

Two Siblings Case with Diagnosis of Autoimmune Polyglandular Syndrome Type 1

Introduction - Objective

Autoimmune polyglandular syndrome type 1 (APS1) is characterized by the classical triad of chronic mucocutaneous candidiasis, hypoparathyroidism and autoimmune adrenalitis. Homozygous mutations in the autoimmune regulator (AIRE) gene localized at 21q22.3 are the etiological cause. In this report, two siblings who had clinical findings apart from the classical triad and were diagnosed with APS1 are presented.

Case 1

A 16 year-old male was admitted with short stature.

Medical History;

- He was shorter than his peers since infancy.
- Loss of hair and eyebrows at the age of 14 (after psychological trauma)
- Parents are first degree cousins
- Targeted adult height: 160.3 cm (-2.58 SDS)
- No history of constitutional short stature in the family
- **His sister had hypoparathyroidism**

Physical examination;

- Weight: 32 kg (-3.17 SDS)
- Height: 143 cm (-4.46 SDS)
 - ❖ Testes 3/3 ml, pubic hair Tanner stage 1
 - ❖ Alopecia, vitiligo, dystrophic changes in the nails,
 - ❖ Mucocutaneous candidiasis

Laboratory findings;

- Glucose: 525 mg/dL
- HbA1c: 7.4 %
- C-peptide: 0.81 ng/mL
- Urine analysis: ketone (-), glucose (++)
- Anti-GAD 37U/mL (N, <10),
- Anti-insulin antibody 2.6 U/mL (N, <10)

Type 1 DM

Investigation of short stature and pubertal delay;

- Bone age 13 years (retarded by 3 years)
- IGF-1 63.7 ng/mL (226-903)
- Peak GH : 10.4 and 12.1 ng/mL
- LH-RH stimulation test revealed a pubertal response

Clinical follow up (22 years)

- Weight 44.3 kg (-3.86 SDS)
- Height 155 cm (-3.44 SDS)
- Pubertal stage Tanner 3, Testes bilateral 15mL
- Metabolic control is achieved with intensive insulin therapy.

Case 2

A 12-year-old girl who was sibling of the case 1 was diagnosed with hypoparathyroidism and hashimoto thyroiditis since the age of three years. She received oral elemental calcium, calcitriol and sevelamer treatments.

Physical examination;

- Weight: 46.8 kg (-0.02 SDS)
- Height: 152.5 cm (-0.37 SDS), No goiter
- Pubertal stage Tanner 4,
- Dystrophic changes in the nails.

The results of the laboratory tests are shown in Table 1.

Diagnosis

- Case 1: Type 1 DM, mucocutaneous candidiasis, alopecia, vitiligo, ectodermal dystrophy
- Case 2: Hypoparathyroidism, ectodermal dystrophy and autoimmune thyroiditis
- APS1 was considered. Results of further laboratory tests are shown in Table 1.

Molecular Genetic Analysis (Exeter University):

- c.769C> T nonsense homozygous variant was detected in exon 6 of the AIRE gene in both patients. Unaffected parents and sister was heterozygous for the same variant.

Table 1. Results of Further Laboratory Tests

	CASE 1	CASE 2		CASE 1	CASE 2
Hb (g/dl)	11.2	11.3	FPG (mg/dl)	220	90
HCT (%)	35.3	33.7	PPPG (mg/dl)	150	113
MCV (fl)	64.7	80	HbA1C (%)	7.4	5.1
MCHC (g/dl)	31.8	33.6	TSH (U/L)	1.1	4.6
			*(0.34-5.6)		
B12 (ng/L)	215	194	ft4 (ng/L)	0.87	0.71
			*(0.54-1.24)		
AST (U/L)	33	13	Anti- TPO	negative	positive
ALT (U/L)	21	13	Anti- T	negative	positive
Ca (mg/dl)	9.4	7	Cortisol (µg/dl)	14.8	7.5
*(8.8-10.8)					
P (mg/dl)	5.5	9	Celiac antibody	negative	negative
*(4-7)					
ALP (U/L)	210	119	Anti-GAD antibody	positive	negative
*(58-213)		*(89-362)			
PTH (ng/L)	33.3	<4.6	Anti-insulin antibody	negative	positive
*(10-63)					
ACTH (µg/dl)	30.3	29.2	Standart dose ACTH	24	23.3
*(0-46)			Peak Cortisol (µg/dl)		

FPG: fasting plasma glucose, PPPG: postprandial plasma glucose

* Normal value ranges by age and gender



Figure 1. Case 1; vitiligo, alopecia (A), Chronic mucocutaneous candidiasis (B), Case 2, Dystrophic changes in nails (C)

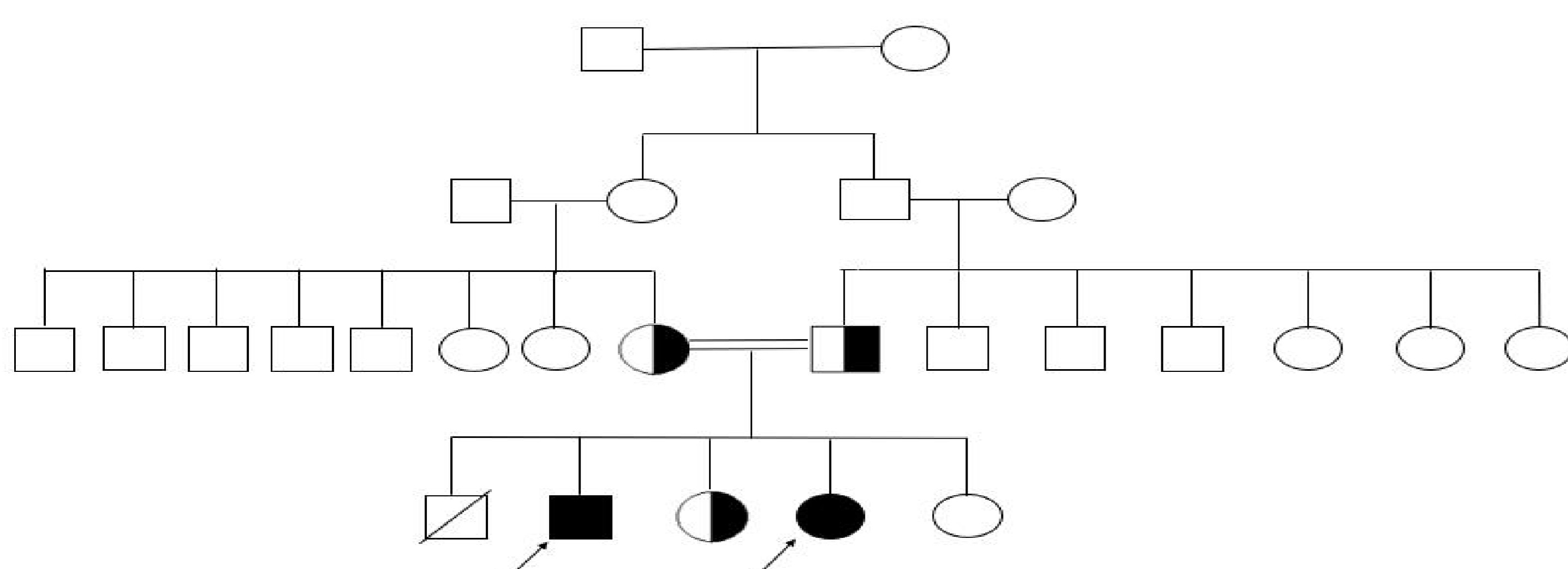


Figure 2. Pedigree

Conclusion

Classical triad of APS1 may not be always present at diagnosis. Cardinal findings may develop at follow-up. Adrenal insufficiency and other autoimmune pathologies (hypogonadism, diabetes, vitiligo, thyroiditis, hypophysitis, chronic atrophic gastritis, malabsorption etc.) should be investigated at diagnosis and later in life.