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SCIENTIFIC LETTERS

MODY 3 diabetes, not every early onset diabetes is type 1 diabetes☆

Diabetes tipo MODY-3, no todo debut es diabetes tipo 1

Hyperglycemia is an increasingly common cause of consultation in paediatrics. Many clinical entities are included under the term of diabetes mellitus.[1]

Type 1 diabetes mellitus is the most common form of childhood diabetes. It represents 95% of all cases of diabetes in Spain among patients under 20 years of age.[2] Maturity onset diabetes of the young (MODY) is a monogenic form of familial early onset diabetes. The diagnosis of MODY requires a high degree of suspicion, with the family history of the patient being taken into account. This disorder is characterized by a dominant autosomal hereditary trait, insulinopenia, and the absence of obesity and insulin resistance and immune markers.[3] Many patients with MODY are mistakenly diagnosed with type 1 or type 2 diabetes.[1]

Maturity onset diabetes of the young is the most common type of monogenic diabetes. All known subtypes of MODY are caused by heterozygous mutations in genes that are crucial for the development or proper functioning of the pancreatic β cells.[4] Developments in molecular genetics have allowed MODY to be classified and diagnosed, with the description to date of at least 14 different genes causing the disease.[5] The most common subtype in the first two decades of life is MODY-2.[1] Patients with the MODY-3 subtype have a more severe defect in insulin secretion, with a greater risk of microvascular complications and a greater need for treatment with oral antidiabetic drugs or insulin.[6] For this reason, and since this disease is unusual in paediatrics, we consider it worthwhile to publish the present case.

A male currently 14 years old was attending and referred from another centre where he had been initially diagnosed with type 1 diabetes at 12 years of age. He had blood glucose 203 mg/dl in the absence of ketoacidosis, and associated polydipsia, polyuria and a three month history of polyphagia, with no weight loss. Initial glycosylated haemoglobin (HbA1c) was 8.9%, with glycosuria and negative glutamic acid decarboxylase (GAD) antibodies. There was no ketonuria. The celiac disease markers were negative, and the thyroid profile was normal. Microalbuminuria proved negative. The other study findings at the start of diabetes, with cardiological, ophthalmological and neurological evaluations were normal. His body weight was 51 kg, with a height of 156 cm, and a body mass index (BMI) of 20.96 kg/m^2. He was at Tanner stage III. The rest of the physical examination proved normal. The patient had a history of hyperglycemic episodes, which were classified as stress hyperglycemia.

The family history revealed type 2 diabetes mellitus in the mother and maternal grandmother.

Treatment was started in the form of multiple-dose insulin with basal insulin (glargine) and bolus insulin (lispro fast-acting insulin analogue), resulting in acceptable blood glucose levels.

In view of the negative GAD antibodies, the study was completed by having blood samples of the child, mother, maternal grandmother and maternal great uncle sent to the Research Unit of Hospital de Cruces (Bilbao, Spain) for the analysis of insulin autoantibodies, GAD autoantibodies and AI2 autoantibodies, all of which proved negative. The patient has a male sibling three years younger, with apparently normal glycemia; no sample was therefore sent at that time.

During the follow-up of our patient, which has been irregular due to localization and transport difficulties, there has been a progressive decrease in his insulin requirements while adequate glycemic control has been maintained, with a rapid decrease in HbA1c (5.8% at 4 months). After negative antibodies were confirmed, and together with the described family history, a MODY study was made, which revealed a heterozygous mutation in exon 4 of the HNF1A gene, consisting of a thiamine duplication in position 789. The mother was also found to present this alteration in heterozygosis. The maternal grandmother and great uncle did not have the mutation. This mutation has not been previously described, but since it results in the formation of an abnormal protein it is likely to be responsible for the disease, this hypotheses being corroborated by the maternal involvement.

With the confirmed diagnosis of MODY-3, rapid insulin was discontinued, the dose of basal insulin was lowered, and treatment with sulfonylureas (gliclazide) 15 mg every

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24 h with progressive dose increments was started simultaneously. The patient currently maintains adequate HbA1c levels. In the most recent blood test, blood glucose was 135 mg/dl, and HbA1c 7%, with a dose increase up to 45 mg daily.

The patient is currently controlled by the diabetes unit of our hospital, with a good clinical course and adequate control of the disease.

One year later, the male sibling was admitted due to a random blood glucose level of 214 mg/dl, glycosuria and HbA1c 8%. Given the background of our patient, and with the suspicion of MODY-3 onset, treatment with sulfonylureas was started. Four days after admission the glycemia values were found to be adequate. The results of the genetic study are pending confirmation.

Since MODY-3 is an unusual form of diabetes in paediatric patients, we consider the publication of this case to be of considerable interest, especially as several members of the same family are affected. We underline the importance of clinical suspicion in establishing a proper diagnosis, since it allowed the treatment to be modified and the disease to be adequately controlled, leading to an improvement in patient quality of life.

Collaboration with the Research Unit of Hospital de Cruces (Bilbao, Spain) proved essential in obtaining a correct diagnosis.

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María José Sánchez Malo[a,*], Marta Arrudi Moreno[a], Gracia María Lou Francés[b]

[a] *Servicio de Pediatría, Hospital Universitario Miguel Servet, Zaragoza, Spain*
[b] *Unidad de Diabetes Pediátrica, Hospital Universitario Miguel Servet, Zaragoza, Spain*

* Corresponding author.
E-mail address: mjsanchezmalo@gmail.com
(M.J. Sánchez Malo).

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Parenteral nutrition: Albumin versus total proteins in the assessment of plasma calcium to adjust parenteral nutrition: A series of cases☆

Nutrición parenteral: albúmina versus proteínas totales en la valoración del calcio plasmático para ajustar la nutrición parenteral: a propósito de una serie de casos

Plasma calcium is the parameter most commonly used to determine patient calcium levels in clinical practice. However, in certain physiological conditions, plasma calcium may not reflect the true clinical situation of the patient. Calcemia (blood calcium concentration) is closely regulated in the body, with total calcium values between 2.2 and 2.6 mmol/l (9–10.5 mg/dl) and ionic calcium values between 1.1 and 1.4 mmol/l (4.5–5.6 mg/dl). Forty percent of circulating plasma calcium is bound to proteins (mainly albumin, but also to globulins), 6% is bound to phosphates, citrate and bicarbonate, and the remaining 54% corresponds to ionic calcium.[1] The total calcium values change when the plasma protein levels change, while ionic calcium remains unchanged.[2,3] Situations where calcemia can be strongly influenced by changes in plasma protein levels include volume overload, malnutrition and nephrotic syndrome. Hypoalbuminemia can also be found in patients with cancer or surgical complications (bleeding, fistula, intestinal perforation, etc.). In these cases, we observe a decrease in total plasma calcium, but not in ionic calcium, a situation known as pseudohypocalcemia.[4] There are other circumstances in which total calcium is hardly evaluable, such as a reduced glomerular filtration rate and alkalosis, since alterations in acid-base equilibrium cause H^+ ions to compete with Ca^{2+} for the protein binding points, though total calcium remains unchanged.[5–7] However, when there are alterations in acid-base equilibrium, the free calcium fraction is modified, and the patients clinically manifest hypocalcemia due to a decrease in ionic calcium, thereby underlining the importance of determining it through laboratory tests.[8] Of note is the high frequency of hypoproteinemia in patients subjected to total parenteral nutrition (TPN) (approximately 85%[9]), which points to the need for strict control in such cases. When interpreting the biochemical parameters of a patient,

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