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 1968-X.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/m^2
  - Tanner Stage 5
  - No Acanthosis Nigricans
  - Normal Blood pressure

Investigations

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 nmol/mol

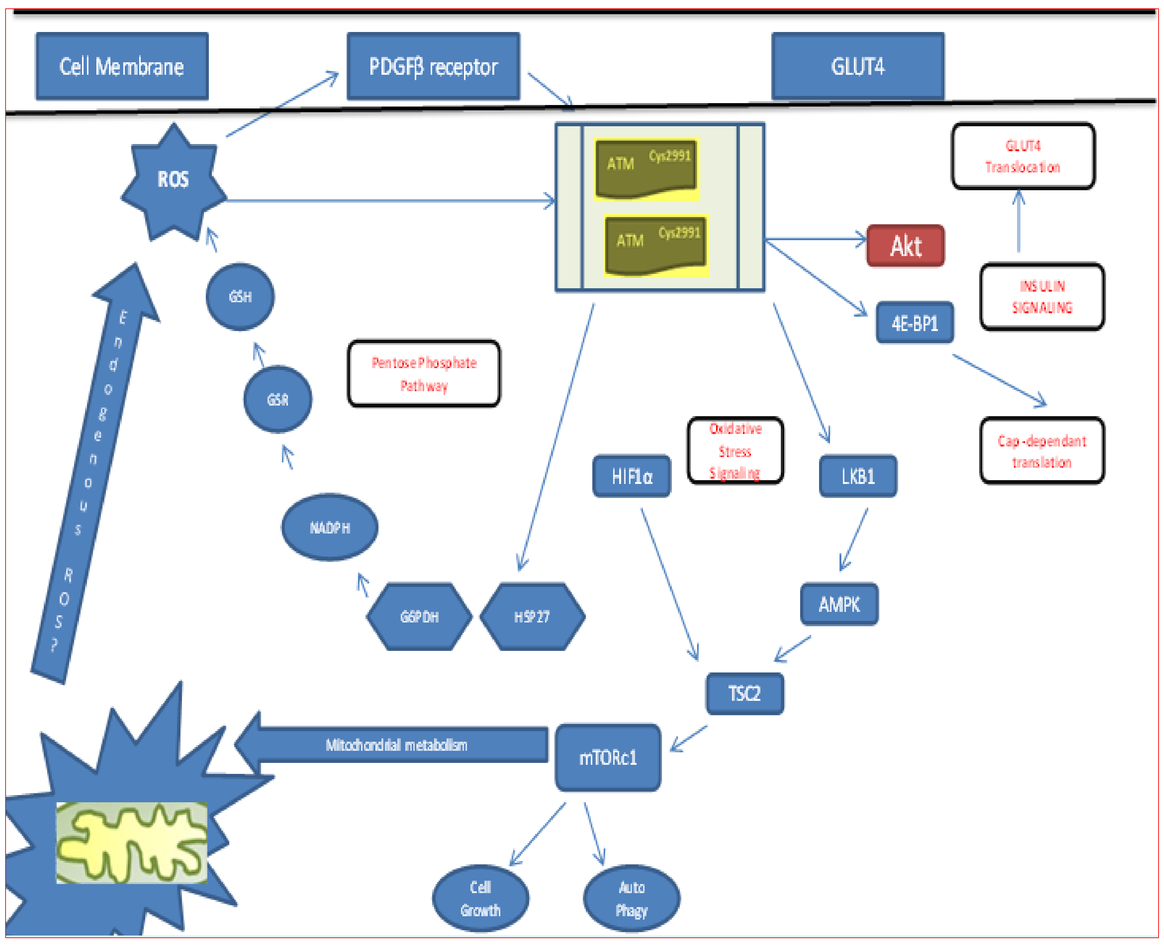
Further investigations	
ALT	209 U/L
Cholesterol	5.3 mmol/L
Triglyceride	2.7 mmol/L
Liver US	Fatty infiltration
Liver biopsy	Findings suggestive of non-alcoholic fatty liver disease

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

Figure1. Schematic diagram showing proposed pathophysiology of diabetes in patients with AT



- 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.

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Diabetes

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