Aneurysmal Bone Cyst – Review

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Abstract

Background: Aneurysmal bone cyst (ABC) is a rare, benign, expansile lesion that produces blood-filled cavities inside the bone. The term, 'Aneurysmal bone cyst' was first time used by Jaffe and Lichtenstein in 1942 [1]. The name is a misnomer, as they are neither aneurysmal nor are, they truly cystic, as these lesions do not have an endothelial lined cyst wall. ABC is a disease of childhood or young adulthood with a median age of 13 years, with an incidence of 0.14 per 105 individuals with slight female preponderance [2].

Pathophysiology: ABC usually present as a solitary lesion either as a primary neoplasm (translocation driven) or a secondary lesion arising adjacent to previous bony lesions like giant cell tumours (GCT), osteoblastomas, chondroblastomas [3]. Few authors have proposed post traumatic hypothesis whereas others feel it could due to an hemodynamic disturbance especially venous impedance.

Primary ABCs: Primary ABC is one where it occurs in a bone without any previously known lesion. But now there has been identification of TRE17 also known as USP6 (ubiquitin-specific protease 6) gene on chromosome 17p13.Pathogenesis of some primary ABC involves transcriptional up-regulation of USP6 when there is the chromosomal translocation t(16;17)(q22;p13) which fuses the promoter region of the osteoblast cadherin 11 gene (CDH11) on chromosome 16q22 to the entire coding sequence of the ubiquitin protease USP6 gene on chromosome 17p13 [4].

Secondary ABCs: Approximately one third of the ABCs appear secondary to other pre-existing bone tumours, most commonly from GCT, which accounts for 19-39% of these cases [5]. Other common precursor lesions are chondroblastomas, chondromyxoid fibroma, fibrous dysplasia, osteoblastomas, haemangioendothelioma, angioma, fibroxanthoma (nonossifying fibroma), solitary bone cyst, fibrous histiocytoma, eosinophilic granuloma, radiation osteitis, osteosarcoma, trauma (including fracture), fibrosarcoma and even metastatic carcinoma [3, 5].

ABCs have been likened to a "blood-filled sponge", composed of blood-filled, anastomosing, cavernomatous spaces, separated by a cyst like wall composed of fibroblasts, myofibroblasts, osteoclast like giant cells, osteoid and woven bone. In approximately one third of cases, a characteristic reticulated lacy chondroid like material, described as a calcified matrix with a chondroid aura, is seen [6]. These are called as "solid aneurysmal bone cyst". The term "solid aneurysmal bone cyst," was coined by Sanerkin et al. in 1983 [7].

Introduction

ABCs are known to commonly involve long bones, posterior elements of the spine and the pelvic bones. ABCs are also seen in the clavicle, scapula, foot and finger bones, thus showing potential to involve almost any part of the skeletal system. Most ABCs are located intramedullary (80%), but more rarely they are localized at the surface, either subperiosteally or cortically. Although intramedullary ABC is typically confined to the metaphysis of the long bones, involvement of the diaphysis is not unusual in surface ABC [3].

Patient usually presents with pain and swelling in the affected area. Sometimes, they may have a pathological fracture at the affected site. Due to the mass effect of the lesion impinging on the spinal cord or exiting nerve roots, spinal column lesions present with pain and neurological deficits. In paediatric patients, sometimes it may affect the growth plate of long bones leading to limb length discrepancy and deformity.

According to the classification of Capanna et al [8], an ABC is classified as Type 1 when it is located centrally and it is well contained inside the bone with no or a slightly expanded outline. It is Type 2 if it causes marked expansion and thinning of its cortical bone outline with involvement of a whole segment. Type 3 ABC involves one cortex with an eccentric metaphyseal location. Type 4 are the least likely to be encountered and can cause superficial erosion of the cortex as it develops subperiosteally and expands away from the bone. Type 5 ones start periosteally, but expand peripherally and toward the bone and penetrate the cortex.

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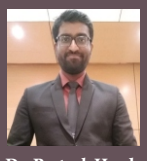
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Radiology-

Typically, they present as sharply defined, expansile, osteolytic lesions with thin, sclerotic rim within the metaphyseal portion of the bone. The lesion is destructive and may expand into the surrounding cortical bone. The mass may elevate the periosteum, but it typically remains contained by a thin shell of cortex. Typically, ABCs are eccentric but may also be central or sub- periosteal.

There are four radiologic stages as described by Dabska and Buraczewski during the development of ABC: initial, active, stabilization and healing. In the Initial phase - the lesion is characterized by a well-defined area of osteolysis with periosteal elevation. Growth phase- lesion grows rapidly with progressive "destruction" of bone and development of the characteristic "blown-out" radiologic appearance. Stabilization phase- "soap bubble appearance" develops, as a result of maturation of the bony shell. Healing phase- results in progressive calcification and ossification, with the lesion transforming into a dense bony mass [9].

Magnetic resonance imaging (MRI) characteristically demonstrates cystic spaces with internal septa with enhancing septal walls within the lesion. On MRI, these cystic spaces appear as "fluid-fluid levels", representing the layering of differing densities of blood. MRI can define perilesional extension, relation with adjacent vital structures and surrounding oedema. Combination of conventional radiographs and MR images are useful for the diagnosis, as well as treatment planning of ABCs as sensitivity, specificity and subsequently, the positive predictive value increases markedly with the combined use of both imaging modalities [10].

Presence of "fluid-fluid levels" is not specific for ABC and can also be seen in many other benign conditions like GCT, chondroblastomas, secondary ABC, fracture through a simple cyst and in malignant conditions of bone like telangiectatic osteosarcoma (TOS) [10,11]. In a study by Mahnken et al., they found that the presence of septa and lobulations were the most important clue for the presence of ABC [10].

Pathology-

Grossly, ABCs appeared as a spongy, blood-filled masses covered by a thin shell of the reactive bone. Microscopically, red blood cells and often pale brown hemosiderin are abundant, filling cyst-like spaces bounded by septal proliferations of fibroblasts, mitotically active spindle cells, osteoid, calcifications, and scattered multi-nucleated giant cells [12].

Differential Diagnosis-

This includes the various benign conditions like unicameral bone cyst, osteoblastomas, chondroblastoma, chondromyxoid fibroma, giant cell tumour and malignant conditions like TOS. In a review of 40 TOS cases, Murphey et al. proposed three imaging features that suggest the diagnosis of TOS over ABC: (1) thick, nodular, and contrast enhancing tissue surrounding the cyst-like spaces on cross-sectional imaging as opposed to the thin non-nodular borders of ABC, (2) the detection of matrix mineralization reflecting an underlying osteoid-producing tumor, and (3) cortical destruction indicative of the more aggressive lesion with associated soft-tissue mass as opposed to the typically well-defined encapsulated margins of ABC and lack of soft-tissue mass[13].

Treatment-

Curettage and bone graft reconstruction of ABC, as described by Jaffe and Lichtenstein, still remains the mainstay of the modern treatment [1]. But now-a-days less invasive and less morbid options are coming up. Traditionally, the following options are available.

Intralesional resection (Curettage)-

Curettage is a less morbid surgical procedure for the treatment of ABCs. Like other surgical procedures of bone, it may be associated with complications like severe bleeding, post-operative fracture, adjacent joint degeneration, local tumour recurrence, long-term pain, growth disturbances and functional compromise [14]. The local control rate can vary among different studies, with some of the studies achieving up to 90% local control rate with curettage alone [15,16]. Now-a-days many centres advocate the use of adjuvants to have better local control rate. Common agents used are chemicals (phenol or hydrogen peroxide), bone cement, argon beam coagulation, cryotherapy with liquid nitrogen or the mechanical effect of high-speed burr.

En- bloc excision-

En- bloc excision or complete resection is associated with low rates of recurrence but significantly high morbidity [17]. Vergel de Dios et al. [18] reported a 21.8% recurrence rate after curettage and did not note any relapses in patients undergoing resection whereas Flont et al. [19] also found no recurrences with en-bloc excision. Morbidities like post- operative pain, limb length discrepancies, muscle weakness, and decreased range of motion were noticed [20]. This procedure is now indicated only in recurrent lesions refractory to less invasive treatment and lesions in locations in which function is not compromised with such a resection such as clavicle, fibula or ulna.

Curopsy-

It was being noticed that some ABC lesions started healing spontaneously, post biopsy. Using this understanding, technique of curopsy was developed. A local recurrence rate of 19 % was reported by Reddy et al. with curopsy as compared to 10 % with curettage only [15]. Under general anaesthesia, percutaneous or with a small 5-10 mm incision, biopsy is performed with the help of core needle and curette or pituitary rongeur. The curette is used to obtain the lining membrane from various parts of the lesion. The procedure causes disruption of internal septations and cyst walls; this induces inflammation inside the lesion and leads to healing.

Sclerotherapy-

Sclerosants, in general, act by direct damage to the endothelial lining, triggering a coagulation cascade and thrombotic occlusion of blood vessels. Sclerotherapy enables minimally invasive treatment of lesions that are deep, difficult to access for surgery and potentially damaging [21]. It can be used in combination with angioembolisation or surgical resection when feasible or as an independent procedure.

Several sclerosing agents have been used, such as absolute alcohol, alcoholic gel, Ethibloc, Aetoxisclerol and Polidocanol.

Kumar Varshney et al. found that Ethibloc (an alcoholic solution) had treatment failure (but no recurrences) in approximately 12% of patients that required a separate procedure, which is comparable to that for extended curettage (approximately 15%) [22]. But multiple sessions can be associated with complications ranging from minor ones like fever, inflammatory reaction to major ones like aseptic bone necrosis, venous leakage in soft tissues, deep venous thrombosis, pulmonary embolism, abscess in soft tissues, osteomyelitis, fractures, epiphyseal necrosis, limb length discrepancy and inflammatory reactions of neurologic structures in spinal locations [23]. Because of these potential side effects, its usage has declined as safer alternatives have been found.

In their study of 72 patients with a mean follow-up of 34 months, Rastogi et al. found a clinical response of 84.5 % with an average of three injections of polidocanol (hydroxypolyaethoxydodecan) per patient [24]. Clinical and radiological improvement continued after the completion of treatment suggesting an ongoing healing process. A recurrence occurred in only two patients (2.8%), both occurring within two years of the end of treatment. Both were successfully treated by further sclerotherapy. In the same institute, a randomized trial was done by Varshney et al., comparing polidocanol sclerotherapy with curettage, high-speed burr, and bone grafting. Group undergoing sclerotherapy had a better healing rate, though the difference did not reach statistical significance. The polidocanal sclerotherapy provides faster pain relief, with a shorter hospital stay, better functional outcomes, and reduced the morbidity and surgical costs [22].

Puri et al. studied 56 cases of primary extremity ABCs which received polidocanol sclerotherapy, with a mean follow up of 62 months. Average of two injections were needed with response rate of 83.6% [PURI - 25]

Possible complications include hypopigmentation, necrosis at the site of the injection in case of extravasation, DVT, pulmonary embolism, osteomyelitis and allergic reactions.

Role of Trans- arterial embolization in ABC-

Trans- arterial embolisation (TAE), as an adjunct or as an alternative to surgery, is particularly useful in cases where surgical excision may result in neurovascular injury, or the lesion is in close proximity to a joint or is located in difficult to approach anatomical regions such as the spine, sacrum or pelvis. It causes immediate devascularisation with subsequent necrosis and tumor lysis.

Indications:

- Pre- operative embolisation- For reduction in intra- operative and post-operative blood loss in hyper vascular tumours and to simplify the excision of tumours [26].
- Combined therapy with Denosumab [27].
- Serial angioembolisation for sacral/ pelvic ABCs [28,29].

Choice of embolic agents depends on the size of the feeder vessels, the location of the tumour, presence of AV shunts and collaterals. Currently, embolising agents of primary use are gel foam, polyvinyl alcohol (PVA) particles, metallic coils and N-Butyl Cyanoacrylate (liquid agent- tissue glue).

Response evaluation:

Response can be seen, both in terms of clinical improvement as well as radiologically. Clinically, pain relief, reduction in swelling and symptoms due to neurovascular compression can be seen. Radiologically, as peripheral sclerotic bone rim formation, decrease of the ABC mass (as per size criteria or tumour volume), disappearance of the double content image (fluid- fluid levels), bone formation or calcification inside the ABC mass and reduction in enhancement on post contrast imaging [30].

One of the possible complications of TAE is non-target embolisation. However, this can be prevented by careful review of the angiograms obtained immediately before embolisation and meticulous care during injection of the embolic agent and using microcatheters advanced selectively into the tumour vasculature. Even with these precautions, TAE may not be done from a particular tumour feeder due to the origin of a vital artery such as the spinal artery. However, overall TAE is a safe procedure [26, 30].

Rossi et al. have reported a series of patients with tumours localized mainly in the axial skeleton, where embolisation had an overall efficacy of 94%, with a relatively low complication rate of 5% [31]. Amendola et al. had no failures in a series of patients treated with embolisation for ABCs of the spine [32]. Donati et al. in turn reported a 75% success rate in ABCs of the sacrum treated only with embolisation [33].

Adjuvant radiotherapy-

Primary or adjuvant EBRT seems to be an effective treatment option for persistent or recurrent ABC. Fractionated doses below 30 Gy may be recommended [34]. However, chronic complications from radiotherapy including secondary malignancies make it a rarely used modality in unresectable and non-responsive lesions.

The other upcoming techniques in managing ABCs are:

1. Percutaneous placement of injection doxycycline: It is an antibiotic with known anti neoplastic properties including the inhibition of matrix metalloproteinase and angiogenesis, both known to play a role in development of ABC [35].

2. Bisphosphonates Therapy: They inhibit osteoclastic bone resorption and osteoclastogenesis and are also known to have a direct anti- tumour and anti-angiogenesis effect [36].

3. Denosumab Therapy: It is a human monoclonal antibody that binds the cytokine receptor activator of nuclear factor-kappa B ligand (RANKL), which essentially initiates bone turnover. RANKL inhibition blocks osteoclast maturation and function and denosumab has been successfully used in the treatment of osteoporosis, skeletal metastases and GCTs as well [37]. Now it's being proposed to be used in ABCs in critical locations and in cases of recurrence after initial surgical treatment [27].

Conclusion-

Aneurysmal bone cyst is a rare, benign disease of paediatric age group, mainly involving the long bones of body but may involve any part of the skeletal system. The management options range from curopsy to resection with the trend moving towards conservative management of these lesions.

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