SPINAL ANEURYSMAL BONE CYST IN CHILDREN: SYSTEMATIC REVIEW OF THE LITERATURE

D.G. Naumov, E.A. Speranskaya, M.A. Mushkin, D.B. Malamashin, A.Yu. Mushkin
St. Petersburg Research Institute of Phthisiopulmonology, St. Petersburg, Russia

Publications on aneurysmal bone cysts of the spine in children for the last 20 years were systematized taking into account different treatment approaches. The results of radiation therapy, local puncture interventions, surgical removal of the tumor, selective embolization, and of their combinations were reviewed based on the data of 19 publications representing 165 pediatric patients.

Key Words: aneurysmal bone cyst, spine, children, treatment.

Please cite this paper as: *Naumov DG, Speranskaya EA, Mushkin MA, Malamashin DB, Mushkin AYu. Spinal aneurysmal bone cyst in children: systematic review of the literature. Hir. Pozvonoc. 2019;16(2):49–55. In Russian.*

DOI: http://dx.doi.org/10.14531/ss2019.2.49-55.

Aneurysmal bone cyst (ABC), also known as hemangiomatous bone cyst, giant cell reparative granuloma, multilocular haematic cyst, and benign bone aneurysm, is a benign lesion characterized by local swelling of bone with formation of cystic cavities separated by fibrous septa and filled with bloody fluid; its cellular structure is represented by proliferation of fibroblasts, giant osteoclast-like cells, and histiocytes [1, 2].

There are two ABC types: primary (de novo) ABCs, which account for 70 %, and secondary ABCs with multiple hemorrhages, which most often develop due to cystic reorganization of giant cell tumor, osteoblastoma, chondroblastoma, or fibrous dysplasia of bone [3].

ABCs account for 1 to 6 % of benign bone lesions, which means 1.4 to 3.2 new cases per 1 million population per year [4, 5]. The vertebral localization of ABCs is found in 8–30 % of cases, accounting for 15 % of all spinal tumors [6]; in this case, the lumbar, cervical, and thoracic spine is affected in 40–45 %, 30 %, and 25–30 % cases, respectively [7].

Despite the primarily benign nature, ABCs can be locally aggressive, reaching Enneking grade III [10], with tendency to exophytic proliferation, which, in the case of spinal localization of tumor, often leads to compression myelopathy and requires combined treatment (Fig. 1) [9].

Treatment of spinal ABCs includes radiotherapy (as adjuvant or monotherapy), local injections (hemostatic agents and glucocorticoids), surgical resection of the tumor, selective arterial embolization, and their combinations [11, 12]. The rate of local recurrences for different treatment options varies from 5 % (en-bloc resection) to 25 % (isolated radiotherapy), being 10–27 %, on average [13].

Despite numerous publications reporting treatment outcomes in adults with ABCs, including spinal ABCs, information about pediatric patients with this tumor is extremely limited. Small clinical cohorts and the lack of systematized publications prevent answering the fundamental question: which treatment option is most effective in children? This is what prompted us to perform this study, the purpose of which was to evaluate the efficacy of current treatments for ABC in children.

The study design was as follows: a systematic review of the literature on treatment of spinal ABCs in children over the past 20 years.

Methodology for Searching and Processing Publications

A systematic review was conducted using medical databases: MEDLINE/PubMed, eLibrary, and Google Scholar search engines, as recommended by PRISMA [14]. At the first stage, three authors independently selected publications using the following keywords: aneurismal bone cyst (ABC), spine, children/pediatric. At the second stage, we analyzed abstracts for compliance with the inclusion criteria and excluded duplicate articles. At the third stage, we reviewed the full-text articles.

Publications were included in the systematic review based on the following criteria:

– date of publication from January 1, 1998 to December 31, 2018;

– follow-up period of at least 12 months after a medical procedure;

– possibility to assess the evidence level of publication [15].

The study also included publications on treatment of ABCs in different age groups, analysis of which enabled quantitating the number of pediatric cases as well as assessing features of their disease and the treatment approach. The scheme for selection of publications for the systematic review is presented in Fig. 2.

The analyzed publications included data of 165 pediatric patients. Detailed characterization of the publications included in the study is presented in the Table.

Results

According to the inclusion criteria, we analyzed 19 publications containing information on 165 cases of spinal ABC

treatment in children. The mean age of patients was 10 years and 5 months. (min 2 years, max 15 years); long-term outcomes were followed-up for 8 years and 4 months (min 1 year, max 21 years), on average.

The distribution of patients by the affected spinal level was as follows: C : C/T : T : L: S – 72 : 1: 44 : 44 : 4.

Depending on the treatment option for ABCs, all patients were divided into five groups:

– Group 1: radiotherapy (monotherapy– 11 cases; adjuvant therapy – 14 cases);

– Group 2: surgical removal, including en-bloc resection – 19 cases and subtotal resection – 55 cases;

– Group 3: embolization – 28 cases;

– Group 4: combination of embolization and surgical removal – 32 cases;

– Group 5: transcutaneous injections – 4 cases.

The outcomes in each group were analyzed according to the following parameters: the rate of local recurrence, changes in the neurological status (in the presence of baseline neurological deficit), changes in pain, and the duration of postoperative follow-up.

Radiotherapy. The largest clinical series that used radiotherapy alone for spinal ABCs in children was presented by Zhu et al. [16] and included 5 cases with a predominant localization of the lesion in the cervical spine (n = 4). Isolated pain without neurological deficit was present in all cases. The course of therapy included 12 to 34 fractions (M = 19) with a total radiation dose of 12 to 60 Gy (M = 33 Gy). The long-term outcomes indicate pain relief within a period of 2 to 4 weeks and no signs of tumor recurrence within a period of 13 to 34 years.

With the same fractionation regimens and total radiation dose of therapy in a series of four cases, Feigenberg et al. [17] observed a persistent reduction in pain and no signs of recurrence in 75% of cases during the follow-up period from 6 years and 7 months to 21 years, while one patient developed angular kyphosis in the cervical spine with a Cobb angle of 60°, which required halo-traction and posterior instrumented fixation at C3–C5, followed by the development of local tumor recurrence. A similar orthopedic complication (a decrease in the vertebral body height with progression of kyphotic deformity) after radiation therapy for an ABC of the T6 vertebra was reported by de Kleuver et al. [18].

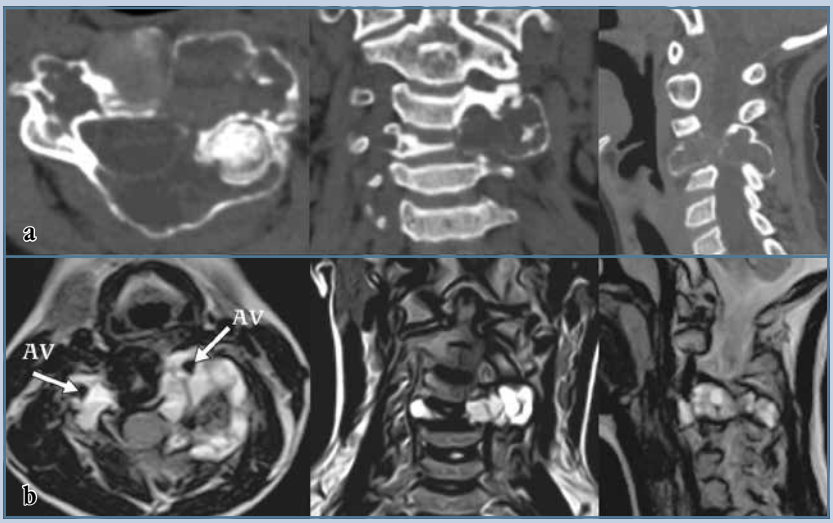

Fig. 1
CT and MRI sections of an aneurysmal bone cyst of the C4 vertebra in a 7 year and 11-month-old child (our own observation): **a** – an asymmetrical decrease in the C4 body height, swelling of the bone structures with thinning and heterogeneity of the end plate contours, and contact lesion of the C3 posterior structures; **b** – a heterogeneous multicavity bilateral lesion with predominant involvement of the left C4 portions, encasing the vertebral arteries (AV – *arteria vertebralis*)

Adjuvant radiotherapy is most often used after subtotal resection of ABCs, which reduces the risk of local recurrence and promotes a decrease in the residual volume of a soft tissue component of the tumor. However, Boriani et al. [8] reported a negative effect of this technique in 33 % of cases in the form of superficial surgical site infection, which required revision surgery.

Given the outcomes of both radiotherapy alone and adjuvant radiotherapy in the treatment of spinal ABCs in children, the following conclusions may be drawn:

– efficacy of this technique amounts to 75 %;

– orthopedic complications, in particular kyphosis progression, occur in 17 % of cases;

–rate of surgical site infections amounts to 33 %.

Surgical resection. According to most authors, the development of neurological deficit is the main indication for surgical removal of spinal ABCs in children [18–20]. Depending on the amount of tumor removal, subtotal and en-bloc resections are distinguished, the results of which differ significantly, primarily in the rate of late recurrence.

Subtotal resection performed by de Kleuver et al. [18] in 19 patients was accompanied by tumor recurrence in 6 (31.5 %) patients, progression of spinal deformity in 4 (21.0 %) cases, persistence of neurological deficit in 2 (10.5 %) patients, and persistence of pain in 1 (5.2 %) case.

Boriani et al. [24] reported a tumor recurrence rate of 7 % in subtotal resection, while en-bloc resection was not accompanied by postoperative complications. Similar results after en-bloc resection were obtained by Zileli et al. [5] in 8 cases: there was no tumor recurrence, persistent pain, and persistent neurologi-

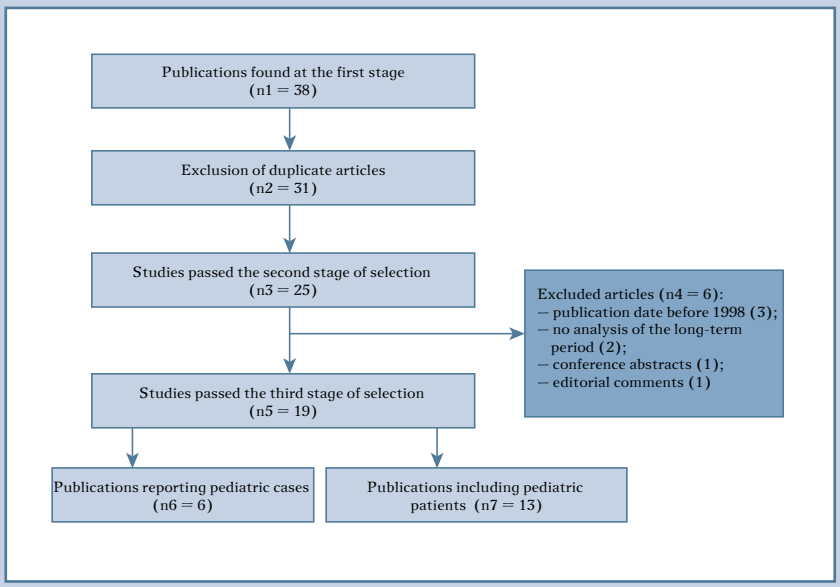

Fig. 2
Schematic diagram of the procedure for selection of publications for the systematic review

cal deficit. Complications included intraoperative CSF leak (1 case) and blood loss ⩾20 % of the CBV (2 cases).

Therefore, surgical resection of spinal ABCs in children is an effective treatment option; however, subtotal resection is associated with a greater rate of local recurrence (up to 32 %) and persistence of neurological deficit and pain (up to 20 %). In turn, en-bloc resection completely eliminates the risk of recurrence; however, this is a highly traumatic procedure, primarily due to intraoperative blood loss.

Embolization. Compared with other techniques, selective arterial embolization (SAE) is a relatively new method for treating spinal ABCs in children. The first results reported by de Cristofaro et al. [25] indicate the appearance of radiographic signs of tumor ossification and a decrease in the pain severity after a single procedure.

The contraindications for SAE include: 1) spinal cord collateral/collaterals from tumor feeding arteries; 2) anastomosis between the vertebral and ascending cervical arteries in cervical ABCs [23].

According to Amendola et al. [27], the use of SAE for spinal ABCs in children provided tumor ossification, relieved pain, and improved the neurological status of patients after 2–5 staged procedures. In this case, the mean duration of hospitalization was 2 days; there was regression of the soft-tissue component and no recurrences in all cases for 4 years and 3 months, on average [27]. In contrast to these optimistic results, Terzi et al. [28] noted the need for surgery in 25 % of cases after 5–7 SAE procedures, due to progression of neurological deficit.

Therefore, SAE of spinal ABCs in children reduces pain and severity of neurological disorders after the first procedure. Regression of the soft-tissue component and tumor ossification have been observed in most cases reported to date and have remained for a long period (M = 3 years and 5 months), but do not exclude the risk of neurological deficit progression.

Embolization followed by surgical resection. As shown above, en-bloc resection of spinal ABCs in children is a highly effective treatment option, but its use is limited by a high rate of vascular injuries, primarily the amount of operating blood loss. However, only one article [29] analyzes absolute blood loss indicators in 8 cases of SAE followed by en-bloc resection: the mean intraoperative blood loss in this study was 841 mL; while in the absence of SAE, it was 940 mL.

A clinical series by Novais et al. [30] included 5 cases of SAE with en-bloc resection of the lesion in the cervical spine; in all cases, there was complete regression of the soft-tissue tumor component and no recurrence for 3 years and 10 months.

Transcutaneous injections. Information on the results of injection administration of glucocorticoids and hemostatic drugs in the treatment of spinal ABCs in children is limited to four cases. The authors note the efficacy of the procedure, 100 % rate of soft-tissue component regression, and tumor ossification, but consider the results only as preliminary [31, 32].

Conclusion

Only 165 cases of treatment for spinal ABCs in children have been reported over the past 20 years, while the domestic literature does not provide any publication directly devoted to treatment of this lesion.

All the reviewed articles reported single clinical cases and small series; in particular, only 6 out of the 19 studies were devoted directly to pediatric patients. In most cases, children were represented by single cases included in a total clinical group.

The role of radiation therapy, which was actively used at the beginning of the analyzed period, has significantly decreased in the last decade. Today, the most effective techniques for treating spinal ABCs in children are en-bloc resection and selective arterial embolization, which have the lowest recurrence rate. However, en-bloc resection is accompanied by high blood loss and risk of injury to nerve structures. Combination of SAE and en-bloc resection reduces the invasiveness of surgery.

The study was conducted without financial support.
The authors declare no conflict of interest.

Table

Characterization of publications included in the review

Author	Age of children (years + months)	Tumor localization (number of cases)	Treatment option (number of cases, children)	Follow-up period (years + months)	Outcome (number of cases)
De Kleuver et al. [18]	13 + 1	C (2) : Th (8) : L (9) : S (3)	SR (19), RT (1), SR + RT(1), SAE (1)	6 + 1	Neurological deficit (3), kyphosis progression (3), pain recurrence (3), tumor recurrence (1
Gladden et al. [31]	3 + 10	C (1)	PI	2 + 7	Ossification and regression of the soft-tissue component
Boriani et al. [9]	12 + 4	C (12) : Th (6) : L (15)	SR (14), SR + RT (12), SAE (4), en-bloc (2), RT (1)	6 + 9	Tumor recurrence (3), superficial surgical site infection (5), progression of spinal deformity (4)
Feigenberg et al. [17]	10 + 5	C (3) : L (1)	RT (4)	15 + 8	No recurrence in all cases
Mohit et al. [26]	10 + 0	C (1)	SAE (1)	1 + 6	Ossification
Deo et al. [23]	2 + 3	C (1)	SR (1)	3 + 0	Late deep peri-implant infection, removal of posterior instrumented fixation. No recurrence for 3 years since primary surgery
Refai et al. [19]	15	C (1)	en-bloc (1)	1 + 0	No recurrence
Novais et al. [30]	11 + 9	C (7)	SAE + en-bloc (5), SR (2)	3 + 10	No recurrence (7), Horner syndrome (1)
Lim et al. [8]	11 + 10	C (1) : Th (2) : L (3) : S (1)	en-bloc (2), Dec (2), Dec + RT (1), SR (1), PI (1)	8 + 2	Tumor recurrence (2)
Zenonos et al. [29]	11 + 4	C (2) : Th (6) : L (6)	SAE + en-block (6), en-bloc (5), SR (3)	4 + 7	Tumor recurrence (2, including en-bloc – 1, SR – 1)
Zileli et al. [5]	13 + 2	C (2) : C/Th (1) : Th (2) : L (4)	en-bloc (8), SR (1)	9 + 6	No recurrence in all cases
Shiels et al. [32]	13 + 5	C (1) : Th (1)	PI (2)	4 + 3	Ossification and regression of the soft-tissue component
Karampalis et al. [21]	9	C (1)	SAE + en-bloc (1)	2 + 0	No recurrence
Amendola et al. [27]	11 + 6	C (3) : Th (1) : L (1)	SAE (5)	4 + 3	Ossification and regression of the soft-tissue component
McDowell et al. [20]	6	C (1)	en-bloc (1)	3 + 11	No recurrence
Boriani et al. [24]	12 + 2	C (22) : Th (16) : L (4)	SAE + SR (19), SR (14), SAE (9)	3 + 2	Recurrence upon subtotal tumor resection (3)
Rajasekaran et al. [22]	8	C (1)	SAE + en-bloc (1)	2 + 3	No recurrence
Zhu et al. [16]	9 + 4	C(4) : L(1)	RT (5)	21+0	No recurrence (3), death after 34 years due to heart disease (1)
Terzi et al. [28]	12 + 6	C (6) : Th (2)	SAE (8)	4 + 5	No recurrence (7), decompression-stabilization surgery (1)

C, Th, L, S – spine regions;
SR – subtotal resection, en-bloc resection;
RT – radiation therapy;
SAE – selective arterial embolization;
Dec – spinal cord decompression;
PI – percutaneous injection.

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Address correspondence to:
Naumov Denis Georgievich
St. Petersburg Research Institute of Phthisiopulmonology,
Politekhnicheskaya str., 32, St. Petersburg, 194064, Russia,
dgnaumov1@gmail.com

Received 15.04.2019
Review completed 25.04.2019
Passed for printing 29.04.2019

Denis Georgievich Naumov, junior researcher, St. Petersburg Research Institute of Phthisiopulmonology, Politekhnicheskaya str., 32, St. Petersburg, 194064, Russia, ORCID: 0000-0002-9892-6260, dgnaumov1@gmail.com;
Elena Aleksandrovna Speranskaya, resident, St. Petersburg Research Institute of Phthisiopulmonology, Politekhnicheskaya str., 32, St. Petersburg, 194064, Russia,ORCID: 0000-0002-4052-8286, el_art@bk.ru;
Mikhail Aleksandrovich Mushkin, orthopedic traumatologist, teaching assistance, Department of traumatology and orthopedics, Pavlov First Saint Petersburg State Medical University, Lev Tolstoy str., 6–8, St. Petersburg, 194064, Russia, mikhail_mushkin@mail.ru;
Denis Borisovich Malamashin, MD, PhD, senior researcher, orthopedic surgeon, St. Petersburg Research Institute of Phthisiopulmonology, Politekhnicheskaya str., 32, St. Petersburg, 194064, Russia, malamashin@mail.ru;
Aleksandr Yuryevich Mushkin, DMSc, Prof., chief researcher, Head of Clinic of Pediatric Surgery and Orthopedics, Head of the Scientific and Clinical Centre for spinal pathology, St. Petersburg Research Institute of Phthisiopulmonology, Politekhnicheskaya str., 32, St. Petersburg, 194064, Russia, aymushkin@mail.ru.