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CASE REPORT: UNCLASSIFIED VERSUS HYBRID FORMS OF DIABETES MELLITUS (DM)

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ABSTRACT

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Background.
The WHO 2019 classification of diabetes mellitus introduced two new subgroups: Hybrid forms and the unclassified. This means that some cases of diabetes mellitus (DM) do not fit into established forms of DM such as Type 1 and Type 2.

Report. This case describes a new form of DM that is different from the two forms of Hybrid forms of diabetes described by WHO in 2019. The patient presented with severe hyperglycaemia, low C-peptide value, no ketonuria and needed large doses of insulin to achieve normoglycaemia. Subsequently, C-peptide became normal and metformin with diet and lifestyle measures controlled the blood glucose. To our knowledge this type of DM has not been classified. We describe this as a third type of Hybrid diabetes.

Conclusion. This adolescent presented with some features of Type 1 diabetes mellitus, but within three years regained normal beta cell function and continuous monitoring shows normal blood glucose values with diet and oral hypoglycaemic drug, Metformin. We describe this as the third type of Hybrid class of diabetes mellitus.

Key words: Hybrid forms of diabetes, Unclassified diabetes, New type of diabetes, C-peptide, Beta cell function.

INTRODUCTION. The classification of diabetes mellitus has been under a state of flux. The first WHO Classification of diabetes mellitus in 1965 described two main types: Insulin Dependent Diabetes Mellitus (IDDM) and Non-Insulin Dependent Diabetes Mellitus (NIDDM).[1] The WHO in 1980 changed this classification to Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM). This was because some of the previously classified cases of NIDDM needed insulin in emergency situation, or as beta cell function detoriates with time.[2]

The 1985 WHO Classification of Diabetes Mellitus introduced a new form of diabetes called, Malnutrition Related Diabetes Mellitus (MRDM).[3] This was however, removed in the WHO 1999 Classification of diabetes for lack of evidence as a specific type.[4] In the current WHO 2019 Classification of diabetes, MRDM is described as Fibrocalculous Pancreatopathy – which is one of the diseases of the exocrine pancreas.[5]

The WHO Classification of diabetes 2019 introduced two new subgroups of diabetes mellitus. These are the Hybrid forms of diabetes and the unclassified.[5,6] The Hybrid forms of diabetes are: slowly evolving immune mediated diabetes of adults, previously called latent autoimmune diabetes of adults (LADA); and ketosis prone Type 2 diabetes which presents with ketosis and insulin deficiency, but later does not require insulin and is not immune mediated. Here we describe a case which presented with features of Type 1 DM: 17 years at onset, low C-peptide value and required large doses of insulin for the control of hyperglycaemia, but over the years regained normal C-peptide values and did not need insulin again. In 2018 we described a similar case, in a 23 years male patient.[7]

CASE REPORT.

BU presented in 2018 at the age of 17 years with Fasting Blood Glucose (FBG) of 13.3 mmol/l (239.4 mg/dl) and glycosuria (++). She was treated for Malaria on account of fever. Her physical examination was normal and her Body Mass Index (BMI) was normal (22.4 kg/m^2). The urinalysis did not show ketones and there was no proteinuria. Investigations: FBC, E/U/Cr, Fasting Lipid Profile and CXR were normal, except for mild anaemia. Her blood sugar was only controlled on large doses of insulin, despite Diabetes Self-Management Education (DSME) and Medical Nutrition Therapy (MNT) as part of her treatment. She required up to 80 iu of insulin in divided doses daily to achieve normoglycaemia.

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Our review in 2018 showed HbA1c of 13.4% and C-peptide of 0.4 ng/ml (0.7 – 1.9 ng/ml). Her insulin therapy was intensified, and in 2019 her HbA1c normalized at 6.4% and C-peptide became normal, 1.0 ng/ml. In 2021 the C-peptide rose to 1.8 ng/ml. Her blood sugar is now controlled on Tab Metformin 500mg tds and diet. Her current BMI is 25 kg/m^2.

DISCUSSION. This patient presented with some features of type 1 DM: age at onset, low C-peptide value and large doses of insulin for the control of hyperglycaemia. However, there was no ketosis and no complications. Follow up has shown progressive improvement in pancreatic beta-cell function and use of Metformin in the treatment. This case does not fit into any of the subgroups described by WHO 2019 Classification of DM. The Hybrid forms of diabetes are: slowly evolving immune-mediated diabetes of adults, previously called latent autoimmune diabetes of adults (LADA); and Ketosis prone Type 2 diabetes, which presents with ketosis and insulin deficiency but later does not require insulin and is not immune mediated. This case does not fit into any of this Hybrid forms of DM.
It is likely that some none autoimmune insult on the pancreatic beta-cells may be temporary and therefore significant beta-cell recovery may lead to reduced insulin requirement. It is envisaged that this patient will not need insulin again and will be controlled on diet, lifestyle modification and oral hypoglycaemic medication. We have described a similar case in a male 23 years patient in 2018.[7] There was no demonstrable ketoacidosis at presentation like in this case. This is proposed as the third type of Hybrid form of diabetes mellitus. C-peptide provides an indirect measure of insulin secretory reserve and beta cell function. It is secreted in equimolar proportion with insulin from pancreatic pro-insulin. It is a useful tool in the diagnosis, classification and management of all types of diabetes mellitus.[8] We measure C-peptide routinely in our centre (Federal Medical Centre Owerri).

Investigations. Table 1 shows the C-peptide values and Glycated Haemoglobin (HbA1c) over time. At presentation in 2017 she had mild anaemia with PCV of 32% (35-54%) which was corrected with haematinics. Her renal function (E/U/Cr) was normal. The C-peptide and HbA1c were not done in the year 2020 because of the Covid-19 pandemic.

TABLE 1. Pattern of C-peptide and HbA1c.

S/no	Year	HbA1c(4-6%)	C-peptide (0.7-1.9 ng/ml)	Remarks
	2018	13.4	0.4	Poor diabetic control and low C-p value
	2019	6.4	1.0	Normal HbA1c and normal C-p value
	2021	9.2	1.8	Poor HbA1c attributed to poor adh to diet.

CONCLUSION. This was diagnosed as a case of Type 1 DM, but within three years assumed normal beta-cell function as evidenced by increased and normal C-peptide values. The control of blood glucose on diet, lifestyle measures and oral hypoglycaemic medication shows that this is not Type 1 DM. This is proposed as a third type of Hybrid form of diabetes.

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