Diabetes – a rare complication of ataxic telangiectasia presenting in childhood

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Introduction

- Ataxia-telangiectasia (AT) is a rare autosomal recessive multisystem disease characterised by progressive neurological impairment, cerebellar ataxia and immunodeficiency, ocular and cutaneous telangiectasia and a predisposition to malignancy
- Several case reports in adult patients suggested co-existence of an unusual form of Diabetes in AT.
- However, there is a lack of clinical data in the associations of Diabetes and cardiometabolic abnormalities in children with AT.

Case Synopsis

- 15.9 yr old, male, South Indian origin
- AT since aged 5 years (homozygous mutations for ATM gene at C1966A->C and 1968X.delI)
- Intellectually normal and attends mainstream school with physical assistance
- 4-week history of polyuria and polydipsia without weight loss
- Father and 5 paternal uncles: Type 2 diabetes mellitus aged <50y

Examination

- Normal Body Mass Index 23.5 kg/m²
- Tanner Stage 5
- No Acanthosis Nigricans
- Normal Blood pressure

At diagnosis

- Fasting glucose 11.5 mmol/L
- Fasting insulin 209 pmol/L
- HbA1c 103 mmol/mol (11.6%)
- Islet Cell antibodies Negative
- GAD antibodies Negative
- Urine C-peptide/Creatinine Ratio 2.84 mmol/mol

Further investigations

- ALT 209 U/L
- Cholesterol 5.3 mmol/L
- Triglyceride 2.7 mmol/L
- Liver US Fatty infiltration
- Liver biopsy Findings suggestive of non-alcoholic fatty liver disease

Management & Progress

- He was started on Metformin 500 mg once daily.
- His fasting glucose maintained between 5-6 mmol/L
- HbA1c of 47 mmol/mol (6.4%) after 1 year
- Dyslipidaemia with raised ALT was noted, and further investigations demonstrated findings suggestive of non-alcoholic fatty liver disease.

Discussion

- Diabetes is a rare complication in AT which is characterised by insulin resistance, negative antibodies, liver dysfunction and dyslipidaemia, without clinical obesity
- Pathophysiology of diabetes in AT (Figure. 1):
  - The ATM gene is found on the long arm of chromosome 11. This gene controls the production of the ATM protein, an essential enzyme involved in cellular responses to DNA damage and other forms of stress in every cell of the body
  - Mutations of the ATM gene in AT leads to disruption of the downstream signalling pathways in the insulin-stimulated glucose transport at the skeletal muscles, and hence glucose clearance.
- Metformin and Thiazolidinediones drugs of choice for AT patients with diabetes
- Our case demonstrated that diabetes and metabolic complications in AT can present in the paediatric age range, and screening should be part of the follow-up of AT from childhood.