

Diabetic Ketoacidosis in an Obese Adolescent Diabetic Patient with Acanthosis Nigricans and without Autoantibodies. Is It Type 1.5 Diabetes?

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Abstract Over the years, adolescents have been diagnosed to be diabetic, the type of which do not fit into the classical types of diabetes – type 1 and type 2. These cases have been reported round the globe. They share features of both types of diabetes like obesity, acanthosis nigricans along with insulin resistance and can even have complications like Diabetic ketoacidosis. The present case study is about a newly diagnosed obese adolescent diabetic patient with acanthosis nigricans presenting with diabetic ketoacidosis who responded to standard treatment of Diabetic ketoacidosis. Subsequently, he was found to have low levels of C-peptide without insulin autoantibodies. Such cases have been variously referred as Double diabetes or 1.5 diabetes in literature and may constitute a subvariant of Diabetes.

Keywords Diabetic Ketoacidosis, Acanthosis Nigricans, Type 1.5 Diabetes, Double Diabetes, Glutamate Acid Decarboxylase (GAD) Autoantibodies

1. Introduction

Though Diabetes mellitus (DM) has been classified into Type1 DM (T1DM) and Type 2 DM (T2DM)¹ over the years several cases have been reported which do not fit into the traditional categories of DM. Such forms of DM have gained the attention of the scientific community from the SEARCH study². Recent data from longitudinally followed cohorts have described the clinical features and taxonomy of some of these syndromes that are “intermediate” between T1DM and T2DM³. The prevalence of both T1DM and T2DM among children and adolescents has been steadily increasing over over the last few decades⁴. However, as the general pediatric population becomes more obese and more ethnically diverse, reliance on phenotypic characteristics for distinguishing

between these types of diabetes is becoming increasingly untenable. At the time of diagnosis, it may not be possible to be certain of the type of diabetes in many cases.⁵

2. Case Report

A 16 year old adolescent male was admitted in the Medicine ward in an unconscious state. The deterioration of his consciousness occurred over a period of 48 hours and was accompanied by fever, cough, respiratory distress, excessive urination and restlessness. The boy was diagnosed to be a diabetic about a month back and was initiated on insulin Glargine and premeal short acting insulin. His fasting blood glucose at initiation of insulin was 357 mg/dl and renal function tests were normal. The patient followed the regime for a few days, but had stopped insulin abruptly when he developed mild fever and cough.

There was no family history of diabetes. The boy had sedentary habits and had a history of weight gain of 11 kg over the last two years.

Examination revealed an obese adolescent with Glasgow Coma Scale of 3/15. His BP was 90/60 mm Hg and low volume pulse with a rate of 124/min. His tongue was dry and extremities were cold. Oral temperature was 101° F. He had deep and hurried respiration - respiratory rate 32/min. Chest examination revealed coarse crepitations on left side. He did not have any abdominal organomegaly. His pupils were 3 mm in diameter and reacted to light. No cranial nerve palsy was detected. He had multiple abdominal striae (Figure 1) and acanthosis nigricans on neck and axilla (Figure 2 and 3).

On admission, his blood glucose level was 654mg/dl. His blood urea and creatinine levels were normal. Serum sodium and potassium levels were 148 mmol/L and 5.6mmol/L respectively. His blood pH and bicarbonate levels were 7.1 and 13 mmol/L respectively. His urine tested positive for acetone. His total leukocyte count was 16,110/ml with a

predominance of neutrophils. Chest X-ray showed patchy opacities in the lower lobe of left lung.



Figure 1. Abdominal striae

The patient was diagnosed to be a case of T1DM with Diabetic ketoacidosis⁶ and pneumonia of left lung. Treatment of DKA was started according to American Diabetic Association (ADA) guidelines¹ with IV fluids – 0.9% Normal Saline and Ringer’s Lactate along with 8 units of short acting Insulin given as IV bolus and 8 units of Insulin given hourly as continuous infusion. Inj Ceftriaxone was given twice daily at a dose of 1 gm IV for pneumonia. An indwelling urethral catheter was placed to measure urinary output.

The patient was monitored intensively with hourly record of blood pressure, urine output and blood glucose. He responded to treatment with improvement of GCS to 15/15 within 12 hours of initiation of treatment. His blood glucose level dropped to 312 mg/dl and serum potassium level was 4.6 mmol/l with a blood pH of 7.34. Urinary acetone was absent.

As the patient had improved and was able to take food orally, oral feeding was initiated along with Inj Glargine and premeal short acting insulin which overlapped the insulin infusion by 6 hours, His blood glucose was 212 mg/dl within 24 hours of initiation of therapy with normal pH and potassium values. His lipid profile was normal. Ultrasonography of abdomen did not reveal any organomegaly or pancreatic pathology.

By 3rd day, the patient was ambulatory, afebrile and was able to take care of himself. He weighed 83 kg with a height of 162cm. His HbA1C level was 11.6%. The patient improved steadily with treatment and was discharged on Day 7 with a combination of Inj Glargine and premeal short acting Insulin along with counseling and instructions of dose

modification according to self blood glucose monitoring.

C-peptide and 8 am Cortisol levels done on follow up at two weeks were 0.78ng/dl.(Range -1.10-5.0ng/dl) and 6.67 pg/dl (Range 4.30-22 pg/dl)respectively. TSH was 2.45 μ IU/ml (Range 0.4 - 4 μ IU/ml). He tested negative for Glutamate acid decarboxylase autoantibodies (GAD). His fasting blood glucose was 102 mg/dl and he was following the insulin regime as was advised at the time of discharge. Repeat Chest X-Ray showed resolution of pneumonia.



Figure 2. Acanthosis nigricans on neck



Figure 3. Acanthosis nigricans on axilla

3. Discussion

An episode of DKA was once considered a hallmark feature that would differentiate individuals with T1DM from those with T2DM. This concept was perpetuated by such statements as "patients with NIDDM [non-insulin-dependent diabetes mellitus] are [not] ketosis prone" ⁷ and "many individuals with type 2 DM [diabetes mellitus] (previously NIDDM) do not require insulin therapy to prevent ketoacidosis" ⁸.

Increasingly, reports have emerged from around the world about DKA occurring in phenotypically T2DM patients especially those who are young and obese⁹. Distinctions between T1DM and T2DM are becoming blurred, both etiologically and clinically. A number of studies have suggested that differences between the two types are not always straightforward, and in many cases, a common pathogenic processes may be evident ¹⁰.

Obesity in children may contribute to the escalation of β -cell destruction, as suggested by the accelerator hypothesis in subjects genetically susceptible to type 1 diabetes ¹¹. Studies have described a subgroup of children and adolescents with a mixture of the two types of diabetes, i.e., subjects who are obese and/or with signs of insulin resistance as well as positive for markers of autoimmunity to β -cells¹². Approximately 70–80% of newly diagnosed type 1 diabetes patients have autoantibodies to Glutamic Acid Decarboxylase (GAD)65 and / or IA-2.¹³ while thirty six per cent of the children with T2DM had at least one detectable beta-cell autoantibody in one series.¹⁴

Thus a gray area has emerged in classification of diabetes especially between obese and adolescent youth who may present with hyperglycemic complications like DKA. The terms "Type 1.5 Diabetes" (T1.5 DM), "Double Diabetes,"(DD), "Latent Autoimmune Diabetes In Youth" (LADY), and "Hybrid Diabetes" characterized by the occurrence of hyperglycemia in overweight/obese children and youth with the combination of markers typical of both T2DM and T1DM, have gained the attention of the scientific community of late.¹⁵ These subjects are usually obese, may have a family history of diabetes, have a low prevalence of autoimmune markers, and lack HLA genetic association¹⁶

C-peptide levels have been used to distinguish between T1DM and T2DM in DCCT. A basal C-peptide level <200 pmol/L was consistent with the diagnosis of type 1 diabetes¹⁷. Baseline C-peptide levels in the type 1.5 diabetic patients were significantly lower than those in patients classified as T2DM and higher than those in patients classified as T1DM¹⁴. C-peptide levels were found to be below normal or even undetectable at presentation with DKA in Type 1.5 DM and also on follow up after remission.¹⁸

Though there are multiple etiological factors for Acanthosis nigricans, it has been associated with childhood obesity.¹⁹ AN has also been described in patients with Type 1.5 Diabetes.²⁰

The present case of DKA in an obese adolescent with acanthosis nigricans and low C-peptide levels without

autoantibodies and family history of diabetes falls in the category between Type 1 and 2 DM – the type of which is increasingly being reported, but does not find mention in the classification of diabetes by any diabetic association. Such cases are likely to present a clinical and therapeutic challenge to the physicians.

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