Abstract

Aim. – To report the first case of fulminant-like type 1 diabetes mellitus in a Hispanic woman from the United States.

Method. – The clinical presentation and laboratory data is presented of a Hispanic woman that was diagnosed with fulminant type 1 diabetes mellitus with a review of the literature.

Results. – An 18-year-old female presented with 1 week of polydyspea and polyuria. The patient was seen by her primary care doctor and found to have an elevated blood glucose. On presentation to the hospital, she was found to be in diabetic ketoacidosis. The laboratory analysis showed a C-peptide of 0.6 ng/mL and a glycohaemoglobin A1c of 6%. The patient had antibodies positive for glutamic acid decarboxylase. The patient was diagnosed with fulminant type 1 diabetes mellitus and was discharged in stable condition on basal/bolus subcutaneous insulin.

Conclusion. – Fulminant type 1 diabetes mellitus is a recently described presentation of diabetes mellitus that has been predominately reported in Japan and other Asian countries. The classical presentation includes rapid onset on ketosis within 1 week of symptoms of hyperglycaemia, with a near-normal glycohaemoglobin and absence of C-peptide. With the majority of case being reported from Asia, it has been hypothesized that there is a genetic determent that predisposes Asian individuals to develop fulminant type 1 diabetes mellitus. The addition of the case to the medical literature expands the focus of fulminant type 1 diabetes mellitus beyond the Asian population and supports the need that further research.

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1. Introduction

Fulminant type 1 diabetes mellitus (T1DM) is a new clinical entity that has a rapid development of hyperglycaemia and keto-sis. In contrast to classical autoimmune T1DM that takes several
months to years to develop signs and symptoms of diabetes, fulminant T1DM takes 1–2 weeks for total beta-cell destruction and progression to hyperglycaemia and ketoacidosis. The majority of research on fulminant T1DM has originated in Japan where 20% of individuals presenting with ketoacidosis are diagnosed with fulminant T1DM [1]. Cases have also been reported from Korea, Philippines, and China [2–4]. With the majority of case reported in the Asian population, researchers have hypothesized that there is a genetic susceptibility in the Asian population. Several investigators have linked genetic marks particularly HLA genes that may increase the risk of fulminant T1DM in the Japanese population versus the Caucasian population [5–7].

Recently, Moreau et al. [8] reported three Caucasian women with fulminant T1DM in France indicating that Caucasians may not be immune to this entity. Currently there is no reported cases of fulminant T1DM in Hispanic individuals or from the USA, we therefore report the first case of an American Hispanic female with fulminant-like T1DM.

2. Case report

A healthy 18-year-old, US born female of Guatemala descent, presented to her primary doctor with 2 weeks of fatigue and 1 week of polydipsia, polyuria, nocturia. The patient reported losing 18 pounds over 2 weeks. She denied any recent infections. A basic metabolic panel ordered by primary doctor had a serum glucose of 934 mg/dL. The patient was directed to the emergency department at our hospital.

The patient had no past medical or surgical history and a significant family history of diabetes mellitus type 2 in maternal grandmother and uncle. The patient was not on any medications prior to admission. She did not smoke, drink alcohol or engage in recreational drug use.

Review of symptoms was positive for what was mentioned in the presenting symptoms and specifically negative for heat or cold intolerance, chest pain, palpitations, shortness of breath, or menstrual irregularities. On initial exam, heart rate 97 beats per minute, blood pressure 99/65, respiration rate 18 breaths per minute, and temperature of 96.5 °F. Her admission weight was 42.6 kg. She appeared healthy in no acute distress. Her mucus membranes were slightly dry. She had no thyromegaly. Her cardiac, pulmonary and abdominal exams were normal. She had normal skin turgor and neurological exam.

Her initial laboratory analysis showed: sodium of 133 mEq/L (136–145), potassium 3.9 mEq/L (3.9–5), chloride 98 mEq/L (98–108), bicarbonate 10.5 mEq/L (24–32), blood urea nitrogen 9 mg/dL (6–23), creatinine of 1.1 mg/dL (0.5–1.2). On blood gas, her pH was 7.24. The anion gap was calculated to be 24.5 mEq/dL (7–15). Urinalysis showed 3+ ketones and 3+ glucose. Her complete blood count showed normal white blood cells, haemoglobin, haematocrit and platelet counts.

The patient was started on an insulin infusion at a rate of 0.1 u/kg/h. Within 12 hours her anion gap had closed and she was transitioned to insulin lispro 10 units daily. The patient was started on a diabetic diet with insulin lispro coverage of four units with meals. Additional blood work showed a HbA1c 6% (3.1–6.5), insulin antibodies less than 0.4 U/mL (0–0.4), islet cell antibodies less than 1.4 (< 1.4), glutamic acid decarboxylase (GAD) antibodies 8.72 U/mL (0.1–4.5), and IA-2 antibodies less than 0.8 (0–0.8), C-peptide 0.6 ng/mL (0.8–3.5) with a serum glucose of 295 mg/dL, TSH 1.88 mIU/L (0.35–5.5), amylase 54 U/L (44–128), lipase 26 U/L (15–60). HLA typing showed the patient to be haplotype DRB1*0407-DQB1*0302.

Based on her clinical presentation and laboratory value she was diagnosed with fulminant-like T1DM. She was discharged in stable condition 3 days after presentation on basal/bolus insulin therapy.

3. Discussion

The diagnostic criteria for fulminant T1DM require: (1) evidence of ketosis or ketoacidosis within about 7 days of hyperglycaemia onset, [2] plasma glucose level greater or equal to 16.0 mmol/L (> 288 mg/dL) and glycohaemoglobin less than 8.5% at initial visit, and [3] urinary C-peptide excretion less than 10 ng/d or fasting serum C-peptide level less than 0.3 ng/mL (< 0.10 nmol/L), or less than 0.5 ng/mL (< 0.17 nmol/L) after intravenous glucagon or after meal at onset [9]. As more cases of rapid onset diabetes with ketoacidosis present, the original definition of fulminant T1DM that included lack of auto-antibodies and evidence of pancreatitis is not always fulfilled. In the Japanese literature, 4.8% of fulminant T1DM are positive for GAD antibodies [10]. Many reports demonstrate no evidence of exocrine pancreas dysfunction. All reported cases do demonstrate near-normal HbA1c, with very high serum glucose and evidence of ketosis or ketoacidosis.

In our current case, this healthy female presented with polydipsia, polyuria, nocturia and weight loss in 1–2 weeks, glucose of 934 mg/dL with ketoacidosis, low C-peptide, near-normal HbA1c level of 6%. The clinical presentation and a majority of laboratory values were consistent with fulminant diabetes mellitus type 1 diabetes. The patient failed to reach the cut-off for a C-peptide level less than 0.5 ng/mL after a meal. We feel that this patient did develop fulminant T1DM and a level of 0.6 ng/mL still indicated near complete destruction of pancreatic beta cells. Because she did not satisfy the strict research criteria for fulminant T1DM, we are using the term fulminant-like T1DM. To our knowledge this is the first case of fulminant-like T1DM in a Hispanic individual and first case in USA. Combine with recent report of fulminant diabetes in Caucasian, our case may indicate that fulminant T1DM may be more widespread and affect people other than of East Asian descent.

Our case is slightly different than those described in the Japanese literature in that she had weight loss and fatigue about 1–2 weeks but polyuria and polydipsia for 1 week. She did not have a history of infection such as a viral upper respiratory tract infection or urinary tract infection. This is in contrast to other published cases, which usually presented with 1 week of symptoms and a preceding infection. The mechanism of her rapid beta-cell destruction remained a puzzle. In the Japanese population, there has been reported cases that also had elevated pancreatic enzymes such as amylase or lipase suggestive of widespread inflammation of the pancreas [5]. Without evidence
of pancreatitis, the resulting hyperglycaemia is the result of isolated destruction for the beta cell in the pancreas. Previously, fulminant T1DM was considered to occur without evidence of autoimmunity or insulitis [1], however population-based studies in Japan have indicated that fulminant onset can have auto-antibodies and autopsy results indicate insulitis if done shortly after onset of ketoacidosis [9]. Our patient had mildly elevated anti-GAD antibodies, which supports that autoimmune may play a role in fulminant T1DM.

Pozzilli et al. described nine patients in a series of 82 Italian patients with newly diagnosed T1DM that had a HbA1c that was less than 7.5%. The conclusion of this article was that this group of patients were different that those observed in Japan because they were positive for auto-antibodies and did not have evidence of pancreatic inflammation and thus did not fit into the diagnosis category of fulminant T1DM. The article did not discuss the presentation of these individuals and was not clear if they presented in diabetic ketoacidosis [11]. The only published cases of non-Asian individuals with fulminant T1DM were from France by Moreau et al. [8].

With the majority of individuals presenting with fevers and flu-like symptoms in Japanese series, a viral cause is possible. Case reports have linked human herpes virus 6, herpes simplex virus, and coxsackie virus with the development of fulminant T1DM [12,13]. Another hypothesis involves T-cell lymphocytes with reactivity to glutamic acid decarboxylase [14]. Different human leukocyte antigen (HLA) haplotypes may also effect the susceptibility to fulminant T1DM versus classical autoimmune T1DM. Imagawa et al. have demonstrated that in Japan, individuals with HLA DRB1*0405-DQB1*0401 are more likely to develop fulminant T1DM, whereas in Caucasian with HLA DRB1*0401-DQB1*0302 increases the risk for classical T1DM [6,7]. The French cohort of patients did not have the gene for HLA DR4 [8]. Our patient fits more with the Caucasian haplotype. The available data from the literature would suggest that this group of individuals are genetically susceptible to the development of fulminant T1DM after an insult or injury. It is still unclear what are the specific genes and environmental factors that lead to this condition.

4. Conclusion

This is the first case of fulminant-like T1DM reported in a Hispanic individual in the United States. This current case adds to the literature of fulminant T1DM and demonstrates that individuals beyond Asia do develop fulminant T1DM. The pathogenesis of fulminant T1DM still needs to be elucidated and the role of autoimmunity, viral infections and genetic susceptibility needs to be clarified with further studies. Certainly more research is needed in the western world to see if fulminant T1DM is more widespread than originally believed. With the addition of more cases of fulminant TDM with evidence of auto-antibodies, it may be determined that autoimmunity is the leading cause of fulminant T1DM.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References