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PATHOLOGICAL FRACTURES OF THE SPINE IN CHILDREN (review of the literature and clinical and morphological monocenter cohort analysis)

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Background. Pathological vertebral fractures are rare and occur in inflammatory, tumor, and dystrophic lesions.
Aim. This study aimed to analyze clinical features and morphological structure of pathological fractures of the spine in children.
Materials and methods. The authors examined and operated 62 children aged 2–17 years for pathological vertebral fractures. We investigated the clinical, radiological, and morphological features.
Results. The average age of children at the time of hospitalization was 10 years. Lesions of thoracic vertebrae prevailed (78%) with the maximum frequency of occurrence at the apex of physiological kyphosis Th_{7-8}. In 10 cases, multiple lesions were noted, including the pathology of other parts of the skeleton. In 69% of observations, clinical symptoms were not dominated by mechanical back pain. Palpation pain (34%) and local spinal deformation (27%) were noted. On average, local kyphosis was 24°. Eleven patients (18%) manifested a neurological deficiency, of which nine fractures were a consequence of the tumor process. In 16% of observations, the fracture of the vertebra was detected to be an accidental X-ray finding. Among the radiation manifestations, all cases (12 patients) registered the decrease in the height of the vertebral body in the form of collapse. Destruction was manifested by various options other than blastic. Therapeutic and diagnostic interventions were performed in 56 patients, and in six children, manipulation was limited to trepan biopsy. The pathological fracture was caused by an inflammatory process in 50% of observations and tumors in 42%, of which 31% is malignant.
Conclusions. Pathological spinal fracture in children should be considered as a syndrome, which in most cases is based on an inflammatory or tumor process. The high frequency of neoplastic, including malignant processes, requires active invasive diagnosis. Therapeutic tactics are determined by the clinical, radiation, and morphological characteristics of pathology.

Keywords: vertebral fractures; spondylitis in child; kyphosis; spine reconstruction children; pathological fractures; tumor of spine.

ПАТОЛОГИЧЕСКИЕ ПЕРЕЛОМЫ ПОЗВОНОЧНИКА У ДЕТЕЙ (краткий обзор литературы и клинико-морфологический анализ моноцентровой когорты)

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Обоснование. Патологические переломы позвонков у детей встречаются относительно редко при воспалительных, опухолевых и дистрофических поражениях.

Цель — анализ особенностей клинической картины и морфологической структуры патологических переломов позвоночника у детей.

Материалы и методы. Изучены клинические и лучевые особенности, морфологическая структура патологических переломов позвонков у 62 детей в возрасте от 2 до 17 лет, обследованных и оперированных в клинике.

Результаты. Средний возраст детей на момент госпитализации составил 10 лет, каких-либо гендерных особенностей выявлено не было. Преобладали поражения грудных позвонков (78 %), наиболее часто на уровне вершины физиологического кифоза $Th_{7–8}$. В 10 наблюдениях отмечены множественные поражения, включая патологию других отделов скелета. В клинической симптоматике преобладали немеханическая (не связанная с движением) боль в спине (69 % наблюдений), болезненность при пальпации (34 %) и локальная деформация позвоночника (27 %) при средней величине локального кифоза 24°. Неврологический дефицит выявлен у 11 больных (18 %), из них у 9 перелом был следствием опухолевого процесса. В 16 % наблюдений перелом позвонка оказался случайной лучевой находкой.

Среди лучевых симптомов патологии снижение высоты тела позвонка отмечено во всех случаях, у 12 пациентов — в виде коллапса. Деструкция проявлялась различными вариантами, кроме бластического.

Лечебно-диагностические вмешательства выполнены 56 пациентам, у 6 детей манипуляции ограничены трепан-биопсией. В 50 % случаев патологический перелом был обусловлен воспалительным процессом, в 42 % — опухолью, из них в 31 % случаев — злокачественной.

Заключение. Патологический перелом позвоночника у детей следует рассматривать как синдром, в основе которого в большинстве случаев лежит воспалительный либо опухолевый процесс. Вследствие высокой частоты неопластических, в том числе злокачественных, процессов необходима активная инвазивная диагностика. Лечебная тактика определяется клиническими, лучевыми и морфологическими характеристиками патологии.

Ключевые слова: перелом позвоночника; спондилит; дети; кифоз; реконструкция позвоночника; патологические переломы; опухоль позвоночника.

Vertebral fractures in the structure of childhood injuries in the Russian Federation account for 0.55% with significant regional variations [1, 2], whereas pathological fractures among them are not officially taken into account. Indirectly, this gap is filled by regional studies that include the prevalence of tumors and tumor-like diseases of the spine; thus this indicator amounted to 1.93 per 100,000 children population in the children population of the Leningrad Region [3].

Pathological vertebral fractures in adults are analyzed much more extensively, enabling the identification of certain patterns. In particular, the destructive and lytic pathology of the cervical spine, which is manifested by a complicated pathological fracture, is caused in more than half of cases by tumor processes [4], and in the overwhelming majority, it is metastatic in nature [5] with a relatively rapid (up to 28 days) manifestation of neurological disorders [6]. Another common cause of pathological vertebral fractures in adults is inflammatory processes, which often have an immunopathological and multilevel nature [7, 8].

The simplest method to verify the etiology of pathological vertebral fractures is a cytological and histological examination of the material from the affected site. Material collection by percutaneous trepanobiopsy is considered as the main method for determining the treatment approach. Its information content reaches 75% in adults and 85% in children [9], whereas computed tomography (CT) navigation enables to increase the effectiveness of the procedure [10].

Among benign tumors leading to a pathological vertebral fracture in pediatric patients, special attention is paid to an aneurysmal bone cyst. The treatment approach of which currently involves the use of exclusively surgical methods, and also

as an independent method, which is repeated embolization or a combination thereof [11, 12].

Among the most common causes of pathological vertebral fracture in children is Langerhans cell histiocytosis. The frequency of neurological disorders in such children is much lower than with pathological fractures in adults [13]. Nevertheless, the relative benignity of Langerhans cell histiocytosis, which according to the international classification of tumors belongs to processes with "nonspecific, limited or unknown malignancy" [14], explains the lack of uniform recommendations for its treatment.

With the rapid development of neurological disorders in the presence of lymphomas and Langerhans cell histiocytosis of the thoracic vertebrae in children, emergency decompression of the spinal cord with simultaneous open biopsy is recommended [15]. At the same time, similar long-term (more than 3 years) orthopedic and oncological results of treatment of neurologically complicated Langerhans cell histiocytosis during 360° spinal reconstruction (stabilization and spinal fusion of the anterior and posterior columns of the spine) were obtained, as well as with isolated posterior decompression with transpedicular fixation, with less trauma of the latter intervention [16]. A positive effect in the form of restoration of the vertebral body over several years can be achieved with curettage in combination with chemotherapy. Also, the use of exclusive methods of chemotherapy and radiation therapy has been described, especially for multilevel lesions, including in combination with neurological manifestations. At that, the absence of the effect of conservative therapy or the rapid increase in neurological symptoms is considered indications of decompression [17–20].

Ewing sarcoma is one of the malignant processes that cause a pathological vertebral fracture in children. In a monocenter analysis of Ewing sarcoma, vertebral lesions were noted in 2 of 27 cases (7.4%) [21].

Thus, pathological spinal fractures in children represent an etiologically diverse group of lesions, united by the syndromic principle. Most of the publications on this subject are either individual cases or limited clinical series focused on a possible oncological etiology of the process in the absence of unity in the choice of therapeutic approach, even in the case of neurological complications.

Having some experience in treating children with pathological spinal fractures, we consider it possible to share the results of our analysis of the clinical and morphological structure of such lesions.

The work aimed to analyze the characteristics of the clinical presentation and the morphological structure of pathological vertebral fractures in children.

Materials and methods

The study design represents a retrospective monocentral 4-year clinical cohort.

The material was obtained based on the following inclusion criteria:

- examination and treatment of patients in the clinic from 1 January 2015, to 31 December 2018;
- under 18 years of age at the time of hospitalization;
- the availability of radiology data confirming a pathological vertebral fracture. The criteria for establishing a diagnosis include signs of a decrease in the height of the vertebral body along with disorders of its bone structure; and
- verification of the pathological process based on morphological, immunohistochemical, bacteriological, and molecular genetic studies of material obtained from the affected area during the examination/treatment in the clinic.

Lesions accompanied by a hyperplastic bone process with an increase in the size of the vertebra without a decrease in the height of its body were excluded from the analysis.

Over the period indicated, the data of 62 children met the listed inclusion criteria.

The study examined the following:

- age and gender structure of the group;
- clinical symptoms, including aspects of neurological status;
- aspects of radiation semiotics of spinal lesions;
- morphological structure of the processes, which led to the pathological fracture; and
- structure and outcomes of the surgical interventions in history.

During the period analyzed, patients with pathological spinal fractures accounted for about 20% of all patients with destructive vertebral lesions treated in the clinic. The average age of patients was 10 ± 0.43 years, and no gender asymmetry in the study group was noted.

Table 1

Main clinical manifestations of pathological vertebral fractures in pediatric patients (n = 62)

Clinical manifestations	Amount (%)
Back pain, including: local (tactile and palpation) provoked by movement	43 (69) 21 (34) 10 (16)
Spinal deformity	17 (27)
Neurological symptoms	11 (18)
Asymptomatic course	10 (16)

Table 2

Frequency of neurologic impairment depending on the nature of the tumor process

Nature of the tumor process	Number of cases with neurological symptoms	Significance of differences
Benign, n = 18	4 (22 %)	Pf* = 0.197 ($p > 0.05$)
Malignant, n = 8	4 (50 %)	

Note. Pf is Fisher's exact test.

Clinical and radiological characteristics of the pathology. At the onset of the disease, an episode of trauma was recorded in 25 (40%) pediatric patients; in other cases, the pathology was identified based on complaints or during examination for a concomitant pathology. Table 1 presents the characteristics of the clinical manifestations of pathological vertebral fractures in pediatric patients.

It is noteworthy that in the presence of back pain, half of the pediatric patients did not report their localization in the pathology zone, and the pain was induced by motor activity only in 16% of cases. With a relatively low overall frequency of neurological complications (8 out of 11 cases), their severity indicated gross motor disorders and corresponded to types A and C on the Frankel scale in 2 and 6 cases, respectively. In 8 out of 11 patients with neurological disorders, the tumor nature of the lesion was further verified in the absence of a significant relationship between neurological disorders and the nature of the oncological process (Table 2).

In all cases, radiation aspects of pathological vertebral fractures were represented by a decrease in the height of the body of the vertebra affected (which was an inclusion criterion), including its collapse in 12 cases with preservation of the contacting upper and lower arch laminae only, sometimes with a complete absence of bone structures. Nine pediatric patients had polysegmental (more than two) vertebral lesions, including five with multilevel lesions. Combined and multiple lesions involving other parts of the skeleton systems were diagnosed in 10 cases.

Analysis of the pathology distribution in individual vertebrae showed a significant predominance of lesions at the apex of the physiological kyphosis of Th_{7-8} (Fig. 1).

The nature of the destructive changes corresponded to the lytic process in 25 patients (including 12 with the vertebral body collapse). In 15 cases, A decrease in the height of the vertebral body was accompanied by its induration (sclerosis). Lytic changes were combined with sclerotic ones

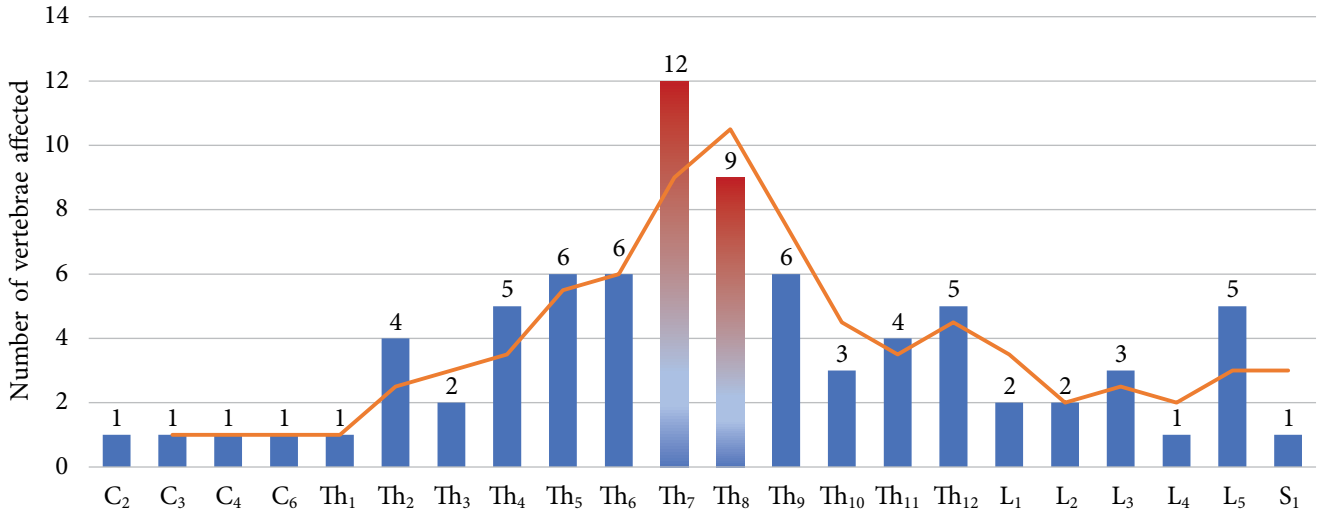


Fig. 1. The level structure of the distribution of pathological vertebral fractures (81 affected vertebrae)

in 13 patients, and destruction was of the nature of the marginal cortical lesion in 9 patients. The extravertebral (paravertebral) soft-tissue component was detected in 12 cases, whereas the epidural propagation with spinal stenosis and spinal cord compression was recorded in 9 cases.

The local kyphotic deformity was noted in 17 pediatric patients (27%), and its average value was 24° ± 3°. According to magnetic resonance imaging (MRI), disks adjacent to the abnormal vertebra were involved in the pathological process in only three cases, and their height and hydrophilicity were reduced.

Despite the clinical presentation, the diagnostic phase in the study group was quite long, including in the presence of neurological symptoms, as the average diagnostic pause was 2.7 months (min 2 months; max 5 months).

Diagnostic and surgical procedures. All patients underwent invasive diagnostic and therapeutic interventions, including trepanobiopsy of the affected vertebra in six cases. In the case of diagnosing a malignant process in the absence of neurologic impairment and indications for spine reconstruction, the child was transferred to an oncology hospital for chemotherapy. The nature of surgical interventions performed in other cases is presented in Table 3.

Indications for surgery, in addition to the proven tumor nature of the process, included spinal deformity, neurological complications, spine instability with a provoked pain syndrome, and insufficient information about trepanobiopsy. Among 26 patients with tumor lesions, the spine instability neoplastic score in the series was 9.2 ± 0.45 points. When conducting anterior reconstruction and posterior instrumental fixation, both stages of the surgery were performed during one surgical session using titanium mesh-cages with autobone for anterior spondylodesis. The posterior instrumental fixation was ensured by the installation of laminar, transpedicular, and hybrid structures.

Morphological structure of the pathology. Fig. 2 presents the results of morphological diagnostics. In the prevalence of inflammatory changes detected in 31 cases (50%), the infectious process was confirmed bacteriologically only in one case (inoculation of *Staphylococcus aureus*). Dystrophic (osteonecrotic) changes, which traditionally could be assessed as Calve disease, were diagnosed in only

Table 3

Structure of surgical interventions

Surgical intervention	Quantity
Posterior instrumental fixation	3
Vertebroplasty	4
Front reconstruction of the spine (titanium mesh-cage [Harms nets] + autobone)	19
Anterior reconstruction + posterior instrumental fixation	30
Total surgeries	56

Table 4

Age structure of the group depending on the pathological process morphology

Morphology	Average age (years)	Difference
Inflammation (n = 31)	9.3 ± 0.47	U_{emp} = 268.5 U_{crit} = 287 (p < 0.05)
Oncology (n = 26)	11 ± 0.73	
Dystrophy (n = 5)	8.8 ± 2/10	–

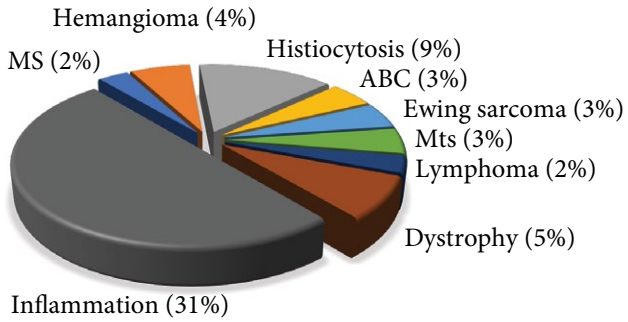


Fig. 2. Etiological structure of the pathology verified according to the histological examination of the material from the affected area. ABC, aneurysmal bone cyst; MS, myeloid sarcoma; Mts, tumor metastasis.

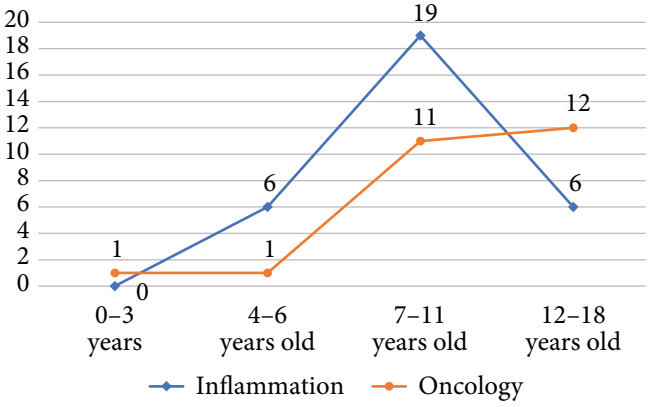


Fig. 3. The number of pediatric patients with inflammatory and tumor lesions of the spine, depending on the age group

five cases (8%). The tumor process was verified in the remaining 26 (42%) pediatric patients, whereas the tumor was malignant in 8 (31%) cases.

An analysis of the relationship of morphological aspects of pathology with age revealed that tumor lesions significantly prevailed compared with inflammatory and dystrophic processes in older pediatric patients (Table 4 and Fig. 3). In particular, a decrease in the frequency of inflammatory lesions was noted in pediatric patients over 11 years of age, and pathological spinal fractures were more common along with the tumor process.

Aspects of postoperative management of patients. During verification of the malignant process, the surgery was considered as the first stage of combined treatment. And immediately after it, the child was transferred under the supervision of an oncologist. In one patient with Ewing sarcoma diagnosed through trepanobiopsy, continued tumor growth was registered, which resulted in fatal outcome, during ineffective chemotherapy.

In the case of the diagnosed inflammatory process, the pathology was considered a vertebral form of nonbacterial osteomyelitis because of which the patient was further observed by a pediatric rheumatologist.

Intraoperative and postoperative complications were recorded in 9 of 56 patients (16%), including the following:

- one case of hemorrhage from epidural vessels in combination with liquorrhea in a pediatric patient with a Th_6 pathological fracture with nonbacterial osteomyelitis, which was stopped intraoperatively;
- one case of transient neurological disorders (independent regression), surgical site infection, and surgical hardware instability (revision interventions and hardware reinstallation were performed) in the early postoperative period (the first 30 days after the surgery);
- four cases of spinal deformity progression (two cases of anterior spinal fusion failure and two cases of contact kyphosis at the upper border of the anterior spinal fusion); and
- three cases of repeat operation because of late complications (more than 3 months after the surgery).

In other patients without intraoperative and postoperative complications, pain and the development of a local destructive process were stopped during the case follow-up. In patients with neurological disorders, complete (four cases) and partial (six patients) regression of symptoms were achieved. However, there were no changes in time in one case.

The restoration of stability of the anterior column of the spine with the formation of a complete anterior spinal fusion (7.5 ± 2.7 months) enabled to dismantle further the posterior metal structure on average within 14 ± 2.2 months.

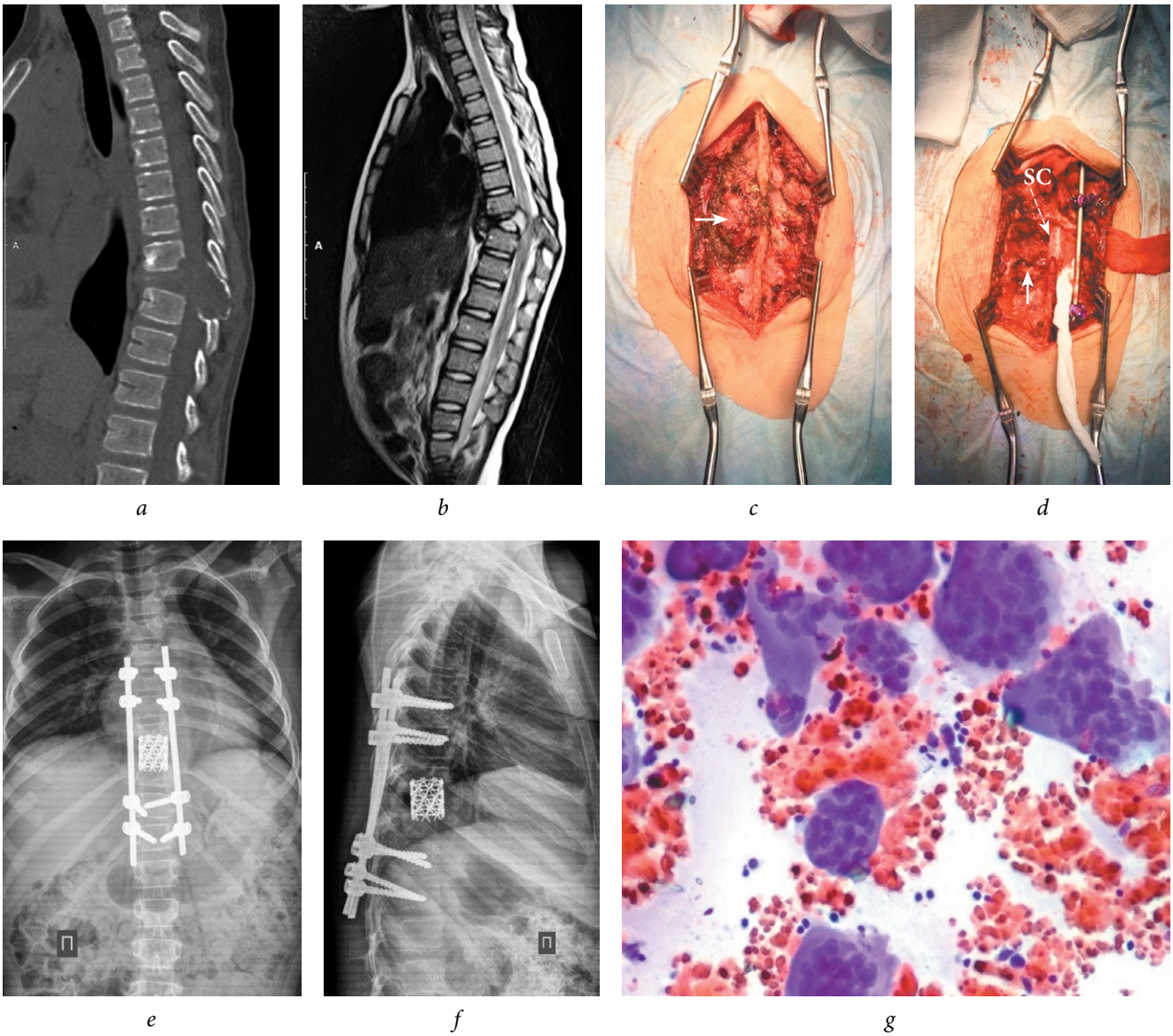
Clinical case

A girl, 8 years old, was hospitalized in the clinic with complaints of back pain and inability to move independently. A space-occupying lesion, Th_9 pathological fracture, and vertebral canal stenosis, as well as lower spastic paraparesis, were diagnosed.

There was an episode of injury (fall) and back pain in history. The patient was hospitalized in the in-patient facility 4 days after the injury; the space-occupying lesion and Th_9 pathological fracture were diagnosed during an examination. Treatment in a federal clinic was recommended, and the waiting period for hospitalization was 2.5 months. During this time, a disorder of movements in the lower extremities occurred, and the child lost the ability to walk.

On admission, there was a serious condition due to lower spastic paraparesis, Frankel type C. The function of the pelvic organs was preserved. CT and MRI (Fig. 4, *a* and *b*) revealed a pathological fracture with osteolytic destruction of the body and the Th_9 arch with paravertebral and intracanal components, vertebral canal stenosis, and spinal cord compression. According to scintigraphy, there was a mild local hyperfixation of the radiopharmaceutical agent (120%).

Because of the presence of neurological disorders, it was decided to conduct a diagnostic and treatment surgery in the amount of reconstruction of the $Th_{8–10}$ spine with total removal of the Th_9 vertebra with a tumor and decompression of the spinal cord. Anterior spinal fusion was performed with a titanium mesh-cage with an auto-rib, and posterior instrumental fixation of $Th_{6–11}$ was performed with deformity correction. The surgery was carried out with the posterior approach; the revision revealed a soft



a *b* *c* *d*

e *f* *g*

Fig. 4. Pathological fracture of the Th_9 vertebra with an aneurysmal bone cyst in an 8-year-old pediatric patient. (*a* and *b*) Preoperative mid-sagittal computed tomography and magnetic resonance imaging sections: osteolytic destruction of the ventral and dorsal elements of the Th_9 vertebra, local kyphosis of 21°, and compression of the spinal cord with the epidural component of the tumor with a myeloblastic lesion. (*c* and *d*) Intraoperative photographs (arrows indicate a tumor and a defect formed after its removal); (*e* and *f*) control postoperative radiographs; (*g*) imprint smear (stained with hematoxylin and eosin, ×100): red blood cells and osteoblast-type giant multinucleated cells. SC, spinal cord

tissue tuberous formation of 6 × 4 cm in size, completely destroying the right half of the arch, articular processes, and the Th_9 vertebral body. Pathological tissues with adjacent intervertebral discs were isolated from the surrounding tissues and removed using electrosurgical and ultrasound bone instruments within adjacent $Th_{8–10}$ vertebral endplates. Spinal cord membranes were circularly released (no signs of invasive growth were detected). The morphological study revealed an aneurysmal bone cyst (Fig. 4, *c*–*g*). Neurotropic and vascular therapy was started, as well as physical therapy classes. The patient was verticalized in an orthosis during positive neurological dynamics after 3 weeks. Partial regression to Frankel type D during the year after the surgery was noted. The patient walked with the help of walkers.

Discussion

Pathological spinal fractures in pediatric patients are relatively rare, but in the structure of patients with destructive lesions of the skeleton, they represent a significant group. A pathological vertebral fracture can be characterized by a clinical presentation similar to traumatic injury and provoked by trauma, although in some cases, there are no symptoms [22].

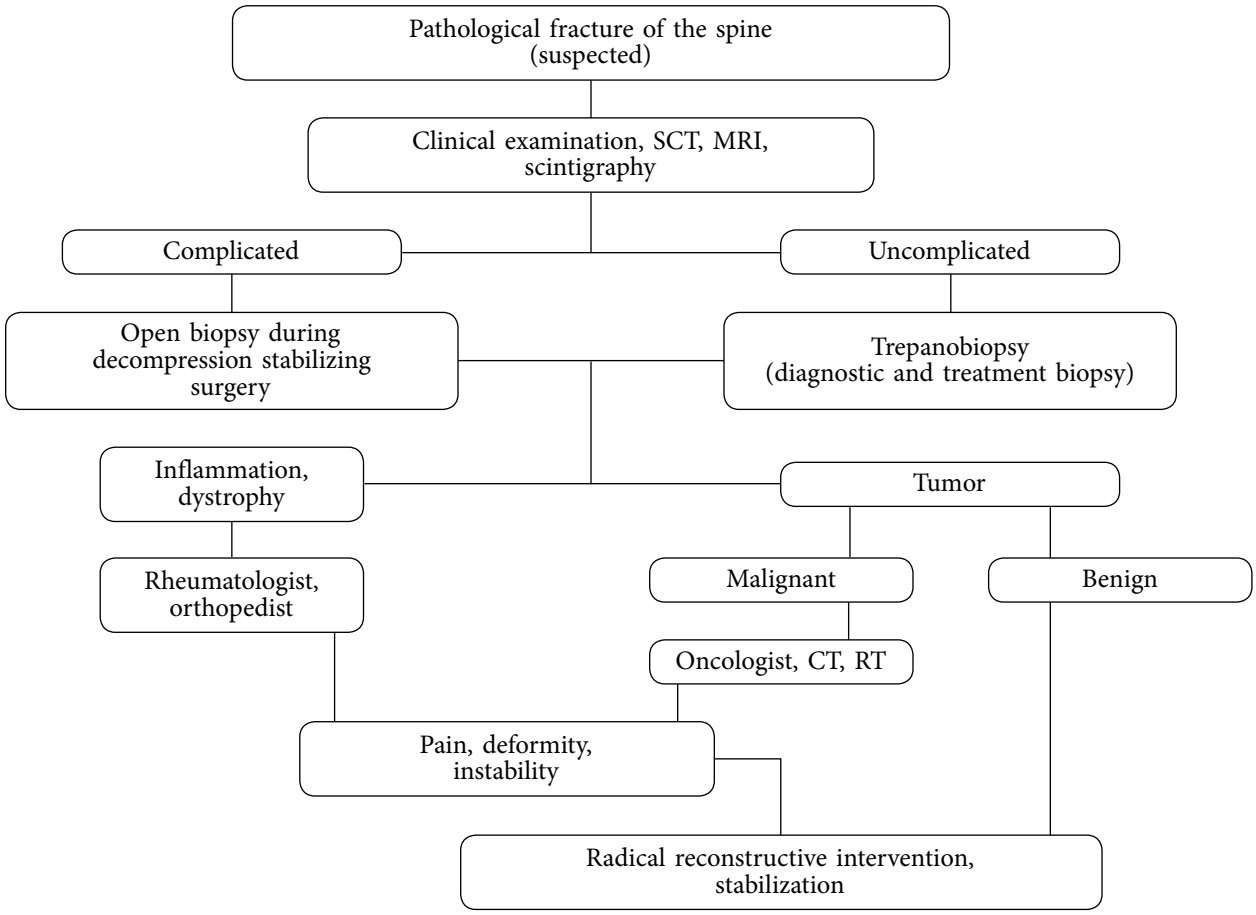


Fig. 5. Tactical algorithm for pathological spinal fracture. SCT, spiral computed tomography; MRI, magnetic resonance imaging; CT, chemotherapy; RT, radiation therapy

If a pathological nature of the process is suspected, an in-depth multistage diagnostic is necessary [23], which according to our data, is long lasting, which is associated with organizational reasons, whereas pathological changes progress, and the treatment pause increases.

Since the causes of a pathological fracture are varied, it is necessary to not only observe the principle of interdisciplinary interaction of specialists such as a pediatric surgeon, orthopedist, oncologist, and rheumatologist but also conduct etiological verification of the disease [24, 25]. In most cases, the material can be obtained through a minimally invasive procedure, percutaneous trepanobiopsy. A subsequent surgical approach is determined by the nature of the process and the complex of vertebrological (instability and deformity), neurosurgical (vertebral canal stenosis and neurologic impairment or risk of it), and oncological criteria.

Taking into account interdisciplinary cooperation, it is advisable to provide diagnostic and surgical care to pediatric patients with a pathological fracture of the spine in a specialized center where the pediatric patient needs to be referred in a short time. And in case of neurological disorders or risk of their development, the patient must be hospitalized urgently. Fig. 5 presents the tactical and therapeutic algorithm for pathological spinal fractures in pediatric patients.

Conclusion

The morphological structure of pathological spinal fractures in pediatric patients is diverse, and processes of an inflammatory (noninfectious) and tumor nature predominate. Since the probability of a malignant process as a cause of a pathological fracture is quite high, the principle of oncological alertness must be observed when choosing the treatment and diagnostic approach.

A pathological vertebral fracture in a pediatric patient is a syndromic category; therefore, the etiological aspect of the material from the affected area should be verified.

Because of the rarity and complexity of the pathology, it is advisable to perform reconstructive surgeries in a specialized center with experience in

such interventions and the possibilities of interdisciplinary interaction (morphologist, surgeon, orthopedist, oncologist, neurosurgeon, and rheumatologist) when deciding on the nature of the treatment.

Additional information

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Conflict of interests. The authors declare no obvious or potential conflicts of interest related to this publication.

Ethical statement. The study was discussed and approved by the ethics committee of the Saint Petersburg Research Institute of Phthisiopulmonology (protocol No. 64/2019). The patients and their legal representatives gave informed consent to the examination, treatment, and publication of the research results in the scientific literature and the use of information in the educational process and other purposes.

Author contributions

V.I. Zorin performed collection and analysis of literature, development of the study design, collection of clinical material, analysis of the results, and writing the article.

A.Yu. Mushkin developed and edited the study design and edited the article.

T.A. Novitskaya reviewed histological preparations and analyzed the results of morphological studies.

All authors made a significant contribution to the research and preparation of the article and read and approved the final version before its publication.

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