Intellectual disability

Congenital hyperthyroidism is most likely the single most preventable cause of intellectual disability, especially in the Southern African context where routine screening is not performed currently.

Anti thyroid hormone resistance

An interesting case of resistance to anti-thyroid hormone treatment in a pregnant patient

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Type 2 Diabetes in a 13year old male

HOSP #	MRN123441843	**WARD**	Paediatric Endocrine clinic
CONSULTANT	Dr. Jody Rusch	**DOB/AGE**	13 y male

Abnormal Result

HbA1c = 6.6%

Presenting Complaint

This patient self-presented to a GP and referred to the Pediatric endocrinologist at Red Cross Children's hospital.

History

The patient, an orphan, had a family history of type 2 DM. The late mother (due to breast CA) and the uncle was confirmed with Type 2 DM. The patient reported self-monitoring of glucose with a point of care device, reported having a glucose at times of 13-14mM. This was thus suspicious for DM2. He reported being active and "running 5-6km on some weekends".

The patient did not report polyuria, but there was a history of polydipsia occasionally.

Examination

BP elevated, pulse regular, BMI 28.3
Acanthosis nigricans was noted, as well as an oily skin.

The rest of the examination was essentially normal.

Anthropometry: not short, overweight

Laboratory Investigations

HbA1c = 6.6%

An OGTT was done, but unfortunately the glucose was out of stock so we needed to make another plan, thus 50% Dextrose (150ml) was given as the 75g glucose equivalent.

Baseline 4.9 mM; 2h 7.8mM

Criteria for interpretation of Oral GTT (WHO guidelines 1999/2007):

Impaired Fasting Glycaemia:
Fasting plasma glucose 6.1 – 6.9 mmol/L
2 hour glucose during 75g OGTT < 7.8 mmol/L Impaired Glucose Tolerance: Fasting plasma glucose < 7.0 mmol/L 2 hour glucose during 75g OGTT 7.8 – 11.0 mmol/L

Diabetes Mellitus: Fasting plasma glucose >= 7.0 mmol/L OR
2 hour glucose during 75g OGTT >= 11.1 mmol/L

Other Investigations

- TSH normal
- Free-T4 = 11.2 pM
- ALT = Normal and no signs of fatty liver disease (although an ultrasound was not performed).

Central hypothyroidism was also suspected. A synacthen stimulation test can be performed to assess the function, but the fact that the TSH is normal, fairly confidently excludes this diagnosis.

Urine protein:creatinine ratio = normal
Ultrasound not done yet to determine whether there's a fatty liver

Final Diagnosis

Diabetes Mellitus type 2 in a child, likely a case of MODY (maturity onset diabetes of the young), although this would likely not present itself in a child with the phenotype of a type 2 diabetic child.

Take Home Message

Diabetes Mellitus type 2 is increasing at an enormous rate, even to the extent that children are starting to become affected.

MODY is caused due to a range of genetic diseases involved in insulin signalling and control. The most wel-known gene is most likely that of glucokinase. However, the most prevalent gene affected in MODY-affected individuals is Hepatocyte Nuclear factor 1 alpha (*HNF1A*) gene. The optimal treatments differ between the different causal genetic defects.

Type	Genetic defect	Frequency	Beta cell defect	Clinical features	Risk of microvascular disease	Optimal treatment
1	Hepatocyte nuclear factor-4-alpha	<10%	Reduced insulin secretory response to glucose	Normal renal threshold for glucose	Yes	Sulfonylureas
2	Glucokinase gene	15 to 31%	Defective glucokinase molecule (glucose sensor), increased plasma levels of glucose are necessary to elicit normal levels of insulin secretion	Mild, stable, fasting hyperglycemia, often diagnosed during routine screening. Not progressive.	Generally no	Diet
3	Hepatocyte nuclear factor-1-alpha	52 to 65%	Abnormal insulin secretion, low renal threshold for glucose	Low renal threshold for glucose, +glycosuria	Yes	Sulfonylureas
4	Insulin promoter factor 1	Rare	Reduced binding to the insulin gene promoter, reduced activation of insulin gene in response to hyperglycemia	Rare, pancreatic agenesis in homozygotes, less severe mutations result in mild diabetes	Yes	

5	Hepatocyte nuclear factor-1-beta	Rare		Pancreatic atrophy, renal dysplasia, renal cysts, renal insufficiency, hypomagnesemia	Yes	Insulin
6	Neurogenic differentiation factor-1	Rare	Pancreatic development		Yes	Insulin

Data from:Naylor R, Philipson LH. Who should have genetic testing for maturity-onset diabetes of the young? Clin Endocrinol (Oxf) 2011; 75:422.

Ramesh SC, Marshall I. Clinical suspicion of Maturity Onset of Diabetes of the Young in pediatric patients diagnosed with diabetes mellitus. Indian J Pediatr 2012; 79:955.

Thanabalasingham G, Owen KR. Diagnosis and management of maturity onset diabetes of the young (MODY). BMJ 2011; 343:d6044.

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Quadruple-H

A case of hyperparathyroidism, hyperthyroidism, hypercalcemia and hypertension