Molecular Genetics and Metabolism Reports 8 (2016) 111–115

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism Reports

journal homepage: www.elsevier.com/locate/ymgmr

Pregnancy in patients with mucopolysaccharidosis: a case series

Fiona J. Stewart [a,*], Andrew Bentley [b], Barbara K. Burton [c], Nathalie Guffon [d], Susan L. Hale [e], Paul R. Harmatz [f], Susanne G. Kircher [g], Pavan K. Kochhar [h], John J. Mitchell [i], Ursula Plöckinger [j], Sue Graham [k], Stephen Sande [k], Zlatko Sisic [l], Tracey A. Johnston [m]

[a] Belfast City Hospital, Belfast, Northern Ireland, UK
[b] University Hospital South Manchester MPS IHSNHS Foundation Trust, Manchester, UK
[c] Lurie Children's Hospital, Chicago, IL, USA
[d] Hôpital Femme Mère Enfants, Lyon, France
[e] Seattle Children's Hospital, Seattle, WA, USA
[f] UCSF Benioff Children's Hospital Oakland, Oakland, CA, USA
[g] Institute of Medical Chemistry and Institute of Medical Genetics, Medical University of Vienna, Vienna, Austria
[h] Central Manchester University Hospitals, Manchester, UK
[i] Montreal Children's Hospital, Montréal, Québec, Canada
[j] Charité - Universitätsmedizin Berlin, Berlin, Germany
[k] BioMarin Pharmaceutical Inc., Novato, CA, USA
[l] BioMarin Europe Limited, London, UK
[m] Birmingham Women's NHS Foundation Trust, Birmingham, UK

ARTICLE INFO

Article history:
Received 2 August 2016
Accepted 2 August 2016
Available online xxxx

Keywords:
Elosulfase alfa
Enzyme replacement therapy
Mucopolysaccharidoses
Pregnancy

ABSTRACT

The mucopolysaccharidoses (MPS disorders) are rare inherited diseases associated with multi-organ accumulation of glycosaminoglycans, leading to musculoskeletal, respiratory, cardiac, neurological, ophthalmological, otolaryngological, and gastrointestinal abnormalities. As a result of improvements in diagnosis, multi-disciplinary care, and therapies such as enzyme replacement therapy and hematopoietic stem cell transplantation, an increasing number of patients with MPS are reaching adulthood and are involved in family planning. Data on fertility and pregnancy outcome in MPS is sparse and comprises primarily isolated case reports. To address this evidence gap, we present a case series on fertility and pregnancy in eight mothers and five fathers with MPS. This case series demonstrates that women with MPS have high-risk pregnancies and deliveries secondary to their underlying disease. However, with appropriate pre-conceptual multi-disciplinary evaluation, optimization and discussion regarding potential risks, combined with regular multi-disciplinary maternal and fetal surveillance in a tertiary center, the outcome of most pregnancies in this case series seems to be favorable with all babies developing normally. Partners of fathers with MPS had uncomplicated pregnancies and deliveries. All children were healthy, with normal growth and development.

1. Introduction

The mucopolysaccharidoses (MPS disorders) are rare inherited lysosomal storage diseases caused by deficiencies in enzymes involved in glycosaminoglycan (GAG) catabolism. The resulting accumulation of GAGs in tissues and organs leads to skeletal and joint abnormalities (hip dysplasia, knee or ankle valgus, kyphosis, scoliosis, atlanto-axial instability, chest deformities, joint stiffness/hypermobility), cardiopulmonary compromise (upper/lower airway obstruction, restrictive lung disease, cardiac valve disease, left ventricular hypertrophy), neurological problems secondary to spinal cord compression, hepatosplenomegaly, and impaired vision and hearing [1]. Cognitive decline occurs in severe forms of MPS I (mainly Hurler [MPS IH], Hurler-Scheie [MPS IHS] syndrome), MPS II (Hunter syndrome), MPS III (Sanfilippo syndrome) and MPS VII (Sly syndrome) [1]. There is wide genotypic and phenotypic heterogeneity among the MPS types. All are autosomal recessive disorders, except MPS II which is X-chromosome linked and typically occurs in males [1].

Recent improvements in diagnosis, multi-disciplinary care, and treatments such as enzyme replacement therapy (ERT) and hematopoietic stem cell transplantation (HSCT) have led to increased life expectancy and a growing number of adult MPS patients. Not surprisingly, MPS adults are considering starting families or are actively pursuing having children. While case reports describing fertility and pregnancy in women with MPS are rare [2–10], even less data exists on fathers

Abbreviations: ERT, enzyme replacement therapy; GAG, glycosaminoglycan; HSCT, hematopoietic stem cell transplantation; MPS, mucopolysaccharidosis.

* Corresponding author at: Northern Ireland Regional Genetics Centre, Belfast City Hospital, 51 Lisburn Road, Belfast BT9 7AB, Northern Ireland, UK.
E-mail address: Fiona.Stewart@belfasttrust.hscni.net (F.J. Stewart).

http://dx.doi.org/10.1016/j.ymgmr.2016.08.002

with MPS. A few case reports have shown that pregnancy and delivery can be problematic in women with MPS [2–5,8]. Small stature, obstructive and restrictive respiratory disease, cardiac issues (mostly valve disease), spinal cord compression, hepatosplenomegaly, and musculoskeletal abnormalities might interfere with normal pregnancy and delivery or exacerbate due to pregnancy [11–18]. Use of steroids (as pre-treatment with ERT to avoid infusion-associated reactions) may cause adrenal insufficiency during pregnancy [19,20]. The majority of published case reports describe pregnancy and/or delivery in women with MPS I [3,4,6,7,9,21–23]. In several of these cases, pregnancy and delivery was successful [6,7,9,10,22]. One report described the case of a woman with MPS IH who had a successful bone marrow transplantation at 14 months of age [3]. Pregnancy was terminated at 9 weeks due to concerns about the patient's health and her ability to care for the baby [3]. Another report described rapid clinical deterioration of a woman with MPS I after discontinuation of ERT during pregnancy and delivery at 29 weeks of gestation of a baby of 1.25 kg [4]. Problems achieving adequate combined spinal-epidural anesthesia and the need for emergency tracheostomy during planned cesarean section has been reported for a 23-year-old woman with MPS IHS who had received ERT for over 10 years [21]. A 37-year-old woman with MPS IS receiving ERT developed signs of pre-eclampsia with hypertension and albuminuria at the end of pregnancy and significant aggravation of preexisting valve disease after delivery [23]. Two case reports discussed pregnancy/delivery in women with MPS IVA. One of the women developed polyhydramnios and dyspnea in the 21st week of gestation and delivered a premature baby of 1.18 kg at 28 weeks [2]. The other case report concerned inadequate pain management during epidural anesthesia for cesarean section, probably due to a combination of kyphoscoliosis, lumbar canal stenosis, and thecal sac compression [8]. Only one published case report discussed pregnancy and delivery in a woman with MPS VI [5]. She developed severe myelopathy in the third trimester of pregnancy due to compression of the cervical spinal cord.

2. Methods

The case series presented here follows eight women and five men with MPS and explores the pregnancy issues associated with their disease. The cases were presented at an advisory board meeting on pregnancy and fertility in MPS patients held April 18th, 2015 in Berlin, Germany, and attended by international MPS experts.

3. Case reports

3.1. Demographics and clinical characteristics (Table 1)

Eight women and five men with MPS were followed at six tertiary care centers in the US, UK, France, Austria, and Germany. The 13 cases involved MPS IHS, MPS II, MPS IV (Morquio syndrome) A and B, and MPS VI (Maroteaux-Lamy syndrome). Each patient depicted in this publication provided written informed consent. The men with MPS II were brothers. Although most of these patients had attenuated phenotypes of MPS they all showed clear manifestations of the disease, including musculoskeletal, respiratory, cardiac, and/or neurological problems. Two patients showed severe short stature, below 125 cm (Table 1). None had psychological or intellectual regression. One of the men with MPS II (case 9) died at 28 years of age, 6 months after undergoing a lung transplantation and less than 2 years after his son was born.

3.2. MPS mothers

Mean age at pregnancy of the eight women was 29.8 (SD 6.5) years (Table 1). Six women had one child. Case 3 (MPS IVA) delivered two children during the observed time interval. Case 8 has three children, of which two were born before MPS VI was diagnosed; only her third pregnancy is reported here. Case 2 (MPS IVA) had a miscarriage and an extra-uterine pregnancy followed by right salpingectomy in the year before the pregnancy. None of the other women had previous pregnancies. None of the partners had MPS.

Fig. 1 provides details on the clinical history and pregnancy outcome of cases 5 and 8. The Appendix provides an overview of all other female cases discussed.

3.2.1. Complications during pregnancy

Complications during pregnancy included lumbar pain (case 6) and migraine (cases 2 and 6) requiring paracetamol use, gastric pain and reflux requiring treatment with omeprazole (case 2), high relative weight gain (18–24% for cases 3, 4, and 5), frequent spotting at 18 weeks (case

Table 1
Demographics and clinical characteristics of the mothers and fathers with MPS.

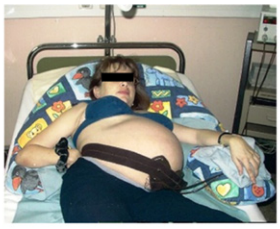
Case	MPS type	Number of children	Age at pregnancy/birth (males), yrs	Height, cm	Weight, kg	ERT/HSCT	
						Throughout pregnancy	During lactation
MPS mothers							
1	IHS	1	22	148	NA	ERT	–
2	IVA	1	41	142	73	ERT	–
3	IVA	2	25	147	41	–	–
			28			–	–
4	IVA	1	35	114	35	–	–
5	IVB	1	31	147	45	–	–
6	VI	1	21	149	75	ERT	–
7	VI	1	32	NA	NA	–	–
8	VI	3[a]	33	146	39	ERT	ERT
Mean (SD)			29.8 (6.5)	141.9 (12.5)	51.3 (17.9)		
MPS fathers							
						At conception	
9[b]	II	1	27	170	51	HSCT (age 17)	
10[c]	II	1	24	168	77	ERT	
11	IVA	1	30	122	NA	–	
12	IVA	1	31	155	NA	–	
13	IVA	3	41, 43, 45	150	85	–	
Mean (SD)			34.4 (8.4)	153.0 (19.3)	71.0 (17.8)		

NA: not available; M: male; F: female.
[a] Only third child (first child after diagnosis of MPS VI) is discussed.
[b] Died at age 28.
[c] Expecting a second child.

MPS IVB: case 5

Clinical history

Thoracic deformity, weak legs, recurrent bronchitis at 3.5yrs
Correction of leg axis bilat. in childhood
Bilateral carpal tunnel surgery at 27 yrs
Bilateral hip endoprosthesis at 28/29 yrs
Bilateral hallux valgus correction
Menarche at 16-17 yrs



Complications during/after pregnancy

High relative weight gain (23%)
Delivery complicated by the large size of the child: ruptured uterus?, blood loss requiring blood transfusion
Baby had breathing problems; neonatal intensive care for 5 days

MPS VI: case 8

Clinical history

Spinal cervical stenosis with myelopathy (decompression surgery)
Mitral/aortic stenosis and insufficiency
Diastolic dysfunction, left atrial dilatation
Moderate restrictive ventilatory impairment
Musculoskeletal: bilateral hip deformation, short stature, joint stiffness
Reduced vision with bilateral cataract
Primary hypothyroidism

Complications during/after pregnancy

Pregnancy complicated by hyperemesis gravidarum resulting in intermittent hypothyroidism (early morning vomiting caused sub-optimal absorption of thyroxin tablets she is taking as substitution therapy for primary hypothyroidism due to Hashimoto thyroiditis)
Deterioration of cardiac problems after delivery
Child: hypotrophy (<3th percentile), hypoglycemia (glucose 30 mg/dL, likely unrelated to mother's MPS), small ventricular septal defect left-right shunt (closed spontaneously), open foramen ovale. Developed normally with normal cardiac function.

Fig. 1. Details on clinical history and pregnancy outcome of cases 5 and 8.

7), hospitalization for atrial tachycardia medication (metoprolol), and adjustment due to hypotension at 23 weeks (case 7). Case 8 had pre-existing primary hypothyroidism for which she received thyroxin substitution therapy; hyperemesis gravidarum during pregnancy resulted in sub-optimal absorption of thyroxin and intermittent hypothyroidism. Most women stopped working early during pregnancy. The husband of case 4 lost his job because he had to assist his wife most of the time during her pregnancy.

3.2.2. Complications during delivery

Deliveries were between 34 and 40 weeks of gestation (Table 2). Two women (cases 2 and 6) had uncomplicated, full-term, spontaneous vaginal deliveries. Seven deliveries (in six women) were planned cesarean sections. In six cases (1, 3 [2 deliveries], 4, 5, 8), this was due to maternal short stature with normal sized babies, leading to cephalopelvic disproportion. Case 5 had blood loss requiring transfusion at delivery with cesarean section at week 37 of gestation. Because of the disproportion of the gravid uterus and the size of the abdomen, the uterine fundus was below the rib cage. After opening of the uterus during cesarean section, the child's head could not be extracted because it was not possible to exert pressure away from the fundus. After several unsuccessful attempts, the child was eventually removed with forceps and born in the cephalic presentation. In the wake of these problems, the uterus began to bleed. In case 7, pre-term delivery at week 37 was required due to maternal aortic stenosis, atrial tachycardia, and a history of nocturnal seizures. Cesarean section was required due to a contracted maternal pelvis and transverse lie of the child. The mode of anesthesia during cesarean section was reported for five cases and included spinal (cases 1 and 7), epidural (cases 5 and 8), and general anesthesia with endotracheal intubation (case 3). No details about the techniques used to perform spinal or epidural anesthesia are available. However, several physicians indicated that the anesthesiologists were well prepared to prevent or manage any complications that may have arisen during anesthesia, due to previous experience with the patient and/or availability of relevant clinical information.

3.2.3. Maternal complications post delivery

Two women had complications after delivery. Case 4 had mastitis and a breast abscess requiring emergency surgery and an umbilical hernia requiring surgical repair. She also had difficulties carrying the child due to her short stature and required special equipment including a baby crib designed for small parents. Case 8 had valve disease before pregnancy for many years without deterioration, but deteriorated significantly after delivery; she will require mitral valve replacement in the near future. At least six women started breastfeeding after delivery (Table 2). Three of the mothers discontinued after several days due to insufficient milk production. Case 3 (MPS IVA), who had two children, had lactation difficulties that were considered by the mother to be related to the small sizes of the babies (2.5 and 2.89 kg). The same problem may apply to case 8 (MPS VI), who had a baby below the 3rd percentile. The reason for the short lactation period in case 2 (MPS VIA) is not clear. Case 5 (MPS IVB) continued lactation for 9 months and reported no problems. Based on this information, we cannot conclude that insufficient milk production is MPS-related.

3.2.4. Neonatal complications

The baby in case 4, who was delivered at 34 weeks of gestation due to the extreme maternal short stature (114 cm), required supplemental oxygen and a feeding tube and 4 weeks of neonatal intensive care. Five days of neonatal intensive care was required for the baby in case 5 due to breathing problems. In case 8, the child had hypoglycemia (glucose 30 mg/dL, which was likely due to the small size [44 cm] of the baby and not related to the mother's MPS), a small ventricular septal defect resulting in a left-right shunt, and an open foramen ovale, but developed normally afterwards, with normal cardiac function.

3.2.5. ERT use during pregnancy

ERT involves intravenous infusion of recombinant enzyme to compensate for enzyme deficiencies in MPS patients. The therapy is currently available for MPS I, II, IVA and VI [1,24]. Four women (cases 1, 2, 6 and 8) continued ERT throughout pregnancy (Table 1) to ameliorate symptoms such as joint pain, chronic migraine, asthenia, and reduced endurance that improved after they started ERT (Table 1). No adverse effects of ERT on pregnancy were reported in any of these cases. Case 8 had ERT infusions during lactation (4 weeks), but avoided breastfeeding in the 24-h period after infusion due to concerns that the enzyme concentration in the milk might increase. The reason why two of the mothers with MPS IVA did not receive ERT during pregnancy is that ERT was not yet available for this indication at the time of pregnancy. Currently, no ERT is available for MPS IVB.

3.3. MPS fathers

The five men with MPS in the case series had a mean age of 30.6 years when their first child was born (Table 1). All had healthy partners. The men with MPS IVA did not receive genetic counseling. One man with MPS II (case 9) had successful HSCT at 17 years of age, but developed pulmonary graft-versus-host disease after 2 months. His brother was treated with ERT at the time of the pregnancy. All pregnancies and deliveries were uncomplicated. The partners of all three men with MPS IVA had a previous miscarriage at 6 weeks or at the end of the first trimester (case 13) of other pregnancies. All children were healthy, with normal growth and development. Case 13 had

Table 2
Pregnancy, delivery and breastfeeding in mothers with MPS.

Case	MPS type	Delivery, weeks of gestation	Mode of delivery	Sex baby	Weight baby, kg	Weight for age %ile	Length baby, cm	Length for age %ile	APGAR	Lactation
1	IHS	37	Planned CS	Male	2.60	5–10th	46	5th	9/9/10	No
2	IVA	40	Vaginal	Male	3.33	25–50th	53	90th	9/10/10	4 days
3	IVA	37	Planned CS	Female	2.50	5th	46	10th	7/8/9	Short time
		38	Planned CS	Female	2.89	10–25th	48	25th	8/9/10	Short time
4	IVA	34	Planned CS	Female	1.95	<3rd	43	<3rd	NA	NA
5	IVB	37	Planned CS	Male	3.29	25–50th	51	50–75th	7/9/10	9 months
6	VI	40	Vaginal	Female	3.36	50th	51.5	75th	10/10/10	NA
7	VI	37	Planned CS	Female	2.37	<3rd	NA	NA	7/8	yes
8	VI	38	Planned CS	Male	2.27	<3rd	44	<3rd	9/10/10	4 weeks
Mean (SD)		37.6 (1.8)			2.73 (0.51)		47.8 (3.7)			

CS: Cesarean section; NA: not available.
Centers for Disease Control and Prevention (CDC) weight and length for age percentiles (%iles) were derived from https://www.cdc.gov/growthcharts/html_charts/wtageinf.htm and https://www.cdc.gov/growthcharts/html_charts/lenageinf.htm.

three children. The partner of case 10 was expecting a second child at the time of data collection.

4. Discussion

Despite the increasing number of MPS patients reaching adulthood, reports on pregnancy remain relatively uncommon. The medical center in France involved in this study had 75 adult MPS patients (≥18 years), including 30 women with MPS I (N = 20), IV (N = 8) and VI (N = 2) and 45 men with MPS I (N = 10), II (N = 22), IV (N = 7) and VI (N = 6). Of these, only two women, with MPS IV and VI, and two men with MPS II had children. One woman with MPS I had an elective abortion at 18 years of age.

Several explanations may account for the relatively low number of pregnancies in MPS patients. These patients may have an increased risk of infertility, but this has not been sufficiently studied. In addition, MPS can severely impact an individual's ability to lead an autonomous lifestyle. Many patients require long-term care or find it necessary to live at home which can hinder development of social or intimate relationships. Female patients must be willing to assume the risks associated with pregnancy and delivery, be able to care for their child and overcome the financial demands related to pregnancy. For example, most women in this case series stopped working during pregnancy and, in one case, the patient's partner lost his job. Consequently, the support of close friends, relatives or family members is critical. Patients may also refrain from having children because they are apprehensive about the risk of passing on the disease to their offspring (which is low if their partner is unaffected). Finally, because of the shortened life span of MPS patients, potential parents may fear leaving their children motherless or fatherless at a young age. Relevant to this point, one of the MPS II fathers in this case series died less than 2 years after his son was born.

The fear of a difficult pregnancy and delivery for women with MPS is not unfounded as demonstrated by the high incidence of complications in this case series and in previous case reports [2–5], although many of the milder complications, such as lumbar pain, migraine, reflux and spotting, are common in pregnancy and may not be related to MPS. Complications during pregnancy can arise from exacerbation of existing clinical manifestations of MPS such as joint pain, cardiac, pulmonary or gastrointestinal disease. The major MPS manifestations that can compromise life are mainly cardiac and respiratory (often due to short stature). Permanent post-delivery worsening of clinical manifestations occurred in one woman within our case series, indicating that pregnancy may have a permanent impact on the mother's health. Despite the many issues the cases encountered during pregnancy and delivery, most children were born healthy, although some neonatal care was required.

MPS patients have significant anesthetic risk secondary to their underlying disease and surgeries require significant planning [25]. Therefore, most physicians preferred a scheduled cesarean section under epidural or spinal anesthesia to a natural delivery (which could require an emergency cesarean section with a higher likelihood of general anesthesia and increased risk). This could partly explain why our cases did not report many respiratory complications. Although no problems with local anesthesia were reported, a recently published MPS IVA case suggested that a combination of kyphoscoliosis, lumbar canal stenosis and cord compression can lead to sub-optimal distribution of epidural anesthetics [8].

Four cases received ERT during pregnancy and no apparent ERT-related adverse effects were reported. More research is needed, however, to assess whether ERT may improve the outcome of pregnancy and to determine the potential benefits and risks of ERT during lactation (only one case received infusions during a very short lactation period). A recently published case report showed uneventful pregnancy and delivery in a woman with MPS I receiving ERT [7]. No recombinant enzyme was detected in breast milk [7]. Several patient registries are collecting information on pregnancy and lactation in patients with MPS I, IVA and VI. The decision to start or continue ERT during pregnancy should take into account the safety category listed on the US and EU ERT labels, as well as the risks of exacerbation of disease associated with cessation of ERT.

5. Conclusions

The present case series demonstrates that women with MPS have high-risk pregnancies and deliveries secondary to their underlying disease. Nevertheless, despite complications during pregnancies, with appropriate pre-conceptual multi-disciplinary evaluation, optimization and discussion regarding potential risks, combined with regular multidisciplinary maternal and fetal surveillance in a tertiary center, the outcome of most pregnancies in this case series was favorable with all babies developing normally. Fertility, pregnancy and parenthood should be discussed regularly with women and men with MPS so that the risks are understood and pregnancies can be planned to minimize these risks. Patients should also be aware of the support that is available, including that from MPS patient organizations, and the need for thorough preconceptual evaluation by a multi-disciplinary team of health care professionals including MPS specialists.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ymgmr.2016.08.002.

Conflicts of interest

The content of this manuscript was based on presentations and discussions during an expert meeting that was coordinated and funded by BioMarin Pharmaceutical Inc. Sue Graham and Stephen Sande are employees of BioMarin Pharmaceutical Inc. Zlatko Sisic is an employee of BioMarin Europe Ltd. All other authors received funding and travel

support from BioMarin Pharmaceutical Inc. to attend the advisory board meeting. In addition, Fiona J. Stewart reports personal fees and non-financial support from BioMarin and Shire, and personal fees from Genzyme, outside the submitted work. Barbara K. Burton reports personal fees and clinical trial support from BioMarin, grants, personal fees and clinical trial support from Shire, personal fees and clinical trial support from Genzyme, personal fees from ReGenX Bio, and clinical trial support from Alexion, Ultragenyx and Cytonet, outside the submitted work. Nathalie Guffon reports grants for clinical trials from BioMarin, Shire, Genzyme, Sobi, and Merk Sereno, outside the submitted work. Susan L. Hale reports grants, personal fees and non-financial support from BioMarin, and grants from Genzyme and Shire outside the submitted work. Paul R. Harmatz reports consulting fees, grant support and clinical trial support from BioMarin, consulting fees and clinical trial support from Shire, consulting fees and clinical trial support from Genzyme, consulting fees and clinical trial support from Alexion, Ultragenyx, and Armagen and consulting fees PTC, Inventiva and Chiesi. John J. Mitchell has participated in BioMarin sponsored clinical trials, and has received travel support and consulting fees from BioMarin.

Acknowledgments

The authors are grateful to Ismar Healthcare NV for their assistance in writing of the manuscript, which was funded by BioMarin Pharmaceutical Inc. The cases described were discussed during an expert meeting about fertility and pregnancy in MPS that was held on April 18, 2015 in Berlin, Germany. This meeting was coordinated and funded by BioMarin Pharmaceutical Inc. The authors all participated in this meeting.

References

[1] J. Muenzer, Overview of the mucopolysaccharidoses, Rheumatology (Oxford) 50 (Suppl. 5) (2011) v4–v12.
[2] H. Salinas, J.R. Preisler, J. Astudillo, S.S.M. Cerda, T. Castillo, F.S. Fernández, R.V. Ide, Síndrome de morquio (mucopolisacaridosis tipo IV) y embarazo, Rev. Chil. Obstet. Ginecol. 70 (2005) 400–403.
[3] C.J. Hendriksz, G.M. Moss, J.E. Wraith, Pregnancy in a patient with mucopolysaccharidosis type IH homozygous for the W402X mutation, J. Inherit. Metab. Dis. 27 (2004) 685–686.
[4] A.T. Anbu, J. Mercer, J.E. Wraith, Effect of discontinuing of laronidase in a patient with mucopolysaccharidosis type I, J. Inherit. Metab. Dis. 29 (2006) 230–231.
[5] H. Bacchus, D.I. Peterson, Pregnancy complicated by myelopathy due to Maroteaux-Lamy syndrome, Am. J. Obstet. Gynecol. 136 (1980) 259–260.
[6] G. Remérand, E. Merlin, R. Froissart, F. Brugnon, J. Kanold, L. Janny, F. Deméocq, Four successful pregnancies in a patient with mucopolysaccharidosis type I treated by allogeneic bone marrow transplantation, J. Inherit. Metab. Dis. 32 (Suppl. 1) (2009) S111–S113.
[7] M. Castorina, D. Antuzzi, S.M. Richards, G.F. Cox, Y. Xue, Successful pregnancy and breastfeeding in a woman with mucopolysaccharidosis type I while receiving laronidase enzyme replacement therapy, Clin. Exp. Obstet. Gynecol. 42 (2015) 108–113.
[8] C. Delgado, C. Kent, M. Sedensky, C. Ciliberto, R. Landau, Management of labor and delivery in a woman with Morquio syndrome, Int. J. Obstet. Anesth. 24 (2015) 383–387.
[9] L.A. Clarke, J.E. Wraith, M. Beck, E.H. Kolodny, G.M. Pastores, J. Muenzer, D.M. Rapoport, K.I. Berger, M. Sidman, E.D. Kakkis, G.F. Cox, Long-term efficacy and safety of laronidase in the treatment of mucopolysaccharidosis I, Pediatrics 123 (2009) 229–240.
[10] Effective epidural anesthesia for cesarean section in parturient woman with type I mucopolysaccharidosis (Hurler's syndrome), Anesteziol. Reanimatol. 6 (2011) 29–31.
[11] K.I. Berger, S.C. Fagondes, R. Giugliani, K.A. Hardy, K.S. Lee, C. McArdle, M. Scarpa, M.J. Tobin, S.A. Ward, D.M. Rapoport, Respiratory and sleep disorders in mucopolysaccharidosis, J. Inherit. Metab. Dis. 36 (2013) 201–210.
[12] E.A. Braunlin, P.R. Harmatz, M. Scarpa, B. Furlanetto, C. Kampmann, J.P. Loehr, K.P. Ponder, W.C. Roberts, H.M. Rosenfeld, R. Giugliani, Cardiac disease in patients with mucopolysaccharidosis: presentation, diagnosis and management, J. Inherit. Metab. Dis. 34 (2011) 1183–1197.
[13] C. Kampmann, C. Lampe, C. Whybra-Trümpler, C.M. Wiethoff, E. Mengel, L. Arash, M. Beck, E. Miebach, Mucopolysaccharidosis VI: cardiac involvement and the impact of enzyme replacement therapy, J. Inherit. Metab. Dis. 37 (2014) 269–276.
[14] C.F. Wippermann, M. Beck, D. Schranz, R. Huth, I. Michel-Behnke, B.K. Jüngst, Mitral and aortic regurgitation in 84 patients with mucopolysaccharidoses, Eur. J. Pediatr. 154 (1995) 98–101.
[15] S.C. Siu, M. Sermer, J.M. Colman, A.N. Alvarez, L.A. Mercier, B.C. Morton, C.M. Kells, M.L. Bergin, M.C. Kiess, F. Marcotte, D.A. Taylor, E.P. Gordon, J.C. Spears, J.W. Tam, K.S. Amankwah, J.F. Smallhorn, D. Farine, S. Sorensen, Cardiac disease in pregnancy (CARPREG) investigators, Prospective multicenter study of pregnancy outcomes in women with heart disease, Circulation 104 (2001) 515–521.
[16] W. Drenthen, E. Boersma, A. Balci, P. Moons, J.W. Roos-Hesselink, B.J.M. Mulder, H.W. Vliegen, A.P.J. van Dijk, A.A. Voors, S.C. Yap, D.J. van Veldhuisen, P.G. Pieper, ZAHARA Investigators, Predictors of pregnancy complications in women with congenital heart disease, Eur. Heart J. 31 (2010) 2124–2132.
[17] K.K. Whitcome, L.J. Shapiro, D.E. Lieberman, Fetal load and the evolution of lumbar lordosis in bipedal hominins, Nature 450 (2007) 1075–1078.
[18] B.H. Heidemann, J.H. McClure, Changes in maternal physiology during pregnancy, Br. J. Anaesth. 3 (2003) 65–68.
[19] P.J. Trainer, Corticosteroids and pregnancy, Semin. Reprod. Med. 20 (2002) 375–380.
[20] J.R. Lindsay, L.K. Nieman, The hypothalamic-pituitary-adrenal axis in pregnancy: challenges in disease detection and treatment, Endocr. Rev. 26 (2005) 775–799.
[21] J. Troko, Y. Poonawala, T. Geberhiwot, B. Martin, Multidisciplinary team approach is key for managing pregnancy and delivery in patient with rare, complex MPS I, JIMD Rep (2016), http://dx.doi.org/10.1007/8904_2016_527.
[22] C.F.M. De Souza, A.A. Silva, M.T.V. Sanseverino, J.A. Magalhaes, S. Fagondes, D. Manica, F.P. Vairo, P. Barrios, R. Giugliani, Pregnancy in a patient with mucopolysaccharidosis type I (MPS I) treated with enzyme replacement therapy: A case report, J. Inherit. Metab. Dis. 38 (Suppl. 1) (2015) S263.
[23] E. Oussoren, F.P.J. Karstens, J.G. Langendonk, M.M.M.G. Brands, A.T. van der Ploeg, Enzyme replacement therapy during pregancy in a Mucopolyssachariadose I Scheie patient, J. Inherit. Metab. Dis. 34 (Suppl. 3) (2011) S208.
[24] C.J. Hendriksz, B. Burton, T.R. Fleming, P. Harmatz, D. Hughes, S.A. Jones, S.P. Lin, E. Mengel, M. Scarpa, V. Valayannopoulos, R. Giugliani, P. Slasor, D. Lounsbury, W. Dummer, STRIVE investigators, Efficacy and safety of enzyme replacement therapy with BMN 110 (elosulfase alfa) for Morquio A syndrome (mucopolysaccharidosis IVA): a phase 3 randomised placebo-controlled study, J. Inherit. Metab. Dis. 37 (2014) 979–990.
[25] R. Walker, K.G. Belani, E.A. Braunlin, I.A. Bruce, H. Hack, P.R. Harmatz, S. Jones, R. Rowe, G.A. Solanki, B. Valdemarsson, Anaesthesia and airway management in mucopolysaccharidosis, J. Inherit. Metab. Dis. 36 (2013) 211–219.