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Review Article

Aneurysmal bone cyst in the head and neck region of the pediatric patients: a review

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ABSTRACT

Aneurysmal bone cysts (ABCs) are benign, vascular and cystic bony tumors which can be rapidly expanding and locally cause destruction of the surrounding tissue. ABCs in the head and neck area are usually found in patients with younger age group. ABC in the head and neck region of children may vary in presentations and severity. ABCs are commonly found in mandible, sinonasal tract and cranium in head and neck region. Imaging and histopathological examinations confirm the diagnosis. Complete surgical excision is the treatment of choice. ABC which is secondary to underlying bone pathology like osteoblastoma may refractory to treatment. ABC in the head and neck region are uncommon and should be considered as differential diagnosis of bony and vascular lesions in the locations like mandible, sinonasal area, cranium, mastoid bone and spine. The review article includes case series, case reports and original research on ABCs manifesting in the head and neck area published in the English language. All literatures identified via Scopus, Google scholar, Medline and PubMed were analyzed individually. Articles of ABCs included according to specified eligibility criteria. The total number of articles were 78 (41 case reports; 37 cases series; 8 original articles). ABCs rapidly grow with expansile manner and result in destruction of bone and surrounding tissue in the head and neck region, so clinicians must think about this clinical entity to diagnose correctly and treat appropriately. The aim of the article is providing a comprehensive review of the ABC in the head and neck region of the pediatric patients.

Keywords: Aneurysmal bone cyst, Head and neck area, Pediatric patients, Surgical excision

INTRODUCTION

Aneurysmal bone cysts (ABCs) are benign intraosseous or rarely lesions of soft tissue in head and neck region of the pediatric age group.[1] ABCs are often considered as locally aggressive lesions with a potential for local recurrence and typically seen in the metaphysis of the long bones and vertebral column.[1] The term aneurysmal bone cyst was first used by Jaffe and Lichtenstein in 1942 to describe two cases of erosive, expansile, blood-filled, cystic lesions in the vertebra of an 18-year-old boy and in the pubic symphysis in a 17-year-old boy.[2] The term ABCs has been accepted all over the world, although this lesion refers to neither an aneurysm nor a bone cyst. ABCs typically affect long tubular bones and spine (1aa). Involvement of ABC in head and neck region is seen approximately in 12% of cases.[3] Approximately 3% of these lesions are seen in the head and neck region with the mandible being the commonest location.[4] Majority of the ABC cases are asymptomatic, but they may present with swelling and local pain.[5] Imaging shows classic osteolytic lesions whereas magnetic resonance imaging (MRI) reveals blood-filled lesions and fluid-fluid levels.[6] Histopathological study confirm the diagnosis.[7] Presently, the treatment of choice for ABCs is surgery such as complete excision, curettage and bone grafting.[8] There is not much literature for ABC in head and neck region of pediatric patients, indicating that these clinical entities are

neglected. This review article discusses the details of the epidemiology, etiopathology, clinical manifestations, diagnosis, treatment and prognosis of the ABC in head and neck region of pediatric patients.

METHODS OF LITERATURE

Multiple systematic methods were used to find current research publications on ABC in head and neck area of pediatric patients. We started by searching the Scopus, Pub Med, Medline, and Google Scholar databases online. This search strategy recognized the abstracts of published publications, while other papers were discovered manually from the citations. A search strategy using PRISMA (Preferred reporting items for systematic reviews and meta-analysis) guidelines was developed (Figure 1). Randomized controlled studies, observational studies, comparative studies, case series and case reports were evaluated for the eligibility. There were total numbers of articles 78 (41 case reports; 37 cases series; 8 original articles). This paper focuses only on ABC in head and neck part of the pediatric patients. The search articles with ABC in adult and elderly age group or lesions of other than head and neck regions are excluded in this review article. Review articles with no primary research data were also excluded. This paper examines the epidemiology, etiopathogenesis, clinical manifestations, diagnosis, treatment, and prognosis of ABC in head and neck region of pediatric patients. This analysis provides a foundation for future prospective trials for head and neck ABC in pediatric age group. It will also serve as a catalyst for additional study ABCs in head and neck part of pediatric age group, allowing early detection and treatment.

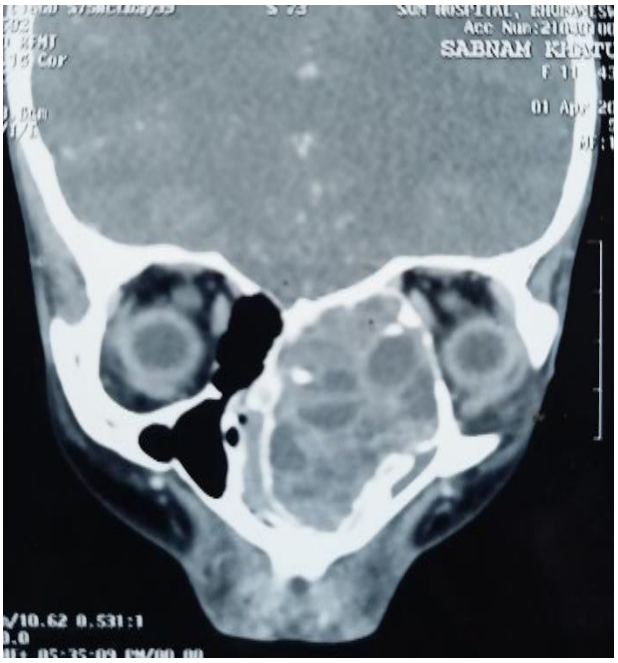

Figure 1: CT scan of the paranasal sinus (coronal view) of expansile growth of aneurysmal bone cyst causing lateral displacement of the left eye ball.

EPIDEMIOLOGY

ABC is an uncommon non-neoplastic expansile osteolytic bone lesion of unknown cause.[1] The prevalence of ABCs is around 1.4 cases per 100,000 persons and they constitute approximately 1% of all tumors of the bone.[9] The incidence of ABC is 0.14 per 100,000 population per year.[10] ABC in the head and neck region are extremely uncommon clinical entity. There is slight female predominance of ABC in comparison to male. ABC is encountered in all age groups, but majority of the cases seen in their second decade of life and 75 to 90% cases of ABC encountered before the age of 20 years.[11] ABC is uncommon after the age of 30 years and highly exceptional after the age of 50 years.[11] In head and neck region, the incidence of ABC in the skull varies from 3 to 6% of all ABCs and usually present as mass over the scalp.[12] Because of several reasons, the exact frequency of ABCs remains elusive.

ETIOPATHOLOGY

As per the definition of world health organization, the definition of aneurysmal bone cyst is benign cystic lesion of bone consisting of blood-filled spaces separated by connective tissue septa containing fibroblasts, osteoclast type giant cells reactive woven bone.[13] The exact etiology of ABC is still elusive. This pathological condition is usually thought as reactive until reports of clonal cytogenetic abnormalities showing neoplastic properties. This lesion usually originates in isolation, although ABC may sometimes be associated with other bony pathology.[14] Approximately 30% of ABCs are secondary to certain lesions such as giant cell tumor, osteoblastoma, chondroblastoma, chondromyxoid fibroma, fibrous dysplasia or non-ossifying fibroma.[15] The exact nature of histogenesis of ABCs are still unclear and it is classified into indeterminate tumor, intermediate malignancy and locally aggressive.[16] It was thought that intraosteous or subperiosteal bleeding due to abnormal venous circulation, activating the osteoclasts and inducing resorption of bone and local remodeling.[17] This theory is no longer approved for primary ABC, which rearrange USP6, on chromosome 17 but remains plausible secondary to ABC which does not show translocation.[16]

The genetic aspect for causation of ABC may predominate, masking the other causal etiologies. Recently genetic and immunohistohemical studies showed that primary ABC is a tumor and not considered as a reactive tumor simulating lesion.[18] Moreover, the neoplastic nature of the ABC was evidenced by showing clonal chromosome band 17p13 translocations which place the USP6 oncogene under regulatory of the highly active CDH11 promoter.[19]

CLINICAL PRESENTATIONS

ABCs may be found at any age group. However, ABCs are commonly seen in young patients in the first and

second decades of life.[20] Approximately 80% of the ABCs are seen before the age of 20 years.[21] ABC primarily seen in young females.[22] ABC often present with pain and sometimes swelling or facial deformity in head and neck region. A short period of pain and swelling in affected bone is the characteristic features, although the clinical presentations are dependent upon the site affected. The main symptoms are edema and/or dull pain in head and neck ABCs. These lesions have rapid growth. Depending on the sites of the ABCs in head and neck region, other symptoms can be seen like headache, vision loss, proptosis, deafness etc.[23] The bony involvement may cause proptosis of the eye.[24] The proptosis of the eye is usually found in case of sinonasal involvement by ABC. Bony involvement particular long tubular bone cause fracture. Spinal involvement may result in pain, torticollis, stiff neck and rarely neurological symptoms.[25] The differential diagnosis of ABC includes vascular lesions, malignant lesions, eosinophilic granuloma, enchondroma or chondromyxoid fibroma, non-ossifying fibroma and fibrous dysplasia.[26] ABCs can be seen in different grades in several other types of lesions such as unichameral cyst, ossifying fibroma, ameloblastoma, giant cell granuloma or even in fracture of the bone. ABC can affect any sites of head and neck region with long bones, spine and pelvis.

DIAGNOSIS

The initial diagnosis of ABC can be done radiographically, with MRI being taken as the first choice for diagnostic tool. The computed tomography (CT) scan is helpful to delineate the bony lesions and extension of the ABC (Figure 1). The diagnosis of ABC should be firmly established and malignant lesions must be ruled out. This implies not only help towards diagnosis of the ABC, but also any underlying bony pathologies inciting the origin of the ABC. The diagnosis of ABC is based on combination of radiological features and histological study. The radiological features of ABCs include cystic bone expansion which shows honey-comb or soap bubble like inner structure. Sometimes radiological findings show destruction of the bone cortex and periosteal reaction.[27] Histological features usually confirm the diagnosis. It is often unwise for a pathologist to render a diagnosis without a thorough inspection of the radiological films. If ABC is suspected radiologically, intra-operative frozen section is usually sought during excision/curettage. This is done to rule out the malignant lesions like telangiectatic osteosarcoma, usually the primary concern in radiological differential diagnosis. The gross pathology of ABC show sponge like, friable, hemorrhagic material which often gritty consisting blood-filled cavities separated by thin, fibrous septa. In case en-block resection of the tumor mass, cysts and cortical destruction can be appreciated. Majority of the ABCs in head and neck area measure between 1 to 10 cm in its maximum diameter.[28] The microscopic picture of ABC shows a stroma consisting of fibroblasts, multinucleate giant cells and bone, as well as cystic spaces usually filled with blood and consisting of increased number of giant cells lining the cavity (Figure 2). Histologically, the cavities lack endothelial cover and full of blood. These are contoured with fibrous septa, enclosing fibroblasts, inflammatory lymphohistiocytic elements, siderophages and osteoclastic giant cells.[29] In initial phase, mitosis may be strong but not abnormal. There are no elastic or smooth muscle fibers. There is reactive osteogenesis inside the immature septa, consisting a thin network of woven or lacy osteoids or more number of mature trabeculae. There is strongly calcified basophil fibrochondroid matrix in more than one-third of cases. The amount of cystic components in ABC can vary. ABC can be divided into types such as classic (95%) and solid (5%).[30] In the head and neck region, the solid type of ABC is usually called as giant cell reparative granuloma, central giant cell granuloma or central ossifying fibroma. The common coexisting lesions with ABC include chondroblastoma and giant cell tumor.[30]

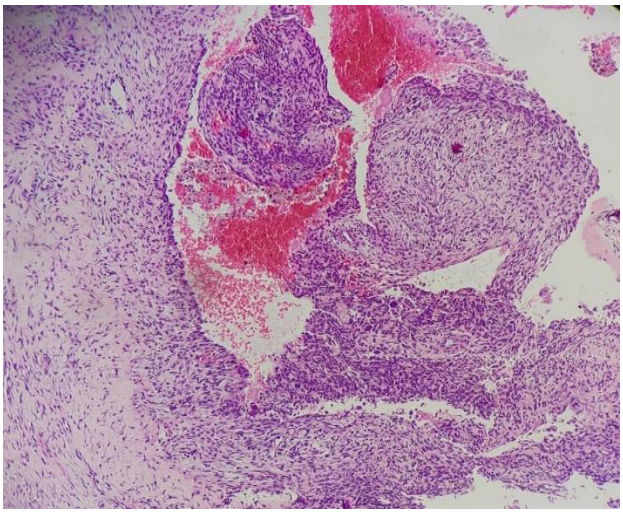

Figure 2: Microphotograph of histopathological picture of the aneurysmal bone cyst.

TREATMENT

Surgical

Surgical excision is the treatment of choice in ABC.[31] Wide resection of the tumor prevent local recurrence but wide resection may require reconstruction which increase the cost of treatment.[32] Currently, En bloc resection is not an option in majority of patients with ABC because of the resulting disability/required reconstructive surgery in this benign disease. So, intralesional curettage with or without bone grafting is still commonly used treatment, but pose a risk of local recurrence of approximately 20%.[32] Marginal resections may be helpful in very expansive form of ABC. Curettage and aspiration of cyst without filling gives good results in comparison to intra-cyst resection. The chance of risk can be minimized by association with curettage to cryotherapy or argon plasma coagulation (with high chance of fracture). In case of fracture or fragilization, osteosynthesis may be helpful if

diagnosis of ABC is certain. Complications for surgical excision of ABC in head and neck regions are uncommon. In some cases, facial paresis may be found following surgical excision of ABC. Facial paresis following surgery can be managed with conservative treatment.

Medical

Local intra-cystic injection of demineralized bone powder, bone marrow, calcitonin, bone substitute and doxycycline are related to contradictory results and sometimes need a large number of procedures. [24,33,34] Injection of absolute alcohol also shows good result with low rate of complications. It may need repeat injection, if cyst shows incomplete result or cure.[35] Intralesional sclerotherapy with alcohol is an effective mode of treatment. Injection of methyl predinsolone acetate should be avoided, as it may exacerbate the lesion.[24] Intra-cystic injection of Ethibloc is found to provide a 70 to 94% rate of cure.[36] However, Ethibloc is no longer available. Radiotherapy is also an effective one, but the chance of malignant transformation limits its use in ABC. However, radiotherapy is sometimes preferred in recurrent spinal lesions inaccessible to other treatment modalities.[37] Interferon alpha-2a therapy is helpful for treatment of vascular tumors in the head and neck region such as ABC and giant cell tumors. It can also be used for controlling unresectable lesions and act as effective adjunct to the surgical excision, when administered before surgery for reducing the tumor size. Chemotherapy is a less common option for ABCs. One study showed that chemotherapeutic agent like denosumab which is a promising alternative treatment for ABCs in head and neck region in pediatric age group.[38]

Artery embolization is an efficient adjuvant treatment for ABCs.[39] It commonly calcify within 2 to 4 months after embolization.[40] This therapy is usually helpful for ABCs in head and neck regions those are difficult to resect because of their locations like deep seated sites. The embolization techniques are often done before surgical resection. The adverse effects of the arterial embolization include ischemia to other vessels, nerves and organs with blood supply from same artery that is embolized.[39]

PROGNOSIS

There is approximately 20% of the patients with ABC show recurrence.[41] The recurrence rate can be reduced by complete surgical excision or surgical excision with cryosurgery.[42] One report shows that selective arterial embolization provides favorable results.[43] As 90% of recurrence after surgery occur within 2 years, close observation with serial radiograph is required for at least two years.[44] The treatment options of ABC have evolved over the years. Resection of the lesion is not an option in majority of cases leaving intralesional procedures like curettage as standard of care.[45] Because of the recurrence rate more than 50%, several adjuvant treatments have been employed. The adjuvant treatments include polymethyl methacrylate (PMMA)/ bone cement, phenol, argon, ethanol and cryotherapy. Less invasive techniques are aggressive biopsy (curopsy), selective arterial embolization, sclerotherapy with ethibloc or polidocanol and systemic treatment with receptor activator of nuclear factor-κ B ligand (RANKL) inhibitors like Denosumab have been tried.[46,47]

CONCLUSION

Aneurysmal bone cyst is expansile, non-neoplastic bony lesion, consisting of sponge like cavities of different sizes which contain either blood or serum. ABC notoriously affects the vertebral column and long bones in the body. Rarely, ABCs seen the head and neck region. ABCs of the head and neck area in pediatric patients pose a diagnostic challenge to otolaryngologists or pediatricians because of their rarity and non-specific symptomatic presentations. As ABCs in the head and neck region often present as a rapidly growing, expansive and destructive lesion, it must be crucial for clinicians or pediatricians for this clinical entity in pediatric patients to diagnose accurately and treat correctly with appropriate method.

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