orphanaesthesia

Anesthesia recommendations for

Maroteaux Lamy syndrome

Disease name: Maroteaux Lamy syndrome

ICD 10: E76.2 (Other Mucopolysaccharidoses)

ORPHAcode: 583

Synonyms: Mucopolysaccharidosis Type VI; MPS VI; arylsulfatase B (ARSB) deficiency

Brief disease summary: Maroteaux Lamy syndrome is an autosomal recessive disease caused by deficiency of the lysosomal enzyme n-acetyl galactosamine 4-sulfatase (aryl-sulfatase B) which is involved in glycosaminoglycan (GAG) degradation [1]. Progressive accumulation of dermatan sulfate in nearly all tissues is believed to provoke the clinical symptoms associated with MPS VI. GAGs are an endotoxin-like molecules that incite an inflammatory response via a tumor necrosis factor pathway and promote apoptotic cell death of chondrocytes [2].

Diagnosis may be incorrect; if uncertainty exists, the diagnosis should be re-evaluated.

Every patient is unique; individual circumstances must always guide clinical care.

Medicine is in progress; new clinical knowledge may not be yet reflected in this recommendation.

Recommendations are not rules or laws; they provide a framework to support clinical decision-making. Although this recommendation has passed a structured review process, it does not meet the formal criteria of a guideline.

Translations may not always reflect the most recent updates of the English version.

Find more information on the disease, its centers of reference and patient organizations on Orphanet: www.orpha.net

A	**AIRWAY / ANESTHETIC TECHNIQUE**	Difficult mask ventilation. Upper airway obstruction from GAG deposits and adenotonsillar hypertrophy. A 'cannot intubate, cannot oxygenate' scenario. Tracheal GAG deposits and tracheomalacia are common. Restrictive and obstructive lung disease may impair ventilation. General anesthesia is preferred with limitations on regional anesthesia use.
B	**BLOOD PRODUCTS (COAGULATION)**	Variability in hemoglobin, serum iron and transferrin saturation occurs in all the MPS subgroups, especially the HSCT and ERT groups. Specific blood products are required for patients post stem cell transplantation. Leukocyte-poor red blood cell products, cytomegalovirus sero-negative, and gamma-irradiated components may be required. An effect of heparin sulfate excess on thrombin has been seen in MPS I but not MPS VI.
C	**CIRCULATION**	The primary cardiac manifestation of MPS VI is progressive valve degeneration with stenosis and/or incompetence. Severe heart failure is common in MPS VI patients in their 20s and 30s due to cardiomyopathy, fibroelastosis, valvular involvement and pulmonary hypertension.
D	**DRUGS**	There are no known interactions between Galsulfase and anesthetic agents. ERT should be withheld postoperatively, as fever due to a minor drug reaction may mimic sepsis or wound infection. Premedication should be used sparingly in the presence of airway obstruction.
E	**EQUIPMENT**	All difficult airway modalities should be available. This includes fiberoptic bronchoscope, supraglottic airway device and videolaryngoscopy. Intraoperative spinal cord monitoring is recommended in the presence of dural thickening, occipito-cervical subarachnoid space narrowing and a dysplastic C1 within the foramen magnum.

Additional disease information

The estimated birth prevalence is 1 in 300 000 live births in Europe [3]. There is no current worldwide incidence rate, and numbers may range according to country or specific ethnic populations studied. The MPS VI prevalence is 0.04 in 100,000 live births in the USA. This represents between 50 and 300 patients in the USA and approximately 1100 patients in the developed world with MPS VI [4].

The inheritance of all types of MPS is autosomal recessive except for MPS type II, which is X-linked. Recently, neonatal screening for MPS was introduced in some regions but in most countries the diagnosis still relies on the clinical suspicion and the results of metabolic, enzymatic, and molecular analyses [5,6].

Rapidly progressive forms usually present before two years of age with severe dysostosis multiplex and coarse facial features. Without proper treatment patients succumb before the second or third decade of life. A more slowly progressive (attenuated) form has been described with later onset, clinical symptoms in fewer systems, less pronounced dysostosis multiplex and longer survival [7-9]. Neonatal examination following diagnosis demonstrates abnormalities in 27% of MPS VI infants: On screening 54.5% were classified as predicted severe, 40.9% as attenuated, and 4.5% as unknown. Imaging abnormalities were present in 41.7% of severe cases and 11.1% of attenuated cases. The most common findings were ASD (13%), valvular thickening (9%), vertebral anomalies (9%), and gastric stasis (13%) [6].

Typically, adult height in the severe phenotype is less than 120 cm and dysmorphic appearance includes coarse facial features, frontal bossing, depressed nasal bridge, enlarged tongue and gingival hypertrophy. Other deformities include thoracic deformities (pectus carinatum), scoliosis or kyphosis (gibbus), macrocephaly, hepatosplenomegaly, protruding abdomen, inguinal and umbilical hernias. The characteristic skeletal dysplasia includes short stature, dysostosis multiplex (in x-ray short, thickened metacarpals, abnormal vertebral bodies, paddle-shaped ribs, and short thick clavicles) and degenerative joint disease [10]. Oral, pharyngeal and upper airway obstruction is common [11]. Both obstructive and restrictive respiratory disease is often present. Obstructive disease is related to bronchial narrowing and tracheobronchomalacia whereas restrictive disease is due to the small stiff thoracic cage and abdominal distension combined with kyphosis, scoliosis, and lumbar lordosis.

Cardiac involvement is frequent and is an important cause of morbidity and mortality [12]. The primary cardiac manifestation of MPS VI is progressive valve degeneration with stenosis and/or incompetence. The most frequent valvular involvement was tricuspid regurgitation (65.7%) followed by pulmonary regurgitation (62.8%) and mitral regurgitation (57.1%) [13]. Abnormal ECGs occur in ¾ of all patients with sinus tachycardia and right and left axis deviation most common. Heart failure may emerge due to cardiomyopathy, fibroelastosis, valvular involvement and pulmonary hypertension. Although coronary artery disease has been described only for MPS I its presence should be considered in patients with MPS I, II, VI, or VII.

Intellect is normal but significant learning issues may arise from hearing and visual limitation. Common neurological manifestations include carpal tunnel syndrome, spinal cord or nerve root compression, optic nerve injury, jugular foramen stenosis and communicating hydrocephalus [14]. Spinal cord compression (SCC) is the result of spinal canal stenosis due to small thickened posterior elements, odontoid dysplasia, thickening of the dura, ligamentum flavum and cruciate ligaments, disk bulging or any combination of these [15]. Stenosis can be exacerbated by the presence of flexion extension instability or gibbous deformity. Patients with MPS VI frequently experience myelopathy associated with SCC during childhood. Patients with SCC in rapidly progressive MPS VI require decompression surgery at a median age of 12

years whereas those with slowly progressive disease did not require surgery until 24 years of age [16].

Visual impairment is common (40% of MPS VI). Corneal opacification of varying severity (38% severe opacification) is frequently seen as well as refractive errors, glaucoma, retinopathy and optic nerve swelling and ocular hypertension [17].

Enzyme replacement therapy (ERT) and hematopoietic stem cell transplantation (HSCT) have been shown to improve the overall survival of MPS patients [18]. The impact of HSCT and ERT on cardiovascular disease has been shown to reduce progression of left ventricular hypertrophy but neither has been shown to influence valvular disease in MPS I, II, and VI. Intravenous ERT by galsulfase (Naglazyme®) may improve certain somatic symptoms but not alleviate neurological symptoms [19]. The enzyme does not reach poorly vascularized sites such as corneas and joint cartilage [20,21].

Evidence supporting the use of bone marrow or HSCT is lacking with only small, noncontrolled studies in MPS VI patients [22,23]. The risk-benefit profile of HSCT in patients with MPS VI is less clear than in other types of MPS and is currently not supported [24,25]. The overall survival rate was 81.3% in MPS VI patients, in which most deaths occurred during the first 3 months post-HSCT [24].

While life expectancy in MPS VI improves with ERT/HSCT therapy, cardiac valve disease progresses and has become more prevalent in adult MPS patients. The most frequent causes of death differ significantly between MPS types with cardiovascular and respiratory failure being predominant in MPS I, II and VI [8].

Typical surgery and procedures

Typical surgery and procedures include diagnostic interventions (MRI, CT), surveillance procedures (cardiac, cervical spine), long-term vascular access provision and disease-specific general surgery [22]. Magnetic resonance imaging (MRI) of the whole spine should be performed annually. MRI brain is indicated when clinical suspicion of hydrocephalus occurs. The frequency can be decreased in asymptomatic adults with stable imaging.

In younger children the most frequent surgical interventions include adenotonsillectomy, middle ear ventilation tubes and inguinal or umbilical hernias [11]. Tracheostomy for upper airway obstruction may be necessary in advanced stages of the disease. With the advent of ERT the requirement for weekly intravenous enzyme administration necessitates central venous access devices (CVADs). Older children present for dental procedures, carpal tunnel surgery, and neurosurgery.

The most common procedures for SCC are laminectomy, laminotomy and open-door laminoplasty (expansion of spinal canal). Often a foramen magnum craniectomy is also performed because the compression involves the upper cervical cord at the foramen magnum [26]. Cardiac surgery for valve repair or replacement is more common in the severe form, but the literature is scarce with respect to cardiac surgery interventions in MPS VI [27,28].

Type of anesthesia

General anesthesia is a difficult and potentially high-risk procedure in MPS VI patients, due to the airway management difficulties and cervical cord impingement [29]. The overall complication rate for all anesthetic procedures was 1.06%. In a large study of patients (2010-

2022) with MPS (11% MPS VI) the anesthetic complication rate was higher for surgical procedures at 3.65% compared to diagnostic procedures, which had a rate of 0.38% [29]. In contrast a similar cohort (2002-2016) demonstrated a complication rate of 25.6% including issues related to airway management (55%), respiratory adverse events (36%), and cardiocirculatory adverse events (9%) and one death [30]. In the updated cohort (2002-2018) from the same institutions, now including 99 patients and 488 anesthetics, at least one anesthesia-related complication occurred in 22.7% of the cases and 32% in MPS VI patients. Spine deformity, immobility, obstructive lung disease, hepatosplenomegaly and scheduled major surgery were associated with an increased risk. Hepatosplenomegaly and immobility imply a progressed disease stage or a poor response to treatment. HSCT was associated with lower risk for events whereas ERT was associated with a minor decrease in risk [18]. Postoperative complications occurred in 13% and included 1 death in a patient with MPS VI. Over the years, with increasing experience of the institutions, the rate of adverse events seems to be decreasing [18].

A statement from the American Pediatric Anesthesia Quality Improvement Initiative (WAKE UP SAFE®) cautions against the use of central neuraxial blocks in MPS. Spinal cord infarction or injury has been reported in 2 patients with MPS IV (Morquio syndrome) but not MPS VI. The recommendation is that extra care must be taken to ensure spinal cord perfusion in patients with MPS undergoing general anesthesia. Factors that are tolerated by normal patients may be poorly tolerated by MPS patients. Such factors include kyphotic curves of the spine, neuraxial anesthesia, and low mean arterial pressure.

Reports of peripheral nerve blocks in patients with MPS are lacking, but may be considered. Whether ultrasound-guided regional techniques are feasible and may allow avoidance of general anesthesia is unknown. Regional anesthesia may be contraindicated in the presence of preexisting neurological impairment [31]. Posterior blocks (erector spinae plane block and paravertebral block), and anterior chest wall fascial plane blocks (serratus anterior, pectoralis I/II, intercostal nerve blocks) have been successful in attenuating median sternotomy pain. Of these, only the transversus thoracis plane block, which targets the anterior cutaneous branches of the second through sixth intercostal nerve innervation of the medial chest wall, has been described in MPS VI [31].

Necessary additional preoperative testing (beside standard care)

Multidisciplinary review is a hallmark of management guidelines for MPS VI [32]. Neurological examination, respiratory function testing, cardiac evaluation, and imaging studies are recommended every 12 months (or earlier if symptoms arise) for MPS VI patients.

Routine neurological examination with assessment of hyper-reflexia is recommended every 6 months after diagnosis. Cervical stenosis should be evaluated by MRI, which is the gold standard to detect compression of the cord, myelopathy, and changes of CSF flow [22].

Pediatric cardiology review, including physical examination, ECG, chest X-ray, and echocardiogram are necessary. Endurance testing includes the 12-minute walk test (12MWT) or the 3-minute stair climb (3MSC), performed before and after ERT and every 12 months. Holter monitoring may be indicated if arrhythmia is suspected.

Evaluation of pulmonary function by forced spirometry and flow-volume expiratory and inspiratory loops should be performed regularly to assess changes in lung volume and obstruction. Comparison to normal values is meaningless but trends are important. There is a general decrease in pulmonary function over time as a result of obstructive and restrictive airway disease and sleep-disordered breathing. While FEV1 and FVC did increase over time,

FEV1 [%Pred] and FVC [%Pred] decreased, with the latter two variables being superior predictors of disease progression as they are adjusted for age, sex and height [33]. Recurrent pneumonia has been reported, and preoperative chest X-ray is worthwhile. Resolution of any active respiratory infections prior to surgery is recommended.

Glycosaminoglycan accumulation in the oropharynx and airway, combined with the typical dysmorphic features, is commonly associated with rhinitis, enlarged tonsils and adenoids, thickening of the epiglottis and narrowing of the trachea and bronchi. Obstructive sleep apnea secondary to upper airway obstruction may lead to failure to thrive, pulmonary hypertension and behavioral and learning problems. Awake fiberoptic nasoendoscopy can be performed to evaluate the extent and severity of airway involvement and may aid anesthetic planning and estimate risk. Polysomnography can be used to assess sleep apnea. Existing adjunctive therapies, such as tonsillectomy and adenoidectomy and NIV, appear to be more effective in ERT-treated subjects [33].

MPS VI can be complicated by severe obstruction of the upper airways often associated with tracheobronchial malacia and complex tracheal stenosis. Cross-sectional imaging using CT or MRI scans is very useful. In general, assessment of the supraglottis is better with an MRI scan, whereas the infraglottis, trachea, and lungs are better assessed by CT scans, as they show cartilaginous structures better and help in assessing the airway caliber, tortuosity, and malacia [34].

Particular preparation for airway management

The airway in MPS patients has a complex anatomy due to MPS deposits, skeletal, and soft tissue abnormalities. Assessment of the airway should be holistic and include multiple parameters. An objective multidimensional score (Salford Mucopolysaccharidosis Airway Score or SMAS) may help to predict and manage difficult airways. Apart from standard airway assessment (MPS type, teeth protrusion, cervical mobility, tongue bulkiness, Mallampati score and thyromental distance), the epiglottis, supraglottis, and glottis are assessed by nasoendoscopy and cross-sectional imaging using CT or MRI. Assessment of the supraglottis is better with an MRI scan whereas the infraglottis, trachea, and lungs are better assessed by CT scans, as they show cartilaginous structures better and help in assessing the airway caliber, tortuosity, and malacia [34, 35]. In a series of patients with MPS undergoing cardiac surgery the Salford scale was used to predict risk. In addition to anesthetic examination, nasoendoscopy, imaging, functional studies, 3D reconstruction, virtual endoscopy, virtual reality and simulation using computerized, physical modeling were described [36].

A difficult airway involving difficult facemask ventilation, difficult laryngoscopy, difficult tracheal intubation, failed intubation, and difficulty in placing and using supraglottic airway devices (SGAs) have all been described [37]. Classic laryngoscopy, FOB-assisted intubation, and VLS-assisted intubations are the most frequent approaches, but all are associated with failed intubations. The frequency of transition to a different (rescue) airway technique or abandoned anesthesia was highest for direct laryngoscopy (24%), conventional fiberoptic intubation (FOI) (17%), videolaryngoscopy (12%) and lowest for FOI through an SGA (0%) [30].

SGAs such as laryngeal mask airways have been used successfully and may serve as a conduit for fiberoptic intubation. Video-assisted laryngoscopy has been used successfully in many MPS syndromes including MPS VI [37]. Patients often have thick nasal and oral secretions, hypertrophied turbinates and a narrow nasopharynx making nasal intubation difficult. The use of an oral airway may fail to relieve or even worsen the degree of airway obstruction due to the high elongated position of the epiglottis.

As difficult bag-mask ventilation and difficult or failed intubation are possible, anesthetic management should be performed by the most experienced anesthetic team with support of an ENT surgeon. Tracheotomy has been successfully used in two scenarios: 1) to safeguard an anticipated difficult airway prior to a planned surgical procedure, and 2) to treat progressive upper airway obstruction. An emergency tracheostomy is an extremely difficult procedure in these patients and may not be feasible if the airway cannot be managed. Tracheostomy may not relieve obstruction if there is diffuse tracheal infiltration and tracheal tortuosity [38].

Endotracheal extubation should only be undertaken after full reversal of the neuromuscular blockade and if the patient is fully awake, coughing efficiently and breathing adequately. Consider intraoperative steroids (dexamethasone) to help reduce postoperative oral mucosal and tongue swelling. Importantly, extubation should be performed in an area where all the necessary personnel and equipment for re-intubation are available immediately.

Although ERT is available, the impact on tracheal deposits has not been documented. By extending the life expectancy of patients with MPS, airway problems may become more prevalent at advanced ages. The potential exists for severe, potentially fatal issues during anesthesia [39].

Particular preparation for transfusion or administration of blood products

Specific blood products are required for patients post-stem cell transplantation. Leukocyte-poor red blood cell products, cytomegalovirus sero-negative, and gamma-irradiated components may be required.

Particular preparation for anticoagulation

Thrombocytopenia related to galsulfase treatment has been reported but significant bleeding diatheses are rare. Dermatan sulfate is structurally related to heparin and has documented antithrombotic properties. Although the excess of dermatan sulfate in MPS VI accumulates primarily in lysosomes and in the extracellular matrix (mainly connective tissue), some can be demonstrated to spill into the circulation where it binds to heparin cofactor II. The serum levels of heparin cofactor II-thrombin complex are used as a marker of several of the MPS syndromes.

An elevated activated partial thromboplastin time (aPTT) has been reported in MPS I (Hurler syndrome) patients but not MPS VI [40]. There is high variability in hemoglobin, mean corpuscular volume, serum iron and transferrin saturation among all the MPS subgroups, with results being higher in the HSCT and ERT group as compared to treatment naïve patients [41].

Particular precautions for positioning, transportation and mobilization

Instability of the atlanto-axial joint and SCC at the upper cervical and thoracolumbar region due to spinal canal narrowing is of prime importance when transporting or moving patients. Awake positioning prior to anesthesia to determine the most appropriate position without signs of neurological impingement is useful. Neck stabilization during intubation and during transition from supine to prone position may be required if atlanto-axial instability is present. Positioning can be difficult due to restricted joint range in elbows, shoulders, hips, knees, and ankles.

Interactions of chronic disease and anesthesia medications

There are no reports on interactions between anesthetic agents and galsulfase. Enzyme replacement infusion reactions including rash, urticaria, headache, hypotension, nausea and vomiting are common and often treated with antihistamines, corticosteroids or antipyretics [42]. A potential interaction with premedication may occur.

Anesthetic procedure

Patients with MPS VI should only undergo anesthesia for imaging or surgery in centers where physicians experienced with the perioperative management of individuals with this disease are available. The parents and patient should receive careful informed consent regarding anesthesia. A difficult intubation should be assumed and planned for. Review of previous anesthetic notes is helpful but changes due to disease progression are common. As MPS VI progresses in spite of ERT, techniques that previously had been successful to manage the airway may not be successful for the current procedure. Central neuraxial regional anesthesia is contraindicated but local or ultrasound-guided regional anesthesia may reduce analgesic requirements postoperatively. Volatile anesthetic induction is preferred to maintain spontaneous respiration until the airway is controlled.

Providing anesthesia for MPS VI patients often requires induction in a fully equipped anesthetic room, with a difficult airway trolley at hand. For imaging procedures, induction of anesthesia in the operating room before transporting the MPS VI patient to the MRI/CT scan suite is advisable. Following major surgery, recovery should be performed in the intensive care unit with extubation in a controlled environment.

Particular or additional monitoring

Neurophysiological monitoring with somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) during scoliosis and cervical decompression surgery has been suggested to reduce the risk of spinal cord injury. It is possible to miss motor deficits and unfortunately parameter changes detected by SSEPs may occur too late to prevent cord damage.

Possible complications

A ‘cannot intubate, cannot oxygenate’ scenario.

Complete airway obstruction, resulting in hypoxemia and cardiac arrest.

Post-obstructive (negative pressure) pulmonary edema.

Failure to maintain airway after extubation, stridor, upper or lower airway collapse.

Need for urgent reintubation or tracheostomy.

Upper spinal cord injury due to dural thickening, occipito-cervical subarachnoid space narrowing and a dysplastic C1 within the foramen magnum.

Postoperative care

There is a risk of upper airway obstruction and there have been reports of post-extubation pulmonary edema presumably due to forced expiration against a narrowed and thickened glottis.

Delayed onset postoperative neurologic deficit has been described following lumbar kyphosis repair [43].

The degree of postoperative monitoring is dependent on the surgical procedure and preoperative condition of the patient. Intensive care is not mandatory, but intensive care facilities should be on site.

If sleep apnea is present, use regional local anesthetic blocks and avoid excessive intraoperative opiates. Continuous oximetry monitoring should be used to detect airway obstruction episodes and desaturation. Consider applying continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP). Postoperative chest physiotherapy has a role in reducing respiratory complications.

Disease-related acute problems and effect on anesthesia and recovery

Acute airway compromise and respiratory failure can be caused by the disease and also as an effect of the anesthetic.

Loss of lower limb MEPs during neurosurgery in the prone position may indicate cord ischemia distal to the operative site. All efforts should be made to increase cord perfusion including increasing blood pressure, surgical repositioning and removal of devices causing cord compression. Failure to regain baseline MEPs should trigger a return to the supine position and awakening of the patient.

Enzyme replacement infusion reactions include rash, urticaria, headache, hypotension, nausea and vomiting and are often treated with antihistamines, corticosteroids or antipyretics [42]. Confusion may occur with reaction to anesthetic agents [44].

Ambulatory anesthesia

Ambulatory (day case) anesthesia is not appropriate for MPS VI patients.

Adult anesthesia

With improved care, the life expectancy of patients with MPS continues to increase. They often need surgical intervention for a variety of indications. The increased life expectancy associated with ERT and HSCT goes along with an increased demand for surgery and anesthesia. Anesthesia becomes progressively more difficult with age even with extended treatment with

ERT [45]. There is general agreement that ERT is effective in reducing urinary glycosaminoglycans and liver and spleen volume, while cardiac and joint outcomes are variable in different studies. Effectiveness on cardiac valves, trachea and bronchi, hearing and eyes is definitely poor, probably due to limited penetration in the specific tissues. ERT does not cross the blood-brain barrier, with the consequence that the central nervous system is not cured by intravenously injected ERT [46].

Surgery in adult MPS patients is considered to be high risk and a wide range of critical clinical situations involving airway compromise have been reported [47]. In adult patients preoperative assessment of conduction disorders (especially atrioventricular (AV) block), aortic valvular assessment and coronary artery status is essential. Cardiac MRI to assess valvular state and function and CT coronary angiography to assess diffuse coronary disease are recommended [48].

Cardiovascular complications in adult MPS patients include cardiac valve infiltration commonly resulting in severe stenosis and/or regurgitation; conduction abnormalities, cardiomyopathy, pulmonary hypertension and coronary artery infiltration [48]. The most common procedure is aortic valve with or without mitral valve replacement [28, 49]. HSCT and ERT have been shown to reduce progression of left ventricular hypertrophy but neither influences valvular disease progression, in particular in MPS type I, II and VI, which remains an unmet need.

Airway abnormalities in adult MPS are varied and complex [37]. There is a progression to difficult intubation as patients get older [50]. Aging can be associated with severe narrowing of the larynx or trachea and with severe obstructive sleep apnea. Mask ventilation and laryngeal mask airway placement do not become more difficult with age. Bone marrow transplantation did not affect airway difficulty, while enzyme replacement therapy was associated with difficult intubations in younger patients. In one series patients over the age of 18 were nearly thirteen times more difficult to intubate when compared to the control group [50].

There is some benefit in airway simulation of intubation involving a computer-generated 3D model, virtual reality and a 3D-printed model of the airway. The role of high-flow nasal oxygen administered as Trans Nasal Humidified Rapid Insufflation Ventilation Exchange (THRIVE) during induction of anesthesia and intubation has been reported [36].

As MPS disorders have historically been considered pediatric diseases, the patient's adult care multidisciplinary team (MDT) may have less experience in managing the broad spectrum of potential critical clinical situations compared with pediatric colleagues [47].

Obstetrical anesthesia

An individualized anesthetic plan for mode of anesthesia prepared in advance is essential. Regional anesthesia (spinal, combined spinal-epidural, or de novo epidural) is preferable but the preparation for conversion to general anesthesia for emergency cesarean section is essential. Both spinal anesthesia and epidural anesthesia have been described in pregnant women with MPS and were effective in a small cohort [51,52]. Either technique may be considered to avoid general anesthesia in a high-risk situation or during pregnancy.

Intrathecal and epidural techniques should be used with extreme caution in patients with MPS VI, due to the anatomical challenges of very short stature, spinal abnormalities causing insertion problems and unpredictability of spread of local anesthesia.

Regional anesthesia is contraindicated in patients with spinal cord compression and may be difficult due to skeletal deformities, short stature, or inability to lie flat. An MPS IVA case

suggested that a combination of kyphoscoliosis, lumbar canal stenosis and cord compression can lead to suboptimal distribution of epidural anesthetics [53]. Bacchus et al. reported a pregnant woman with MPS VI who had myelopathy due to compression of the cervical spinal cord by thickened dura [54]. During the last trimester, she had severe neurologic deterioration with spastic quadriparesis and impairment of sphincter function. There was no improvement 2 months after delivery, so a cervical laminectomy and longitudinal splitting of the dura from C-5 to the foramen magnum was done with good return of function.

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