The vertebral syndrome in various types of mucopolysaccharidosis: clinical features and treatment

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The paper presents recommendations on the assessment and treatment of vertebral pathology in patients with various types of mucopolysaccharidosis. The recommendations are based on literature data and the authors’ own experience. The purpose of the publication is an invitation to the discussion in the format of an expert consensus.

Key Words: mucopolysaccharidosis, vertebral syndrome, spinal pathology.

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The opportunities of targeted therapy have attracted attention not only to mucopolysaccharidosis (MPS) but also to growing trends in improving the quality of life, in particular due to timely neurosurgical and orthopedic interventions.

More than a year and a half has passed since the establishment of an inter-rater group for treating MPS patients within the Association of Traumatologists and Orthopedists of Russia. Now, it is time to review the preliminary results.

We briefly describe the main tasks faced by the group’s experts:

1) recruitment of a multidisciplinary team of experts (geneticists, pediatricians, general practitioners, orthopedists, neurosurgeons, anesthesiologists, neurologists, rehabilitation physicians) to assess the syndromic status of the entire nosologic group and a particular patient; substantiation of rehabilitation approaches, including the surgical one;

2) preparation of a federal clinical guidelines draft;

3) coordination of interdisciplinary patient logistics;

4) planning of multicenter and survey studies based on intra- and inter-rater assessment.

At the 11th All-Russian Congress of Traumatologists and Orthopedists of Russia held in Saint-Petersburg, April 11–13, 2018, there was a second round table discussion on syndromic assessment of the status of MPS patients and aspects of early diagnosis and approaches in treatment of the orthopedic pathology. The presented paper is the first product of the expert group. The authors will gratefully welcome all comments and suggestions.

General methodology of guidelines

The clinical guidelines on the diagnosis and treatment of spinal pathology in different MPS types were developed by a group of experts based on the evidence-based medicine principles. Information was searched in the Medline (Pubmed version), Embase (Dialog version), and Cochrane Library electronic databases, based on a systematic review of the literature, using, in particular, a consensus of study’s author opinions.

MPS belongs to the group of orphan diseases, which excludes large cohort and randomized studies; therefore, only expert opinions published within the last two decades can be used to develop protocols for the diagnosis and treatment of spinal disease.

Design

An analysis of publications devoted to this problem demonstrated that almost all of the publications were based on series of clinical cases. No studies that might be attributed to an ASMOK (Association of Medical Societies for Quality of Medical Care and Education) level exceeding 2+ and to I or II evidence level were found. Accordingly, all guidelines in this document are of evidence level C or less.

The purpose of this study is to develop the algorithm for treatment of vertebral syndrome in patients with different types of MPS.

The paper is presented mainly in the form of tables for the most vivid presentation of the material. We have already used this form, and, in our opinion, it is very convenient for perception and practical application. The features of selection and analysis of the material are deliber-ately not considered in the presented guidelines.

Methods used to assess the quality and strength of evidence are as follows:

– consensus of experts;

– assessment of the evidence level in accordance with a rating scheme (Table 1).
Definitions and classification

MPS is a group of complex heterogeneous progressive diseases caused by deficiency of lysosomal enzymes involved in the glycosaminoglycan degradation pathway [1]. Depending on the deficiency in one of the 11 lysosomal enzymes (chondroitin sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, and/or hyaluronate), seven main MPS types are distinguished (Table 2). The manifestations are associated with impaired utilization and accumulation of glycosaminoglycans in lysosomes of cells in all organs [2]. According to the international classification of hereditary skeletal diseases [3], all MPS types belong to the group of lysosomal storage diseases involving the skeleton (multiple dysostosis).

Multisystem phenotypic symptoms. Products of abnormal metabolism cause physical development delay, coarsening of facial features, mental retardation, skeletal dysplasia, hepatosplenomegaly, frequent respiratory infections leading to respiratory failure, cardiovascular disorders, eye diseases, hard hair growth, and changes in the skin [4, 5]. All MPS types, except for, probably, MPS III, are associated with these somatic symptoms.

Neurocognitive disorders (including mental deficiency, adaptive behavior and motor skill learning, impaired attention and memory, delayed speech development), which are usually associated with sleep disorders and epileptic seizures that often occur in MPS III, can also be observed in patients with MPS I, II, and VII [6].

Secondary neurological symptoms, often in the form of motor deficit, develop in the following cases [7–10]:

1) in stenosis at the foramen magnum level with spinal cord compression, hydrocephalus, and Chiari I malformation;
2) in kyphotic (kyphoscoliotic) deformity of the thoracolumbar spine, often resulting in vertebromedullary conflict;
3) in peripheral nerve lesions associated with tunnel syndromes (the most common manifestation is carpal tunnel syndrome).

Treatment of these symptoms usually involves surgery. The clinical and radiological features of vertebral syndrome in MPS are as follows [17–25]:

- underdevelopment of the axial muscles;
- increased physiological kyphosis;
- disc protrusion, anterior disc herniation;
- hypoplasia, wedging of the apical vertebrae;
- hypermobility of spinal motion segments;
- progressive kyphosis/kyphoscoliosis at the thoracolumbar junction level;
- cervical stenosis (untypical of MPS type III and VII).

The clinical and radiological features of cervical stenosis in MPS are as follows:

- laminar hypoplasia (especially in C1);
- thickening of soft tissues in the craniovertebral junction area (dura mater, ligaments, cellular tissue);
- dysplasia/hypoplasia, odontoid retroflexion;
- C1–C2 instability;
- true spinal stenosis;
- foramen magnum stenosis;
- spinal cord compression;
- disc protrusion;
- syringomyelia, Arnold-Chiari I malformation;
- combination of factors.

Dysplasia/hypoplasia, odontoid retroflexion, and C1–C2 instability cause segmental instability [8, 10, 16–18, 26–28].

A review of spinal changes in MPS, which are able to cause secondary neurological manifestations, is presented in Table 3.

The objectives and basic principles of conservative treatment of children with different MPS types are presented in Table 4.

The follow-up protocol for patients with MPS is provided in Table 5.

The system for assessment of cervical spinal cord compression to determine the indications for surgery in patients with MPS type VI, based on the clinical neurological status, somatosensory
The basic principles and surgical treatment approach for spinal pathology in MPS are presented in Tables 7 and 8.

Fig. 1 shows the surgical treatment approach for spinal pathology in patients with different types of MPS. Surgical correction of spinal pathology in MPS is performed with allowance for the features of vertebral syndrome (Table 9).

**Limitations to the use of guidelines for surgical treatment of spinal pathology in MPS**

The main purpose of the described approaches is to preserve the patient's motor activity, quality of life, and social adaptation. Therefore, the main contraindications to complexity of positioning with head fixation application of the guidelines include:

- compromised concomitant pathology, including that caused by the underlying disease, which is life-threatening or having significant limitations for the expected survival period;
- communication gap with parents regarding the goal of an oriented treatment strategy;
- infectious processes in the exacerbation period.

**Conclusion**

Spinal pathology is one of the leading syndromic manifestations of MPS. The spinal dysmorphism syndrome complex includes three typical syndromes: stenosis of the craniovertebral junction, most typical of MPS type I, II, and VI; craniovertebral instability (which is often combined with stenosis) in MPS type IV; and kyphosis/kyphoscoliosis in MPS type I, IV, and VI.

A key component of early screening for vertebral syndrome is assessment of the patient's neurological and motor status. The most accepted tools are the modified scale of the Japanese Orthopaedic Association (mJOA), Nurick scale, 6-minute walk test, and 3-minute stair climb test.

Deterioration of the neurological status and quality of life in the setting of confirmed stenosis and instability as well as progression of spinal deformity underlie prognostically vital indications for surgical correction.

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**Table 2**

| Type/syndrome          | Clinical manifestations                                                                                                                                 |
|------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| MPS I/Hurler           | Multiple dysostosis, disproportionate dwarfism, multiple contractures in joints, carpal canal syndrome, os odontoideum, atlantoaxial instability, acetabular dysplasia, *cova valga bilateralis*, genu valgum, stenosing ligamentitis |
| MPS I/Hurler-Scheie, Scheie | More mild manifestations of Hurler syndrome                                                                                                               |
| MPS II/Hunter          | Multiple dysostosis, disproportionate dwarfism, multiple contractures in joints, carpal canal syndrome, os odontoideum, atlantoaxial instability, acetabular dysplasia, *cova valga bilateralis*, genu valgum, stenosing ligamentitis |
| MPS III/Sanfilippo     | Only mild somatic manifestations, subnanism, moderate contractures (mainly in the elbow joints)                                                          |
| MPS IV/Morquio         | Severe skeletal dysplasia, multiple dysostosis, disproportionate dwarfism, hypermobility of joints, os odontoideum, atlantoaxial instability, *cova valga bilateralis*, acetabular dysplasia with impaired hip joint relationships, genu valgum, foot deformities, chest deformities |
| MPS VI/Maroto-Lamy     | Multiple dysostosis, disproportionate dwarfism, contractures in joints, carpal canal syndrome, os odontoideum, atlantoaxial instability, acetabular dysplasia, *cova valga bilateralis*, genu valgum, stenosing ligamentitis, chest deformity |
| MPS VII/Sly            | Multiple dysostosis, disproportionate dwarfism, contractures in joints, os odontoideum, atlantoaxial instability, acetabular dysplasia, chest deformity |
| MPS IX/hyaluronidase deficiency | Subnanism, periarticular hypertrophy, nodular synovial masses with effusion in joints, acetabular erosion                                                      |
Decompression and occipital-cervical fusion are indicated in patients with instability and stenosis at the craniovertebral junction level.

Stable segment-by-segment fixation of the spine is indicated for local kyphotic/kyphoscoliotic curves, within five spinal motion segments.

Spinal fixation by dynamic systems is preferable for extended spinal deformities.

The guidelines do not concern the possibility of age and interdisciplinary continuity, detailed planning of the treatment approach with assessment of a perioperative risk, and desire to solve orthopedic and neurosurgical tasks within one session. These circumstances underlie the need for multidisciplinary and multicenter studies.

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### Table 3
Spinal changes in mucopolysaccharidosis (MPS) [17–25, 29–30]

| Type of MPS/syndrome | Craniovertebral stenosis | Occipital-cervical instability | Thoracolumbar kyphosis | Scoliosis |
|----------------------|--------------------------|-------------------------------|------------------------|----------|
| MPS I/Hurler         | ++*                      | +                             | ++                     | +        |
| MPS I/Hurler-Scheie, Scheie | ++                    | –                             | +                      | +        |
| MPS II/Hunter        | ++                      | –                             | +                      | +        |
| MPS IV/Morquio       | +                       | +++                           | +                      | +        |
| MPS VI/Maroto-Lamy   | +++                     | +                             | ++                     | +        |

* Without bone marrow transplantation (+ for patients after transplantation of hematopoietic stem cells).

### Table 4
Objectives and basic principles of conservative treatment of children with different types of mucopolysaccharidosis [31–34]

| Improvement of neurological condition* | Anticholinesterase drugs, anticonvulsants, dehydration. Currently, there is no effective treatment of neurological complications |
|---------------------------------------|--------------------------------------------------------------------------------------------------|
| Improvement of orthopedic status      | Corset therapy, massage, exercise therapy, orthotics, orthopedic correction of pathological arrangements, contractures, etc. |
| Social adaptation**                   | Physical and functional rehabilitation, training to use assistive devices — verticalizers, braces, devices |

* The most valid tools for assessing the neurological status of patients with different types of mucopolysaccharidosis are the modified scale of the Japanese Orthopedic Association (mJOA), Nurick scale, 6-minute walk test, and 3-minute stair climb test.

** Scored integrative assessment of disabilities and role limitations is often performed using the Functional Independence Measure (FIM) scale.

### Table 5
The recommended protocol to follow-up patients with different types of mucopolysaccharidosis [8, 17, 36–39]

| Examination                                                | Examination rate |
|------------------------------------------------------------|------------------|
| Clinical examination by a neurologist and an orthopedist   | 6 months         |
| X-ray of the cervical spine (upright and lateral projections, flexion, extension) | 2 to 3 years |
| X-ray of the thoracic and lumbar spine with involvement of the hip joints (upon progression) | 2 to 3 years (every 6 months) |
| MRI of the cerebral and spinal conductive pathways (tractography, if possible) | 1 year |
| Functional MRI of the cervical spine with flexion and extension | 1–3 years |
| CT of the craniocervical junction + cervical + thoracic + lumbar spine + CT of the upper respiratory tract and lungs | Before surgery |
Table 6
The system for assessment of spinal cord compression at the craniovertebral junction level to decide the need for surgical treatment [35]

| Score | Test results |
|-------|--------------|
|       |              |

Clinical neurological examination

0  -- normal neurological findings;
1  -- increased/decreased tendon reflexes, lateral differences in muscle reflexes;
2  -- pyramidal tract signs: Babinski reflex, Gordon reflex, Oppenheim reflex, muscle twitching;
3  -- paresis or weakness of the upper and/or lower limbs

Somatosensory evoked potentials of the median nerve

0  -- normal;
1  -- prolongation of at least one of the interpeak latencies: N9/P13, N9/N13b, or N13a/N20 (> 2.5 SD)*;
2  -- lack of P13 and/or N13b (subcortical);
3  -- lack of N20 (cortical)

MRI

0  -- no spinal cord compression;
1  -- spinal cord compression (no CSF in any direction);
3  -- myelomalacia signs

* N9/P13: brachial plexus – caudate nucleus; N9/N13b: brachial plexus – caudate nucleus; N13a/N20: caudal spinal cord – cortex.

Table 7
Basic principles of surgical treatment of spinal pathology associated with different types of mucopolysaccharidosis [40–50]

| Surgical treatment principles                  | Indications                                                                 |
|------------------------------------------------|-----------------------------------------------------------------------------|
| Decompression and stabilization                | Stenosis, instability, and stenosis combined with instability at the craniovertebral junction level, mechanical neurological instability |
| Deformity correction with instrumented stabilization of the spine | Progression of spinal deformity, worsening of somatic and neurological statuses |

Table 8
Surgical treatment approach for spinal pathology in mucopolysaccharidosis [22, 46–47, 50, 61–62]

| Spine region | Deformity correction | Spinal cord decompression |
|--------------|----------------------|---------------------------|
| Cervical     | +/-                  | +                         |
| Thoracic     | +                    | +/-                       |
| Lumbar       | +                    | -                         |
Assessment of the syndromic status and risk of surgical treatment

Discussion of the step-by-step protocol of surgery with assessment of the patient’s functional state (ECG, blood pressure, saturation, RF, blood loss volume) and spinal cord (dynamics of spontaneous somatosensory and motor evoked potentials based on IONM data)

Monitoring of indicators at all surgical stages: after intubation, during turning and positioning, decompression, correction, fixation (depending on surgery type), and extubation

Features of the anesthetic protocol and intensive care:
- IONM before turning after intubation;
- difficulty of positioning with head fixation (Mayfield frame, halo);
- readiness for complex intubation using fiber optics and a video laryngoscope;
- ultrasound monitoring for central venous catheterization;
- postoperative follow-up in the intensive care unit

— possibility of completion at each step;
— coordinated actions of a multidisciplinary team

Fig. 1
Surgical treatment approach for spinal pathology in patients with different types of mucopolysaccharidosis [63–66]: RF – respiratory function; IONM – intraoperative neuromonitoring

Fig. 2
MRI (a) and CT scans before (b) and after (c) surgery in a 6-year-old child with cervical stenosis associated with mucopolysaccharidosis type IV (Morquio A): spastic tetraparesis
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Fig. 3
Appearance and radiological findings of a 3-year-old child with kyphosis associated with mucopolysaccharidosis type IH: a – before surgery; b – structural changes in the apical vertebral bodies; c – signs of spinal cord compression; d – after correction and instrumented fixation of deformity at the T9–L4 level; e – after surgery

Fig. 4
Appearance and radiological findings of a 6-year-old child with scoliotic deformity associated with mucopolysaccharidosis type IVA: a – before surgery; b – after correction and posterior instrumented dynamic fixation of deformity at the T5–L2 level

Таблица 9
Variants of surgical correction for spinal pathology with allowance for vertebral syndrome features

| Spinal pathology                                                                 | Features of orthopedic correction                      |
|---------------------------------------------------------------------------------|--------------------------------------------------------|
| Instability, stenosis, and combination of instability and stenosis at           | Decompression and posterior instrumented fixation      |
| the craniovertebral junction level; foci of myelopathy (Fig. 2)                 | (occipital-cervical fusion)                            |
| Local (no more than five spinal motion segments) spinal deformities, local kyphosis | Stable segmental fixation of the spine                 |
| of more than 20°, and scoliosis of more than 40° (Fig. 3)                       |                                                        |
| Extensive (more than five spinal motion segments) spinal deformities, kyphosis   | Dynamic spine fixation                                 |
| of more than 20°, and scoliosis of more than 40° (Fig. 4)                       |                                                        |
References

1. Muenzer J. Overview of the mucopolysaccharidoses. Rheumatology (Oxford). 2011;50 Suppl 5:v1–v12. DOI: 10.1093/rheumatology/ker394.

2. Clarke LA. Mucopolysaccharidosis Type I. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews(R)(Internet). [Seattle (WA): University of Washington, Seattle, 1993–2019. 2002 Oct 31 [updated 2016 Feb 11].

3. Bonafe L, Cormier-Daire V, Hall C, Lachman R, Mortier G, Mundlos S, Nishimura G, Sangiorgi L, Savarirayan R, Sillence D, Spranger J, Superti-Furga A, Warman M, and NusSMA Study Group. Nosology and classification of genetic skeletal disorders in 2015 revision. Am J Med Genet A. 2015;167A:2869–2892. DOI: 10.1002/ajmg.a.37565.

4. Leone A, Rigante D, Amato DZ, Casale R, Pedone L, Magarelli N, Colosimo C. Spinal involvement in mucopolysaccharidoses: a review. Childs Nerv Syst. 2015;31:203–212. DOI: 10.1007/s00386-014-2578-1.

5. Muenzer J, Beck M, Eng CM, Escolar ML, Giugliani R, Guffon N, Harmatz PR, Kamin W, Kampmann C, Koseoglu SF, Link B, Martin RA, Molter DW, Munoz Rojas MV, Ogilvie JW, Parini R, Ramaswamy U, Scarpa M, Schwartz J, Wood RE, Wraith EH. Multidisciplinary management of Hunter syndrome. Pediatrics. 2009;124:e122–e129. DOI: 10.1542/peds.2008-0999.

6. Shapiro EG, Jones SA, Escolar ML. Developmental and behavioral aspects of mucopolysaccharidoses with brain manifestations – Neurological signs and symptoms. Mol Genet Metab. 2017;125:1–7. DOI: 10.1016/j.ymgme.2017.08.009.

7. White KK. Spinal deformities in mucopolysaccharidosis type I. J Pediatr Orthop. 2010;30:41–48. DOI: 10.1097/bpo.0b013e3181defb34.

8. Lachman R, Martin KW, Castro S, Basto MA, Lammers AE, Hislop AA, Flynn Y, Haworth SG. The beaked, notched, or hooked vertebra: its significance in infants and young children. Radiology. 1994;197:767–765. DOI: 10.1148/radiology.194.4.7657697.

9. Swischuk LE. The beaked, notched, or hooked vertebra: its significance in infants and young children. Radiology. 1976;95:661–664. DOI: 10.1148/95.6.661.

10. Langer LO Jr, Carey LS. The roentgenographic features of the KS mucopolysaccharidosis of Morquio (Morquio-Brailsfords disease). Am J Roentgenol Radium Ther Nucl Med. 1966;97:1–20. DOI: 10.2214/ajr.97.1.1.

11. Tandon V, Williamson JB, Cowie RA, Wraith JE. Spinal problems in mucopolysaccharidosis I (Hunter) syndrome. J Bone Joint Surg Br. 1996;78:958–944. DOI: 10.1302/0301-620X78B6.1279.

12. Berleman U, Jeszenszky DJ, Buhler DW, Harms J. Mechanisms of retrolisthesis in the lower lumbar spine. A radiographic study. Acta Orthop Belg. 1999;65:472–477.

13. Leone A, Giugliemi G, Cassar-Pullicino VN, Bonomo L. Lumbar intervertebral instability: a review. Radiology. 2007;245:62–77. DOI: 10.1148/radiol.2451051359.

14. Levin TL, Berdon WE, Lachman RS, Anyane-Yeboa K, Rual-Shapiro C, Roye DP Jr. Lumbar gibbus in storage diseases and bone dysplasias. Pediatr Radiol. 1997;27:289–294. DOI: 10.1007/s002470051351.

15. Thorne JA, Javadpour M, Hughes DG, Wraith E, Cowie RA. Craniovertebral abnormalities in Type VI mucopolysaccharidosis (Maroteaux-Lamy syndrome). Neurosurgery. 2001;48:489–492. DOI: 10.1227/00006123-200104000-00001.

16. Vougioukas VI, Berlis A, Kopp MV, Korinthenberg R, Spreer J, van Velthoven V. Neurosurgical interventions in children with Maroteaux-Lamy syndrome: Case report and review of the literature. Pediatr Neurosurg. 2001:35:35–38. DOI: 10.1159/000050938.

17. Rigante D, Antuzzi D, Ricci R, Segni G. Cervical myelopathy in mucopolysaccharidosis type IV. Clin Neuropathol. 1999;18:84–90.

18. Mut M, Cila A, Varli K, Akalan N. Multilevel myelopathy in Maroteaux-Lamy syndrome and review of the literature. Clin Neurol Neurosurg. 2005;107:230–235. DOI: 10.1016/j.clineuro.2004.05.003.

19. Tong CKW, Chen JC, Branham DW, Roye DP Jr. Lumbar gibbus in storage diseases and bone dysplasias. Pediatr Radiol. 2001;31:1264–1268. DOI: 10.1007/s002470101522.

20. Nurick S. The pathogenesis of the spinal cord disorder associated with cervical spondylosis. Brain. 1972;95:587–100. DOI: 10.1093/brain/95.1.87.

21. Lammers AE, Hulsop LA, Flynn Y, Haworth SG. The 6-minute walk test: normal values for children of 4–11 years of age. Arch Dis Child. 2008;93(6):464–468. DOI: 10.1136/adc.2007.125653.

22. Harmatz P, Mengel KE, Giugliani R, Vanayannopoulos V, Lin SP, Parini R, Guffon N, Burton BK, Hendrikssz CJ, Mitchell J, Martins A, Jones S, Guelbert N, Vellodi A, Hollik C, Slaor P, Decker C. The Morquio A Clinical Assessment Program: baseline results illustrating progressive, multisystemic clinical impairments in Morquio A subjects. Mol Genet Metab. 2013;109:54–61. DOI: 10.1016/j.ymgme.2013.01.021.

23. Harmatz P, Ketteridge D, Giugliani R, Guffon N, Teles E, Miranda A, Yu ZF, Swidler SJ, Hopwood JP. Direct comparison of measures of endurance, mobility, and joint function during enzyme-replacement therapy of mucopolysaccharidosis VI (Maroteaux-Lamy syndrome): results after 48 weeks in a phase 2 open-label clinical study of recombinant human N-acetylgalactosamine 4-sulfatase. Pediatrics. 2005;115:e661–e689. DOI: 10.1542/peds.2004-1025.
53. Alden TD, Amatino HI, Dalla Corte A, Lampe C, Harms PR, Vedolin L. Surgical management of neurological manifestations of mucopolysaccharidosis disorders. Mol Genet Metab. 2017;123:41–48. DOI: 10.1007/jmgm.2017.09011.

54. Borlot F, Arantes PR, Quiao CR, Franco JF, Louren o CM, Bertolotti DR, Kim CA. New insights in mucopolysaccharidosis type VI: neurodevelopmental perspective. Brain Dev. 2014;36:585–592. DOI: 10.1016/j.braindev.2013.07.016.

55. Charrow J, Alden TD, Breathnach CA, Frawley GP, Hendriksz CJ, Link B, Solanki GA, Alden TD, Burton BK, Giugliani R, Horovitz DD, Jones SA, Yasin MN, Sacho R, Oxborrow NJ, Wraith JE, Williamson JB, Siddique I. The mucopolysaccharidoses: a systematic review. J Inherit Metab Dis. 2014;37:69–78. DOI: 10.1007/s10545-013-9630-2.

56. Whitley CB, Belani KG, Chang PN, Summers CG, Blazar BR, Tsai MY, Bradley WG Jr, Scalzo D, Queralt J, Nitz WN, Atkinson DJ, Wong P. Normal pressure hydrocephalus evaluation with cerebrospinal fluid flow measurements at MR imaging. Radiology. 1996;198:523–529. DOI: 10.1148/radiology.198.2.8596861.

57. Kachur E, Del Maestro R. Mucopolysaccharidoses and surgical cord compression: a report and review of the literature with implications of bone marrow transplantation. Neurosurg. 2000;47:223–229. DOI: 10.1097/00006123-200007000-00016.

58. Lee C, Dineen TE, Brack M, Kirschje J, Rupp M. The runcome VM. Perioperative risk reduction for vertebrologic surgeries in patients with hereditary spinal deformities: mid-term results. J Pediatr Orthop. 2013;95:2957–2963. DOI: 10.1097/BPO.0b013e3182819154.

59. Taylor C, Brady P, O’Meara A, Moore D, Dowling F, Fogarty E. Mobility in Hurler syndrome. J Pediatr Orthop. 2008;28:163–168. DOI: 10.1097/BPO.0b013e3181649e25.

60. Ransford AO, Crockard HA, Stevens JM, Modagheghi S. Occipito-atlanto-axial fusion in Morquio-Brailsford syndrome. A ten-year experience. J Bone Joint Surg Br. 1996;78:397–413. DOI: 10.1302/0301-620x.78b4.780307.

61. Haddad FS, Jones DHA, Yellodi A, Kane N, Pitt MC. Carpal tunnel syndrome in the mucopolysaccharidoses and mucolipidoses. J Bone Joint Surg Br. 1997;79:5756–5782. DOI: 10.1097/0301-620x.78b4.7547.

62. Weisstein JS, Delgado E, Steinbach LS, Hart K, Packman S. Musculoskeletal manifestations of Hurler syndrome: long-term follow-up after bone marrow transplantation. J Pediatr Orthop. 2004;24:97–101. DOI: 10.1097/00004694-200401000-00019.

63. Garriédo E, Torallo-Cervecio F, Adams CI. Combined spinal arthrodesis with instrumentation for the management of progressive thoracolumbar kyphosis in children with mucopolysaccharidosis. Eur Spine J. 2014;23:2751–2757. DOI: 10.1007/s00586-014-3186-1.

64. Dedo O, Thacker MM, Rogers KJ, Otto M, Belthur MV, Baratela W, Mackenzie WG. Upper cervical fusion in children with Morquio syndrome: intermediate to long-term results. J Bone Joint Surg Am. 2013;95:1228–1234. DOI: 10.2106/JBJS.R.01135.

65. Riabykh SO, Shusharina VL, Ochirova PV, Tret’iakova AN, Riabykh TV. Perioperative risk reduction for vertebrologic surgeries in patients with hereditary diseases of the connective tissue. Genij Orthopedii. 2015(4):48–52. DOI: 10.18019/1028-4427-2014-4-48-52.

66. Safiullinov MS, Skripnikov AA, Riabykh SO, Ochirova PV. Score evaluation of intraoperative neurophysiological monitoring results of spinal deformity surgical correction in syndromically caused systemic skeletal pathology. Genij Orthopedii. 2017;23(2):201–205. DOI: 10.18019/1028-4427-2017-3-2-201-205.

67. Pavlova OM, Burtshev AV, Gubin AV, Riabykh SO. Posterior cervical screw fixation in children: the treatment experience. Hir. Povozon. 2017;14(3):27–31. DOI: 10.18019/1028-4427-2017-3-2-27-31.

68. Burtshev AV, Gubin AV, Riabykh SO, Kotel’nikov AO. The vertebral syndrome in various types of mucopolysaccharidosis. IRP: POSYONOMIYA 2019;16(2):81–91.
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