Int J Diabetes Dev Ctries (July–September 2016) 36(3):374–375
DOI 10.1007/s13410-015-0406-0

CASE REPORT

Fulminant type 1 diabetes occurring in a child in association with acute hepatitis A infection: case report and review of literature

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Received: 3 July 2014 / Accepted: 19 May 2015 / Published online: 4 June 2015

Abstract Fulminant type 1 diabetes is a recently described form of T1DM presentation, reported mainly from Japan. This mode of presentation is very rare among Caucasians and is not reported from India before. We report a child presenting with fulminant type 1 DM in association with acute hepatitis A virus infection.

Keywords Fulminant type 1 diabetes · Hepatitis A

Introduction

Fulminant type 1DM is a recently recognized pattern of type 1 diabetes presentation reported mostly from Japan. It is characterized by an abrupt onset of diabetes with ketosis or ketoacidosis, near-normal HbA1c level at presentation, complete beta cell destruction at onset, and absence of islet-associated antibodies [1]. Fulminant type 1DM is considered as a subtype of type 1B diabetes. Owing to the heterogenous nature of T1B DM, there is appreciable variability in its mode of presentation. Ethnic variability has a significant role in the incidence of fulminant T1DM. Fulminant T1DM is rare among Caucasians and is not reported from India before. Viral infections are known to trigger T1DM. Reports of Hepatitis A precipitating T1DM are very rare.

Case report

A 3-year-old girl was brought with fever of 2 days duration and lethargy abdominal pain and vomiting for 1 day. She did not have any osmotic symptoms or loss of weight prior to the present episode. She had contact to hepatitis A viral hepatitis in the household at the same time. On evaluation, she was found to have high blood sugars (378 mg/ dl) and strong ketonuria. There was no acidosis. She was hemodynamically stable. Her heart rate was 104/min, respiratory rate 24/min, blood pressure 96/69 mm of Hg. Her weight was 12 kg (between 5th and 10th percentile) and height was 88 cm (10th percentile). Her serum sodium and potassium were 131 and 3.1 mEq/l, respectively. Her serum creatinine was 0.5 mg/dl and blood urea was 16 mg/ dl. Her liver function test showed a serum total bilirubin of 3 mg/dl, SGOT 760 IU/l, SGPT 340 IU/ l, and ALP of 560 IU/l. Serum lipase was 138 (normal 73–393 u/l) and did not suggest exocrine pancreatic damage. She improved with intravenous fluid administration, potassium replacement, and intravascular insulin infusion. Ig G HAV was done which was positive (HAV IgG 3.8 S/CO, >1.0 reactive by CMIA (chemiluminescent microparticle immunoassay)). Even though Ig M HAV is the marker of acute infection, Ig G was done because the antibody test was done 6 weeks after the episode and the patient had no history of hepatitis A in the past and was not immunized for hepatitis A. Anti GAD 65 antibody was negative (4.6 IU/mL by EIA (<10 negative)). Her HbA1c at admission was 6.2 %. Her fasting serum C peptide level was undetectable. She was discharged on a subcutaneous basal bolus insulin regimen

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with a bedtime basal insulin injection and three pre-meal bolus insulin injections. On follow-up, her blood sugars were fairly controlled and she required 0.5 units of insulin/kg of body weight daily. Her liver function test subsequently normalized.

Discussion

This report highlights a rare presentation of fulminant type 1 diabetes associated with acute hepatitis A infection. This is also the first report of fulminant type 1 diabetes from India to our knowledge. Fulminant type 1 diabetes accounts for up to 20% of all ketotic onset diabetes mellitus in Japan [2]. Balasubramanian et al. reported that none of the 55 recent onset type 1 DM patients from North India had fulminant type 1 diabetes [3]. Fulminant type 1 diabetes is very rare among Caucasians [4].

HLA polymorphisms strongly confer susceptibility or resistance to type 1 diabetes. Susceptibility polymorphisms may be different for Caucasians and for Japanese. While DR4-DQ4 is not a susceptibility factor for Caucasians, for Japanese, DR4-DQ4 confers susceptibility [5]. Imagawa et al. found that the frequency of HLA-DR4 was significantly higher in fulminant type 1DM unlike the frequency of HLA DR 9. In contrast, HLA-DR9 but not DR4 was more frequent in typical type 1A diabetes. Haplotype DR4-DQ4 was significantly more frequent, and DR8-DQ1 was less frequent in fulminant type 1DM. In type 1A diabetes, DR9-DQ3 was significantly more frequent [6]. In India while HLA DR 3 confers susceptibility to type 1DM and DR 2 protects from type 1DM, HLA DR 4 is very common in the background population, but it does not confer susceptibility to type 1DM [7]. Balasubramanian et al. could not identify any patient with fulminant type 1DM in a study of 55 recent-onset type 1DM in North India. HLA DR 4 did not impart susceptibility in this population [3]. Differential susceptibility of HLA DR 4 in part may explain the differences in incidence of fulminant type 1DM in different ethnic groups. Viral infections can precipitate fulminant type 1DM. IgA antibody titres to enterovirus are found to be significantly higher in fulminant type 1DM than in typical type 1A DM [8]. Pregnancy is another condition known to precipitate fulminant type 1 DM. Shimizu et al. reported 22 patients with fulminant type 1 DM with ketosis presenting during pregnancy or within 2 weeks postpartam [9]. Viruses may trigger type 1 DM by several mechanisms. Reports of hepatitis A viral infection triggering type 1 diabetes is very scarce in the medical literature. Adi FC reported nine patients with new-onset DM associated with an acute infectious hepatitis epidemic in Nigeria [10]. Makeen AM reported three patients who developed diabetes mellitus and presented with diabetic ketoacidosis within weeks of acute hepatitis A infection [11]. Another report of fulminant type 1 DM associated with acute hepatitis A was published from Korea [12].

Present report shows that fulminant type 1 DM occurs in India as well. Enteroviral infection, particularly hepatitis A viral infection, is more common in developing world; such infections may in part contribute to the increasing incidence of type 1 diabetes in this part of the world. There can also be regional variability in occurrence of fulminant type 1 DM between different parts of India as these are genetically diverse populations.

References

1. Tanaka S, Kobayashi T, Momotsu T. A novel subtype of Type 1 diabetes mellitus. N Engl J Med. 2000;342:1835–7.
2. Imagawa A, Hanafusa T, Uchigata Y, et al. Fulminant type 1 diabetes: a nationwide survey in Japan. Diabetes Care. 2003;26:2345–52.
3. Balasubramanian K, Dabadghao P, Bhatia V, Colman PG, Gellert SA, Bharadwaj U, et al. High frequency of type 1B (idiopathic) diabetes in North Indian children with recent onset diabetes. Diabetes Care. 2003;26:2697.
4. Pozzilli P, Visalli N, Leslie D, IMDIAB Group. No evidenca of rapid onset (Japanese) type 1 diabetes in Caucasian patients. Diabetologia. 2000;43:1332.
5. Ikegami H, Ogihara T. Genetics of insulin dependent diabetes mellitus. Endocr J. 1996;43:605–13.
6. Imagawa A, Hanafusa T, Uchigata Y, Kanatsuka A, Kawasaki E, Kobayashi T, et al. Different contribution of class II HLA in fulminant and typical autoimmune type 1 diabetes mellitus. Diabetologia. 2005;48:294–300.
7. Bhatia E, Melira NK, Taheja V, Vaidya MC, Ahuja MMS. HLA-DR antigen frequencies in a north Indian type 1 diabetic population. Diabetes. 1985;34:565–7.
8. Imagawa A, Hanafusa T, Makino H, Miyagawa JI, Juto P. High titres of IgA antibodies to enterovirus in fulminant type 1 diabetes. Diabetologia. 2005;48:290–3.
9. Shimizu I, Makino H, Osawa H, Kounoue E, Imagawa A, Hanafusa T, et al. Association of fulminant type 1 diabetes with pregnancy. Diabetes Res Clin Pract. 2003;62:33–8.
10. Adi FC. Diabetes melitus associated with infectious hepatitis in Nigeria. Br Med J. 1974;1:183–5.
11. Makeen AM. The association of infective Hepatitis type A (HAV) and Diabetes mellitus. Trop Geogr Med. 1992;44(4):362–4.
12. Hwang Y-C, Jeong I-K, Chon S, Oh S, Ahn KJ, Chung HY, et al. Fulminant Type 1 diabetes mellitus associated with acute hepatitis A. Diabetes Med. 2010;27(3):366–7.