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LATE ONSET OF TYPE 1 DIABETES MELLITUS-CASE REPORT AND GENERAL CONSIDERATIONS

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Type 1 diabetes mellitus is an autoimmune condition arising from the destruction of pancreatic insulin-producing beta cells. The affection is most common in children and young peoplebut it can occur at any age. We describe the clinical case of 65 years-old women diagnosed in 2017 with type 1 diabetes mellitus.The patient presented at the " Nicolae Malaxa" Clinical Hospital Bucharest for weight loss, polyuric-polydipsic syndrome, physical asthenia. Biochemical determinations have highlighted: blood glucose: 308 mg/dL, diabetic ketoacidosis (pH: 7.12), *glycated hemoglobin*: 10.6%, pancreatic C-peptide-0.12 ng/mL, autoantibodies to glutamic acid decarboxylase>2000 IE/mL Insulin therapy in basal bolus regime has been initiated associated with lifestyle intervention with a favorable evolution in terms of glycemic control. Type 1 diabetes mellitus diagnosed in the adults may have similar clinical and biological characteristics to that occurring in younger ages and rapid insulin requirement is predictive for severe endogenous insulin deficiency. Type 1 diabetes mellitus is associated with other autoimmune diseases such as thyroid diseases and in the case presented the patient was diagnosed with Hashimoto thyroiditiswith euthyroidism three years before the onset of type 1 diabetes.International recommendations underline the importance of screening for thyroid disease for all patients with type 1 diabetes mellitus and also for celiac disease in adult patients in the presence of symptoms, signs and laboratory findings suggestive for this affection.

Keywords: late onset of type 1 diabetes mellitus, autoimmune diseases, screening.

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is an autoimmune condition arising from the destruction of pancreatic insulin-producing beta cells. The affection is most common in children and young people[1]. In 2019 International Diabetes Federation (IDF) published the 9th edition of the Diabetes Atlas which mentions that more than 1.100.000 children and adolescents bellow 20 years have T1DM[2].The incidence of new-onset T1DM in those over 20 years of age is unknown. In 2013 Hawa MI and coworkers published in *Diabetes Care*astudyabout theadult-onset autoimmune diabetes in Europe. It was a cross-sectional study in which 6151 diabetic patients were included, recruited between 2004 and 2007 from nine European countries. All patients were clinically evaluated (waist and hip circumferences, blood pressure) and laboratory tests such as:lipids, lipoproteins and specific autoantibodies -glutamic acid decarboxylase (GAD) antibodies, antibodies to insulinoma-associated antigen-2 and zinc-transporter were performed.The results of the study showed that adult-onset autoimmune diabetes is not rare and it was reported in 9.7% of this cohort of diabetic patients diagnosed between 30 and 70 years[3]. Two years latera review on the global epidemiology of T1DM in young and adults has been published. The authors analyzed 70 articles published between 1982 and 2014. The authors concluded that: "*Few studies on epidemiology of T1D in adults are available worldwide, as compared to those reporting on children with T1D. The geographical variations of T1D incidence in adults are parallel to those reported in children. As opposed to what is known in children, the incidence is generally larger in males than in females*" [4].

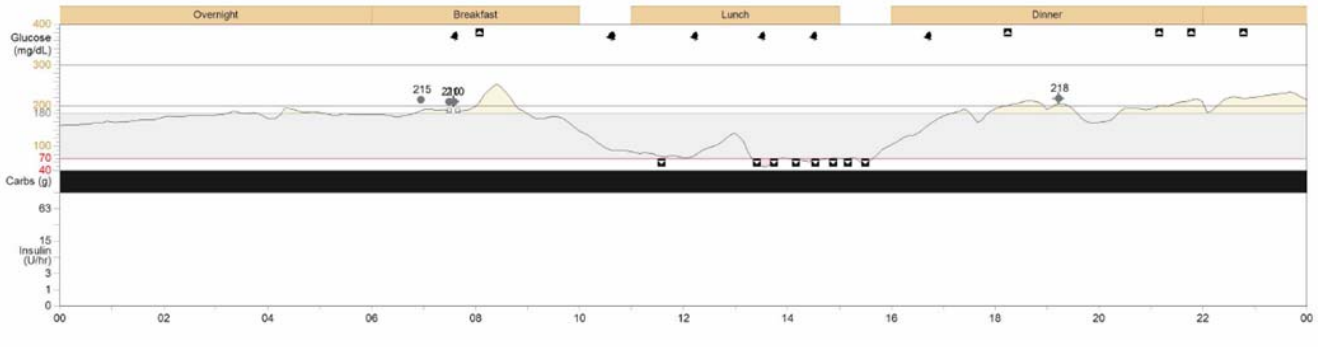

Figure 1. Asymptomatic hypoglycaemia on CGM recording.

CASE REPORT

A 62-year old woman was admitted in the "Nicolae Malaxa" Clinical Hospital Bucharest in June 2017 for weight loss (8 kg in a month), polyuric-polydipsic syndrome, physical asthenia. The patient has a heredo-colateral history of diabetes. At the admission the patient was overweight (height: 167 cm, weight: 73 kg, body mass index: 26.17 kg/m^2), with mediocre general condition, dehydrated skin, no neurological signs. Biochemical determinations have highlighted: blood glucose: 308 mg/dL, diabetic ketoacidosis (pH: 7.12), glycated hemoglobin (HbA1c): 10.6%, total cholesterol: 211 mg/dLSpecific treatment (endovenousinsulin infusions, repeated fast insulin) was initiated, which led tocorrection of diabetic ketoacidosisand lowering of blood glucose levels. Associated investigations included determinations of pancreatic C-peptide–0.12 ng/mL (reference values: 0.78–5.19 ng/dL), autoantibodies to GAD>2000IE/mL (reference values -<10 IE/mL) were also performed.Associated conditions: hypertension in treatment with angiotensin converting enzyme inhibitor drugs, dyslipidemia in treatment with statins and chronic autoimmune thyroiditis.Hashimoto thyroiditiswas diagnosed in 2014 (anti-thyroid peroxidase antibodies-TPOAbs>1200 UI/mL, reference range<60 UI/mL). The patient had euthyroidism (thyroid stimulating hormone:2.137µU/mL, reference range: 0.55– 4.78 µU/mL, free thyroxine: 1.16 ng/dL (reference range: 0.89–1.76 ng/dL) and thyroid ultrasound scan showed no evidence of structural alteration.Insulin therapy (rapid-acting and long-acting insulin analogs) in basal bolus regimen has been initiated associated with lifestyle intervention (medical nutrition therapy and physical activity) with a favorable evolution of blood glucose and HbA1c (values between 6.3–7% during 2018–2020). Because the recurrent asymptomatic hypoglycemia was suspected, continuous glucose monitoring (CGM) was recommended for this patient. The CGM recording revealed the presence of asymptomatic hypoglycaemia, which is why insulin doses have been adjusted.

DISCUSSION

T1DM is common form of diabetes in childhood and adolescence but it can occur at any age; onset of diabetes in the present case was at the age of 62 years. Patients with T1DM are not typically obese or overweight but the two conditions cannot exclude the diagnosis. It should be noted that the patient was overweight at the time of diagnosis.

T1DM may have similar or different clinical and biological characteristics in late onsetcompared to young onset. The rate of beta cells destruction is higher in children and adolescents, and smaller in others patients (mainly adults). In most situations, children may present diabetic ketoacidosis as the first manifestation of the disease; adults may retain sufficient beta cells function to prevent ketoacidosis[5].For the describedpatient, the onset of diabetes was with polyuria, polydipsia, marked weight loss and ketoacidosis. In practice in some situations in later life, patients with T1DM are frequently treated as having type 2 diabetes mellitus (T2DM) and clinicians should take into account the fact that T1DM diagnosed in the adults may have similar clinical and biological characteristics to that occurring at younger ages andrapid insulin requirement is predictive to severe endogenous insulin deficiency[1].

T1DM is associated with other autoimmune diseases such as thyroid disease (Hashimoto thyroiditis, Graves disease), primary adrenal insufficiency (Addison disease), celiac disease and vitamin B12 deficiency (pernicious anemia)[7,8]. T1DM may occur with other autoimmune diseases

such autoimmune hepatitis, dermatomyositis, myasthenia gravis[9, 10, 11, 12]. In 2019 Hughes JW and coworkers published in *Diabetes Care* a study about the prevalence of autoimmune diseases in adults with T1DM. In the study were included 1.212 adults of the Washington University Diabetes Center during the period 2011 to 2018. The results of the study showed that autoimmune diseases incidence and prevalence increase with age and female sex strongly predict autoimmune diseases risk. In patients included in the study the most common autoimmune disorders associated with T1DM were thyroid diseases, collagen vascular diseases and pernicious anemia. Authors recommend that. "*Individuals who are diagnosed with T1DM at older ages, particularly women, should be monitored for other autoimmune conditions*"[13]. At the same timeAmerican Diabetes Association recommends routine screening for thyroid disease for all patients with T1DM, screening for celiac disease in adult patients in the presence of symptoms (abdominal pain, diarrhea, malabsorption) or sign and laboratory manifestations suggestive for this affection (osteoporosis, iron deficiency anemia, vitamin deficiencies). The American Diabetes Association suggest measurement of vitamin B12 levels in patients with T1DM and peripheral neuropathy or unexplained anemia[7]. In the case presented the patient was diagnosed three years before the onset of diabetes with Hashimoto thyroiditiswith euthyroidism.

CONCLUSION

T1DM diagnosed in the adults may have similar clinical (polyuria, polydipsia, marked weight loss)and biological (ketoacidosis) characteristics to that occurring at younger ages and rapid insulin requirement is predictive for severe endogenous insulin deficiency. T1DM is associated with other autoimmune diseases such as thyroid diseases and this was also the case for the patient described above.International diabetes associations recommend screeningfor thyroid disease for all patients with T1DM, screening for celiac disease in adult patients in the presence of symptoms,signs and laboratory findings suggestive for this affection.

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