Comparison of Clinical and Laboratory Characteristics Between Adult-Onset Type 1 Diabetes and Latent Autoimmune Diabetes in Adults

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Although they do not initially require insulin, diabetic adults presenting autoantibodies against β-cells (anti-GAD antibody [GADA] and anti–islet cell antibody [ICA]) more rapidly develop the need for insulinization, a fact characterizing latent autoimmune diabetes in adults (LADA) (1,2). Differences between LADA and type 2 diabetes (3–6) and between children and adults with type 1 diabetes (7) have been reported. In contrast, few studies are available comparing type 1 diabetes diagnosed during adulthood with LADA, with the results not being consistent (4,5,8). Therefore, the aim of the present study was to investigate clinical and laboratory parameters in patients with LADA compared with patients with adult-onset type 1 diabetes.

RESEARCH DESIGN AND METHODS

— Among the diabetic adults (age at diagnosis >35 years) seen at our service and investigated with GADA upon diagnosis (no routine ICA analysis was performed) (2), 54 patients with LADA (individuals not requiring insulin for at least 1 year after diagnosis and positive for GADA) (1,2,4,5) and 45 patients with type 1 diabetes (individuals with ketoacidosis or hyperglycemia accompanied by polyuria, polydipsia, and weight loss immediately requiring insulin after diagnosis and GADA positive) (1,4) were selected. BMI, presence of arterial hypertension, C-peptide, insulin resistance by homeostasis model assessment (9,10), GADA and anti-TPO antibody (TPOA) titers, and triglyceride and HDL cholesterol levels at diagnosis were compared between the two groups. The characteristics of the patients are shown in Table 1.

Some investigators have demonstrated that not all patients classified as LADA show the same evolution, with a subgroup showing characteristics similar to type 2 diabetes except for the presence of autoantibodies (11,12); however, a clear distinction of these patients at diagnosis is still not possible. Differentiation based on BMI (12) does not seem adequate (3,13), and no well-established cutoff exists regarding the antibody combination and titers that would best differentiate these patients (3,11). Thus, as done in most studies (1,2,4–6), we did not subdivide patients with LADA.

GADAs were tested by radioimmunoassay, with a level ≤1 unit/ml being considered negative. Serum C-peptide and insulin concentrations were measured by immunofluorimetry during fasting, and glycemia was determined in the same sample. TPOAs were assayed by chemiluminescence, with a level ≤15 units/ml being considered negative. The results are expressed as means ± SD unless otherwise indicated. Differences in continuous variables between groups were estimated using a nonparametric Mann-Whitney *U* test. For dichotomous variables, Fisher's exact test was used. Logistic regression was used to determine potential confounding covariables. A P value <0.05 was considered significant.

RESULTS

— LADA patients displayed a higher BMI, higher C-peptide levels, and arterial hypertension; elevated triglycerides (>150 mg/dl) and reduced HDL cholesterol (<45 mg/dl) were also more common (multivariate analysis). C-peptide levels were >0.3 nmol/l (14) in all LADA patients versus 51.4% of type 1 diabetic patients ($P < 0.01$). Insulin resistance evaluated with the homeostasis model assessment of insulin resistance (9,10) was lower in type 1 diabetic patients (multivariate analysis). No difference in GADA titers or extrapancreatic autoimmunity evaluated based on TPOA measurement was observed between the two groups. The results are shown in Table 1.

CONCLUSIONS

— Our study showed differences between patients with adult-onset type 1 diabetes and LADA in terms of BMI, arterial hypertension, triglyceride and HDL cholesterol levels, C-peptide levels, and insulin resistance. LADA was associated with a higher BMI, higher C-peptide levels, greater insulin resistance, and a higher prevalence of arterial hypertension and hyperlipidemia. No difference in GADA or TPOA titers was observed. Hosszufalusi et al. (4) did not demonstrate differences in BMI, waist-to-hip ratio, HDL cholesterol, total cholesterol, triglycerides, presence of arterial hypertension, β-cell function (in patients

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Abbreviations: GADA, GAD antibody; ICA, islet cell antibody; LADA, latent autoimmune diabetes in adults; TPOA, anti-TPO antibody.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Characteristics of the patients at diagnosis*

	LADA	Type 1 diabetes	*P* value
n	54	45	
Sex (male:female)	31:23	28:17	
Age at diagnosis (years)	40.2 ± 3.9	39.7 ± 3.5	0.54
BMI (kg/m^2)	27.2 ± 3.1	23.1 ± 2.9	<0.001
Arterial hypertension (%)	36	11	0.012
Fasting glycemia (mmol/l)*	10.5 ± 2.3	11.4 ± 2.9	0.1
Triglycerides >150 mg/dl (%)	35	18	<0.05
HDL cholesterol <45 mg/dl (%)	45	22	<0.05
HOMA-IR (pmol/l × mmol/l)	2.4 ± 1.8	1.3 ± 1.2	<0.001
C-peptide (nmol/l)	0.61 ± 0.18	0.28 ± 0.14	<0.001
Presence of TPOA (%)	24	20	0.65
TPOA titer (units/ml)	82 ± 31	75 ± 22	0.24
GADA titer (units/ml)	17.3 ± 6.8	16.1 ± 5.7	0.39

Data are means ± SD unless otherwise indicated. *At the time of laboratory evaluation (up to 3 days after diagnosis). HOMA-IR, homeostasis model assessment of insulin resistance.

with a recent diagnosis), or genotypic characteristics between these two groups of patients. In that study, patients with LADA differed in terms of the more common presence of isolated autoantibodies (GADA or ICA) and less pronounced deterioration of β-cell function. Similar to the present results, GADA titers did not differ between the two groups. A previous study has shown differences in the genotypic characteristics of patients with LADA and type 1 diabetes, but most cases with type 1 diabetes were diagnosed at <20 years of age (5). Another study analyzing patients >20 years of age at diagnosis revealed that GADA-positive patients with insulin deficiency (C-peptide <0.3 nmol/l after stimulation) differed from those without deficiency in terms of clinical characteristics (younger, lower BMI, and higher HbA_{1c} levels), humoral autoimmunity to other organ-specific autoantibodies (higher prevalence of IA2 antibody, anti-thyroid, and anti–parietal cell antibodies), as well as HLA class II genes.

Our data contribute to the distinction of adult-onset autoimmune diabetes into a more rapidly progressing form (similar to classical type 1 diabetes) and a more slowly evolving form accompanied by a deterioration of β-cell function (LADA) as previously proposed (4,12).

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