KYPHOSCOLIOSIS CAUSED BY LYMPHANGIOGENIC FORM OF GORHAM – STOUT DISEASE WITH AXIAL SKELETAL LESION

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The paper presents a clinical observation of a child with lymphangiogenic form of spontaneous osteolysis (Gorham – Stout disease) associated with massive destruction of the rib cage and progressive kyphoscoliotic deformity. Staged surgical treatment under the therapy with osteoclast inhibitors resulted in the deformity correction and significant improvement in the quality of life. The prognosis remains unclear due to the risk of osteolysis progression.

Key Words: spontaneous osteolysis, children, Gorham-Stout disease, GSD, hylothorax, kyphoscoliosis, osteoclast inhibitors.

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Many rare skeletal diseases have become better understood due to advance in the medical science. Publications dealing with this issue increasingly more often go beyond the mere description of pathology: now it is possible to not only passively observe the natural course of the disease, but also to evaluate the effect of selective therapy, which provides at least inhibition of the process, if not cure. However, orthopedic complications of these diseases are an independent serious medical problem.

A few years ago, a group of researchers including one of the authors of this article published the literature review and their own clinical observation of spine lesions in a patient with the gemangiogenic form of the spontaneous osteolysis or Gorham – Stout disease, GSD) [1]. Vascular embolization relieved pain and enabled avoiding active surgical manipulations in a 14-year-old girl, and the subsequent targeted treatment with osteoclast inhibitors for three years showed the long-lasting stabilization of the process and its asymptomatic course.

The new case is characterized by lymphangiogenic pathology of the axial skeleton in a GSD patients with massive involvement of the spine and rib cage in the process.

Patient S., 8 years old, was admitted to the pediatric surgical clinic of the St. Petersburg Research Institute of Phthisiopulmonology (StPIP) complaining of the deformity of the spine and rib cage. A child was born from the second pregnancy, which was accompanied by gestational pyelonephritis and anemia. Perinatal period was uneventful (first labor at the gestational age of 40 weeks, birth weight 3410 g, length 53 cm, vaccinates), the development corresponded to the age at least up to 1.5 years, but during this time period the patient had several episodes of SARS complicated by obstructive syndrome.

Pediatric surgeon was consulted at the age of 1 year 8 months (30.09.2009) due to the pathology discovered during X-rays examination for SARS, which was considered as hypoplasia of the rib VII on the left. X-ray control in 4 months (13.01.2010) showed more clear picture of hypoplasia of the rib VII on the left with pronounced pulmonary pattern enrichment, reduced volume of the left lung field, abnormal structure of the left pulmonary hilum, and reaction of the paracostal pleura, which was classified as a pleural effusion.

The patient's overall state worsened, there were symptoms of SARS and obstructive syndrome, and the child was admitted to Pediatric Pulmonology Department of the Republican Hospital at the place of residence, where he was first diagnosed with the left-sided pleuritis and then spontaneous chylothorax on the left (Fig. 1a, b). Rib cage pathology was regarded as Poland's syndrome with hypoplasia of the ribs VI–VII–VIII on the left with underlying type IV Ehlers-Danlos syndrome (no genetic research has been conducted, diagnostic criteria apparently included grade I–II scoliosis, grade I insufficiency of the mitral and tricuspid valves, and false cords of the left ventricle.

Patient's state progressively worsened and chylothorax increased after ineffective drainage of the pleural cavity on the left (13.01.2011). For this reason, revision of the thoracic cavity and ligation of the thoracic lymphatic duct on the left was carried out through the thoracotomic approach (26.01.2011) followed by thoracotomy, ligation of the thoracic lymphatic duct on the right after another 2 months (04.03.2011). Antibacterial therapy was carried out. Control examination (03.05.2011) showed US signs of liquid in the pleural cavity on the right (not less than 121 ml) and left (up to 8 ml). Child's mother refused further treatment.

Later on, orthopedist was consulted at the place of residence with complaints of spinal and thoracic deformity. The child was admitted to several federal medical institutions. No radiopharmaceutical hyperfixation was observed during osteoscintigraphy, spondylograms (29.12.2014) showed kyphoscoliotic deformity with the left-sided scoliotic arch of 88° and a kyphosis of 83° with the apex at T6. The pathology was regarded as a lymphangiogenic variant of the Gorham-Stout disease with progressive destruction (resorption) of the ribs and progressive kyphoscoliosis (Fig. 1c). Interdisciplinary consultation decided to administer osteoclast inhibitors followed by operation. The patient received two courses of pamidronic acid drugs (Pamidronate Medac) at a dose of 30 mg for 3 days (90 mg per cycle) repeated every 3 months. During this treatment, osteolysis did not worsened. However, progression of spinal deformity was observed.

In March 2015, the patient was admitted to the pediatric surgical clinic of the StPIP with the diagnosis of Gorham-Stout syndrome (lymphangiogenic osteolysis) for operation. Complications included osteolysis of the ribs VI–VII–VIII on the left; grade IV progressive left-sided thoracolumbar kyphoscoliosis (Fig. 1, 2). There was pronounced body imbalance in the frontal plane: the boy had to tilt his head to the left in order to maintain vertical position. Adaptive capabilities were dramatically reduced, the boy was hardly capable of walking a few minutes within the department. Since the patient had

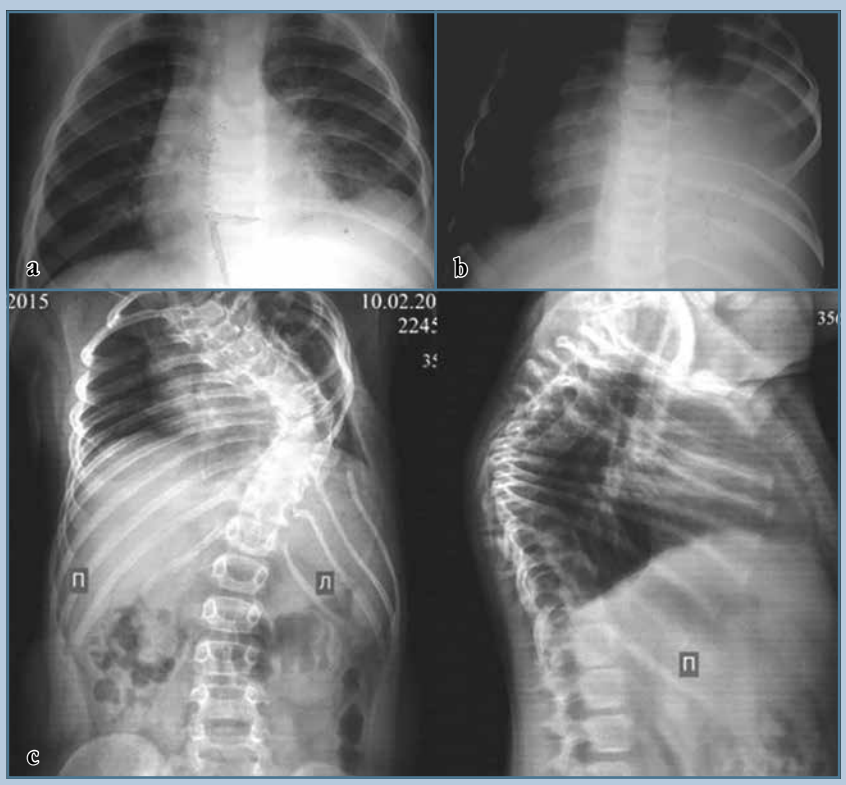

Fig. 1
Survey radiographs of the ribcage of patient S. at the age of 1 year 7 months **(a)**, 3 years **(b)** and spine at the age of 7.5 years **(c)**: initially detected blurred contour of the rib VII on the left **(a)** later on transforms into its complete disappearance and thinning of the ribs VII and IX with the left-sided chylothorax **(b)**, development of severe combined deformity with the apex at T6; **(c)** — left-sided scoliotic curve T3—T11 — 88°, thoracic kyphosis T4—T8 — 83°

asymmetric defect of the framing function of the rib cage with underlying progradient lysis of the ribs VI–VII–VIII on the left, which is a contraindication to the use of spinal brace therapy and thoracoplasty, and high age-related growth capacity, we decided to perform a palliative surgery, posterior unilateral instrumented spinal fixation with a dynamically adjustable system. The operation was performed on the 09.04.2015 (Fig. 3a).

1. Posterior hybrid instrumented correction of thoracolumbar spine with the transpedicular fixation using a Domino-type connector (CD Horizon Legasy 4,5 tools) and 3-level Luque sublaminar fixation in the subapical segments.

2. Open biopsy of the soft tissue of the posterior surface of the left portion of the rib cage (at the area of resorbed ribs).

The attempt to separate vertebral arches at the apex of the deformity showed that they are strongly porous and unsuitable for the use of any supporting elements.

Histological study of the operational material showed soft tissue having typical structure. No increase in VEGF (vessel endothelial growth factor) level was detected.

The child received four courses of therapy with pamidronic acid throughout the year under the supervision of cardiorheumatologist.

The patients was re-hospitalized in March 2016 for the staged correction of

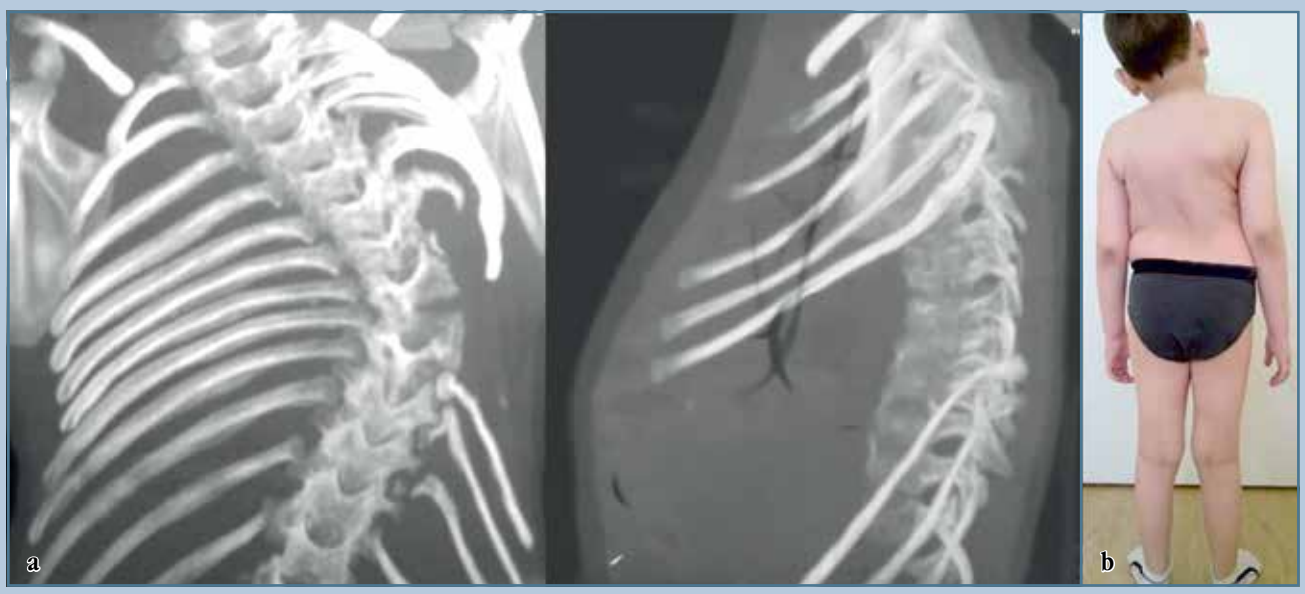

Fig. 2
3D-CT of the spine and thorax **(a)** and appearance of patient S. **(b)** at the age of 7.5 years: total resorption of the ribs VI–VII–VIII on the left, spine deformity, pronounced body imbalance in the frontal plane, the child had to tilt his head to the left in order to maintain vertical position

spinal deformity. There were no subjective complaints at admission, the child's condition was satisfactory. Despite the reduced exercise tolerance, there was a significant increase in adaptation capabilities: boy could walk almost without restrictions. Local signs: moderate body disproportion, including rib cage and thoracic spine deformity. Hypertrophic postoperative scars. Lower limbs, D < S by 1.0 cm, active and passive joint movements are not restricted and painless.

Staged correction of scoliotic deformity: distraction in the Domino system was made on 04.03.2016 (Fig. 3b). The postoperative period was uneventful. The wound healed by primary intention. The treatment with osteoclast inhibitors was continued at the place of residence for 10 months. During this time, the boy grew by 6 cm, there were no radiological signs of continued osteolysis. Staged remounting of the posterior metal structures is planned.

Discussion

Basic data about the modern interpretation of Gorham's disease were described in the Spine Surgery journal a few years ago [1]. It is a rare disorder, whose location is usually limited to spontaneous bone(s) resorption area [4]. It is based on VEGF hyperproduction, leading to uncontrolled proliferation of vascular endothelial cells (blood and/or lymphatic) with gradual replacement of bone tissue with connective one, which is accompanied by bone resorption with underlying increase in blood or lymph inflow, altered tissue pH, and other cascade mechanisms. Overproduction of VEGF was not confirmed in our case, which however does not contradict the diagnosis, since this examination result is quite possible at different stages of the disease and in different tissues [6, 8].

Clinical presentation of the GSD is variable and is directly related to location and type of the pathology [1]. Disease symptoms are nonspecific, the most typical signs include local pain and, more rarely, swelling and dysfunction of the involved portion of the segment. The disease may be asymptomatic and present with complications, such as tooth loss, pathological fracture, neurological deficit and deformities, when the spine is involved [3, 8]. Respiratory failure (respiratory distress syndrome) is usually associated with the development of chylothorax with involvement of the rib cage and thoracic lymphatic duct. Relatively rare development of elephantiasis with dilatation of the regional lymph vessels is observed in the case of involvement of the peripheral bones [5, 6].

So far, there is no common approach to the treatment of GSD patients and tactics are chosen depending on the severity and spread of the process.

Surgical techniques are used in the case of intrathoracic complications (chronic or recurrent chylothorax), necessitating pleurectomy, thoracentesis, ligation and/or embolization of the thoracic duct [3, 8].

Orthopedic surgical treatment is usually necessitated by the loss of the supporting ability of extremities. In this case, it is advisable to perform stabilization

and reconstruction of the involved segments in the stable phase of the disease, anticipating the possibility of osteolysis progression [3, 7, 8]. Rachiopathy is not common in GSD patients, but it is not casuistic as well (more than 10 % of cases). However, the issues of its treatment are not separately covered in publications.

The available literature data on the possible options of medical treatment for GSD (with bisphosphonates, genetically engineered drugs, interferon alfa-2, etc.) were summarized above [1], but the mere fact that there are such a diverse approaches rather indicates that it is a test therapy. In our study, inhibition (arrest?) of bone resorption process was due to the use of selective osteoclast inhibitors. Therapy with these drugs proved to be effective and will be continued.

As for the vertebral syndrome, in our opinion, the situation may develop in two directions in the following years:

– we deliberately have not used true dynamic VEPTR systems for spine fixation, since they are directly contraindicated in patients with severe kyphosis and unpredictable state of the rib cage carcass: if the supporting ability of the vertebrae above and below the resorption area is preserved, staged remounting of the metal structures may require spine strengthening with the second system on the contralateral side;

– if resorption of the ribs and vertebrae starts progressing, it will result in quite a difficult situation. In this case, the course of the disease will determine, whether the problem will be solved surgically by orthotics, external fixation (HALO-pelvic), or in any other way.

We leave this issue for possible discussion on the pages of the journal and for the analysis of long-term follow-up results.

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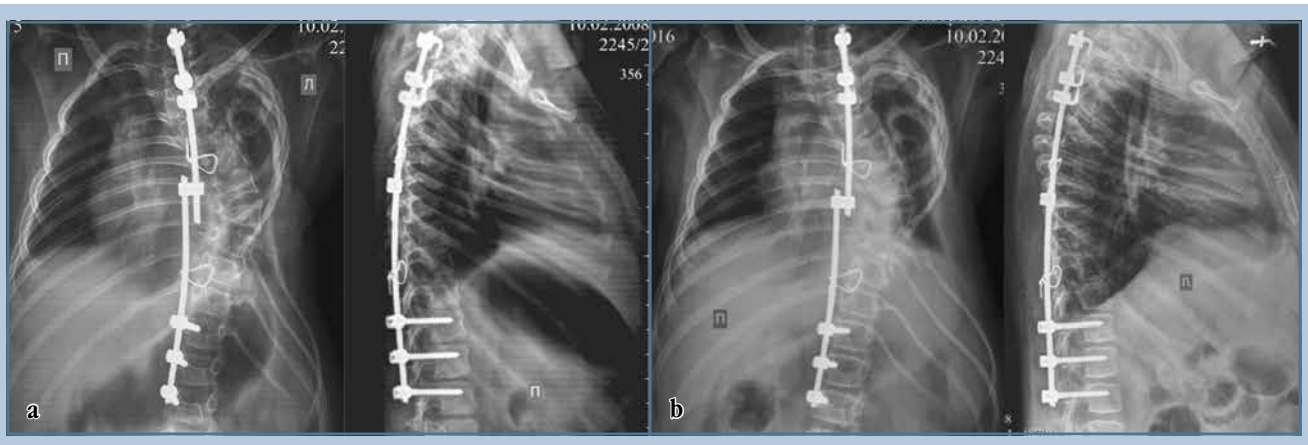

Fig. 3
Staged radiographs of the spine of patient S. immediately after the unilateral posterior instrumented hybrid correction with Domino-type connector (CD Horizon Legasy 4,5 tools) and 2-level Luque fixation in the subapical segments **(a)** and staged distraction performed in 10 months **(b)**: apart from preserved correction and missing ribs, staged control shows blurred structure of the apical vertebrae along with the absence of bone resorption around the lower bearing screws

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