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Early-Onset Type 2 Diabetes Misdiagnosed as Type 1 Diabetes in a 15-Year-Old Nigerian Girl: A Case Report

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Abstract

Type 2 diabetes mellitus (T2DM) is emerging as a new clinical disorder among children and adolescents. Although there is increasing prevalence of this clinical entity among adolescents worldwide, its diagnosis among Nigerian children and adolescents is still uncommon, hence, the reason many physicians still misdiagnose T2DM in adolescents as type 1 diabetes mellitus for reason of age of onset. Here, we present a 15-year old, overweight, girl who presented with history of polyuria, polydipsia and weight loss; her blood glucose level was 14.3 mmol/l, glycated haemoglobin 12.4% and glycosuria (3+), with no ketonuria or proteinuria. She was initially diagnosed as type 1 diabetes and managed with multiple doses of insulin by the pediatric team until she was later reviewed by the endocrinology unit. The diagnosis was later changed to early-onset T2DM (Youth-onset T2DM) based on a BMI of 29.75 kg/m^2, presence of acanthosis nigricans, absence of ketosis, preserved beta-cell function as shown by normal serum C-peptide levels, absence of anti-glutamic acid decarboxylase (GAD) antibodies and islet cell antibody, and also response to oral anti-diabetic agents while her insulin therapy was discontinued. Therefore, a possibility of T2DM should be suspected in childhood and adolescent with diabetes associated with overweight or obesity, relatives with T2DM and features of insulin resistance (IR) like acanthosis nigricans, hypertension, dyslipidaemia, non-alcoholic fatty liver disease (NAFLD), hyperandrogenism, or polycystic ovarian syndrome (PCOS).

Keywords

Type 1 Diabetes Mellitus, Type 2 Diabetes Mellitus, Adolescent,

Misdiagnosis, Acanthosis Nigricans, Nigerians

1. Introduction

Until recently, immune-mediated type 1 diabetes mellitus (Type 1A) was the only type of diabetes considered prevalent among children, with only few cases of children considered to have type 2 diabetes mellitus or other forms of diabetes. Type 2 diabetes mellitus (T2DM), which was once considered a rare condition in childhood and adolescent population, now accounts for about 15% to 45% of all newly diagnosed cases of diabetes in children and teenagers [1] [2]. The epidemic ofT2DM in childhood and adolescent is the result of a variety of factors, the most important of which appears to be an increase in the rate of obesity in children [2].

Typically, children with immune-mediated type 1 diabetes are not overweight and have recent weight loss, polyuria, and polydipsia. However, as the population is becoming increasingly overweight, the percentage of children with type 1 diabetes who are obese is increasing [3] [4] [5]. In a comparison of youth with type 1 and T2DM, 96% of those with T2DM, versus 24% of children with type 1 diabetes, were overweight or obese at diagnosis. This epidemic of type 2 diabetes in childhood and adolescence has created difficulty in distinguishing the aetiology of diabetes in some children without advanced laboratory evaluation. Distinguishing between type 1 and type 2 diabetes in an overweight or obese adolescent, therefore, may be challenging, especially in ethnic/racial minorities, and also among developing countries like Nigeria with low incidence of type 2 diabetes among youths [6] [7]. In such patients, a detailed family history and measurement of islet auto-antibodies 65 and anti-glutamic acid decarboxylase 512 are recommended, and plasma or urinary C-peptide concentrations also may be helpful [8] [9] [10]. The differences in the treatment modalities between individuals with T2DM compared to T1DM and the profile of co-morbidities, underscores the importance that specific type of diabetes be established. Otherwise, misclassification can have serious clinical and psychosocial consequences. Incorrectly diagnosing T2DM in a young patient with T1DM could be life threatening if the situation is managed with oral diabetes medication rather than insulin. Likewise, misdiagnosing T1DM as T2DM can result in unnecessary life-long treatment with insulin, when alternative glucose lowering therapies may be more appropriate.

While there is heterogeneity in the presentation of both type 1 and type 2 diabetes, there are certain clinical features that suggest type 2 diabetes. Obesity is a hallmark of type 2 diabetes, with up to 85% of affected children either overweight or obese at diagnosis [5]. Occasionally, obesity may be masked by significant weight loss in the months or years before diagnosis. A family history of diabetes is usually present; 45% - 80% of patients has at least one parent with dia-

betes and may have a history of diabetes over several generations. Of the patients, 74% - 100% has a first- or second-degree relative with T2DMin contrast to only 5% of patients with T1DM [11]. Of note, diabetes in the parent or other relative may not be recognized until the child is diagnosed. Acanthosis nigricans is a disorder associated with insulin resistance and obesity, is common in youth with type 2 diabetes. It is described as a darkened, thick, velvety appearance to the skin found typically in folds or creases (nape of the neck, axilla, groin, and over flexor surfaces) and present in 90% of patients with type 2 diabetes and can be the most easily visible clinical indicator of insulin resistance. The frequency of acanthosis nigricans in obese adolescents or hyperinsulinemic children varies considerably by ethnicity. Up to 90% of obese or hyperinsulinemic children in Native American populations had acanthosis nigricans, whereas it was present in less than 5% of non-Hispanic white counterparts [11]. Typically, children with type 2 diabetes are usually diagnosed over the age of 10 years, that is, in the middle to late puberty. As the childhood population becomes increasingly overweight, type 2 diabetes may be expected to occur more in younger prepubertal children, hence clinicians need to be aware of this possible increasing occurrence.

2. Case Report

A 15-year old high school leaver presented at the paediatric clinic with a month history of weight loss, polyuria and polydipsia. The paternal grandmother had type 2 diabetes, the father was newly diagnosed with diabetes, and mother had systemic hypertension; her other clinical details are as shown in **Table 1**. The fasting plasma glucose (FPG) was 14.3 mmol/L, glycated haemoglobin (HbA1C) 12.4% and glycosuria (3+) but no ketonuria or proteinuria (**Table 2**).

The girl was the third of three children in a semi-affluent family with none of the siblings having diabetes. She attained menarche at the age of 12 years and had a regular menstrual cycle. Findings on examination were those of an overweight adolescent (BMI-29.75 kg/m^2), waist circumference was 96 cm, hip circumference 104 cm and waist-hip ratio was 0.92; no facial acne or evidence of hirsutism but had widespread acanthosis nigricans (at the nape of the neck, axilla, infra-mammary area, and at the groin) (**Figure 1**).

Table 1. Summary of case history.

Features	Patient
Age	15 years
Medical history at presentation	Polydipsia, Polyuria, weight loss BMI: 29.75 kg/m^2
Family history	Paternal grandmother: Diabetic Father: Newly diagnosed with diabetes & morbid obesity Mother: Hypertension & obesity
Ethnicity	Nigerian and Yoruba extraction

Keys: BMI: Body mass index.

Table 2. Clinical characteristics at presentation.

Test	Result	Normal range
Casual plasma glucose (mmol/L)	14.3	3.0 - 5.5
Glycated haemoglobin (HbA1C) [%]	12.4	3.5 - 6.4
Urinalysis; Glucose Ketone Protein	 3+ Negative Negative	
Urea (mmol/L)	4.4	3.5 - 6.5
Creatinine (μmol/L)	72	60 - 120
Anti-GAD 65 abs	Negative	
Islet cell abs512	Negative	
Serum C-peptide (ng/mL)	5.58	0.9 - 7.1
Electrolytes (mmol/L)	Sodium –136 mmol/L, Potassium –3.8 mmol/L, Bicarbonate –19 mmol/L	135 - 145 3.5 - 5.0 18 - 22
Fasting lipid profile (mmol/L)	TC: 3.0 HDL-C: 0.8 LDL-C: 2.0 TG: 0.5	3.0 - 5.5 >1. 29 <2.5 <1.69

Keys: HbA1C: Glycated haemoglobin; Anti-GAD abs: Anti-Glutamic acid decarboxylase antibodies; TC: Total cholesterol; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; TG: Triglycerides.

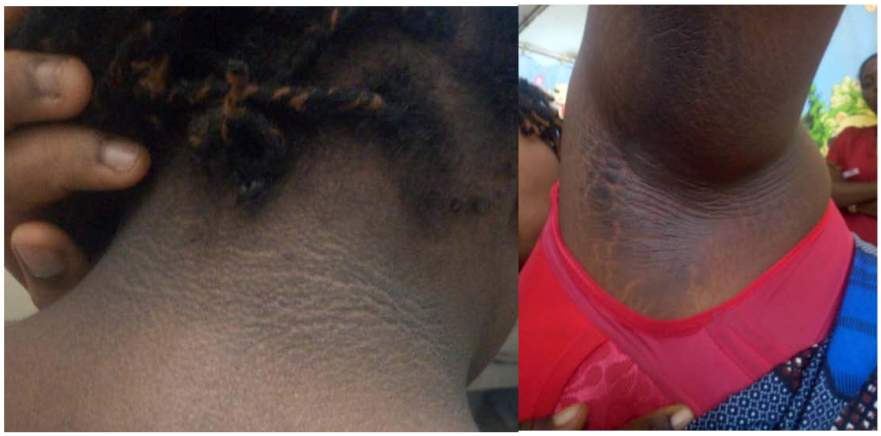

Figure 1. Acanthosis nigricans on the nape of neck & armpit.

An initial diagnosis of type 1 diabetes was made by the paediatric team based on the patient's age, and subsequently managed with multiple doses of soluble insulin. However, this initial diagnosis was revised when she was reviewed by the endocrinology unit that noted the presence of peripheral stigma of insulin resistance, i.e. acanthosis nigricans. Coupled with the patient's raised BMI, a provisional diagnosis of T2DM in an adolescent was made. Tests for antibodies to glutamic acid decarboxylase 65 (anti-GAD65) and islet cell antigen 512 (ICA512) were all negative; there was preserved beta-cell function as shown by

normal serum C-peptide levels. With the above results, a definitive diagnosis of Type 2 diabetes in adolescent was made; hence patient's insulin therapy was discontinued.

The patient and parents were adequately counseled and patient was placed on dietary control. She was advised to stop consumption of high-calorie drinks such as carbonated drinks, processed fruit juice; to reduce consumption of food with high glycaemic index such as cassava flakes, short grain rice, white bread, table sugar, etc. and to increase consumption of food with low glycaemic indexes such as vegetables, beans, porridge, grainy bread, soya beans and milk. She was also counseled to reduce her food portion and increase her physical activities with the aim of achieving, as close as possible, the weight appropriate for her age. This was done in addition to Metformin with good glycaemic response.

3. Discussion

Type 2 diabetes mellitus had always been considered a disease of older adults, while type 1 diabetes mellitus, was considered a disease of children [12]. Perhaps, this misconception is the main reason why our patient was misdiagnosed and managed as a case of type 1 diabetes, based solely on her age being. In recent times, there has been an increase in the incidence of T2DM in children and adolescents all over the world. This increase is directly proportional to a rise in prevalence and degree of obesity in adolescents, especially in regions where the diet has become more westernized with high glycaemic index [13] [14]. Increased consumption of these foods highin glycaemic index (GI) and glycaemic load (GL) lead to a resultant insulin resistance and impairment of pancreatic function.

Our patient was a 15-year old overweight female of African origin with a BMI of 29.75 kg/m^2; she had a family history of diabetes in at least two generations. Positive family history is a common finding in children and adolescents with type 2 diabetes [11]. However, diabetes in the parent or other relative may not have been diagnosed or recognized until the child is diagnosed. This was true in our patient whose father although morbidly obese, was only diagnosed on routine screening after this index patient was diagnosed of diabetes. Patients with T2DM can present in various ways, from being asymptomatic to being very ill, with or without the classic symptoms of polyuria, polydipsia, weight loss, hyperglycaemia and glycosuria with or without ketosis [15]. Many patients with T2DM whether adult-onset or early-onset usually present with one or more chronic microvascular complications of diabetes at or shortly after diagnosis [16]. However, our patient did not have any finding suggestive of such complications. Microvascular disease is the hallmark of hyperglycaemia diagnosed at a young age. In Japanese children, incipient retinopathy was detected in 36% of the cases at the time of diagnosis, and in 39% of the cases at 2 years follow-up, while microalbuminuria was observed in 39% at 2 years follow-up [17]. Hence, young people with type 2 diabetes are more likely to develop microvascular complica-

tions compared with type 1 diabetes [17]. Also, the long-term risk of cardiovascular disease in young people diagnosed with type 2 diabetes is worse than those diagnosed later in life [18]. As our patient is female, this is in keeping with female preponderance, that is, females have a higher incidence of type 2 diabetes than males, with a female to male ratio of 1.8 - 2:1.7 [5] [19]. Girls tend to reach puberty earlier and puberty is associated with fat accumulation, contributing to greater insulin resistance in girls than in boys of a similar ages; they also carry more subcutaneous fat than boys. Also, physical activity levels also tend to be lower among adolescent girls than boys and this may be adding to greater prevalence and incidence of obesity and diabetes. The peak age of onset of T2DM in children coincides with pubertal timing because the mean age at diagnosis is 12 to 16 years, with an earlier onset in girls [11] suggesting that physiological insulin resistance during puberty may play an important role. One of the markers of insulin resistance that is commonly found in adolescents with T2DM is acanthosis nigricans which our patient had. However, other markers of insulin resistance like hypertension, dyslipidaemia, polycystic ovarian syndrome (PCOS), were absent in our patient.

The primary prevention of T2DM is directed toward the obesity pandemic and involves reversing eating and entertainment trends in homes, schools, and communities that have resulted in excess caloric intake and marked decrease in energy expenditure by children and adults. The American Diabetes Association (ADA) recommends testing in overweight children and teens (BMI > 85th percentile for age and sex, weight for height > 85th percentile, or >120% of ideal body weight) who have any two of the following characteristics: type 2 diabetes in first- or second-degree relatives; African American, American Indian, Asian, Latino, or South Pacific Islander race or ethnicity; and evidence of insulin resistance or a condition associated with insulin resistance (e.g. acanthosis nigricans, PCOS, hypertension). Further, the ADA recommends that testing begins at 10 years of age or at puberty (whichever occurs earlier), that testing be repeated every 2 years, and that fasting plasma glucose testing be performed [11].

Regarding therapy, because Metformin is the only oral hypoglycaemic agent approved for paediatric use, other oral anti-diabetic agents used in adults are yet to be validated and approved for use among children and adolescents [20]. Treatment of T2DM in the paediatric population remains challenging because of the difficulty of successfully employing lifestyle changes. Hence, measures that combine dietary changes, exercise, and behavioural modification should be put in place to manage diabetes in this category of patients.

4. Conclusion

With an increasing number of reported cases of T2DM in adolescents, a high index of suspicion is needed to correctly diagnose diabetes in children with non-congruent clinical findings. Moreover, clinicians need to be aware that type 2 diabetes is not necessarily adult-onset and more education and seminars

should be conducted to sensitize the primary care physicians to give consideration to such condition in children and adolescent with diabetes. Also, it is important for clinicians to routinely screen overweight children with family history of diabetes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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