

# **Mucopolysaccharidoses and Pregnancies**

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**Short overview on the literature  
Austrian experience and case reports**

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# Overview

- Introduction – what is special in MPS ?
- MPS and pregnancies – examples from the literature
- Published case report: severe form of MPS IVA
- Case reports from USA and Austria with MPS IVA, MPS IVB
- What can we learn - summary and conclusions

# Introduction: What is special ?

- MPS are multi-system disorders
- MPS are clinically very heterogeneous
- MPS patients with attenuated forms can survive until late adulthood
- MPS patients with multi-disciplinary care and new treatments (BMT, HSCT, ERT) can survive longer
- **MPS patients are getting older and have new perspectives for their life and family planning !**

# Examples from the literature - 1

## MPS I (Hurler / Scheie):

1. female patient with intermediate form of MPS I:
  - BMT at the age of 4 yrs
  - Gave birth to 4 girls between the age of 18-26 yrs
2. Female patient with severe form of MPS I:
  - Diagnosis at the age of < 1 yr old
  - BMT at the age of 14 months
  - Pregnant at the age of 21 yrs, but termination at 9 weeks of gestation
3. Female patient with severe form of MPS I:
  - Diagnosis at the age of 5 yrs
  - Enclosed in the ERT – extended study
  - Gave birth to a girl of 1, 250 g at 29 weeks of pregnancy

# Examples from the literature - 2

## MPS I (Hurler / Scheie):

4. **Ongoing prospective study by Genzyme** analysing pregnancy and birth in MPS I patients who continued **ERT during pregnancy and lactation**
  - First female patient with MPS I-Scheie has completed the study
  - Gave birth to a boy of 2,500 g at 37 weeks of pregnancy (caesarean section)
  - Good development in the first 12 months
  - Focus on breastfeeding and ERT outcome
5. Female patient with MPS I
  - **Successful epidural anaesthesia** with ropivacaine seems to be possible and safe

# Examples from the literature - 3

## MPS VI (Maroteaux-Lamy):

### 7. Two sisters with MPS VI

- Diagnosed at the age of 35 yrs (145 cm) and 38 yrs (140 cm)
- The eldest had 2 children
  - Both born with caesarean section due to maternal hip malformation
  - Pregnant of 3<sup>rd</sup> child, refused ERT

### 8. Female patient with MPS VI

- Pregnant at the age of 25 yrs
- Development of myelopathy at 36 weeks of pregnancy (1 week bed-rest)
- After another 13 days, she gave birth to a health boy by caesarean section

# Examples from the literature - 4

## MPS VI (Maroteaux-Lamy):

9. Turkish female patient with MPS VI

- Married woman with 2 children

10. Two brothers with MPS VI

- Diagnosed at the age of 38 yrs (161 cm) and 40 yrs (168 cm)
- The younger married with a daughter at the age of 33 yrs

# Examples from the literature - 5

## MPS II (Hunter):

### 11. Female patient with mild manifestations of MPS II

- 28 yrs old
- 148 cm
- Her brother with MPS II died at the age of 25 yrs
  - Her enzyme activity was in the same ranges as her brother
- Gave birth at 38 weeks of pregnancy
  - Girl of 2,600 g
  - Died at 11 months due to other problems than MPS II (severe pulmonary vein stenosis and large atrial septal defect)



# Examples from the literature - 6

## MPS III (Sanfilippo):

### 12. Female patient with MPS IIIB

- 23 yrs: Married
- 28 yrs: Gave birth to a healthy girl
- 36 yrs: Mental retardation became evident
- 57 yrs: Diagnosed with MPS IIIB

One of her brothers was also affected

- Until the age of 49 yrs: Worked in non-demanding jobs
- 54 yrs: Institutionalised
- 66 yrs: Diagnosed with MPS IIIB

# Case report from the literature:

## “Severe form of MPS IVA (Morquio A) and pregnancy”<sup>1</sup>

### Phenotype of Morquio A patients<sup>2</sup>

Severe form	height: <120 cm
Intermediate form	height: 120 – 140 cm
Mild (attenuated) form	height: > 140 cm

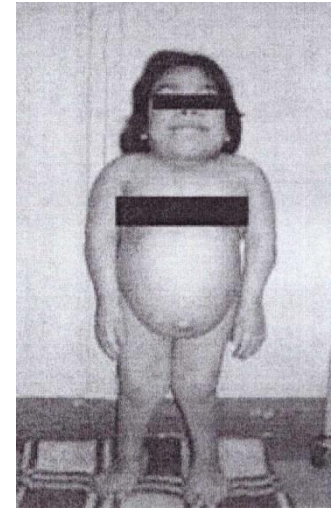
1. Salinas HP et al. Rev Chil Obstet Ginecol 2005;70:400-3;
2. Montano AM et al. J Inherit Metab Dis 2007;30:165-74

# Mother's parameters I

- Age: 24 years
- Diagnosis: 8 years (urine)
- Definitive diagnosis: 21 years
- Instability of the cervical spine (C1/C2) because of dysplasia of the dens axis, not operated
- Corneal opacity, not operated
- Regular menstruation cycle
- First pregnancy: first consultation after 16 weeks of amenorrhoea

# Mother's parameters II

- Size: 87.5 cm
- Weight: 23 kg
- Waist size: 94 cm
- Pectus carinatum
- Insufficiency of the mitral and tricuspid valves
- Abdomen with umbilical hernia
- Extreme genua valga



# Period of pregnancy

- Ultrasound: female foetus, all other parameters normal
- During the stay (21<sup>st</sup> week of gestation): development of polyhydramnios and dyspnoea, then weekly controls
- Birth: 28+3 weeks of pregnancy, spontaneous contractions started, decision for caesarean section
- Regional anaesthesia

# Baby's parameters

- Female
- Weight: 1,180 g
- Length: 38 cm
- APGAR: 8/9
- Exogenous surfactant factor application
- Anaemia of premature child
- Hyperbilirubinaemia
- Apnoea
- Bronchopulmonary dysplasia

# Another mother with severe form of MPS IVA – Morquio A from USA

- MPS suspected before birth
  - Sister of patient was diagnosed with Morquio at 22 months
  - Morquio A diagnosed after birth
- Decision to become pregnant not easy:
  - Independent life
  - Working full time
  - Driving a SUV
  - Walking on her own
  - Caring for herself



[www.gofundme.com/kmj554](http://www.gofundme.com/kmj554), January 23<sup>th</sup>, 2015

## Mother's parameters:

- Menarche delayed
  - Patient: 15 yrs
  - Sister with Morquio A: 18 yrs
- Age at pregnancy: 35 yrs
- Height: 114.3 cm
- Weight: 34.9 kg
- Weight gain during pregnancy:
  - At 9 weeks: 0.91 kg (2.6%)
  - At delivery: 6.4 kg (18.2%)

## Father's parameters:

- Height: 173 cm
- Age at pregnancy of wife: 33 yrs



*18<sup>th</sup> week of  
pregnancy*



# Planning the next steps

- High risk pregnancy doctor 2 hours away, specialised in dwarfism
- Tests before agreement by the doctor:
  - Heart
  - Sleep study
  - Respiratory
- Accepted by an anaesthesiologist as part of the team
- Anaesthesia: endotracheal, but awake and sitting when going into airways
- Planned delivery: Caesarean section
- Agreement: Life of the mother before the baby

## Uneventful pregnancy without any problems until week 33 with monthly controls



In the 31<sup>st</sup> week of pregnancy, the anaesthesiologist „didn't want to push out luck“, delivery was planned for the 34<sup>th</sup> week

# Baby's parameters

- Female
- Weight: 1950 g
- Size: 43 cm
- Problems with the daughter after birth:
  - Oxygen feeding tube
  - For weeks at the neonatal intensive-care unit (NICU)
- Problems with the mother after several weeks
  - Mastitis and breast abscess: emergency surgery needed
  - Belly button hernia: surgical repair needed



Private fotos

# After the happy end...

## Mother reflections

- When I had all the tests done, I had an idea of some of the things that could happen to me and/or the baby
- Death was a big part of it
- I am thankful how great things ended up but I would never take that risk again



*Special baby bed for the small mother, daughter with 1, 2 and three months*

# **Austrian mother with an attenuated form of MPS IVB – Morquio B**



- MPS suspected: 3,5 years: thoracic deformity, weak legs, recurrent bronchitis
- MPS diagnosed: 6 – 7 years
- History of operations:
  - correction of leg axis bilat. in childhood
  - Carpal tunnel syndrome bilat. (27 yrs)
  - Hip – Endoprosthesis bilat. (28 and 29 yrs)
  - Hallux valgus bilat.





*one day before delivery*

## Mothers parameters:

- Menarche: 16 – 17 yrs
- contraception: contraceptive pill and menstrual cycle meter
- Age at pregnancy: 31 yrs (not planned)
- Height: 147 cm
- Weight: 45 kg
- Weight gain during pregnancy: 10,5 kg (23 %)

Fathers height: 179 cm

## Around the Birth:



- From the beginning on a Caesarean section was planned because of bilateral hip endoprotheses
- First planned date: two weeks before the calculated date
- Second planned date: 37+4week of pregnancy („big baby“)
- Lumbar anaesthesia because of risks of endotracheal anaesthesia in MPS

## After birth



- boy, 3292 grams, 51 cm. Delivery complicated by the big size of the child, disproportion due to the small abdomen of the mother: high blood loss with need of blood transfusions for the mother
- Baby: APGAR: 7/9/10.
- Umbilical cord blood: pH = 7,35
- breathing problems
- neonatal intensive care for 5 days
- Breast feeding: for 9 months
- Now: healthy strong boy





## **Two pregnancies in a mother with attenuated form of MPS IVA – Morquio A**

- MPS suspected: 3 yrs, when first operation was performed due to hip dislocation and knock knees
- MPS diagnosed: 13 yrs
- History of operations:
  - 3 yrs: first hip operation bilateral
  - 14 yrs: subtrochanteric derotation osteotomy bilateral
  - 25 yrs: hip endoprosthesis bilateral
- Additional diagnosis since 2014: multiple sclerosis, therefore enzyme replacement therapy (ERT) was not started yet



*Daughters, 11  
and 14 yrs old*

*(private foto)*

## Mother's parameters:

- Menarche: 15 – 16 yrs
- Contraception: contraceptive pill until pregnancies
- Age at pregnancies: 25 and 28 yrs
- Height: 147 cm
- Weight: 41 kg
- **Weight gain during pregnancy:**
  1. child: 6 kg (15 %)
  2. child: 10 kg (24 %)

## Father's parameters:

- Height: 183 cm

## About first pregnancy and birth:

- From the first visit to the gynaecologist, a Caesarean section was planned because of the bilateral hip endoprosthesis
- Amniocentesis: no pathological result
- Date of delivery: 21 days before the calculated date
- Endotracheal anaesthesia during operation
- **Baby's parameters** (37<sup>th</sup> week of pregnancy):  
Girl, 2500 g, 45 cm, APGAR score: 7,8,9
- Breast feeding: only short time, not enough breast milk

## About second pregnancy and birth:

- Amniocentesis was not performed („it is not possible to investigate for MPS“)
- Date of delivery: 14 days before the calculated date
- Caesarean section under endotracheal anaesthesia was performed
- **Second baby's parameters** (38<sup>th</sup> week of pregnancy):
  - Girl, 2970 g, 47 cm, APGAR score: 8,9,10
  - Ten days in hospital due to aspiration of amniotic fluid
- Breast feeding: again only short time, not enough breast milk

# Why not ?

## Father with MPS IVA – Morquio A



*MPS IVA, private photo*

- Born: 1969
- 150cm, 85kg
- Suspected: at 1½ years
- Diagnosed: 2003/2014
- Disability: 100%  
(since 1997)
- Restricted: mobility,  
hearing, finger  
movement
- Operations: eyes
- Married since 2006
- **3 children (2 girls, 1  
son), 1 miscarriage**

# Pregnancies in MPS ? - Conclusions

- Nevertheless, even in such patients pregnancy can be successful with the right preparation and a selected medical team before starting
- To stay close to a specialised clinic seems to be vital
- Such a pregnancy can only be handled in a family with several supporting relatives
- The time efforts and the financial problems should not to be overlooked
- In one of the described cases, the woman could not work during most of the pregnancy, the husband lost his work because he stayed most of the time with his wife
- The special crib shows that some of the problems managing a child perhaps start after birth

# Complications arise from:

- Little knowledge about pregnancy in MPS
- No adequate genetic counselling
- Atlanto-axial instability: worsening of myelopathy
- Worsening of lumbar lordosis
- Worsening of other maternal affected organs (heart, heart valves, lungs...)
- „Right“ time for the delivery - disproportion of the baby's size compared with the mother's trunk
- Caesarean section with anaesthesia (endotracheal intubation vs. epidural anaesthesia)
- Medical regimen for HSCT/BMT and gonadal toxicity
- Uncertain handling of ERT ...

# Conclusions

- Pregnancies “happen” to MPS-patients (women and men)
- In most cases without any help for reproduction
- Often without any genetic counselling or carrier screening of the partner
- In attenuated forms, we often hear by chance from children after the delivery, often through caesarean section
- Patients with late onset of mental deterioration can also have a family and children





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**[www.mps-austria.at](http://www.mps-austria.at)**