UBC. Calculating bluish fibrochondroid areas indicate ABC. In the absence of these characteristics, differential diagnosis is difficult in case of fracture, and comparison between radiologic and clinical findings is most contributive [21].

Telangiectatic osteosarcoma should be systematically screened for, and biopsy is essential before treating ABC [10,22]. The aspect is often highly misleading and diagnosis histologically difficult. Differential diagnosis in favor of osteosarcoma is based on findings of atypical cells and mitoses and a more irregular osteoid matrix; these are to be looked for in the biopsy material as a whole. Molecular biology can be called in, using FISH (fluorescence in situ hybridization) to show rearrangement of USP6 in primary ABC [21].

Giant cell tumor (GCT) is almost never seen before closure of the growth cartilage and tends to involve the epiphyseal-metaphyseal region of the long bones; these are sometimes the only points differentiating ABC from GCT. Strong P63 expression is also more often associated with GCT than ABC [21].

Eosinophilic granuloma, osteoblastoma or malignant tumor may be mistaken for ABC in spinal locations, and only biopsy enables diagnosis.

Non-ossifying fibroma (NOF) and solid ABC could appear fairly similar according to some authors. Although NOF is bulging and off-center on the long bone metaphysis, it is generally asymptomatic, with a full aspect on MRI, and biopsy is rarely useful.

Solid ABC cannot be distinguished morphologically from giant cell reparative granuloma or from brown tumor in hyperparathyroidism.

2.6.3. Natural history

ABC, although benign, can leave severe sequelae, and diagnosis and treatment need to be early. It shows highly variable evolutivity; three forms have been distinguished: quiescent, active and aggressive. It sometimes resolves spontaneously or after simple biopsy (Fig. 8A, B) [10]. In other cases, the cyst may become aggressive, entirely destroying one end of the bone, raising fears of malignancy (Fig. 7A, B). Evolution involves 3 or 4 phases:
osteolysis with cortical destruction and raising of the periosteum; periosteal reaction with a neoplastic ossified border creating a swollen aspect in the bone; stabilization with the appearance of sepa; then cicatrization with variable calcification, ossification and remodeling. After healing, the bone recovers a normal aspect, although non-evolutionary cysts often persist.

ABC shows malignant transformation only in case of irradiation [22,23]. Rare cases of malignant tumor have been described developing at the site of an ABC treated several years previously [10,22].

More often than in UBC, growth disorder can induce limb-length discrepancy or axial deviation when the ABC crosses the growth plate, spontaneously or following treatment.

Certain spinal forms may lead to neurologic complications, either due to tumor growth or following fracture.

Most ABCs resolve after treatment, and most local recurrence is in children, aggressive forms or central lesions.

2.6.4. Treatment

Once diagnosis is established, we wait, if possible, for 4 to 6 weeks after the biopsy before initiating treatment, to allow the trepanation orifice to fill and, in some cases, the cyst to begin involution [22].

No treatments, other than wide resection, guarantee cure. Other methods show failure rates of 15 to 30%, so that the least aggressive techniques are implemented first, sometimes associated to osteosynthesis in case of severe fragility [10,22].

Radiation therapy is effective, but the risk of malignant transformation limits its use to a few absolutely exceptional cases, such as recurrent spinal lesions inaccessible to other treatments [23].

Isolated embolization can treat certain ABCs, notably in the spine or sacrum. It may need to be repeated. It requires the presence of afferent vessels, and is not free of risk such as accidental ischemia of visceral organs or the spinal cord [25]. Preoperative embolization helps reduce risk of hemorrhage in ABC of the spine, sacrum or pelvis [10,22,24).

Methylprednisolone acetate injection is to be avoided, as it may exacerbate the lesion [10,22].

Intralysyntic injection of demineralized bone powder, bone marrow, calcitonin, bone substitute or doxycycline have given contradictory results and sometimes require a large number of procedures [10,22,26,27].

Intracystic injection of Ethibloc was reported to provide a 70 to 94% rate of cure [28]. Ethibloc, however, is no longer available, and other techniques have proved less dangerous [22,28,29]. In 2010, Varshney reported a randomized study in which polidocanol (Aetoxysclerol®) sclerotherapy showed success comparable to surgery, with fewer complications [27]; a mean 3 injections were required (Fig. 10A–C).

Absolute alcohol also shows good treatment efficacy with a low rate of complications. It may require repeat injection, if the cyst remains insufficiently filled [29]. It is our present technique of choice, due to its simplicity, harmlessness and efficacy.

Simm et al. succeeded in calcifying a sacral ABC, resistant to embolization, by zoledronic acid perfusion, without need for subsequent surgery [30]. Denosumab has been proposed in ABC, especially of the spine, but without details of treatment duration or long-term results [31].

Surgery was classically the treatment of choice in ABC [10,22,23,27]. Wide resection guarantees against local recurrence, but at the cost of reconstruction problems and of possible complications that the benign nature of ABC cannot justify. Marginal resection may still be used in very expansive forms. In less aggressive forms, subperiosteal resection limits the risk of local recurrence compared to simple curettage, and periosteal conservation facilitates reconstruction. If the tumor leaves a continuous boney wall, curettage and filling by graft, cement or bone substitute also provides good results, but with a 10 to 30% risk of local recurrence. Percutaneous curettage and cyst aspiration without filling provides results comparable to intracyst resection. Recurrence risk can be limited by associating curettage to cryotherapy or argon plasma coagulation (with increased risk of fracture). In case of severe fragilization of fracture, osteosynthesis may be considered if diagnosis is certain.

Certain teams continue to prefer surgery, but we ourselves reserve it to cases in which sclerotherapy cannot be implemented due to location, or to more aggressive forms, where it may be the only option.

3. Conclusion

UBC and ABC are common benign lesions affecting similar populations and with similar clinical and radiological aspects. Differential diagnosis may be difficult but is mandatory, as treatment is different. In UBC, complications mainly consist of fracture. In ABC, they concern rather the osteolytic potential of the lesion and the impact on growth. Biopsy is indispensable in ABC, to rule out telangiectatic sarcoma. In both forms, if there is no threat of fracture, percutaneous injections are the attitude of choice; otherwise, osteosynthesis is required.

Disclosure of interest

The author declares that he has no conflicts of interest concerning this article.

For editorial reasons, the following references are limited to recent publications. More complete bibliographies are to be found in the articles by Docquier and Cahuzaq for UBC and Cotalladora and Docquier for ABC [2,3,10,22].