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VITAL HEALTH SOLUTIONS

Type 1.5 Diabetes

Type 1.5 diabetes (also known as latent autoimmune diabetes of adulthood [LADA], or slow-onset type 1 diabetes) is an autoimmune form of diabetes diagnosed in adults, who do not immediately require insulin for treatment, are often NOT overweight and have little or no insulin resistance. Antibodies are present that attack the beta cells. LADA accounts for approximately 10% of people with diabetes, making it probably more widespread than type 1 diabetes. It is estimated that almost 20% of those initially diagnosed with type 2 diabetes, actually have LADA.

Characteristics of type 1.5 diabetes:

- * initially presents as type 2
- * absence of DKA/ketosis
- * responds well to oral anti-hyperglycemic agents
- * normal C-peptide level (0.9-4.3 ng/dL)
- * absence of obesity, dyslipidemia, hypertension
- * usually no family history of type 2 diabetes
- * positive autoantibodies
- * insulin dependency often occurs

Who should be tested for LADA:

- * thin adults (under age 50) with type 2
- * symptoms similar to type 1 at diagnosis
- * those with absence of metabolic syndrome (HTN, central obesity, lipid abnormalities)
- * those with other autoimmune diseases, such as:
 - celiac sprue
 - graves
 - hashimoto's thyroiditis
 - pernicious anemia
 - premature gonadal failure
 - hypoparathyroidism

Comparing Clinical Features:

	Type 2	Type 1.5	Type 1
Pathophysiology	<ul style="list-style-type: none"> * peripheral insulin resistance * decreased beta cell mass and function * decreased insulin secretion 	Latent autoimmune destruction of the pancreatic beta cells	Autoimmune destruction of pancreatic beta cells
Symptoms	Usually none	Dependent on level of beta cell destruction	Increased thirst, urination, weight loss
Typical Age of Onset	Adult	Adult	Youth or Adult
Ketoacidosis	Usually absent	Absent at diagnosis (may occur later)	Rapid onset
Autoantibodies	Negative	GAD-65 islet cell antibodies (ICA)	<ul style="list-style-type: none"> * GAD-65 * Islet-cell antigen-2 (IA-2) * Insulin autoantibodies (IAA) * Islet cell antibodies (ICA)
CV Complications (vs euglycemia)	2-4X higher	2-4X higher	increased risk of CV morbidity and mortality (esp women)
Microvascular complications	Increased	Increased	Increased
Insulin Dependence	Over time, if at all (50% will require insulin after 10 years)	Within 6 years (50% will require insulin after 4 years)	At diagnosis
Insulin Resistance	Yes	Some	No
Treatment	Meal plan Activity Oral & Injectable meds 30-40% need insulin later	Meal plan Activity Oral meds work until beta cells destroyed Insulin later	Meal plan Activity Insulin/Symlin at diagnosis

Diagnosis of type 1.5 diabetes:

- * established by the presence of increased levels of pancreatic auto-antibodies in those with recently diagnosed diabetes.
- * Commonly tested autoantibodies indicative of latent disease progression:
 - Glutamic Acid Decarboxylase (GAD-65)*
 - Islet cell antibodies (ICA)
 - Tyrosine Phosphatase (TPA)
- * presence of auto-antibodies not only confirms diagnosis, but also predicts insulin dependency within 3 years of diagnosis:
 - GAD 92%
 - ICA 86%
 - TPA 75%
- * If diagnosed, evaluate C-peptide to determine degree of beta cell destruction and medication management

If all 3 immune markers (GAD, ICA and TPA) are present, there is a 100% chance of being insulin dependent after 3 years.

In type 1 diabetes, the person usually tests positive for all 3 autoantibodies. Those with type 1.5 diabetes experience a slower progression and become insulin dependent at a later stage because in type 1 diabetes, there is a presence of HLA-DR4-DQ8 antigens that are more prevalent and these antigens are thought to cause rapid progression of beta cell destruction and early insulin dependence. In type 1.5, immune tolerance to beta cell antigens may occur and this protects beta cells from rapid destruction, there is slower progression to insulin dependency and the person is usually older at onset.

What is GAD-65*?

- * enzyme produced by pancreatic beta cells
 - * strong predictor of insulin dependence in diabetes
 - * GAD is the most sensitive marker
 - if positive: diagnose type 1.5
 - if negative, check ICA or TPA
- UKPDS measured GAD and ICA:
- entire group: 10% were GAD+
6% were ICA+
 - 25-34 yo: 34% were GAD+
21% were ICA+

Treatment Goals for type 1.5 diabetes:

- * control blood glucose as in types 1 & type 2 diabetes
- * same recommendations for meal plan, physical activity and blood glucose monitoring
- * improving blood glucose will improve pancreatic function
- * preserve beta cell function in order to
 - have better glycemic control and less retinopathy
 - prevent complications

Summary:

Type 1.5 diabetes is a common form of an autoimmune condition, that is usually initially diagnosed as type 2 diabetes. Type 1 diabetes may be suspected in young adults who are not obese, have no family history of type 2 diabetes, have no lipid abnormalities, and who may lose control of blood glucose levels early with oral agents. Confirmation is made by obtaining a GAD auto-antibody and C-peptide testing.

Although testing for LADA is not indicated in all individuals with type 2 diabetes or in those with obvious type 1 diabetes, testing for it may help tailor treatment so that early administration of insulin can be initiated, which would help preserve beta cells function longer, versus other oral medications. Since many oral diabetes medications work by forcing the pancreas to produce more insulin (such as sulfonylureas), this treatment would actually be speeding the demise of the beta cells. In addition, a lower carbohydrate diet would be even important in order to reduce the work load of the pancreatic beta cells. Overall, by knowing for sure if one has type 1.5 diabetes, vs. type 2 diabetes, with proper lifestyle and medications, the lifespan of the LADA pancreas can be extended (from 5 years to maybe 10 years or more).

Additional Notes:

Zhao, Y. Journal Clinical Endocrinology Metabolism 2014: Patients diagnosed with LADA demonstrated beta-cell preservation when administered sitagliptin along with insulin, compared with insulin alone