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Case Report *Volume 6 Issue 1*

LADA in Children: Time to Rethink

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Abstract

LADA is a diagnosis of autoimmune hyperglycaemia in adults requiring very low insulin doses. LADA presents in between a spectrum between T1DM and T2DM and hence poses a diagnostic difficulty. We present two cases of siblings diagnosed as T1DM on insulin therapy Case 1 has very low insulin requirement for over 24 months with C-peptide in the normal after 2yrs of onset of the disease. And the 2nd case having a similar presentation being euglycemic for 6 months without any insulin for the duration. LADA may be defined as an entity occurring in adults however a similar presentation can occur in children and should be kept in mind while evaluating and treating such children, especially ones with prolonged need for low insulin dose.

Keywords: LADA; Autoimmune Spectrum; Children

Abbreviations: LADA: Latent Autoimmune Diabetes in Adults; TIDM: Type I Diabetes Mellitus.

Background

Latent autoimmune diabetes in adults (LADA) is a condition of hyperglycaemia in autoimmune positive adult having low insulin requirement. There is an increasing number of this diagnosis and has been also called as type 1.5 diabetes. However there no current guidelines for diagnosing LADA but the Immunology of Diabetes Society have proposed the following criteria [1]:

- Age of onset in adults > 30 years
- Positive islet cell autoimmunity
- Absence of requirement of Insulin (at least for initial 6 months)

The most characteristic feature of LADA is the age of presentation and has been described the world over as occurring in adult population. The autoimmune destruction of pancreas cells is very slow in LADA resulting in the low insulin requirements and higher C-peptide values than Type 1 Diabetes [2]. This is in turn result in the absence of the acute presentation of polyuria, polydipsia and ketoacidosis seen with very low insulin level.

Case Report

Case 1

An 8yrs old girl was diagnosed type 1 diabetes mellitus 2yrs back, when she had presented with mild diabetic ketoacidosis in another hospital. Her HBA1c was 11.7mmol/L at the time of admission and blood sugars above 400mg/dl. She was admitted and treated as per the diabetic protocol and discharged on regular insulin of total daily dose of insulin of 16units/day. However soon her insulin requirement reduced and since the last 18 months she has been on regular insulin 4 units for breakfast and 3 units in the evening. She was referred to our institution for diabetic management and appropriate diagnosis.

She now weighs 20kg, 120.cm tall, HBA1C -9.4mmol/L. She takes regular insulin twice a day, a total of 7 units (0.35units/kg/day).On further work up her TSH -1.46 µU/mL, GAD-65 – 19.03 IU/ml, C-peptide – 1.36 ng/ml, TTG> 200 RU/ml.

Her insulin dose-adjusted A1c (IDAA1C) was <9. Due to high value of the IgA TTG the child was advised an endoscopy, the biopsy a result of which was mild villous atrophy and mild increased in intraepithelial lymphocytes.

Case 2

A 4year 11month year old girl, sibling of the first case, weighing 15kg had increased frequency of micturition 6 months back and was tested for diabetes mellitus owing to the history of T1DM. Her urine result for any infection was negative. However her blood sugars were high, ranging between 250-350mg/dl, HBA1C was 8.6mmol/L at the time, there was no acidosis at the time. She was started on regular insulin twice a day but was subsequently stopped due to blood sugars being maintained in normal range. The child was brought to us by the parents with concerns about her future need for insulin and a diagnosis.

On evaluating her HBA1C -6.8 mmol/L, TSH -3.46 μU/mL, free T4- 1.16ng/ml, GAD-65 – 122 IU/ml, C-peptide – 1.87 ng/ml, TTG- 92.6 RU/ml.

She was advised an endoscopy in view of the raised anti-TTG to diagnose Celiac disease. Biopsy results reported mild villous atrophy and shortening, increased intraepithelial lymphocytes (>30 lymphocytes/100 enterocytes). Lamina propria showed moderate infiltrate of lymphoplasmacytic cells forming occasional lymphoid aggregations. There was history of diabetes in her elder sister.

Discussion

TIDM results from autoimmune destruction of pancreatic cells resulting in progressive hyperglycaemia and it is estimated that only 20-30%cells remain functional at the time of diagnosis [3]. The remnant cells are responsible for the need for reduced levels of insulin requirement or remission seen in some children commonly known as the honeymoon period. However with time the volume of these cells decline and the child requires higher insulin doses. Partial remission is seen in about 40-50% and can last as long as 24 months [4], but there is a progressive fall in the C-peptide indicative of the reduction of beta cells.

The final diagnosis of our first case was unclear despite her having a typical presentation of diabetic ketoacidosis (mild) at the onset, as progressive insulinopenia which is the hallmark of TIDM was not documented even after 2yrs of onset of hyperglycaemia evidenced by the normal C-peptide values, this presentation is seen in LADA. In LADA the autoimmune destruction of beta cells is very slow, hence the patients have very minimal insulin requirement for prolonged durations.

Our case1 was a diagnostic dilemma due very low insulin requirement which was considered as a honeymoon period but prolonged for over 2yrs, but with a normal C-peptide level which is more a feature of LADA along with positive antibodies and seen in T1DM. The child presented with glycosuria, normal values of C-peptide, was non obese which are features seen in MODY or type 2 diabetes mellitus (T2DM), but these were ruled out due to positive antibodies which is absent in both the above.

The only other case of LADA in a child has been reported in Turkey in 2004 of an 8yr old girl who had progressively worsening hyperglycaemia and went on to develop autoimmunity after 4yrs of onset [5]. Most often LADA is diagnosed as T2DM who go on to develop need for insulin within a few years as the beta cell destruction progresses in adults beyond 30yrs. Only near normal C-peptide value differentiate T1DM and LADA. A lot of patients with TIDM and LADA have a similarity of being HLA-DR3/DR4 positive [6], suggesting both the conditions maybe being a part of the same spectrum of disorder.

Autoimmunity in T1DM is associated with other immune diseases and thyroid autoimmune disorder is the most common followed by celiac disease. Autoimmunity being the underlying feature in LADA warrants screening for other autoimmune conditions as in TIDM [7]. Recent data in adults have reported increased BMI as a modifiable risk factor for onset of LADA, however such studies are not presently available in the pediatric population [8].

LADA is currently a diagnosis reserved for the adult population but may well be present in the pediatric population and diagnosed as a phase of remission, or undiagnosed due to asymptomatic hyperglycaemia. There is a need to differentiate LADA from T1DM despite insulin being the treatment modality in both, because the natural course of LADA is much slower than T1DM with lower insulin requirements. The parents need to make aware of this while treating so that they do not develop a false sense of security and stop monitoring or treatment or both. The paediatricians and endocrinologists should keep in mind a possibility of such a diagnosis in children with atypical physical or biochemical presentations.

Key Points

- Similar presentation of LADA in children can be missed due to overlapping features with T1DM.
- C-peptide will be a useful tool for making the diagnosis and predicting the need for insulin.
- Children with LADA can also have associated other autoimmune conditions and should be monitored.

What's new?

- Similar presentation of LADA in children can be missed due to overlapping features with T1DM.
- C-peptide will be a useful tool for making the diagnosis and predicting the need for insulin.
- Children with LADA can also have associated other autoimmune conditions and should be monitored.

Ethical approval

The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee Informed consent was taken from the parents.

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