

Recent Trends in the Management of Aneurysmal Bone Cyst

A Systematic Review

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا أنك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Contents

Title	Page No.
List of Tables	i
List of Figures	ii
List of Abbreviations	v
Introduction	1
Aim of the Work.....	2
Review of Literature	
Aneurysmal Bone Cyst.....	3
Diagnosis	9
Management.....	19
Patients and Methods	55
Results	59
Discussion	68
Conclusion.....	72
References	73
Arabic Summary	—

List of Tables

Table No.	Title	Page No.
Table (1):	Characteristics and management of aneurysmal bone cyst and telangiectatic osteosarcoma.....	17
Table (2):	Denosumab in the treatment of patients with aneurysmal bone cyst	41
Table (3):	Output from all papers used in the study	61
Table (4):	Dosage and follow up	62
Table (5):	Rate of healing, complication, recurrence and failure	63
Table (6):	Number of patients in each study combined with healing rate.....	64
Table (7):	Comparison between the studied treatments regarding rate of healing	65

List of Figures

Fig. No.	Title	Page No.
Fig. (1):	Aneurysmal bone cyst of the distal femur metaphysis.....	3
Fig. (2):	Illustration of the aneurysmal bone cyst classification.....	8
Fig. (3):	Aneurysmal bone cyst of the proximal humerus.....	11
Fig. (4):	The three components of an aneurysmal bone cyst.....	13
Fig. (5):	Microscopic section shows solid proliferation of spindle cells, cystic spaces without any endothelial lining filled with blood.....	15
Fig. (6):	Histologic images of the aneurysmal bone cyst (ABC).....	17
Fig. (7):	An (ABC) of the pelvis which recurred after intralesional excision and autologous bone grafting.....	26
Fig. (8):	Algorithm for the management of aneurysmal bone cyst.....	26
Fig. (9):	Evolution of an ABC of the distal femur after ethanol 96% injection.....	27
Fig. (10):	Aneurysmal bone cyst of the left proximal humerus.....	28
Fig. (11):	Aneurysmal bone cyst of L3.....	28
Fig. (12):	Plain radiograph of the patient showed an osteolytic lesion in the proximal humeral diaphysis.....	30
Fig. (13):	Repeat magnetic resonance imaging 6 weeks after the initial one	31

List of Figures (Cont...)

Fig. No.	Title	Page No.
Fig. (14):	Fluoroscopy picture taken during the 5 th injection of polidocanol.....	31
Fig. (15):	Complete clinical response after bisphosphonate therapy (Pamidronate) of an aneurysmal bone cyst in a 13-year old boy.....	34
Fig. (16):	Complete radiological response after bisphosphonate therapy (Pamidronate) of an osteoblastoma tumor in a 12-year old girl.....	35
Fig. (17):	Clinical failure of bisphosphonate therapy (Zoledronic acid) for an aneurysmal bone cyst in 19-year old man.	36
Fig. (18):	Representative axial and sagittal CT-scan images of the patient prior to treatment and 3 months after treatment ossification of the ABC	38
Fig. (19):	Denosumab-induced bone calcification on computed tomography lean and contrast medium decrease 6- magnetic resonance imaging in a 16-year	42
Fig. (20):	A 16-year-old girl with pelvic aneurysmal bone cyst presenting fluid blood levels and contrast medium enhancement at baseline.....	43
Fig. (21):	A 12-year-old boy presenting with ulnar aneurysmal bone cyst.....	43
Fig. (22):	Imaging history of Case 1, reporting CT scan and MRI performed before ABC treatment, after embolization and after treatment with denosumab	46
Fig. (23):	X-ray presenting with pathological fracture.....	49

List of Figures (Cont...)

Fig. No.	Title	Page No.
Fig. (24):	Axial and sagittal computed tomography of the thoracic spine before treatment revealing the lytic lesion involving the vertebral body and left pedicle of T2.....	52
Fig. (25):	Axial and sagittal computed tomography and magnetic resonance imaging revealing new bone formation with in the lesion following treatment.....	53
Fig. (26):	Literature search flow chart.....	60
Fig. (27):	Comparison between the studied treatments regarding rate of healing.....	65
Fig. (28):	Comparison between the studied treatments regarding rate of complications.....	67
Fig. (29):	Comparison between the studied treatments regarding rate of recurrence.	67

List of Abbreviations

Abb.	Full term
<i>ABC</i>	<i>Aneurysmal Bone Cyst</i>
<i>BP</i>	<i>Bisphosphonate</i>
<i>CT</i>	<i>Computed Tomography</i>
<i>ECM</i>	<i>Extracellular Matrix</i>
<i>GCT</i>	<i>Giant Cell Tumour</i>
<i>GCTB</i>	<i>Giant Cell Tumor of the Bone</i>
<i>LCH</i>	<i>Langerhans Cell Histiocytosis</i>
<i>LN</i>	<i>Liquid Nitrogen</i>
<i>MMP</i>	<i>Matrix Metalloproteinases</i>
<i>MR</i>	<i>Magnetic Resonance</i>
<i>MRI</i>	<i>Magnetic Resonance Imaging</i>
<i>NF-KP</i>	<i>Nuclear Factor K- Light chain of B Cells</i>
<i>NGS</i>	<i>Next Generation Sequencing</i>
<i>ONJ</i>	<i>Osteonecrosis of the Jaw</i>
<i>RANKL</i>	<i>Receptor Activator of Nuclear Factor-Kappa B Ligand</i>
<i>RAS-Protein</i>	<i>Cellular Signaling Mechanism</i>
<i>ROM</i>	<i>Range of Motion</i>
<i>SAE</i>	<i>Selective Arterial Embolization</i>
<i>SVABC</i>	<i>Solid Variant of Aneurysmal Bone Cyst</i>
<i>TOS</i>	<i>Telangiectatic Osteosarcoma</i>
<i>UBC</i>	<i>Unicameral Bone Cyst</i>
<i>Usp6</i>	<i>Ubiquitin-Specific Protease</i>

INTRODUCTION

Aneurysmal bone cysts (ABCs), were first described by Drs. Jaffe and Lichtenstein in 1942 when they described pelvic and spine lesions that when exposing the lesion and opening in to its thin wall, the surgeon was immediately confronted by a large hole containing much fluid blood.

The name aneurysmal bone cyst has proven to be a misnomer, however, as these lesions are neither aneurysmal nor truly cystic, as they lack an endothelial wall. Instead, these benign expansile lesions produce cavities within the bone that fill with blood and are lined by proliferative fibroblasts, giant-cells, and trabecular bone.

ABCs were historically believed to result from increased venous pressure causing extravasation of cellular and blood contents into cyst-like voids in the bone.

More recently, identification of a genetic driver a translocation induced up-regulation of (the ubiquitin-specific protease USP6 (Tre2) gene has defined at least a subset of ABCs to be a primary neoplasm.⁽¹⁾

AIM OF THE WORK

The target of this study is to describe the efficacy of new line treatment modalities of (Aneurysmal Bone Cysts) compared between them according to:

- Long term outcomes and healing rate.
- Recurrence rates.
- Complications after therapy.

ANEURYSMAL BONE CYST

Definition:

Aneurysmal bone cyst (ABC) is a locally destructive, expansile benign neoplasm of bone, with a tendency for local recurrence. Although it is most common during the first two decades of life and it usually arises in the metaphysis of long bones, it can affect any age group and any bone. ⁽²⁾

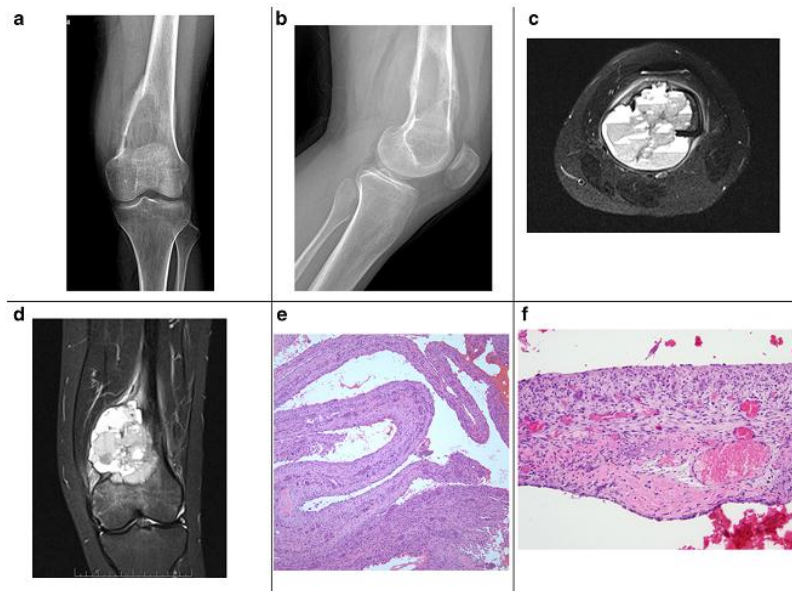


Fig. (1): a–f Aneurysmal bone cyst of the distal femur metaphysis. a AP knee X-ray with large, eccentrically located expansile lesion at the distal femur metaphysis with thin cortical borders and trabeculations. b Lateral knee X-ray with similar findings to a. c MRI knee, axial cross-sectional image revealing multiple, clear fluid-fluid levels and peri-lesional edema. d MRI knee, coronal cross-sectional image revealing expansile lesion abutting and displacing surrounding soft tissue. e Low power histology of ABC showing unlined, undulating cyst wall containing scattered giant cells. f Higher power histology of ABC showing mineralizing osteoid within a wall/ septation. ⁽¹⁾

Incidence:

An ABC is a solitary, expansile, radiolucent lesion usually located in the metaphyseal region of the long bones. Fortunately, ABCs are seen much less often than simple bone cysts, and they represent only 1% of all primary bone tumors sampled for biopsy.

The annual incidence of primary ABCs approximates 0.1 per 109 individuals. Nearly 70% of affected patients are aged 5 to 20 years, and approximately half of these cysts occur in the second decade of life, although the lesion has been reported in infants. No sex predilection is reported. ⁽³⁾

Aneurysmal bone cysts can be located throughout the skeleton, and the most common sites are the femur, tibia, spine, humerus, pelvis, and fibula, with approximately half of reported cases occurring in the long bones of the extremities. Although they usually arise in the metaphyseal region of the bone, ABCs may sometimes cross the physis into the epiphysis or extend into the diaphysis. Approximately 20% of ABCs involve the spine.

They may occur anywhere between the axis and the sacrum and can cause spinal cord compression or spinal deformity.

In the vertebra itself, the cyst may be found in the body, pedicles, lamina, and spinous process. Involvement of 2 or more adjacent vertebrae is not uncommon. Aneurysmal bone

cysts may also occur in the maxilla, frontal sinus, orbit, zygoma, ethmoid, temporal bone, mandible, sternum, clavicle, hands, and feet. ⁽³⁾

Pathogenesis

Campanacci et al. ⁽⁴⁾ described the lesion as a response to local hemorrhage. An initial insult produces intraosseous bleeding, leading to the formation of a cyst. The cyst walls may house capillaries that hemorrhage into the newly formed cavity, producing osteolytic and repair tissue, which may ultimately explain the lesion's predilection for rapid, aggressive expansion.

It was proposed that the ABC is a reactive lesion rather than a true neoplasm and that vascular disturbances in bone lead to increased intraosseous pressure, causing local destruction and distension of bone ⁽⁴⁾.

Recently, primary ABCs have now been identified as an independent neoplasm. The oncogenes responsible for ABCs are formed secondary to gain-of-function translocations of t(16;17)(q22;p13) involving a gain-of-function of TRE17/USP6 (ubiquitin-specific protease USP6 gene).

In ABCs, this mutation causes the induction of matrix metallo-proteinases (MMP) activity via NF-kB. MMPs function to degrade extracellular matrix (ECM) components, allowing for the growth and rapid expansion of ABC lesions. Despite the oncogenic activation of USP6 gene in ABC, the tumor is generally thought to have no malignant potential. ⁽¹⁾

ABC is characterized by a USP6 gene rearrangement in the majority of cases and, as indicated by a recent NGS- based study, potentially in all cases. Twelve different fusion partners have so far been identified, including CDH11, CNBP, COL1A1, CTNNB1, EIF1, FOSL2, OMD, PAFAH1B1, RUNX2, SEC31A, STAT3 and THRAP3. CDH11-USP6 translocation is the most common, found in approximately one third of ABCs, while the frequency of other fusion partners is not known, due to the large number of fusion partners and small number of analyzed cases. All these translocations lead to up-regulation of USP6 in cells in which it is not normally expressed, via the so-called promoter swapping mechanism ⁽²⁾.

Pathophysiology:

Much debate exists regarding the nature of ABCs. *Dabska and Buraczewski*⁽⁵⁾ were among the first to comment on the pathophysiology and natural history of the ABC. They divided its progression into four phases, with the initial phase described as: **(1) Osteolysis** of the marginal part of the bone with discrete elevation of the periosteum. **(2) The growth phase** is characterized by the progressive destruction of bone. Demarcation of the lesion is poor during this phase; bony shells and septations may not be obvious on plain radiographs. **(3) The stabilization phase** is defined by the classic ABC appearance: an expansile lesion with a distinct bony shell and osseous septations. **(4) In the healing phase**, progressive ossification of the lesion is obvious and results in a bony mass with a somewhat irregular structure.