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Aneurysmal Bone Cysts: Diagnosis and Treatment

G Burnei [*1,2], Viorel Tandea[3], Burnei Cristian[4,5],Grigore Serban-Radu[6,7], Raducan Ionut Daniel[7,8]

[1]*Macta Clinic, Constanta, Romania*
[2]*Tinos Clinic, Bucharest, Romania*
[3]*Pediatric Surgery Department,"Grigore Alexandrescu" Clinical Emergency*
[4]*"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*
[5]*Clinical Emergency Hospital, Bucharest, Romania*
Hospital for Children, Bucharest, Romania
[6]*Permanence Center Medisys, Arad, Romania*
[7]*"Vasile Goldis," Western University of Arad, Arad, Romania*
[8]*Medical Center ART, Arad, Romania*

***Corresponding Author:** G Burnei, Macta Clinic, Constanta, Tinos Clinic, Bucharest, Romania*

ABSTRACT

Background Context: *Aneurysmal bone cyst is a benign lytic tumour structure with a lower rate than the simple bone cyst and it is 1% of the total of the primary bone tumours.*

In the medical practice the treatment includes multiple therapeutic methods. All these methods have constantly followed the reduction of recurrences and the transition from minimum invasive surgical techniques.

Purpose: *The paper presents diagnosis data, methods of treatment and analyses the rate of therapeutic recurrences between the different methods of treatment preferred by various authors. There are also presented therapeutic methods from personal experience.*

Method: *The data studied from the literature have briefly been preserved and presented such as to reveal the essence of radiological and imaging exploration, the diagnosis and treatment. There have been also recorded therapeutic methods less agreed by some authors, and therapeutic methods with 0 recurrence rate.*

Conclusions: *Since 1942, when Jaffe and Liechtenstein described and communicated the treatment method, there have been made remarkable progresses: regression rate has dropped from more than 50% to 0-5 %.*

Each ABC must be differentially treated according to the shape, sizes, position on different body segments, the combination with evolutive complications and if the cyst recurred.

Sclerotherapy and the cause-related treatment is a first intention treatment. Currently, the curettage and other additional times are still the only standardized methods

Keywords: *aneurysmal bone cyst; differential diagnosis, spontaneous evolution, first intention treatment, standardized treatment.*

INTRODUCTION

Definition

It is a benign cystic bone lesion, solitary, expansive and destructive, septate in multiple cavities, of variable sizes, containing blood, trabecular bone, fibroblasts and osteoclastic giant cells. The content of the simple bone cyst is formed of serous citrine fluid and it has a membrane [1]; aneurysmal bone cyst (ABC) is not tapestried with a cystic membrane.

Incidence

It is frequently localized in the metaphyseal area of long bones and it occurs much more seldom than the simple bone cyst. ABC is 1% of the total of primary bone tumours confirmed by biopsy and it has an annual incidence of 1 case of 10 (raised to the power of 10) persons. Regarding the location on segments, it occurs most frequently in the pelvic limbs, 35%: femur 13% and tibia 22%. The increased rate also occurs in the thoracic limbs, about20%, as well as in the spine cord, 16-20%. It may occur in the maxillary, mandibula, stern, clavicula, hand and legs in the frontal or orbital sinus or in the temporal and ethmoid zygomatic bones.

ABC occurs in children and young adults, more frequently in the age group between 10 and 30 years old, and much more seldom in children under 10 years old. There is no predilection for

male or female gender. The differenced recorded in one way or another are insignificant.

Clinical Aspects

Clinical manifestations occur in relation to the sizes. ABC is a tumour structure, destructive and expansive, therefore the first signs are local pain and tumefaction in the immediate neighbourhood of the joint. Later, the growth disorders occur and they affect the growth cartilage, causing joint pains and claudication or invasion of the joint cartilage, fractures on the pathological bone or neurological symptoms, if the aneurysmal cyst is seated in the spine cord and produces the spinal cord or nerves compression.

Genetic Data

ABC has 2 forms, primary and secondary. The primary form is genetically determined, and the secondary form occurs after some bone tumours; chondroblastomas, chondromyxoid fibroma, nonossifying fibroma, giant cell tumour or fibrous dysplasia. The secondary form is30 % of the aneurysmal bone cysts and are not considered neoplasms as the patients do not have the translocation present in primary form.

The primary forms of aneurysmal bone cyst are genetically determined by hazards present on the segments 7p16p and 17p11-13 specific to the USP6 oncogene and to theCDH11 promoter. The most frequent translocation described t (16-17) (q22; p13) determines the juxtaposition of the CDH 11 promotor region on 16p22. This mutation determined the activation of the MMP-matrix metalloproteinase by NFkB. The activated MMPs degenerate the components of the ECM- extracellular matrix and allow quick growth and expansion of lesions in the aneurysmal bone cyst [2]. It is believed that the tumour has no malign potential.

Radiological and Imaginary Data

The characteristic image has been described by Jaffe as a lesion where ‘the bone seems blown-out’ or ‘ballooned outside the normal profile’ and covered by a thin layer of neoplasm periosteal bone. ABC is the most frequently localised, 80 % of the cases, in metaphysis of long bones and it is eccentrically situated; it rarely occurs in the centre or subperiosteal. In the spinal cord, there occur frequent component elements of the vertebral arch, but they can also expand somatically. The ABC periodical assessment allows to establish the evolutive phase. Capanna divides the cyst radiological evolution in 3 phases [3]: inactive, active and aggressive. The inactive phase has a characteristic cystic area delimited by aperiosteal reaction occurring lake a sclerotic border. The active cyst has a suddenly interrupted discontinuous bone film and the delimitation of the configuration is taken by the periosteum. The circumferential appearance of the cortical bone is areolar. The aggressive cyst shown no signs of reparatory osteogenesis and a well-defined endosteal image. The radiological appearance is of total destruction.

CT has the role of clarifying the radiological identified images especially when those lesions occur in the spinal cord. The need of tomography becomes much clearer to determine if the ABC has invaded the vertebral disc or medullar canal. CT emphasizes the fluid-fluid levels, if the patient can stand still enough time to allow the sedimentation of the sanguinolent content; the cyst chambers do not have an active flow connected to the medullar canal flow and therefore the fluid -fluid levels occur. The CT and CT-3D allow the surgeon to determine the critical points of the intervention and to select the most appropriate intervention and method of synthesis or the necessary implants in case of a required surgery.

IRM provides valuable clues related to [4] :

- cyst development stages (inactive, active or aggressive)

- medulla compression

- presence of fluid-fluid levels becoming much more easily clear

- determination of the differential diagnosis; can help to exclude or to confirm some proliferative lesions such as atypical osteosarcoma or the telangiectatic osteosarcoma that can radiologically imitate the ABC or of other cystic lesions by relieving the multicysticappearance or the hypointensity of the marginal line.

- cyst walls; it shows better the cyst walls and improves the contrast.

- the fluid-fluid levels; the images are much clearer by enhancing the double density;

- the oedema of the soft adjacent tissues; the lesion is ABC representative.

- lesion expansion; lesion limits are shaped more warning the surgeon on some vascular or nervous risks.

IRM with contrast agent helps differentiating the classical shape from the solid shape.

Certain Diagnosis

The presence of a deformity where a bone segment has the configuration of a 'soap bubble' where the fluid-fluid levels are imaginary identified, is not pathognomonic for the aneurysmal bone cyst.

These aspects can also be met in the simple bone cyst, osteoblastoma, giant cell tumour and the telangiectatic osteosarcoma. The certain diagnosis is established based on the histological exam confirmed by the immunohistochemical exam.

Macroscopically, ABC includes porous tissue with free air and blood covered by a thin bone layer.

Microscopically, there are present: red blood cells, fibroblasts, trabecular bone, hemosiderin and polynucleate giant cells.

Biopsy may be performed though open access, by puncture or curettage.

The standard method is made by open access. This method allows to take a sample from the area with the clearest changes macroscopically viewed.

Aspiration biopsy with a fine needle is less invasive and it is probatory in ABC, but there may occur cases of undiagnosed telangiectatic osteosarcoma.

Biopsy percutaneous curettage has turned on a special interest after having noticed some healed ABCs only as a result of biopsy [5,6]. This method of diagnosis and treatment had been practiced for a long time in the East-European countries. Curettage must provide biopsy material from several parts of the cyst and to quantitatively destroy enough of the cyst internal architecture in order to cause healing. In order to cause healing, the smaller cysts are selected, less aggressive and with images suggesting a primary ABC [5]

Endoscopic curettage destroys the cyst internal configuration and causes the reshaping of cortical affected by the cyst [7]. Cyst healing is radiologically determined and the relapse rate is unknown.

Differential Diagnosis: the Aneurysmal Bone Cyst versus the Telangiectatic Osteosarcoma

Any cystic bone lesion in which the bone seems 'ballooned' outside the bone shape and shoes fluid-fluid levels required the differentiation of the benign lesions from the malign lesions. The ABC has to be differentiated by the telangiectatic osteosarcoma (TOS). It is an extremely difficult issue and it particularly regards the microscopical and complementary exam and imaginary data.

Microscopic examination with a low-resolution power cannot make the difference because the images are identical; only the high-resolution power examination emphasizes the malign appearance present in ABC by identifying the sarcomatous cells and in the ABC are enhances fibroblasts.

The differential diagnosis between the ABC and the telangiectatic osteosarcoma is suggested by the following criteria [8]:

- on the cross-section, the cystic lesion in the ABC has a thicker, nodular shape compared to the thinner and non-nodular, continuous shape, present in the ABC.

- in ABC the bone matrix is mineralized by osteoid tissue collections caused by the tumour, while in the ABC there are not shown osteoid tissue collections.

- destruction of the cortical present in the ABC accompanied by the invasion of the soft tissue shows an aggressive tumour combined to the ABC where the cystic lesion is well-delimited encapsulated and without invading the soft parts.

Spontaneous Evolution

The untreated bone cyst evolves extensively and destructively and can be registered in several possible cases: growth disorders by the invasion of the growth cartilage; in varus and valgus deviations and shortening of that segment.

Invasion of the adjacent flow is followed by the limitation of movements and by vicious anchyloses. Usually, massive destructions and joint invasion endoprosthesis. If the destructive lesions are at a distance equal to or greater than 2 cm, the reconstruction would be appropriate especially when the patient is under 12 years old. The fracture to the pathological bone. More frequently, fractures occur in the proximal extremity of the femur. They involve the base of femoral neck, the pertrochanteric, intertrochanteric and subtrochanteric area. These fractures require the treatment of the entire cyst-fracture lesion complex. The access shall be minimum, the reduction manoeuvres shall be minimum and the synthesis shall be as short as possible to avoid vascular lesions. Consolidation of stabilization shall be provided by a monoplane external fixator that will be kept for 3 or 4 weeks.

Spontaneous healing is an exception possibility [9]. The decision to remain in standby shall be taken into account when the aneurysmal bone cyst is in a stage and when it has a seat not involving a fracture risk and subsequent destructive lesions. Usually, after determining the ABC diagnosis, it is recommended a treatment.

Treatment

Jaffe and Lichtenstein, in the original description of the ABC stated as method of treatment the curettage and the bone graft [10]. This was the standard treatment for many years [11]. After this treatment, relapses had an increased rate, higher than 50%. Thus, to improve the results, over the years, the curettage was accompanied by other therapies that have considerably increased the rate of healing. Relapses have decreased up to 5 % and some authors have communicated 0 relapsed cases [12]. The current guidelines take into account sclerotherapy as a first intention treatment and consider the medical treatment. These treatments have a minimum risk, low costs and are easy to bear.

Simple Methods of Treatment Entered in Armamentarium

Guidelines and Trends

Sclerotherapy

Is a method that determines the sclerosis of the vascular endothelium and triggers vessel coagulation cascade and obstruction.

Percutaneous Shots with Polidocanol. This sclerotic method is the most often used. Intralesional injected polidocanol has a rate of healing close to that estimated for the intralesional curettage with high speed drill-graft and sometimes even bigger [13]. It causes no major complications and the functional results are better. For each shot are inserted 2-4 ml/Kg body under fluoroscopic control. There is an average of 4 shots every 7 days. There can be given several shots. Clinical and radiological assessment is made until healing. Brosjo used this method of treatment in a group of 38 patients with ABC. The number of shots varied from1 to 11 in combination to the moment when healing was determined. 37 patients of 38 healed up and it was found that the sizes of a patient's cyst increased after repeated shots. The patient was operated and healed up [14] .

Percutaneous Shots with Surgiflo and Alcohol. Surgiflo is used as a fibrosing and haemostatic agent in arteriovenous malformations. Intralesional injected Surgiflo has a therapeutic effect every 1-2 shots. Ghanem injected intralesional Surgiflo in 16 patients with active and aggressive aneurysmal bone cysts. Its use is an alternative treatment with a certain effect. Only 2 patients of 16 have been injected twice. All healed up and 3 patients showed complications, shortening of pelvic limbs [15].

Percutaneous Shots with Etibloc. Etibloc injection causes lysis of the vascular endothelium and the rate of healing is of 92 % [13]. (Varshney) **Attention!**

Although the results are very good, the etibloc administration is followed by serious complications; aseptic bone necrosis, cerebellar stroke followed by death. Therefore, its use is rejected by physicians and patients.

Etiopathological Treatment

Percutaneous Shots with Doxycycline. This antibiotic stops the matrix metalloproteinases and angiogenesis, both playing a role in bone expansion [16]. Shiels communicates a relapse in 20 cases treated by this method that occurred after 20 months. This method is still under consideration [17].

Bisphosphonates stop the osteoclasts and reduce bone resorption. It is possible that they cause apoptosis and the resorption of tumour cells. It is recommended in the inoperable tumours and can cause lesion sclerosis [18]

RANKL inhibitors (receptor activator of nuclear kappa B lingand). Denosumab is a direct RANKL inhibitor and it was proposed as an adjuvant therapy in the treatment of aneurysmal bone cyst [19]. The treatment reduces the pain and it is well-tolerated and causes the resolution of some radiological signs and of some neurological systems. The cure of an aneurysmal bone cyst seated in the sacral bone was recorded [20]. It is recommended to be used in adolescents and adult people. As side effects have been mentioned infections, eczemas, hypocalcaemia and mandibula necrosis.

Standardized Methods of Treatment

Curettage and Other Additional Times

Curettage and bone graft. In the original description of the ABC, Jaffe mentioned the curettage and the bone graft as a treatment. This method of treatment is still actual nowadays, but it is associated with other surgery times to reduce the increased relapse rate. After curettage and bone graft, the relapse rate is of 59 % [21].

Curettage, as a single surgical time, is applied in the small cysts, up to 4 cm3.Intraoperative lavage with phenol or the obliteration with cement or alomatrix increases the rate of healing.

In 9 children and adolescents with ABC with a volume smaller than 4 cm3, I made a curettage and obliteration with cement. One of the 9 patients was diagnosed with acetabular ABC seated in the caudal half. The lesion was located in the ischiadic area of acetabula and it had a clinical onset at the age of 5 with limping gait. After 2 months, the pain and the antalgic position of the hip reappears, with the apparent limb length inequality. IRM with contrast agent determined the presence of a lytic lesion of acetabula suddenly developed intraarticular and in the iliac fossa: the ABC diagnosis was made. A surgery was performed and the interacetabular chondro-sanguineous laceration and the osteo- sanguineous laceration were evacuated from the internal iliac fossa. The cyst was curetted and obturated with cement, the lesion measuring of about 4 cm and outside the carrying surface. The histopathological exam has certified the ABC diagnosis. (fig 1) In other 5 patients, I have performed curettage and obliteration with alomatrix. All the ABC cases amounting 4 cm (cubic) curetted and obturated with cement or alomatrix healed up.

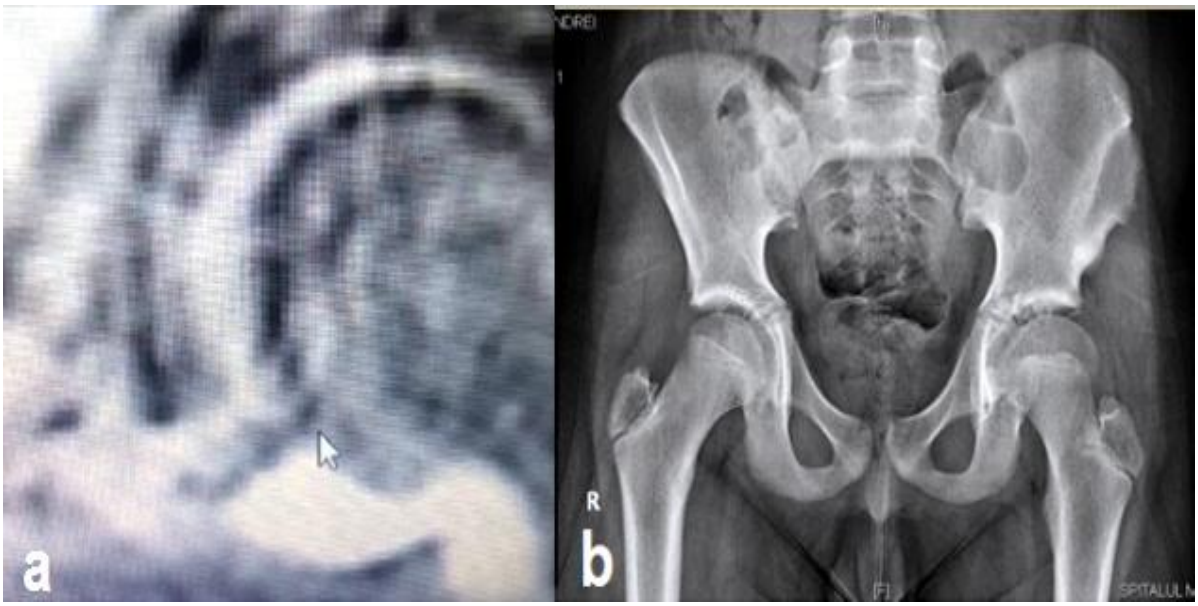

Fig1. *Left acetabular ABC a) IRM with contrast agent: distal lytic acetabular lesion with intraarticular effusion in the pelvic space expanded in the iliac fossa b) Pelvis radiography 7 years after the surgery. In the caudal area of the left acetabula is noticed a small area with increased intensity related to the cyst obturated with cement. The implant has been slowly and gradually incorporated until it almost disappeared. The joint mobility is within the normal limits.*

Curettage – intralesional reaming with a high-speed drill and bone graft reduces the relapse rate. This combination allows, by the intralesional reaming, to mechanically remove the septa, level the orifices that communicate with the medullary canal and mobilise the aggressive cells. This association reduces the relapse rate to 3-10 % [22, 23]

Curettage and coagulation of bone surfaces. Argon beam resulted from gaseous inert argon causes a unipolar electric power causing the drying and coagulation of the cyst bone areas. The argon technology is not present in most of the operating rooms and it is not familiar to surgeons. It reduces the relapse rate to 20 % and if the curettage is it is combined with a high-speed reaming, the relapse rate will be reduced to 7,5 % [24]. Use of the argon beam may increase the rate of the fractures to pathological bone, as a result of the desiccation and coagulation effect resulting in the reduction of bone resistance.

Curettage and phenol lavage**.** Phenol has the role to biochemically remove the neoplastic cells remained after curettage. The relapse rate drops from 41%, when the curettage is used alone, to 7 % if the curettage is combined with phenol" sterilization" [25].

Curettage and cryosurgery. Cryosurgery consists in using the nitrogen in liquid for or aerosols. This causes a freezing temperature and destroys the toxic cells responsible for expansion by freezing them. It is a less used method because of the possible complications: postoperative

fractures, cutaneous necroses or deep infections. relapse rate is reduced between3 and 5 % from 17,6 % when the nitrogen is used.

Curettage and cement obturation. The cement used in ABC increases the bone resistance reduced by the presence of cyst and it reduces the relapse rate by the thermal effect caused until its cementation.

After curettage and cementation, the relapse rate is of 17% comparing to curettage and graft, where relapses occur in a ratio of 37% [26]. The cement in children may have a long-term effect if used in cysts larger than 4 cm*(cubic). It may remain inert and cannot be able to be absorbed. This increases the risk of fractures to pathological bone. As well, the non-absorbed cement is like a foreign body and it may generate a local infection.

Curettage – intralesional reaming with high-speed drill – electrocauterization –

intraoperative lavage with peroxide, saline solution, betadine – obturation with alomatrix. Moreover, this combination has 2 surgical times, lavage with peroxide, saline solution, betadine and the obturation with alomatrix. Intralesional reaming with high-speed drill and the electrocauterization mobilizes and partially destroys the neoplastic cells responsible for the extension and deterioration of the bone cortical. During cauterization, on the cyst walls and on the electrosurgical scalpel remain masses of the tissue containing 'toxic' cells. The masses on the lamp are removed by scraping the blade; the ones on the cyst walls are mobilized and removed by interoperative lavage with peroxide, saline solution, and beta dine. This 'sterilization' is completed by under pressure cleaning with compresses or wicks so that the cyst wall is continuous when palpated with the index finger tip. The BMP obturation, preferably with alomatrix, induces a regeneration process more intense than the autogenous one and heals the bone cortical within a variable time in relation to child's age.

Between 2004 and 2016 I operated 25 patients with ABC aged between 9 and 18 years by using method. After an average follow-up period of 8,6 years, I haven't had any relapse. 6case of the 25 cases were with a fracture to pathological bone: 4 to the femur and one per shoulder and radius. To avoid shortening and deviation in varus of the femur neck I have used TEN stems or TEN stems and external fixator for 30 day.

Treatment of Need

Radiotherapy may be used in the relapsed, inoperable ABCs or when they are seated in areas difficult to be accessed for a surgery. It is the role to destroy the cells responsible for the cyst occurrence. The results of radiotherapy are good in a ratio of 80-100% [21,27]. Radiotherapy used as assisted therapy runs the risk of deteriorating and marginalizing the function. Therefore, it is recommended to use it only in the inoperable cases and in the cases where embolization has failed. It is advisable that the therapeutic dose is minimum: 3000-5000 c Gy[28]. Radioisotopes intralesional inserted run high risks and ere no longer used.

Metal Implants

When we face an ABC-fracture lesion complex and the decision is taken, from various reasons, to treat the fracture first and then the cyst, we may be surprised by the cure of both the fracture and the cyst. I have found that both lesions healed in 3 patients with femur fracture on ABC, as a result of the osteosynthesis of fracture with centro-medullary stems. The surgical intervention was made by Al. Pesamosca, my teacher, and its goal was to treat the fracture within a first time and then to treat the cyst in the second time. I have also assessed 2 out of the 3 patients after 11 years and the healing of the lesion complex was obvious. Personally, I have treated a patient at the age of 14 with femur fracture on the ABC, seated in the 1/3 distal femur, who has been healed.

Based on these observations, in 2 patients aged 15 and 17, who had ABC in COA in fracture imminence, located femoral and inter- and subtrochanteric, I have applied nails gamma cuie to avoid fracture, and the cysts healed.

Other authors have radiologically noticed different grades of healing of this lesion after inserting some K wires in the cystic structure [29].

TEN stems used in the osteosynthesis of active ABC and larger than 4 cm under fracture imminence inactivate the cyst and reduce its sizes (fig. 2). In the case of cysts smaller than 4 cm (cubic) the stems may determine healing.

In the literature there are papers mentioning the ABC treatment by draining the cyst with grooved screws or with grooved screws and BMP.

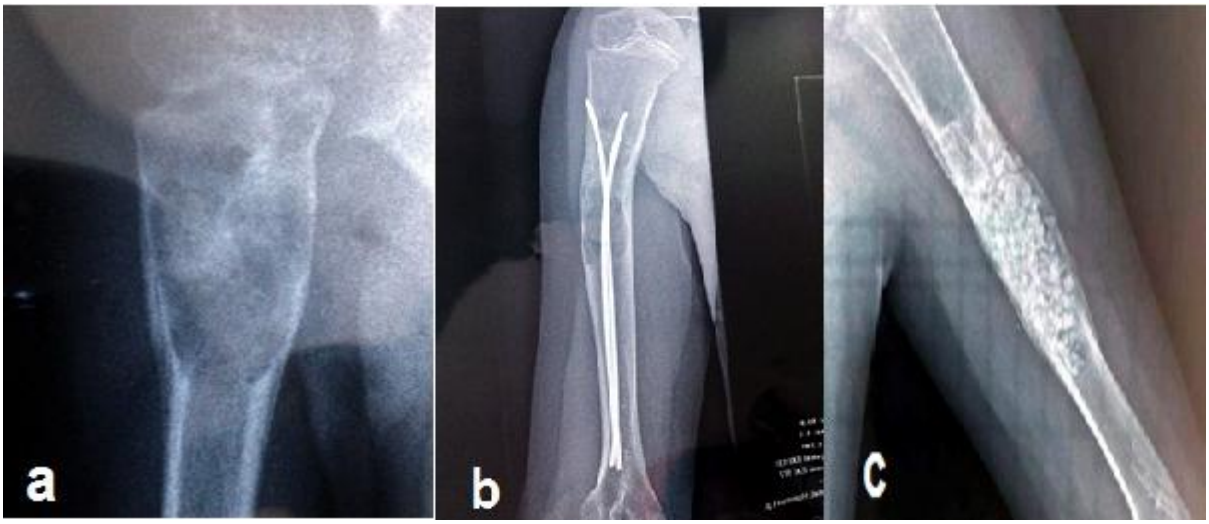

Fig2. *a) ABC ⅓ proximal of the right bone arm with a fracture imminence in a 7 years old girl b) 5 years from the TEN centro-medullary osteosynthesis. The cyst had a diaphyseal descension, it has been reduced and became inactive, and in the proximal area occurred a normal structure c) 6 years after the synthesis, the persistent lytic area was treated by curettage – intralesional abrasion with a high-speed drill - electrocauterization –intraoperative lavage with saline solution, peroxide, betadine and obturation with BMP.*

Embolization

Arterial selective embolization may be used as an adjuvant method in the treatment of ABC difficult to be surgically accessed or with high bleeding risk. There are recorded favourable results in 94% of the cases although sometimes it is necessary to repeat embolization twice or three times. The possible complications after embolization are transitory paralysis in ABCs with rachidial or tegmental necrosis localization [30]. Embolization of these cysts shall take into consideration the avoidance of any obturation of Adamkievicz artery, which might cause an irreversible paralysis [31].

This method has limited indications considering that it is sometimes hard to identify the tumour vascularization and sometimes these vessels provide the vascularization of other vital or functionally important organs.

Cyst Resection

The full excision of the cyst reduces the relapse rate to 0-5%, but there have occurred major complications compared to curettage and other combined times: limb inequality, muscle stiffness, limitation of the adjacent joint mobility, etc. This intervention shall be considered in relapses that failed to respond to the minimum invasive treatment and their localization is not in contact with the growth cartilage. Currently, this intervention is deemed to be old-fashioned.

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