Clinical Characteristics of Latent Autoimmune Diabetes in Youth (Type 1.5 DM)

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Purpose

Diabetes mellitus (DM) was mostly type 1 DM (T1DM) in childhood, but recently there is an dramatic increase of type 2 DM (T2DM). Sometimes it is not easy to classify DM based on clinical features, especially in the case having both type 2 clinical phenotype and autoantibody positivity. It is named as type 1.5 DM (T1.5DM) or latent autoimmune diabetes in youth, or slowly progressive type 1 DM. This study was designed to evaluate the clinical characteristics of childhood DM according to the classification and to evaluate the clinical course of T1.5DM who initially had autoantibody positivity and type 2 DM clinical phenotype.

Methods

A total of 91 subjects who were diagnosed and could be followed-up at Dankook University Hospital between 2001 and 2015 were enrolled in the study. Study subjects were classified into 3 groups: T1, T1.5, and T2DM. Clinical features as well as laboratory findings were compared among groups. Mann-Whitney U test, Kruskal-Wallis test, and Chi-square test were used for statistics using IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA).

Results

Among 91 subjects, type 1, 1.5, and 2 DM were 51 (56.0%), 7 (7.7%), and 33 (36.3%), respectively. Age at diagnosis and BMI Z scores were lower (age at diagnosis 8.61 vs. 13.18 vs. 13.59 years old, p<0.001; BMI Z scores -1.22 vs. 0.78 vs. 0.91, p<0.001), and DKA at diagnosis were the most common in T1DM. Serum c-peptide levels were significantly lower in T1DM (0.52 vs. 1.92 vs. 3.62 ng/mL, p<0.001). Autoantibody positivity was 92.2% in T1DM, among them GAD autoantibody and insulin autoantibody were common. In T1.5DM the mean duration was 4.56 years, among them 43% of patients needed intensive insulin treatment of more than 0.5 U/kg/day during follow-up.

Table1. Clinical and laboratory characteristics of the study subjects

	T1DM (n=51)	T1.5DM (n=7)	T2DM (n=33)	P		
				Among groups	T1.5 DM vs. T1DM	T1.5 DM vs. T2DM
Age at diagnosis (years)	8.61 ± 4.16	13.18 ± 3.42	13.59 ± 2.49	<0.001	0.009	0.917
Follow up duration (years)	4.45 ± 3.27	4.56 ± 3.76	3.12 ± 2.79	0.149	0.834	0.344
Sex (male:female)	25:26	7:0	15:18	0.027	0.013	0.011
BMI Z score at diagnosis	-1.22 ± 1.47	0.78 ± 0.91	0.91 ± 1.51	<0.001	0.001	0.416
DKA at diagnosis	35/50 (70%)	1/7 (14.3%)	2/32 (6.2%)	<0.001	0.008	0.457
pH at diagnosis	7.23 ± 0.16	7.38 ± 0.11	7.38 ± 0.03	0.003	0.114	0.654
Serum c-peptide / Glucose ratio	0.0014 ± 0.002	0.0097 ± 0.012	0.0177 ± 0.019	<0.001	0.001	0.128
GAD Ab positivity	42/49 (85.7%)	5/7 (71.4%)	0/33 (0%)	<0.001	0.312	<0.001
Islet cell Ab positivity	1/35 (2.9%)	2/5 (40%)	0/29 (0%)	<0.001	0.036	0.018
Insulin Ab positivity	18/50 (36%)	4/7 (57.1%)	0/32 (0%)	<0.001	0.411	<0.001
IA-2 Ab positivity	22/30 (73.3%)	3/4 (75%)	0/27 (0%)	<0.001	1.0	0.001
HbA1C at diagnosis (%)	12.54 ± 2.01	11.51 ± 2.34	11.64 ± 2.79	0.258	0.354	0.9
Initial fructosamine (umol/L)	639.3 ± 188.1	579.0 ± 119.0	462.1 ± 211.0	0.009	0.471	0.271
Initial glucose (mg/dL)	462 ± 203	299 ± 140	271 ± 138	<0.001	0.035	0.654
Initial serum c-peptide (ng/mL)	0.52 ± 0.45	1.92 ± 1.07	3.62 ± 2.02	<0.001	0.002	0.049
Initial treatment (None : Insulin only : Insulin and OHA : OHA only)	0 : 50 : 1 : 0	0 : 2 : 3 : 2	1 : 5 : 8 : 19	<0.001	<0.001	0.483
Recent treatment (None : Insulin only : Insulin and OHA : OHA only)	0 : 48 : 3 : 0	0 : 3 : 2 : 2	2 : 0 : 10 : 21	<0.001	<0.001	0.001

Table 2. Clinical and laboratory characteristics of patients with T1.5DM

	Group 1				Group 2				
Variables	Pt 1	Pt 2	Pt 3	Mean ± SD	Pt 4	Pt 5	Pt 6	Pt 7	Mean ± SD
Sex	M	M	M		M	M	M	M	
Age at diagnosis (yr)	14.2	14.49	8.49	12.4 ± 3.2	9.03	18.32	14.55	13.2	13.78 ± 3.83
Initial BMI z score	0.49	0.82	1.11	0.8 ± 0.3	2.64	0.004	0.05	0.04	0.77 ± 1.26
Initial HbA1c (%)	9.9	13.1	8.4	10.5 ± 2.4	9.2	14.2	13.8	12	12.3 ± 2.28
Initial serum c-peptide (ng/mL)	0.1	2.4	3.57	2.02 ± 1.87	1.6	2	2.4	1.36	1.84 ± 0.46
Initial serum C-pep/Glucose ratio	0.005	0.011	0.036	0.02 ± 0.02	0.003	0.006	0.008	0.003	0.01 ± 0.002
GAD Ab	-	+	+		+	+	-	+	
Islet cell Ab	N/A	+	+		-	-	-	N/A	
Insulin Ab	+	-	-		-	+	+	+	
IA-2 Ab	N/A	+	+		+	N/A	-	N/A	
FU duration (yr)	11.68	1.36	6.09	6.38 ± 5.17	4.38	0.91	1.88	5.66	3.21 ± 2.19
Initial treatment	OHA, LI	OHA, LI	OHA		OHA	OHA,LI	OHA,LI	Insulin	
Recent treatment	MI	MI	MI		OHA	OHA,LI	OHA	OHA,LI	
Time to insulin (yr)	7.64	0.66	2.7	3.67 ± 3.59					
HbA1c at insulin tx (%)	9.7	8.4	10.2	9.43 ± 0.93					
Serum c-peptide at insulin tx (ng/mL)	0.1	2.8	1.2	1.37 ± 1.36					
Serum C-pep/Glu ratio at insulin tx	0.0004	0.016	0.004	0.007 ± 0.01					
Recent HbA1c (%)	8.1	10.1	11.5	9.9 ± 1.71	5.9	7.6	5.8	11.1	7.6 ± 2.48
Recent serum c-peptide (ng/mL)	0.1	1.9	0.1	0.7 ± 1.04	4.1	3.13	20.4	1.85	7.37 ± 8.74
Recent serum C-peptideep/Glu ratio	0.0004	0.008	0.0003	0.003 ± 0.01	0.034	0.024	0.2	0.025	0.07 ± 0.09

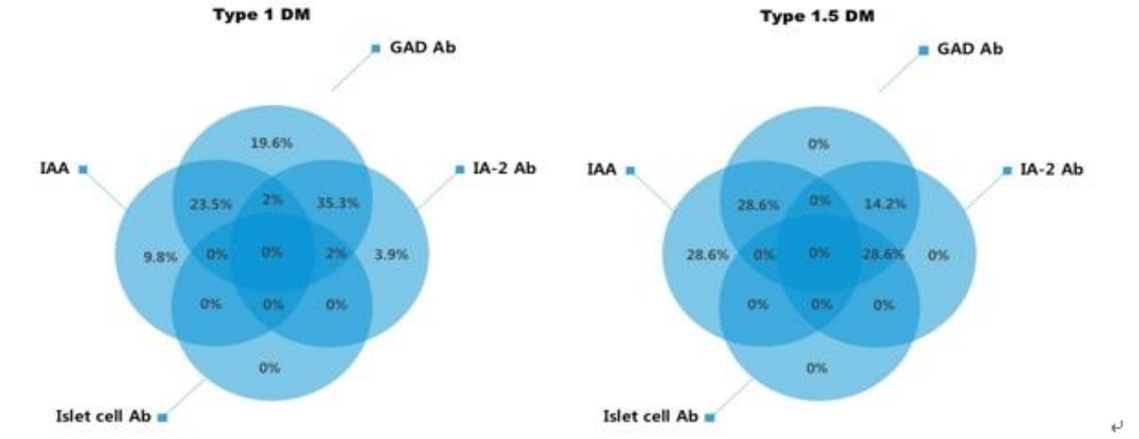

Fig. 1. Distribution of autoantibodies in T1 and T1.5 DM.

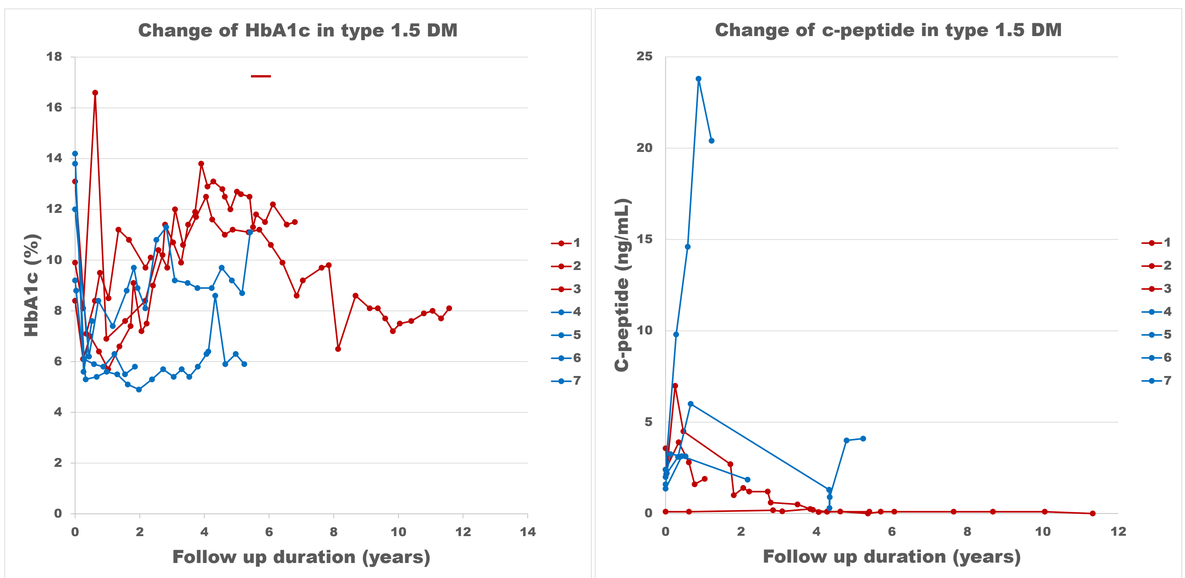

Fig. 2. Change of HbA1c & serum c-peptide in T1.5 DM during follow-up.

Conclusion

It is valuable to check initial autoantibody status in patients with diabetes mellitus for classification and management. It is important to closely monitor patients with T1.5DM because they might need intensive insulin treatment within several years.

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