ENCHONDROMATOSIS WITH CERVICAL SPINE INVOLVEMENT IN CHILDREN: SMALL SERIES AND REVIEW

D.B. Malamashin[1], A.Yu. Mushkin[1, 2], D.A. Glukhov1, V.P. Snishchuk[1, 3]
[1]St. Petersburg Research Institute of Phthisiopulmonology, St. Petersburg, Russia
[2]Pavlov First Saint Petersburg State Medical University, St. Petersburg, Russia
[3]Leningrad Regional Children's Clinical Hospital, St. Petersburg, Russia

Objective: to present different variants of the clinical course and surgical treatment of an extremely rare vertebral pathology — enchondromatosis with involvement of the cervical vertebrae in children. Two cases of local and multiple forms of bone dyschondroplasia with damage to the cervical vertebrae, accompanied by orthopedic and neurological complications in children aged 7 and 11, are described. As a result of the operation, complaints were completely stopped in one child and neurological disorders were eliminated in another. The diagnosis was verified histologically. The results were followed up for more than 2 years and 1 year after the operation, respectively. Present-day data on Ollie's disease in children are presented. Indications, timing and volume of surgical intervention for bone dyschondroplasia are determined individually, depending on the size, location, and number of enchondromas. However, if the cervical spine involvement is complicated by increasing pain and neurological disorders, it is precisely decompression of the spinal cord that should be set as a priority aim of the surgery.
Key Words: Ollie's disease, multiple bone chondromatosis, dyschondroplasia, children, spinal deformity, spinal cord compression.
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Enchondromatosis is a rare congenital systemic skeletal disease relating to a heterogeneous group of metaphyseal chondrodysplasias. Ollier was the first to describe it as bone dyschondroplasia. Synonyms of this term are dyschondroplasia and multiple enchondromatosis. Additionally, according to the author's name, it is called Ollier disease [1–5]. Enchondromas occur as single or multiple masses. They are characterized by enchondral ossification disorder with the preservation of non-calcified cartilage foci, which increase and may become malignant in the process of growth [6, 7]. In a disease today described as Ollier disease, unlike the Maffucci syndrome (both conditions belong to the group of dyschondroplasias), bone lesions are not accompanied with skin manifestations of neoangiogenesis.

The incidence of Ollier disease is less than 1 : 100 000 [4, 8, 9]. Despite the sufficient number of published articles in the last 10 years devoted to individual cases of the disease [6, 7, 10–14], there is not enough data on spinal lesions. This fact enables us to share our observations.

The objective is to present different variants of the clinical course and surgical treatment of an extremely rare vertebral pathology.

From 2013 to 2019, two boys aged 7 and 11 underwent surgery. They complained of neck pain, limited range of motion, and neurological disorders. The survey of the patients and their parents did not reveal any peculiarities of family and obstetric history.

Case 1

Patient M. was first examined by an orthopedist at the age of 7 y.o. concerning complaints of gait disturbances. A month later, the child complained of weakness in the upper extremities, mainly in the right, which was manifested by the inability to hold a spoon on his own while eating. After being examined by a neurologist, the child was hospitalized in the neurological unit, where radiodiagnostics was performed for the first time. The diagnostic findings were the reason to send the patient to our clinic.

The main complaints upon hospital admission were neck pain, severe loss of head tilt and rotation, weakness in the right arm, and gait disturbances. From the clinical point of view, tenderness was noted during palpation of the neck, primarily in the upper neck. Clinical and biochemical blood tests were within normal limits. Neurological examination revealed a spinal cord lesion from the C4 segment with right-sided hemiparesis (mixed in the arm and spastic in the leg) and spinal cord irritation on the left without pelvic organ dysfunction.

No pathology was detected by chest X-ray. A cervical spine CT scan (Fig. 1a–c) revealed a nodule formation originating from the arches of the C2–C3 vertebrae, sharply narrowing the spinal canal. MRI of the cervical spine (Fig. 1d–f) showed severe compression by pathological lesion of the spinal cord and the neural foramen on the right at the C2–C3 level.

Due to the progression of focal neurological symptoms, a decision was made on therapeutic and diagnostic lesion resection. A bone block containing a lesion originating from the blocked arches of the C2 and C3 vertebrae was resected through the posterior approach. Con-

sidering that the resection area was limited only to the vertebral arches, without affecting the intervertebral joints, and the clinical symptoms were accompanied only by manifestations of spinal cord compression, without complaints typical of the instability of this area, it was decided not to perform additional instrumental fixation. To stabilize the posterior column, the laminectomy defect was blocked with a bone graft (rib autograft) fixed on ligatures to the C1 arch and the remains of the C3 arch.

The lesion was presented by dense bone-cartilaginous tissue of irregular shape, originating from the vertebral arches (Fig. 2). Histological examination of the surgical specimen found hyaline cartilage tissue containing ossificans.

The postoperative period proceeded without complications; the child was discharged on the 10th day after surgery with pronounced improvement. Short-term and long-term results of radiation and clinical studies are presented in Fig. 3.

Let us give attention, to the clinical effect of the operation, namely to the complete relief of all components of pathological symptoms: pain, neurological disorders, and restoration of the full range of movements in the cervical spine. There is no recurrent tumor; the spinal canal is not narrowed. We state the presence of local C2–C4 kyphosis, equal to 4°. Its value does not change between tests conducted 1 month and 1 year after surgery, despite the almost complete resorption of the autograft (Fig. 3e, f). For more than two years, the patient is still under the supervision of the clinic's doctors.

Case 2

Patient A., 11 years old, was admitted to the hospital complaining of cervical spine pain, weakness in the right arm, and numbness of the fingers of the right hand. The examination revealed a painful lesion of the proximal metaphysis of humerus, physical inactivation in the right shoulder joint, multiple exostoses of the upper and lower extremities, and *genu valgum*.

According to the anamnesis, at the age of 1 year 6 months, the patient was first diagnosed with a neoplasm of the right scapula and the fifth rib on the left. At the age of 1 year 9 months, the patient underwent resection of the left radius exostosis. Available morphological conclusion on the surgical specimen – enchondroma. Later, the patient was followed up by an orthopedist at the place of residence with chondrodysplasia. At the age of 10 years and 11 months, the patient consulted a neurologist in connection with the onset of right ptosis and myosis (Horner's syndrome). No pathological changes were detected by the brain MRI.

X-ray and MRI scans of the cervical spine detected signs of a voluminous paravertebral lesion on the right at the C7–T2 level, compressing the dural sac and the right apex (Fig. 4). There also was exostosis of the right scapula body (1.8 × 1.3 cm in size).

CT scans of the cervical and upper thoracic spine in the right costovertebral angle at the C7–T1 level showed a lesion with clear uneven contours, bone density, heterogeneous structure, 2.7 × 4.5 × 3.4 cm in size, sharply deforming the adjacent vertebrae. The boundary between it, the head of the first rib, the root of the arch, part of the arch, and the T1 transverse process on the right was not differentiated. The lesion prolapsed into the spinal canal up to 7 mm, compressing the dural sac. There was hypoplasia of the head of the second rib on the right; multiple bone exostoses were found in the area of the shoulder blades, ribs, and collarbones (Fig. 5).

Considering the anamnestic and clinical-radiology data, Ollier disease was found. It was decided to perform surgery because of the onset of neurological disorders. A posterior approach was performed in the area of transverse and articular processes of the C7–T1 vertebrae; a bone-cartilaginous conglomerate extending to the costovertebral angle was found. An approach to the tumor was made through the long back muscles. A right-sided hemilaminectomy was performed at the C7–T1 level with a costotransversectomy of the 1st and 2nd ribs. The tumor was spreading into the spinal canal and compressing the dural sac and spinal cord roots. Decompression was performed, as well as foraminotomy

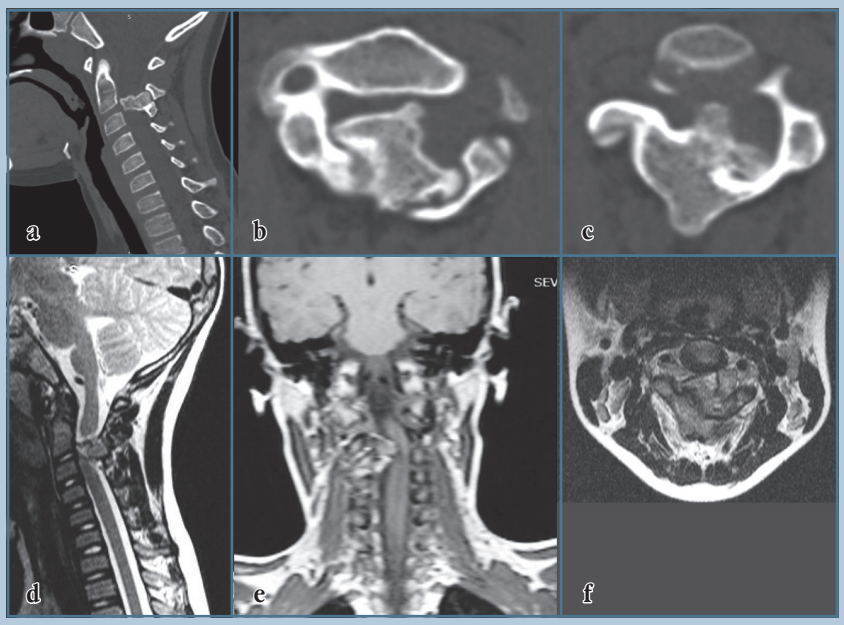

Fig. 1
CT **(a–c)** and MRI **(d–f)** of the cervical spine of the patient M., 7 y.o., before operative treatment (explanations are in the text)

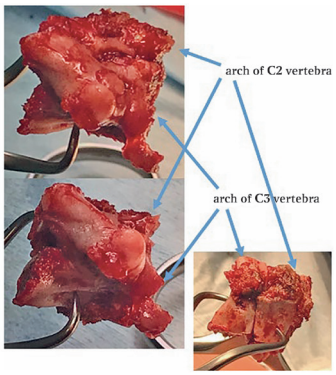

Fig. 2
Macroscopic picture of a tumor resected by a block with fragments of the C2–C3 arches

on the right with resection of the intracranial component. Meanwhile, a marginal defect containing tissue of similar consistency was found in the body of the T2 vertebra. The defect was resected. The operative exploration revealed the spread of bony-cartilaginous outgrowths anteriorly with a decrease in the right hemithorax volume. Resection of the bone block with pathological tissues was performed in an extrapleural manner.

According to the analysis of histological specimens, the pathological tissue was determined as chondroma (Fig. 6).

After 14 days, the lesion of the proximal metaphysis of the right humerus, histologically verified as chondroma, was resected (Fig. 7). No signs of malignancy were found in the resected specimens.

Against the background of a rapid and almost complete regression of neurological symptoms and pain syndrome, the patient was discharged within two weeks under the supervision of an orthopedist and a neurologist at the place of residence. The patient has no signs of recurrence of tumors or the onset of any new complaints for up to 12 months after surgery. Regrettably, the touch with the patient was subsequently lost.

Fig. 3
Postoperative radiological **(a–h)** and clinical **(i–l)** studies of the cervical spine of the patient M., 7 y.o.: lateral X-ray, day 3 after surgery **(a)**; sagittal **(b)**, axial **(c)** sections and 3D CT **(d)** in a month after the surgery; sagittal **(e)** and coronary **(f)** MRI sections; axial **(g)** and sagittal **(h)** CT sections a year after the surgery; photos **(i–l)** showing the complete recovery of movements of the cervical spine (2 years after the surgery)

Discussion

The main reason for enchondromatosis is unknown. The presence of changes (mutations) in the *IDH1*, *IDH2,* and *PTHR1* genes associated with Ollier disease and Maffucci syndrome, has been proven. Simultaneously, in Ollier disease (OD, OMIM 166000), the mutation is present only in the enchondromas. It is caused by somatic mosaicism. It means that the mutation is detected only in part and not in all cells [8].

Previously, it was believed that the disease mainly affects girls [1, 8, 15, 16]. Currently, not only the identification of enchondromatosis in 2.4–5.0 % of all primary tumors and skeletal dysplasia in adults has been proven, but also the predominant detection in men with the possibility of almost half (48 %) cases of malignancy of one or more nidus. It is considered that the growth of lesions or the onset of pain syndrome as signs of malignancy [2, 11, 18]. In women, a combination of the disease with tumors of the ovarian genital cord is possible [8, 19].

In 13 % of cases, the disease manifests itself in the first year of life with neoplasms in the extremities, deformity, limitation of motion, shortening of bones, gait disturbances, pain, and the abolition of function [20]. Pathological fractures may arise [4, 9, 15].

According to the number of affected bones, there are monostotic, oligostotic,

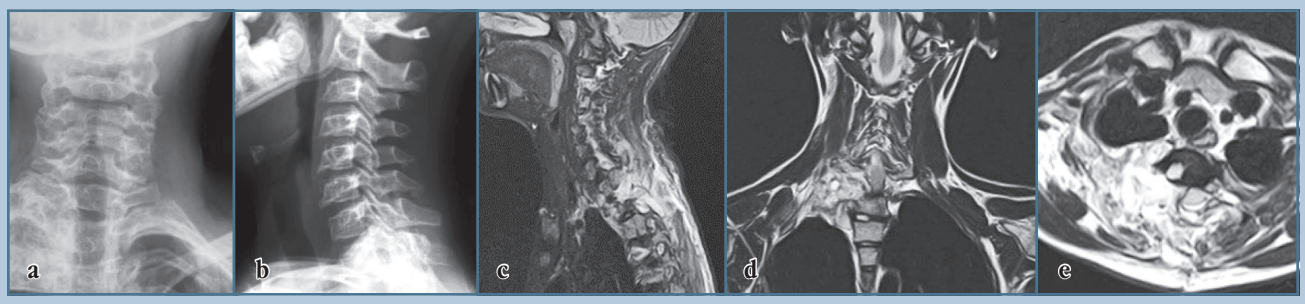

Fig. 4
X-rays **(a, b)** and MRI **(c–e)** scans of the cervical and upper thoracic spine of the patient A., 11 y. o.: lesion at the C7–T2 level on the right, spreading in the paravertebral manner, occupying the upper hemithorax and narrowing the spinal canal

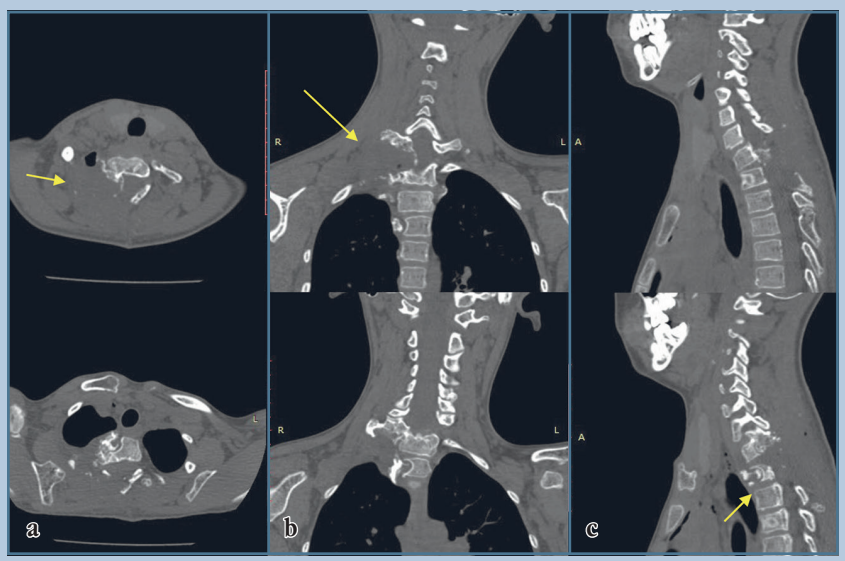

Fig. 5
Axial **(a)**, coronary **(b)** and sagittal **(c)** CT sections of the cervical spine of the patient A., 11 y.o.: pathological lesion with structureless bone inclusions deforming the vertebrae and spinal canal

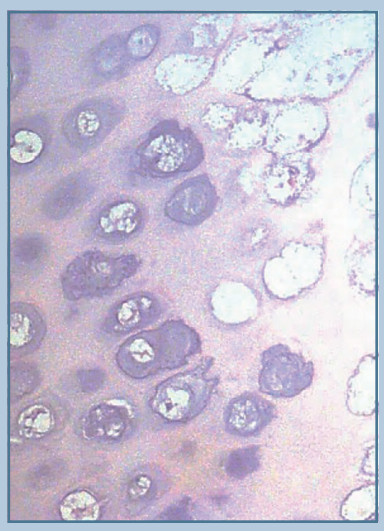

Fig. 6
A section of hyaline cartilage with moderate anisocoria of cartilage cells: hematoxylin and eosin stain, mag. 200

and polyostotic lesions. A.A. Arenberg's classification suggests the identification of four forms according to the localization of the lesion [17]:

1) acroform – lesion of small bones of the distal segments of the extremities (hands, feet);

2) a monomelic variant – a lesion of the bones of one limb with an adjacent part of the shoulder girdle or pelvis;

3) unilateral or predominantly unilateral form; foci are localized on one side, or there is significant inequality of the lesion with the predominant involvement of one half of the body;

4) bilateral form (the most common); areas of cartilage are found in both halves of the body; they are usually located asymmetrically.

Lesions of the peripheral skeleton (metaphyses of long tubular bones, the pectoral and pelvic girdles) are typical of the disease, while in the axial skeleton the ribs are affected more often (18 %) [10, 15, 20–24]. Extremely rarely (less than 6 %) the spine is affected, which is accompanied by severe deformities [11, 14], including fatal complications due to hypoventilation and pneumonia [25].

Treatment of the disease poses significant difficulties, especially with large deformities, multiple foci, and rare localizations, which include the spine. There is no pathogenetic therapy. In the onset of pain, neurological disorders, and signs of malignancy, surgical treatment

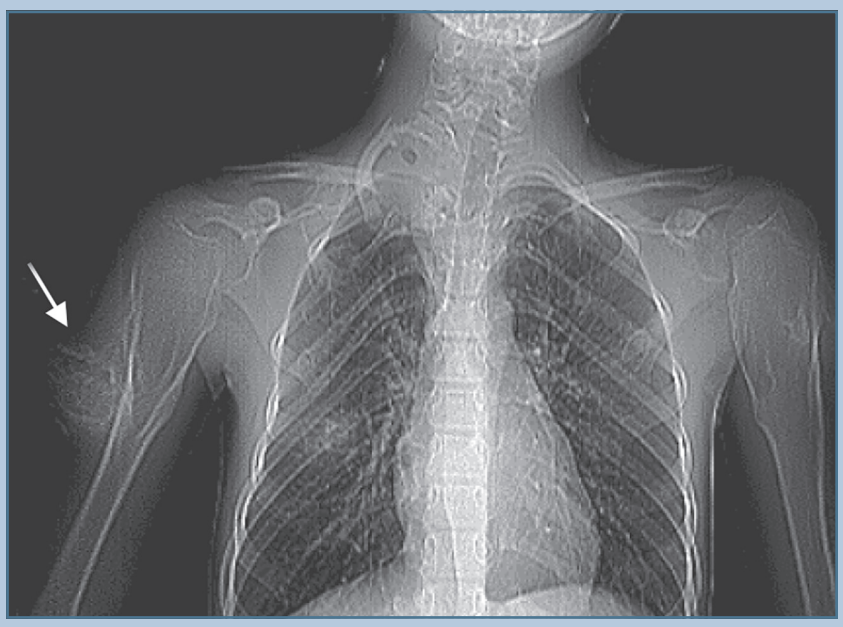

Fig. 7
Extraosseous lesion of the proximal metaphysis of the right humerus (indicated by an arrow) associated with deformation of the proximal parts of both shoulder bones

is the only effective option. Nevertheless, the variety of clinical manifestations of enchondromatosis and its complications does not provide clear algorithms for the management of such patients. In addition, the disease prognosis is difficult to evaluate due to the wide clinical variability [8, 22, 23].

The given clinical examples illustrate some features of a spinal lesion in this pathology:

1) the disease can occur both in the form of an isolated focus with a significant bone component and associated with multiple non-ossifying lesions; it mostly corresponds to the typical Ollier disease;

2) apparently, the localization of enchondromas in the cervical spine is not exclusive: this is evidenced by the clinical observations of colleagues [11, 14]. We consider that this may be due to the anatomical features of this area, suggesting peculiar mechanisms of segmentation disorders with a large number of zones of interstitial cartilage formed during embryogenesis. These cartilages, respectively, become a potential source of formation of enchondromas;

3) intracanal growth of enchondromas results in compression of the dural sac and neural structures which requires decompression; the tumor localization affects the extent of the surgery. In case 1, radical removal with decompression surgery of the dural sac was sufficient to achieve a good long-term clinical and functional result, even though there was no instrumental fixation of the upper neck. In case 2, the features of the process distribution (intracanal location of the tumor with spread to the stellate ganglion zone) when planning the volume of surgery were aimed at improving the neurological status.

Conclusions

Supervision and treatment of children with bone enchondromatosis do not currently have a clear sequence of actions. The patients are under the care of a pediatrician, oncologist, geneticist, and orthopedist. The latter usually decides on the tumor resection. Indications, timing, and scope of surgical treatment are defined individually, depending on the size, localization, number of enchondromas and their complications, and the tendency of nodes to become malignant (secondary chondrosarcomas). As can be seen from our data and other papers, when the cervical spine is affected, indications for surgery are usually caused by an increasing pain syndrome, deformity, and neurological disorders. This means that they are practically urgent. Most of them are primarily caused by compression syndrome. In this regard, decompression should be the priority goal of such surgeries. In these cases, a limited laminectomy without affecting the intervertebral joints may not require additional stabilization of the spine. Nonetheless, with a significant destabilization of the posterior column of the cervical spine, the need for its implementation should hardly be doubted.

The study had no sponsors. The authors declare that they have no conflict of interest.

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Address correspondence to:
Malamashin Denis Borisovich
St. Petersburg Research Institute of Phthisiopulmonology,
32 Politekhnicheskaya str., St. Petersburg, 194064, Russia,
malamashin@mail.ru

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Denis Borisovich Malamashin, MD, PhD, orthopedic surgeon, senior researcher, Clinic of Pediatric Surgery and Orthopedics, St. Petersburg Research Institute of Phthisiopulmonology, 32 Politekhnicheskaya str., St. Petersburg, 194064, Russia, ORCID: 0000-0002-7356-6860, malamashin@mail.ru;
Aleksandr Yuryevich Mushkin, DMSc, Prof., chief researcher, Head of the Scientific and Clinical Centre for Spinal Pathology, Head of the Clinic of Pediatric Surgery and Orthopedics, St. Petersburg Research Institute of Phthisiopulmonology, 32 Politekhnicheskaya str., St. Petersburg, 194064, Russia; Professor of the Department of traumatology and orthopedics, Pavlov First Saint Petersburg State Medical University, 6–8 L'va Tolstogo str., St. Petersburg, 197022, Russia, ORCID: 0000-0002-1342-3278, aymushkin@mail.ru;
Dmitry Aleksandrovich Glukhov, postgraduate student, orthopedic surgeon, St. Petersburg Research Institute of Phthisiopulmonology, 32 Politekhnicheskaya str., St Petersburg, 194064, Russia, ORCID: 0000-0002-6880-8562, dmitriy.a.glukhov@gmail.com;
Viktor Pavlovich Snishchuk, neurosurgeon, chief external expert for pediatric neurosurgery of the Leningrad Region Healthcare Committee, Leningrad Regional Children's Clinical Hospital, 6 Komsomola str., St. Petersburg, 195009, Russia; St. Petersburg Research Institute of Phthisiopulmonology, 32 Politekhnicheskaya str., St. Petersburg, 194064, Russia, ORCID: 0000-0003-0933-8502, v_p_s@list.ru.