Diabetes mellitus in a 16-year-old boy developing multiple neuro-endocrine dysfunctions in the course: is it type 1 diabetes or Wolfram syndrome, or both?

Maristella Santi, Christa E. Flück, Claudia Böttcher

Department of Pediatrics (Division of Pediatric Endocrinology and Diabetology), Inselspital, Bern University Hospital, Switzerland.

The authors have nothing to disclose / corresponding author: maristella.santi@insel.ch

Introduction

- Autosomal recessive mutations in the Wolfram syndrome type 1 gene are responsible for the classical Wolfram syndrome.
- The gene encodes wolframin, a membrane glycoprotein, which helps to regulate the calcium homeostasis in the endoplasmic reticulum.
- Wolfram syndrome is characterized by early-onset, non-autoimmune diabetes mellitus (DM).
- The associated symptoms, like optic atrophy, diabetes insipidus, sensoneuronal deafness, urinary tract abnormalities, neurologic degeneration manifest with inconstant severity, as well as variable age of onset, often delaying the precise diagnosis.

Results

- The DM was difficult to control (hemoglobin A1c levels between 8.1-9.7%) despite high-doses of insulin were used (1.7 IU/kg/day).
- Repeat antibody testing for type 1 DM revealed positivity for anti-insulin-antibodies.
- Family history was positive for type 2 DM.
- During follow-up, the patient showed multiple neuro-endocrine dysfunctions over the following decade (Fig. 1 and 2).
- Poor response to a 6 months course of low-dose testosterone stimulation at age 15 years.

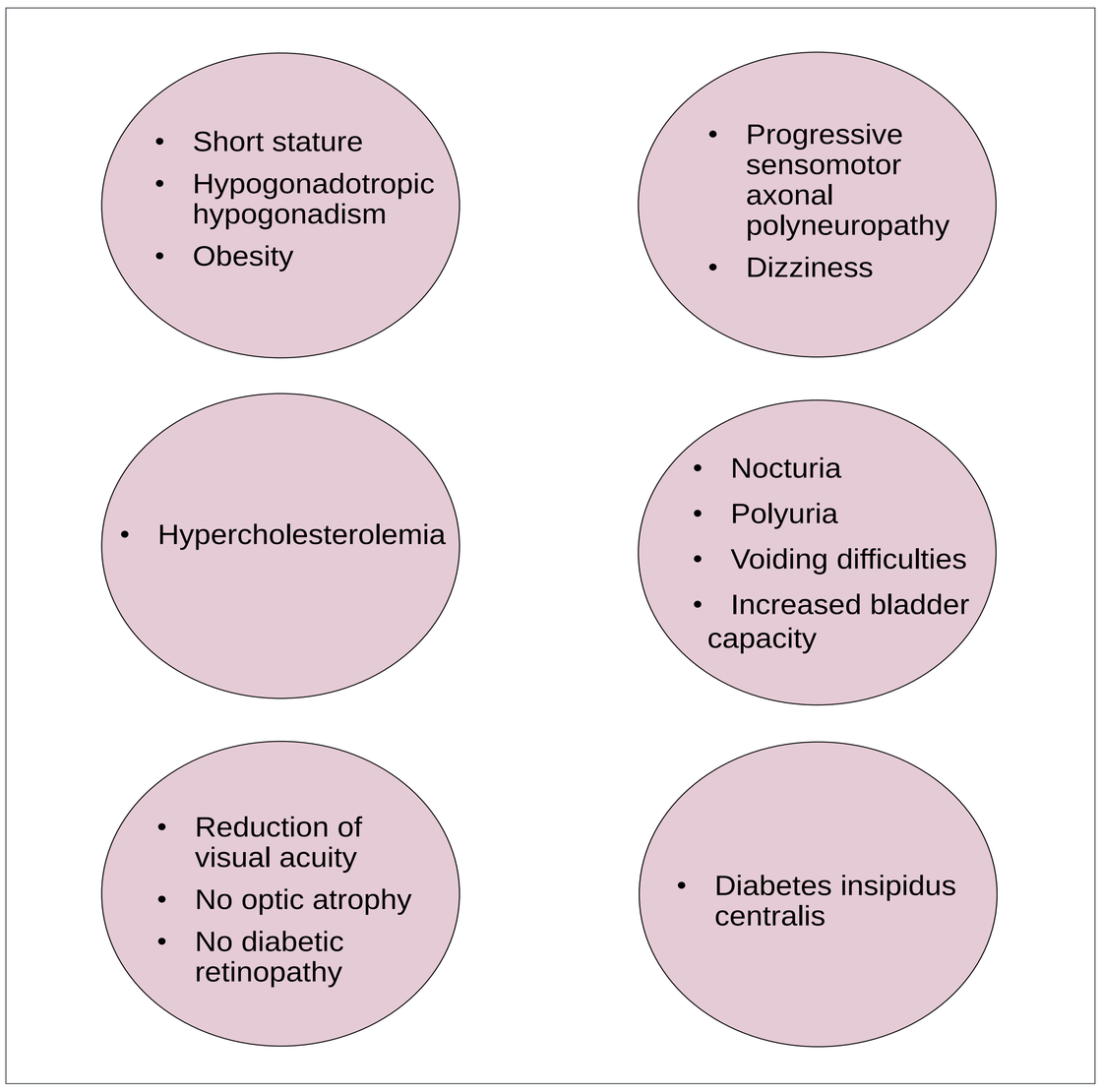

Fig. 2: Multiple neuro-endocrine dysfunctions at the age of 16 years.

Objective

- We report the case of a 16-year-old boy who presented with insulin-dependent DM without ketoacidosis at the age of 5 years and developed multiple neuro-endocrine dysfunctions over the following decade.

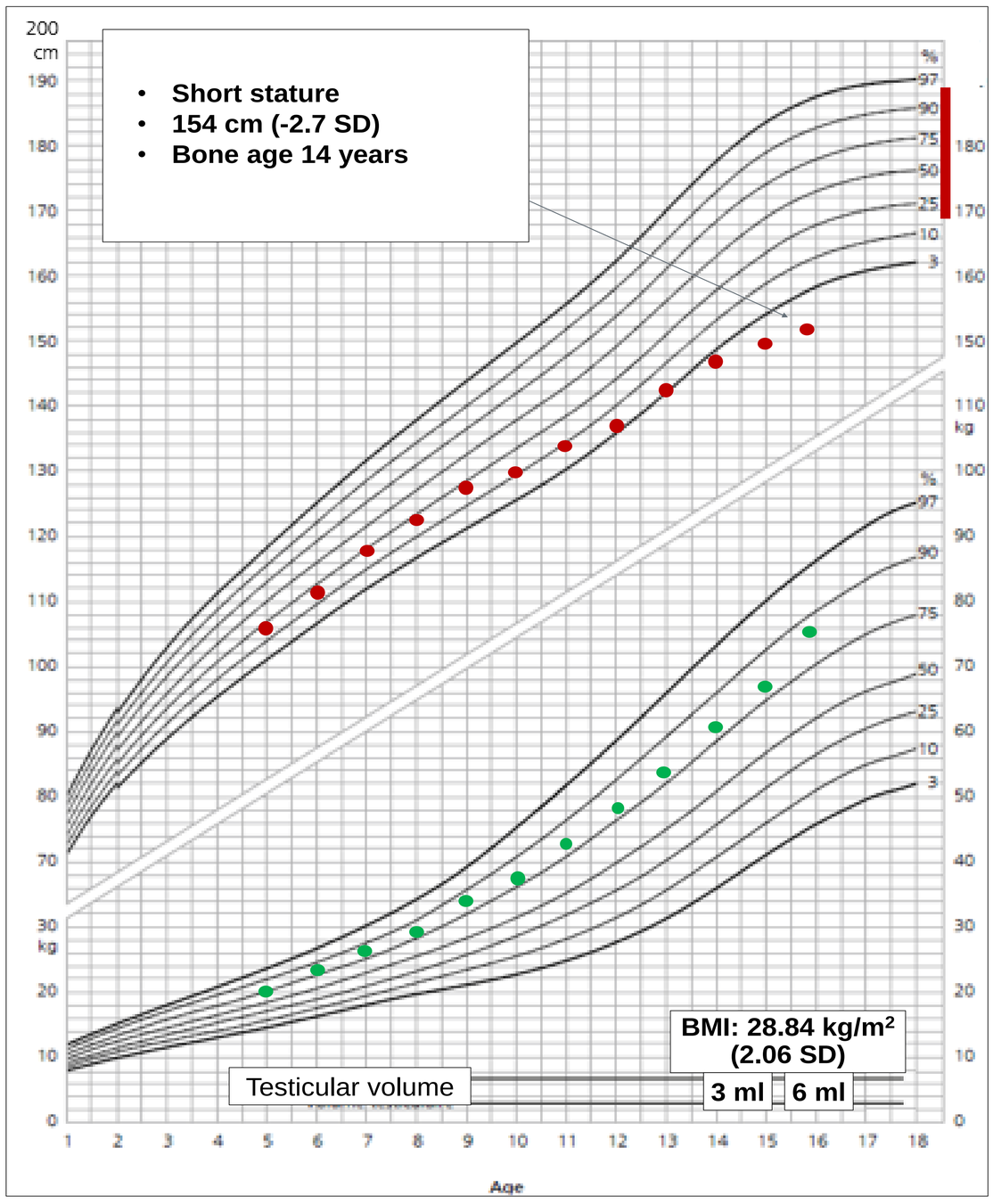

Fig. 1: Growth charts up the age of 16 years. BMI, Body mass index. SD, standard deviation.

- Renal function, hepatic function, thyroid function, audiologic examination and magnetic resonance imaging of the brain were normal.
- **Array CGH analysis: arr(1-22)x2,(X,Y)x1**, no imbalance was detected.
- Molecular DNA sequencing of the wolframin gene is pending.

Conclusion

- Importance of careful clinical vigilance for atypical features in children having non-autoimmune diabetes mellitus.
- Not only typical monogenic forms should be considered, but also mitochondrial causes such as Wolfram syndrome.
- Wolfram syndrome requires specific genetic workup and clinical monitoring.
- Diagnosis of Wolfram syndrome may have therapeutic implications, GLP-1 receptor agonists may improve metabolic control.