Recent Trends in the Management of Aneurysmal Bone Cyst

A Systematic Review

Submitted for Partial Fulfillment of Master Degree of Orthopedic Surgery

By

Hussein Mohamed Ahmed Gomaa
M.B.B.Ch.
Faculty of Medicine, Ain Shams University

Under Supervision of

Prof. Dr. Rafeek Ahmed Sadek
Professor of Orthopedic Surgery
Faculty of Medicine, Ain Shams University

Dr. Ashraf Mohamed El Seddawy
Lecturer of Orthopedic Surgery
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2019

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to ***Allah****, the Most Kind and Most Merciful.*

I'd like to express my respectful thanks and profound gratitude to ***Prof. Dr. Rafeek Ahmed Sadek,*** *Professor of Orthopedic Surgery, Faculty of Medicine, Ain Shams University, for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to ***Dr. Ashraf Mohamed El Seddawy,*** *Lecturer of Orthopedic Surgery, Faculty of Medicine, Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I would like to express my hearty thanks to all ***my family*** *for their support till this work was completed.*

Hussein Mohamed

List of Contents

List of Tables

List of Figures

List of Figures (Cont...)

List of Figures (Cont...)

List of Abbreviations

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

INTRODUCTION

Aneurysmal bone cysts (ABCs), were first described by Drs. Jaffe and Lichenstein 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)*

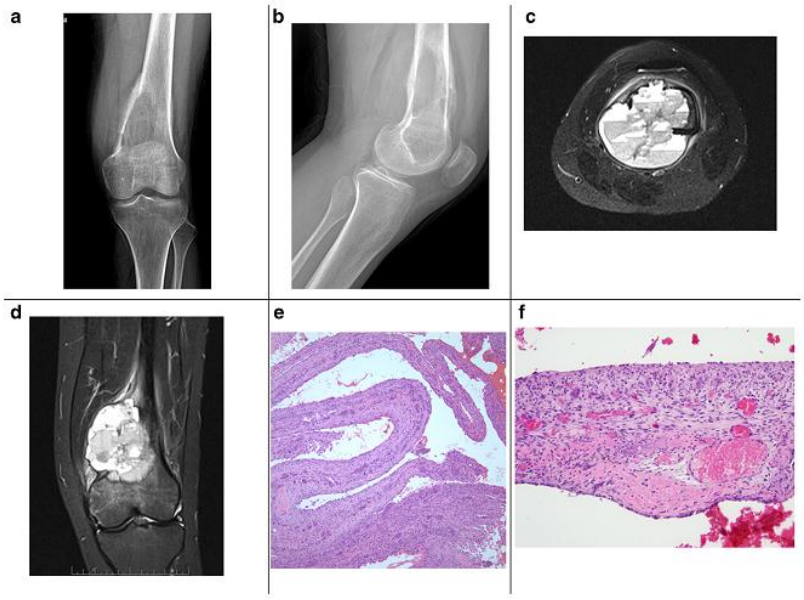

Fig. (1): a–f Aneurysmal bone cyst of the distal femur metaphysis. a AP knee X-ray with large, eccentrically located expansile lesion at the distal femur metaphysis with thin cortical borders and trabeculations. b Lateral knee X-ray with similar findings to a. c MRI knee, axial cross-sectional image 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-proteinas (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.