Is Autoimmunity on the Increase in Type 1 Diabetes Mellitus (T1DM)?
Presentation of Multiple Autoimmune Disorders at Diagnosis of T1DM

D Elangaratnam, S Punniyakodi, V R Puthi
Department of Paediatrics, Peterborough City Hospital, UK

Introduction

- T1DM results from autoimmune destruction of pancreatic beta islet cells and up to 1/3 of patients develop autoimmune polyglandular syndrome (PAS)
- Autoimmune hypothyroidism (AIHT) is the most common disorder associated with T1DM with a prevalence between 5-31.5%
- Autoimmune non glandular problems like coeliac disease (CD) occur in 1 - 8.3% in children with T1DM
- Approximately 50 T1DM susceptibility genes have been identified and these genes also carry a potential risk for various autoimmune diseases occurring simultaneously or within a narrow time interval and might explain associated endocrine autoimmune diseases in one third of all T1DM patients
- We present two patients presenting at diagnosis with PAS and CD

Case Reports

Case 1
- 9 year old girl presented in diabetic ketoacidosis with a 3 month history of polyuria and polydipsia
- Initial TSH 97.5 mU/L (NR: 0.3-5.0) and Free T4 1.3pmol/L (NR: 12-22)
- Thyroid peroxidase antibody (TPO Ab) was normal and repeat TSH 75.6 mU/L and FT4 of 3.8 pmol/L, confirmed the diagnosis of AIHT
- Tissue Transglutaminase (tTG) >128 U/ml (NR: <10). She was heterozygous for HLA DQA1*05:01/DQB1*02:01 and negative for HLA-DQ8 (HLA-DQB1*03:02), consistent with a diagnosis of CD

Case 2
- 10 year old girl presented with two week history of polyuria, polydipsia and high blood glucose
- Initial TSH 9.2 mU/L and repeat test showed TSH 63.3 mU/L which confirms the diagnosis of AIHT
- Positive family history for CD
- Tg level was 170 U/ml and jejunal biopsy showed features of villous atrophy confirming CD

T1DM & Hypothyroidism

- HLA DQ Polymorphism (HLA-DQA1, DQB1, DQ2 and DQ8) can significantly modify the risk for CD and AIHT
- HLA-DQ8/DQ2 is known to increase the risk of developing anti-thyroid antibodies and CTLA-4 gene polymorphism may play significant role in synergy with Human Leucocyte Antigen (HLA) for the development of AITD
- Studies reported that 50% of children with elevated TPO Ab hypothyroidism in 3-4 years
- Majority of children with T1DM do not have symptoms of hypothyroidism
- Recurrent hypoglycaemias can be a presenting feature of hypothyroidism in T1DM due to decreased hepatic glucose production

T1DM & Coeliac Disease

- HLA DQ2 and DQ8 genes increase the risk for developing T1DM and CD
- HLA DQ2 is prevalent in 20-30 % of population, and only a minority develop CD suggesting an additional non HLA linked genetic involvement
- TNF α is a major factor responsible for damaging small intestinal epithelium and increases the T1DM level
- TNF α has synergistic action with IL-6 to increase the HLA DQ gene expression which allows more gliadin into small intestinal epithelium and modulate the inflammatory response which leads to development of CD
- More than half of the children with T1DM who develop coeliac disease may be asymptomatic IgA anti-tTG antibodies has high sensitivity (95-98%) and high specificity (95%) to detect CD in T1DM

Prevalence of Organ Specified Autoantibodies and Autoimmune Diseases

Discussion

- T1DM patients exhibit increased risk of other autoimmune disorders, especially AIHT and CD in children
- Early detection of antibodies(anti-tTG Ab and Anti-TPO Ab) and latent organ specific dysfunction at the diagnosis or later in evolution of T1DM, is strongly advocated
- Metabolic control can be affected by concomitant autoimmune conditions in children with T1DM, hence early detection and management reduces the morbidity
- Presentation of both autoimmune polyglandular and non glandular disease at diagnosis is rare, suggesting a complex interplay of genetic (HLA and non HLA linked genes, environmental and immunological factors

Conclusion

References


Soni, A., Shaw, E. J., Natarajan, A. and Ng, S. M. (2014), Children and youth with type 1 diabetes developing concomitant autoimmune disease do not exhibit worsening metabolic control or growth impairment. Practical Diabetes, 31: 3-4 years.