

Genetic Susceptibility in Autoimmune Polyglandular Syndrome - Type 3 Variant

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NOTHING TO DISCLOSE

INTRODUCTION

- Autoimmune polyglandular syndrome type 3 (APS3) comprises a wide spectrum of combinations of autoimmune endocrine disorders other than adrenal insufficiency. It includes the association of autoimmune thyroid disease (ATD) with type 1 diabetes (T1D), which is known as APS3 variant (APSA3v). Genes linked to joint susceptibility for APS3v have been reported in few cases.
- We report a 10-year-old girl with Graves' disease (GD) who developed T1D after six years of the diagnosis.

CASE REPORT

- A 10-year-old girl was diagnosed with GD at 3-years of age.
- Treated with Carbimazole but had frequent relapse when medication was stopped.
- Her mother has T1D, and two of her aunts were diagnosed with ATD.
- Summary of Follow up in Endocrine clinic after initial diagnosis:**

(5) 6 Months
(3/11/12)

- Relapse – Clinically.
- FT4: 17.04 / TSH = 0.016
- Increased carbimazole dose to 5 mg OD

(6) 3 months
(22/1/13)

- Palpitations
- Abnormal TFT FT4: 35 / TSH = <0.005
- Propranolol
- Divided the carbimazole dose into 2.5 BID

(7) 1 months
(20/2/13)

- Improving symptoms
- FT4: 24 / TSH <0.005
- Continue on same carbimazole + propranolol regimen

(8) 4 months
(8/6/13)

- Patient stopped propranolol
- TFT FT4: 17.8 / TSH = 0.034 (normalized)
- carbimazole is 2.5 mg BD
- Counseling done for treatment strategies, and parents decided to go for surgery

- After more than 6 years of diagnosis, she was admitted for surgery as definitive treatment, rather than radioactive iodine, because she had an active thyroid eye disease. She was in euthyroid status.
- On admission, she reported classic symptoms of T1D.
- Investigations revealed BG: 26.3 mmol/l, pH= 7.35, HCO₃=22, Urine: +2 ketones, +3 glucose, HbA1C of 10% and a persistent hyperglycaemia (18-27 mmol/l), which was well controlled by insulin treatment.
- Cortisol: 472 nmol/l, Celiac screening: -ve, T1D antibodies: +ve

(1) 1 week:
(12/3/07)

- On propranolol + carbimazole (5 mg) TID
- Improving symptoms
- FT4: 30.14 / TSH <0.005

(2) 1 month
(16/4/07)

- Diagnosed as Grave's based on positive antibodies
- FT4: 9.97 / TSH = 0.015
- Stopped propranolol
- Decrease carbimazole to BD

(3) 6 months
(10/9/07)

- FT4: 12.27 / TSH = 5.26
- Decrease carbimazole to OD

(4) 6 months
(1/4/08)

- Relapse.
- FT4: 30.42 / TSH = 0.009
- Returned to carbimazole to BD
- Continued on carbimazole with another relapse in 2011-2012 when tried again to wean it off,

DISCUSSION

- In a cross sectional study, 60% of APS3v patients developed GD before the onset of T1D, and 30% developed GD after the onset of T1D; while only 10% of patients developed both simultaneously.
- Insidious onset of diabetes was more common in APS3v patients who developed GD first, suggesting an influence of GD on the speed of B-cell destruction.
- A number of genes were reported in association with APS3v, including: HLA class II, CTLA-4, FOXP3, Insulin VNTR, PTPN22 and IL2R α /CD25 genes.

CONCLUSIONS

- The reported cases of APS3v with genetic association provide potential illustration of genes linked to joint susceptibility of APS3v, and if these genes could be clustered in certain families or ethnic groups, screening for at risk group would be possible.
- Our patient has a strong first-degree family history of autoimmune endocrine disorders; therefore, genetic testing was planned for the family.

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