SSIEM Official Satellite Symposia
28 to 30 August 2015, in Lyon (France)

This conference is part of the Educational Program of Excellence on CDG created by the Portuguese Association for CDG (APCDG, www.apcdg.com).

It is organized in partnership with several associations and/or country CDG patient advocates: CDG Australia, CDG Brazil, CDG Czech Republic, CDG Denmark, Foundation of Glycosylation (the FoG) Canada, CDG Denmark, CDG Italy/Ireland, CDG Israel, Les ptits CDG France, CDG Spain, CDG Sweden, CDG USA, CDG UK charity and CDG The Netherlands.

©Foundation of Glycosylation and Portuguese Association for CDG and related rare metabolic diseases (APCDG-DMR, Portugal). 2015. All rights reserved.
This and other resources available at:
www.apcdg.com
Endocrine aspects in PMM2-CDG: diagnostic approach and management

Miski Mohamed
Introduction

• PMM2-CDG (CDG 1A)
• Endocrine system
• Endocrine problems in CDG
  • Growth
  • Thyroid dysfunction
  • Sexual development
PMM2-CDG (1A)

- Phosphomannomutase 2 deficiency
- 1: 20,000-50,000
Multisystem disease

Cardiac (cardiomyopathy)

Muscle

Hormones

Intestinal absorption (protein losing enteropathy)

Coagulation factors (bleeding, thrombosis)

Brain development

Kidney (proteinuria)

Liver
Classical/infantile presentation

Feeding problems
Failure to thrive
Hypotonia
Psychomotor retardation
Ataxia (vermis hypoplasia)
Abnormal fat distribution
Endocrine abnormalities
Abnormal liver function
Coagulation defects
Pediatric/adult presentation

Psychomotor retardation
Speech delay
Ataxia
Retinitis pigmentosa
Cataract
Endocrine abnormalities
Coagulation defects
Endocrine system
Hypothalamic - Pituitary - Thyroid Axis

TRH = Thyroid Releasing Hormone
TSH = Thyroid Stimulating Hormone
Endocrine dysfunction in CDG

• **Hormones** are glycosylated

• Binding/transport proteins in blood are glycosylated
  • Thyroxin binding globulin (TBG) is glycosylated
    • Hypothyroidism

• The **receptors** on the target cells are glycosylated
  • Insulin receptor
    • Hyperglycemia due to insuline resistance
Growth

• Failure to thrive
  • First year of life mainly due to feeding problems
  • Protein loss in gut
  • Growth factor/Insulin like growth factor (IGF)

Growth hormone therapy
HYPOTHYROIDISM

Intolerance to Cold
Receding Hairline
Facial & Eyelid Edema
Dull-Blank Expression
Extreme Fatigue
Thick Tongue - Slow Speech
Anorexia
Brittle Nails & Hair

Hair Loss
Apathy
Lethargy
Dry Skin (Coarse & Scaly)
Muscle Aches & Weakness
Constipation
Menstrual Disturbances

Late Clinical Manifestations
Subnormal Temp
Bradycardia
Weight Gain
↓LOC
Thickened Skin
Cardiac Complications

Thyroxine supplementation therapy
Discriminative features of hypothyroidism in CDG

- Constipation
- Low basal body temperature
- Dry/itchy skin
- Decreased sweating
- Thinning of the eyebrows
- Goiter
- Depression
Hypogonadotropic hypogonadism

- Brain problem
  - Low LH/FSH
- Gonads are not stimulated to make enough hormones
  - Deficiency of estrogen or testosterone
    - **Girls**
      - Delayed menstruation
      - No breast development
    - **Boys**
      - Low testicular volume
      - Low sperm count

LH/FSH supplementation therapy
Conclusions

• Hypothyroidism is hard to diagnose in PMM2-CDG
  • Symptoms overlap
  • TSH elevation are common in PMM2-CDG and normalize without intervention in 2/3 of the patients
  • FT4 is most reliable because not glycosylated
  • low FT4 in combination with clinical symptoms → treat for hypothyroidism
  • TBG is not an usefull marker and often abnormal in patients → no clinical consequence!

• Growth hormone defiency is frequent in PMM2-CDG
  • Can be supplemented but often not neccesary

• Secondary sexual deveopment
  • Check for hormones
  • Supplement FH/LSH if needed
Acknowledgements

E. Morava
T. Gardeitchik
H. Claahsen-van der Grinten
D.J. Lefeber
R.A. Wevers
Foundation Glycosylation (FoG) is the official sponsor of the videos targeted to the “SSIEM Official Satellite Symposia – Second World Conference on Congenital Disorders of Glycosylation (CDG): a challenging story of sugar trees”:

The Foundation Glycosylation (FoG) founded by Duncan Webster (Canada), is the official sponsor of the videos of all oral session that will be given during the conference. This material will be available in the Youtube channel dedicated to “SSIEM Official Satellite Symposia – Second World Conference on Congenital Disorders of Glycosylation (CDG): a challenging story of sugar trees” at:

For more information about the work of this organization which is focused on research to ALG9 -CDG (CDG -1L), visit the following link: http://www.thefog.ca/main.html

ACKNOWLEDGMENTS

• All speakers
• All participants
• Associations
• Organizations
• Domaine Saint Joseph
• All Volunteers
• Pf Pascale de Lonlay and Nathalie Seta
• Dr Maria A Vilaseca and Pf Jaeken
• Biocommunicat