Aneurysmal Bone Cyst: A Review of Management

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ABSTRACT

Aneurysmal bone cyst is a rare lesion that is most often found in young adults and children. It can have an unpredictable behavior, with a high recurrence rate after treatment. Treatment is based on personal and institutional experience and preferences. Standard treatment consists of curettage (manual + motorized high-speed burr) plus local adjuvants and bone grafting to fill the void. In anatomical locations that are difficult to reach surgically, percutaneous procedures (injection of sclerosant agents, radiofrequency thermal ablation (RFTA)) or selective arterial embolization (SAE) are used. Medical management with bisphosphonates (BPs) or denosumab has also been advocated. Minimally invasive surgical procedures such as “curopsy” and percutaneous demineralized bone matrix (DBM) and/or autologous bone marrow concentrate (BMC) grafting...
Aneurysmal bone cyst (ABC) was first described in 1942 by Jaffe and Lichtenstein. It is a rare lesion with an incidence of 1.4 per 100,000 individuals and represents 1% of primary bone tumors. It generally affects children and young adults under 20 years of age, with no clear sex prevalence. The most common sites of the lesion include the femur, tibia, humerus, and posterior elements of the spine (mainly lumbar, less frequently at the thoracic and cervical levels).

Clinical and radiographic presentation. Pain is the main symptom, associated with swelling and local tenderness; neurological symptoms caused by compression of the nerve roots are also common in cases of spinal localization. A pathologic fracture can sometimes be the initial presentation of ABC in indolent cases, even if less commonly than in unicameral bone cyst (UBC). Limb deformity and length discrepancies can also be present, since ABC is more common in the pediatric population with open growth plates.

ABCs are locally aggressive lesions that destroy and deform the bone. On X-ray examination, they appear as cystic lesions located eccentrically, with a thin layer of cortical bone. On magnetic resonance imaging (MRI), they show multiple internal trabeculae with a multi-locular appearance (“soap bubble” sign), with layers of varying thickness and cavities filled with blood of different densities (multiple “fluid-fluid levels”). Computed tomography (CT) can be helpful in better defining the osseous borders of ABC. While the MRI features (soap bubble appearance and fluid-fluid levels) are very characteristic (except in the solid variant) of ABC, they are not pathognomonic, since they are also seen with other lesions, such as UBC, giant cell tumor of bone (GCT-B), and telangiectatic osteosarcoma (Fig. 1a,b). Also, ABC may be either a primary lesion or superimposed upon another tumor, such as chondroblastoma, GCT-B, chondromyxoid fibroma, non-ossifying fibroma (NOF) or fibrous dysplasia; secondary ABCs account for nearly 30% of all ABCs.

Etiology. The etiology of ABC is still controversial. It was initially believed to be caused by a periosteal trauma that disrupted the vascular system, increasing venous pressure and resulting in an expansile vascular lesion that resorbs and expands, but alterations of the ubiquitin-specific protease USP6 and/or osteoblast cadherin 11 CDH11 genes have recently been identified, confirming a tumoral pathogenesis even if such genetic alterations occur in only two-thirds of primary ABCs.

Histology. For a diagnosis of ABC, needle biopsy (by trocar needle) (Fig 2) or incisional biopsy is recommended; even if the results of MRI are character-
istic, biopsy is mandatory to exclude telangiectatic osteogenic sarcoma, which can resemble ABC on imaging.9,10 Macroscopically, with the use of a trocar needle, uncoagulated blood can be withdrawn, while serous-hemorrhagic fluid can be appreciated in chronic lesions. Thus, there are similarities between UBC and ABC, and a diagnosis can be difficult to establish based solely on a cytological smear.14 Microscopically, ABC has calcifying bluish fibrochondroid areas, while areas of cement-like flakey substances are more characteristic of UBC.15 Histologically, two subtypes have been described. The classic type accounts for 95% of all cases and is characterized by honeycombed vascular spaces separated by fibrous septae that contain numerous capillaries, fibroblasts, osteoclast-type giant cells, and filaments of osteoid tissue. In contrast, the solid variant of ABC is characterized by a more fibroblastic and fibro-histiocytic proliferation phenotype, and smaller and less abundant vascular spaces. A mixed variant has also been described. Histopathologic examination of ABC can reveal fibrous septae, osteoclast-like giant cells around woven bone trabeculae, cavernous blood-filled spaces, and thin-walled vessels, and a differential diagnosis with other lesions that are characterized by the presence of osteoclastic giant cells (GCT-B, brown tumor, and NOF) is needed.16 Histologically, criteria that can be used for the diagnosis of primary ABC include (1) presence of blood-filled spaces; (2) membranes composed of spindle-shaped mononuclear stromal cells; (3) lack of organization in stromal cells; (4) osteoclast-like giant cells scattered throughout the lesion; (5) focal concentrated aggregates of giant cells; and (6) absence of a chondroid matrix and the plump mononuclear cells typical of GCT-B.17

**MANAGEMENT OF ABC**

There are different options for the treatment of ABC including surgical resection of the lesion, curettage with or without bone grafting, optional adjuvant therapy, endovascular treatment by selective arterial embolization, external-beam radiotherapy, and percutaneous directed therapies, including sclerotherapy, thermal ablation, cemen- toplasty and percutaneous injection of bisphosphonate or doxycycline.1 The local recurrence (LR) rate varies depending on the treatment. However, recurrence is generally much more common in ABC than is juxtaphyseal or periarticular in young children (less than 10 years old), and within the first 2 years after surgery.17,18

**En bloc excision**

En bloc excision has a low risk of LR, but at a cost of high iatrogenic morbidity. Several studies have reported that local control of the disease is achieved in 95-100% of cases after complete en bloc resection of ABC.4,6,19 Lampasi et al.20 described 3 young patients who underwent fibular en bloc excision of ABC and reconstruction with contralateral fibular autologous graft (1 case) or allograft (2 cases). At a mean follow-up (FU) of 11.6 years (range 3.1-27.5), there was no LR and no significant differences in subjective scores, growth disturbance, alignment, stability or bone reconstitution between the resection group and the curettage group (6 patients). However, the number of procedures, including for the removal of hardware, complications (two minor) and duration of immobilization/orthoses were greater in the resection group; also, movement of the ankle was restricted in one patient.20 Flont et al.21 did not observe LR in 26 patients who underwent en bloc excision, although the resection group showed a higher prevalence of possible remaining symptoms, such as postoperative pain, dysmetria, and muscle weakness, and decreased range of motion compared to the intralesional treatment group. For this reason, en bloc resection is considered when ABC recurs after repeated intralesional treatments, when ABC is localized in expendable segments without compromising function, or when irreparable damage to a joint is already present.21

In 2009, Abuhassan and Shannak22 described subperiosteal resection in a series of 8 patients with ABC of the distal fibula; the mean size of the resected specimen was 5.12 cm (range 3.5-8.0) and none of the patients received instillation of bone marrow, autogenous bone graft, allograft or any synthetic bone substitutes. All had complete regeneration of the bone defect within 3 to 9 months after surgery, and no joint instability or LR at a mean FU of 11.5 years (range 2-18), with no difference in the range of movement, alignment or stability of the ankle when compared with the opposite side.22 Mostafa achieved similar results with the same technique, which obviously can be proposed only for expendable non-weight-bearing bone (i.e., the fibula).23

*Figure 2. Needle biopsy under CT control of aneurysmal bone cyst of the acetabulum.*
Curettage

Intralesional curettage, with or without adjuvant procedures and/or bone grafting, is the treatment of choice for ABC (Fig. 3a-c). Before the introduction of local adjuvants, some authors reported LR in up to 59% of patients with intralesional curettage alone.7 The use of polymethyl methacrylate cement (PMMA), motorized high-speed burr, argon beam, phenol and cryotherapy has dramatically reduced the incidence of LR. The tumor is exposed through a cortical window with a longitudinal length that should be almost the same dimension as the ABC. To minimize bone loss, the tumor is generally approached through the thinner or more damaged cortex; bone windows should be elliptical, with the major axis on the long axis of bone to reduce stress-risers.

Most of the tumor is removed with manual instruments (angled curettes, rongeurs, forceps), and a motorized high-speed burr is then used to “polish” the ABC walls. In a series of 40 patients, Gibbs et al. reported local control of almost 90% at 7.2-years FU with curettage plus high-speed burring without any other adjuvants.24 Dormans et al. reported a healing rate of 82% without LR with their four-step surgical technique that included the use of high-speed instruments.25 Wang et al. observed one case of LR among 31 patients who were treated with curettage plus high-speed burring plus bone grafting, and concluded that high-speed burring as the sole adjuvant to intralesional curettage seems to be a reasonable approach to achieving a low LR rate for ABC.26 On the other hand, other studies have reported that the use of high-speed burring does not lead to a statistically significant reduction in LR.17

Argon beam coagulation has also been proposed as an adjuvant procedure. A beam of argon gas produces a unipolar electric current that superficially dessicates and coagulates tissues.27 A reduction in the recurrence rate has been noted when manual curettage was augmented with the use of an argon beam coagulator. Cummings et al. reported a LR rate of 0% with argon beam coagulation after manual and motorized curettage.28 Steffner et al. found a drop in the LR rate from 20.6% after manual and motorized curettage alone to 7.5% with the addition of an argon beam, albeit with an increase in the rate of post-operative fracture from 0% to 12.5% due to desiccation and osteonecrosis in the argon beam group.29

Another adjuvant is phenol, or carbolic acid, which is an aromatic organic compound produced from petroleum that is used in the production of plastics and pharmaceuticals. It is used as an
adjuvant in intralesional treatment of benign (ABC, chondroblastoma, GCT-B) or low-grade malignant (low-grade chondrosarcoma) bone tumors. It kills neoplastic cells remaining in the wall of the lesion after curettage. Capanna et al. reported a recurrence rate of 7% after curettage plus phenol versus 41% after curettage alone in a mixed series of benign lesions,\textsuperscript{16} while Bitzan et al. reported no local recurrence when phenol was used as an adjuvant in ABCs.\textsuperscript{11} On the other hand, Keçeci et al. found no differences in the recurrence rate of ABCs by manual curettage alone, manual and motorized high-speed curettage, and manual and motorized high-speed curettage plus phenol in a retrospective study on 85 patients.\textsuperscript{32}

Cryotherapy has also been proposed as an adjuvant to augment intralesional curettage in benign or low-grade malignant bone tumors.\textsuperscript{11} Freezing is achieved with liquid nitrogen, which has a boiling point of -195.79°C. When it is poured through a funnel into the tumor cavity, it has a physical effect on tissues thanks to the sudden decrease in temperature that leads to a rapid increase in cell volume and eventual rupture of the cell membrane. Marcove et al. treated a series of 51 ABCs (34 primary and 17 secondary) with curettage followed by cryosurgery with liquid nitrogen; they reported a LR rate of 17.6%, with a reduction to 4% when a second cryosurgery was performed.\textsuperscript{34} Schreuder et al. reported one LR out of 27 cases (3.7%) after curettage, cryotherapy with spray nitrogen and bone grafting.\textsuperscript{43} More recently, the same group reported 80 consecutive cases treated with curettage and cryosurgery with a minimum FU of 2 years; they found 4 LRs for a recurrence rate of 5%, all of which were successfully treated with a second curettage and cryotherapy.\textsuperscript{36} Despite the low LR rate, cryotherapy with liquid nitrogen has possible complications such as post-operative fracture, soft tissue necrosis (including skin), and wound infections in 8 to 14% of cases.\textsuperscript{11,36} Moreover, it is difficult to handle correctly, and several devices have been developed to deliver freezing thermic shock, with improved handling and safety with respect to liquid or spray nitrogen; cold is created and controlled through the use of different gases and transmitted to tissues through probes for which the temperature is controlled.

Following curettage, the tumor cavity can be left empty or filled. Bone grafting is usually preferred for the biological potential of being re-inhabited by the host’s cells and being replaced by the host’s bone over time, while cementation with PMMA is preferred for immediate mechanical stability and strength; it also has a further adjuvant effect due to the exothermic reaction of polymerization while the cement hardens.\textsuperscript{37,38} Ozaki et al. reported LR rates of 17% after curettage and cementation and 37% after curettage and bone grafting, with a significant difference in the cumulative 10-year relapse-free survival between groups.\textsuperscript{39} In a comparative study on the effect of PMMA versus bone grafting in a pediatric population, Wallace and Henshaw reported similar rates of complications and LR.\textsuperscript{38} Mankin et al. reported similar LR rates with the use of bone graft or PMMA.\textsuperscript{19} The use of PMMA in the pediatric population raises concerns about long-term effects: it has no potential for bone incorporation and re-growth, can cause stress-shielding with an eventual risk of pathological fracture, and can be a substrate for infection.\textsuperscript{38}

Another option for filling the defect is with bioactive glass, which is an osteoconductive bone substitute with biostimulative, antimicrobial and neo-angiogenic properties. The bioactive glass BG-S53P4 (commercially BonAlive, BonAlive Biomaterials Ltd, Finland) was approved as a bone substitute in Europe in 2006. It has been cleared to be safe and well-tolerated, with good long-term results in benign bone tumors, in both adults and children.\textsuperscript{40} Syvänen et al.\textsuperscript{38} reported only 2 cases of LR (11%) in a series of 18 skeletally immature patients who were affected by ABC and treated with bio-glass; both patients were male, with large lesions close to the physes of the femur (one proximal, one distal), and had been previously treated with bone allograft. No disturbance of bone growth was observed. Moreover, the long-lasting resistance of bio-glass to compressive forces could be beneficial in the case of LR. While bio-glass can be considered a good alternative to fill the cavity after tumor excision, it has not yet been shown to affect the tumor or influence the LR rate.

Moreover, demineralized bone matrix (DBM) and autologous bone marrow concentrate (BMC) have been proposed as a graft to stimulate bone regeneration and subsequent ABC healing, even without extensive curettage of the lesion. DBM has osteoinductive and osteoconductive properties, and BMC supplies osteoprogenitor cells. Autologous percutaneous marrow grafting was first described by Lokiec et al. as an alternative to methylprednisolone injection in UBCs to improve the consolidation rate and reduce the number of procedures,\textsuperscript{41} while Delloye and co-workers introduced the combined use of DBM and autologous bone marrow aspirate for the treatment of ABCs.\textsuperscript{42,43} At the same time, Rosenthal et al. described excellent results in nonunions, bone cysts (ABC and UBC) and fibrous lesions with allogenic or xenogenic DBM.\textsuperscript{44} This approach has since been developed into BMC and extended to other benign lesions: the combined use of DBM and BMC in the treatment of UBCs was proposed, and a higher healing rate compared to a single injection of steroids was reported.\textsuperscript{45} Excellent results have also been reported in the treatment of ABCs.\textsuperscript{46,47}

Cuproxy

Cuproxy, or “biopsy with intent to cure”, is a percutaneous procedure that merges minimal invasiveness and a favorable percentage of success. Spontaneous healing of ABC has been observed after a fracture or a biopsy alone. Therefore, Reddy et al. proposed percutaneous limited curettage at the time of biopsy, which includes obtaining the lining membrane from various quadrants of the cyst, as a biopct and curative procedure.\textsuperscript{48} In cases of ABC, they observed a healing rate of 81% after cuproxy and of 90% after curettage, with a statistically significant difference in LR rate (19% in the cuproxy group vs. 10% in the curettage group, \(p=.04\)). However, cuproxy is a single procedure and curettage is performed following a previous biopsy. Biestecker et al. speculated that an ABC was a secondary lesion of bone reactive to hemodynamic disturbances,\textsuperscript{7} and Marcove et al. suggested that arresting this hemodynamic disturbance should induce healing and prevent recurrence.\textsuperscript{14} Therefore, healing may occur either spontaneously or after biopsy or fracture. Reddy et al. supported the
hypothesis that destruction of the internal cyst architecture alters the hemodynamics and induces healing, and this is the rationale that underlies treatment with curepsy or curettage without any adjuvants. Part of their success rate can be due to the appropriate selection of patients as candidates for curepsy (small lesions with imaging results suggesting low aggressiveness). To date, there have been no other reports on this technique.

Percutaneous Intracystic Sclerotherapy

Percutaneous treatment is a less-invasive option that is considered to be the treatment of choice in several centers due to the highly demanding surgical difficulties in some anatomical areas, with high complication and LR rates, ranging from 10 to 44%. Alcohol solutions are used as sclerosant agents in many pathologies such as arteriovenous malformations (AVMs) (Fig. 4a-c), lymphangiomas, renal cysts, and hepatic metastases. Sclerosant agents damage the endothelial lining, trigger the coagulant cascade and result in thrombotic occlusion of blood vessels. One of the most popular is the alcoholic solution of Zein (Ethibloc®; Ethicon, Inc., Sommerville, NJ, USA), which has been shown to provide high healing rates in the treatment of ABCs, but has also been associated with an unacceptable complication rate, including frequent minor complications such as local inflammatory reactions (in up to 94% of patients) and major complications such as aseptic bone necrosis, pulmonary embolism, deep venous thrombosis, and cerebellar infarct leading to death.

Lambot-Juhan et al. reported the efficacy and safety of percutaneous sclerotherapy with absolute alcohol (ethanol 96%) in a series of 29 children, with a good response in 59%, a partial response in 31% and a poor response in 10%. None of the children experienced any inflammatory reaction or post-procedure pain. One complication occurred as a transitory radial paralysis after injection of a humeral ABC because of the extravasation of alcohol. Although none of our patients has experienced bradycardia during the procedure, extreme care should be taken since there is a potential risk of pulmonary artery spasm and even cardiac arrest if alcohol enters the systemic circulation.

Another sclerosing alcohol is polidocanol, which is used in varicose veins of the extremities, in esophageal varices, in intestinal AVMs and in hydrocele. Rastogi et al. treated 74 ABCs with 3% polidocanol. After a mean of 3 injections (range 1-5) and 12 months (mean) of treatment (range 6-18 months), they found a reduction of ABC dimensions of 76.6% and a clinical response of 84.5%, with a LR rate

Figure 4. (a) X-ray of a humeral aneurysmal bone cyst, (b) MRI of the humeral bone cyst, (c) percutaneous injection of sclerosant agents.
of 2.8% (2 patients, both healed after another injection of polidocanol). The overall results suggested that sclerotherapy was less invasive, with a shorter hospitalization stay, and as effective as open surgery, but safer. Potential complications with the use of polidocanol include hypopigmentation, necrosis at the site of injection in the case of extravasation, pulmonary embolism, osteomyelitis, allergic reactions and anesthetic complications. Polidocanol is relatively contraindicated for patients with skin conditions at the site of injection, heart disease, asthma or pregnancy. It should not be injected intra-arterially because severe necrosis can occur, and should not be used if the lesion causes neurovascular compression requiring surgical treatment. Brosjö et al. reported 37 good results in 38 cases after a median of 4 (range 1–11) injections, with 3 minor local inflammatory reactions.

**CT-guided thermal ablation**

Thermal ablation is widely used as a minimally invasive percutaneous treatment with a curative or palliative effect in several tumors, including benign bone tumors such as osteoid osteoma, and bone metastases. The increase in temperature can be achieved by radiofrequency (radiofrequency thermoablation, RFTA), microwave, high-intensity focused ultrasound, or LASER. Thermal ablation includes cryotherapy (cryoablation), in which tumor necrosis is achieved by freezing instead of heating, and can also be used percutaneously with the modern systems described previously. RFTA is the most frequently used technique; it consists of a high-watt electric generator (150–250 W) that produces alternating current of high-frequency radio waves that pass between the electrodes. Heat is produced by resistance that causes ionic and molecular agitation in the tissues surrounding the probe, inducing coagulation necrosis and cell death. It usually operates in a monopolar mode (interstitial electrode at the tip of the probe inserted into the tumor, grounding pads on the skin). Such percutaneous treatment requires guidance through imaging, and CT scan is the gold standard.

RFTA is considered to be safer and easier to use than other traditional surgical treatment methods to cure ABC because it causes fewer post-operative complications and reduces the need for hospitalization. It is also indicated in the presence of contraindications for the use of opioids and NSAIDs non-steroidal anti-inflammatory drugs such as during pregnancy, if collateral effects have developed, or if there are contraindications to surgical treatment due to poor health of the patient or when the tumor is located in anatomical regions that are surgically difficult to treat. In all these cases, percutaneous procedures are the treatment of choice. Zarzour et al. reported significant pain reduction and no complications or LR in 20 cases of painful ABC in different anatomical locations treated with percutaneous RFTA (11 cases) or percutaneous RFTA plus cementation (9 cases).

**Doxycycline foam**

Recently, the percutaneous administration of doxycycline foam as an antitumoral agent has been described. Doxycycline is an antibiotic with antitumoral properties. It inhibits osteoclastic functionality and neoangiogenesis, and promotes osteoclastic apoptosis and healing of micro- and macroscopic lymphatic malformations. Intraluesional injection of doxycycline has been reported to give a good healing response with a low LR rate (5%), although the exact mechanism of action in ABC is not yet known. Daly et al. reported that doxycycline had osteotropic and toxic effects on matrix-metalloproteinases which play a role in bone-destroying osteoclastic activity. Moreover, a direct action as an inhibitor of tumoral cell growth and neoangiogenesis and as a promoter of the osteoblast population in bone metastases has been described. Doyle et al. used intraosseous injections of doxycycline to successfully treat recurrent ABC in the spine of a 12-year-old boy. Shiel et al. reported the percutaneous injection of doxycycline foam and found a reduction in the LR rate, especially for juxaphyseal lesions. However, doxycycline foam can lead to complications, particularly in soft tissues, with local necrosis and damage. In addition, it does not provide structural support when used in a protein foam delivery system, and multiple procedures are required (mean 5 injections; up to 14 prior to ABC resolution). For these reasons, the use of doxycycline as an adjuvant to curettage and bone grafting with calcium phosphate (which is an osteoconductive, absorbable bone substitute that encourages bone to grow onto its surface as it slowly resorbs over time) has been proposed to allow for a single-stage procedure, with reduced LR rates, decreased risk of soft tissue injury and improved structural support. There were no changes in either the porosity or mechanical properties of the bone substitute due to the use of doxycycline as an adjunct. On the other hand, Woon et al. recently postulated based on a small series that a single injection of doxycycline should be considered a viable primary treatment option for ABC.

**Bisphosphate intravenous systemic therapy**

Bisphosphonates (BPs) inhibit osteoclastic bone resorption and are routinely used in the treatment of metastatic bone involvement secondary to several types of tumors. Preclinical and clinical evidence has indicated that BPs have direct anti-neoplastic activity, both directly, by inducing apoptosis and inhibiting tumor cell adhesion and invasion, and through indirect means such as the inhibition of angiogenesis. Cornels et al. hypothesized that BPs could be a potential therapeutic option in the management of symptomatic benign bone tumors, and treated 8 patients (5 with ABC) with standard pharmacological doses proposed for the treatment of osteoporosis. At a mean FU of 21 months, they reported complete ossification of the tumor in 3 cases, partial ossification with symptomatic relief in 4 cases, and 1 failure in a large ABC in the posterior arc of C2 that required resection and vertebral stabilization. Kieser et al. reported 6 patients with spinal ABC treated with systemic BPs, under the same inclusion criteria and treatment protocol as Cornels et al.; they achieved 1 complete ossification and 3 partial ossifications with no residual symptoms, while 2 patients required surgery because of progression of neurologic dysfunction at a lumbar location and an unstable C2 lesion.

**Denosumab**

Denosumab is a monoclonal human antibody that binds to the cytokine receptor activator of nuclear factor-
kappa B ligand (RANKL), which essentially initiates bone turnover. RANKL inhibition blocks osteoclast function, and denosumab has been successfully used in the treatment of osteoporosis, skeletal metastases and more recently GCT-B.16 Satisfactory results in the treatment of the latter and immunohistochemical similarities between ABC and GCT-B have led to the speculation that denosumab could also be useful in cases of ABC. While there are still few papers on this point, they show promising results.6,60,61 Pelle et al. reported a case of a 5-year-old child with ABC of the sacrum treated with denosumab to avoid peri-operative risks and complications, with pain relief and neurological deficit recovery at 2 and 6 weeks from treatment, respectively, with a significant reduction in volume by MRI.60 Lange et al. described 2 vertebral ABCs in children (8 and 11 years old) that were successfully treated with denosumab after failed embolization, with healing of the lesions at 4 months.67 Palmerini et al.66 noted clinical and radiological improvements in their multicentric study, at a mean FU of 23 months (range 3-55) and with a median of 8 (range 3-61) denosumab administrations. After 5 months of treatment, in 7 of their 9 patients, the ABC was surrounded by a clear bony rim on CT scan and the uptake of gadolinium contrast was decreased on MRI.2 Patients required surgery. At the latest FU, 2 patients had discontinued denosumab and 5 were still receiving denosumab; all had no evidence of disease progression.16 Denosumab can be used as a neo-adjuvant therapy to facilitate subsequent surgery, in ABC as well as in GCT-B; its use is associated with a dose-dependent risk for the development of osteonecrosis of the jaw.

Endoscopic Curettage

Endoscopic surgery has recently been proposed as an alternative treatment in ABC management. It may give an accurate evaluation of the tumor through a direct view of the cavity (for a cystic tumor). Direct visualization can avoid possible remnants without excessive curettage, which may be associated with intra-operative fractures and bone fragility. Also, from an aesthetic point of view, small stab incisions should be better than a surgical open scar.70 The surgical technique has been well described by Aiba et al. in 2018.70 Under fluoroscopic guidance, the ABC is localized. The position and number of skin incisions depend on the site and dimensions of the tumor. The bone cortex is punctured with Kirschner wire and then enlarged up to 7-8 mm with cannulated drills. An arthroscope is inserted and the tumor is curetted manually with angled curettes and forceps, and motorized shavers or burrs. The arthroscope and instruments are interchangeable to allow for an adequate view and achieve complete curettage. Post-operatively, patients with ABC localized to bones of the lower extremity are allowed weight-bearing of 50% for one month and then partial weight-bearing of 60% up to the 3rd month, when bone healing is usually confirmed by X-rays. Patients with ABC of the upper limb are restricted to non-contact sports. Aiba et al.70 treated 37 patients with endoscopic curettage between 2003 and 2014. Seven LRs (18.9%) required re-endoscopic treatment in 4 cases or open curettage and bone grafting with a bone substitute in 2 cases (all with successful healing), while 1 asymptomatic case was simply observed. Contact with physis was associated with LR, while age under 10 was associated with residual ABC.

Selective arterial embolization

ABCs are usually vascularized by one or more pathological feeding arteries. Selective arterial embolization (SAE) has been described as an associated technique to reduce intra-operative bleeding, and as primary treatment when surgery is not indicated in several benign bone and soft-tissue tumors. It was proposed for the treatment of ABC in the 1980s.5 Rossi et al. reported a high percentage of disease control (94%); a second or third procedure was necessary in 39% of cases, and 5% of patients reported complications such as skin necrosis and transient paresthesias.71 A high percentage of local control has been reported in spinal localizations, and SAE has been proposed as the treatment of choice in spinal ABC.66,72 Terzi et al.73 reported that 73.9% of ABCs of the mobile spine had healed with SAE at a mean FU of 3 years (range 0.5-10). The number of procedures necessary to achieve (clinical and radiographic) healing varied from 1 to 10 (average 4). Despite these results, SAE has limited indications because of the difficulty of identifying the afferent vessels to the ABC, which are frequently not discernable from the nutrient vessels to tissues and vital organs, with major concerns about ABC of the rachis, where the artery of Adamkiewicz can be inadvertently embolized, leading to irreversible neurologic damage.74

Radiotherapy for aneurysmal bone cysts

Radiation therapy (RT) can be another alternative for the treatment of ABCs, and satisfactory results have been reported in the literature.2,14,72 RT is not currently indicated as primary treatment for ABC, and is reserved for cases of repeated LR, when surgery is not indicated or difficult to perform, or as an alternative to SAE in the spine because of the risk of irreversible neurologic damage, as already mentioned.74 RT can also be considered after incomplete resection or curettage, to achieve better local control. In addition to having a direct necrotic effect on tumor cells, it causes thrombosis and the obliteration of small vessels with a subsequent reduction of the blood supply to ABC, leading to a decrease in size and eventually ossification. RT also has a direct analgesic effect.75,76 It includes both “classic” external beam RT (EBRT) and the intralesional injection of radionuclides.

While several studies have reported that EBRT achieved a local control rate of up to 100%, all of them included only a small series of patients. In 1970, Biesecker et al. reported 4 cases of ABC that were primarily treated with EBRT (1 LR), and 7 cases that were secondarily treated with EBRT for LR after curettage, with control of the disease in all cases; the overall LR rate at 4-year FU was 9% for EBRT, compared to 45% for surgery.77 In 1995, Marcove et al. reported a series of 11 ABCs treated with primary EBRT alone; the local control rate was of 90% for EBRT (versus 63% for surgery), but one patient developed radiation-induced sarcoma.78 Feigenberg et al. reported no LRs nor development of secondary malignancies in 9 patients at a median FU of 17 years, with only 1 case of major complication (dorsal kyphosis from vertebral body collapse that required surgical stabilization at 10 months from EBRT).77 Boriani et al. reported complete remission in all patients with ABC of the mobile spine treated with EBRT alone (3 cases or...
curettage plus EBRT (14 cases), even though patients who underwent surgery plus RT showed the highest incidence of late axial deformity. Basarir et al. described the outcome of 56 children with ABC; the local control rate following EBRT was 79% (50% in 2 cases of primary RT and 83% in 12 cases of EBRT as an adjuvant to surgery) versus 81% for surgery alone. More recently, Zhu et al. reported 12 patients treated with EBRT at a mean FU of 20 years (range 3-36): pain relief was achieved in all patients within 4 weeks after EBRT, while radiological ossification of ABC was achieved within 2 years, and none of the patients showed late complications of RT. Heyd and Seegenschmidt reviewed 44 studies in which 196 ABC lesions were treated with EBRT. Of these patients, 90% experienced relief of symptoms (87% CR and 3% partial remission (PR)). An optimal scheme (total dose and fractioning) is essential to avoid adverse reactions to EBRT. Since ABCs most often affect young patients, radio-induced complications include growth disturbances besides skin problems, myelopathy and carcinogenesis. The total dose should be between 26 and 30 Gy, delivered in daily fractions of 1-2 Gy, with a small radiation field, with the use of low- or intermediate-dose megavoltage three-dimensional conformal RT, which has the capacity to penetrate deeper into tumors with less scattering to surrounding tissues.

Percutaneous intralesional injection of radionuclide has also been proposed in the treatment of ABC of the axial skeleton. The proven radiosensitivity of ABCs, and the ability to effectively control disease within a cavity of phosphorus-32 chromic phosphate colloid, a radiopharmaceutical that is used for the management of several radiosensitive intra-articular diseases (rheumatoid synovitis, recurrent hemorrhages cause by hemophilia), led Bush et al. to speculate that the cellular lining of ABCs might respond to radionuclide injection: 5 patients with large ABCs were managed with injection of 32P chromic phosphate under CT guidance: all lesions ossified at a mean FU of 2 years, with only a single minor complication (leakage of a small amount of the radiopharmaceutical, which was cleared by the patient without any negative effects).

Calcinon

Direct intralesional injection of calcitonin for ABC treatment was first described by Szendroi et al. in a study that included 7 patients. The treatment protocol consisted of three injections per week for 5 weeks. They achieved complete healing in 3 cases and partial healing in 3. In one case treatment was discontinued due to hypersensitivity reaction in a hypervascularized ABC. Afterwards, Gladden et al. first described the combined use of calcitonin and methylprednisolone for the treatment of ABCs.

Oliveira et al. retrospectively described their results in 47 patients with a minimum FU of 2 years. Exclusion criteria were secondary ABC, ABC located in the spine, initial surgical treatment, and incomplete radiographic evaluation. At time of the procedure, all cases were biopsied with an 11-gauge trocar needle, the cyst walls were manually scarified with the tip of the needle to break the septa and the hematic content was aspirated. A solution of calcitonin 200 IU and methylprednisolone 120 mg was then injected into the lesion. A pressure dressing was maintained for 3 days; X-rays or CT scan were taken monthly, and the procedure was repeated if no satisfactory healing of the lesion occurred after 2 months. A mean of 2.8 procedures were performed for each patient (85% of patients required up to 4 procedures, 1 (2%) required up to 6, and 1 (2%) required up to 7), and the average length of treatment was 10 months (range 2-60 months). Ninety-one percent of patients showed satisfactory results and 72% showed complete ABC healing at a mean FU of 45 months. The LR rate was 10.6% during FU, and a percutaneous procedure was repeated with success in 3 patients; 2 required surgical treatment because of disease progression, while 1 experienced a pathological fracture and the lesion subsequently healed.

Conclusions

ABC is a benign bone tumor with unpredictable behavior and a high recurrence rate after treatment. A histological diagnosis is mandatory, as telangiectatic osteogenic sarcoma may mimic ABC. Treatment is also mandatory, even in indolent cases, due to local aggressiveness with progressive bone destruction and deformation, and subsequent functional impairment. Standard treatment is curettage (manual + motorized high-speed burr) plus local adjuvants and bone grafting to fill the void. In anatomical locations that are difficult to reach surgically, percutaneous procedures (injection of sclerosant agents, RFTA) or SAE are used, and medical management with BPs or denosumab has also been advocated. Minimally invasive surgical procedures such as “curepsy” and percutaneous DBM and/or autologous BMC grafting have been proposed. Due to the lack of high-level comparative studies, treatment is based on personal and institutional experience and preferences, with the need to balance the cost and morbidity of treatment itself against the recurrence rate. On one hand, invasive procedures seem to have a lower recurrence rate and shorter treatment duration. On the other hand, less-invasive percutaneous or medical therapies have a lower complication rate at the cost of a longer / repetitive treatment.

The authors’ preferred techniques are manual and high-speed burr curettage plus adjuvant and bone grafting with or without prophylactic osteosynthesis in large lesions with a risk of impending fracture; percutaneous injection of a sclerosant agent (polidocanol) or DBM plus autologous BMC or curepsy plus DBM in skeletally immature patients; and SAE as a preoperative procedure to reduce intraoperative bleeding in cases of large lesions and as primary treatment in spinal lesions, if it can be performed safely.

References

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Aneurysmal Bone Cyst: A review of Management


