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Case Report

Group B Coxsackie virus Induced Fulminant Type I Diabetes - Case Report Highlighting a Pathological Scenario of Serious Concern -

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ABSTRACT

Type 1 Diabetes (T1D), is a severe disease, representing 5-10% of all reported cases of diabetes worldwide. Fulminant Type 1 Diabetes Mellitus (FT1D) is a subtype of type 1 diabetes mellitus that is largely characterized by the abrupt onset of Diabetic Ketoacidosis (DKA) and severe hyperglycemia without insulin deficiency. Viral infections have been hypothesized to play a major role in the pathogenesis of Fulminant Type 1 Diabetes Mellitus (FT1D) through the complete and rapid destruction of pancreatic beta cells. Coxsackie viral infection has been detected in islets of 50% of the pancreatic tissue recovered from recent-onset Type 1 Diabetes (T1D) patients. In this report we have highlighted a case where the patient developed a Group B Coxsackie virus infection culminating in the development of Fulminant Type 1 Diabetes Mellitus (FT1D).

Keywords: Fulminant diabetes; Coxsackie virus; Diabetic ketoacidosis; Hyperglycaemia; Polyuria

ABBREVIATIONS

T1D: Type 1 Diabetes; FT1D: Fulminant Type 1 Diabetes; DKA: Diabetic Ketoacidosis; CV-B: Coxsackie Virus B; SGOT: Serum Glutamic-Oxaloacetic Transaminase; SGPT: Serum Glutamic Pyruvic Transaminase; GGT: Gamma-Glutamyltransferase; CRP: C-Reactive Protein

INTRODUCTION

Type 1 Diabetes (T1D) is a severe disease, representing 5-10% of all reported cases of diabetes worldwide [1]. It is characterized by a defect in insulin production form the pancreas as a result of selective and massive destruction of islet cells or of their functional impairment [1]. Its principal signs and symptoms include polyuria, polyphagia, polydypsia, weight loss, weakness and recurrent infections [2]. The annual incidence of Type 1 Diabetes [T1D] varies widely from one country to another but is, however, in steady increase across the globe, especially among children and young adults [3].

Fulminant Type 1 Diabetes Mellitus (FT1D) is a subtype of type 1 diabetes mellitus that is largely characterized by the abrupt onset of Diabetic Ketoacidosis (DKA) and severe hyperglycemia without insulin deficiency [3]. Viral infections have been hypothesized to play a major role in the pathogenesis of Fulminant Type 1 Diabetes Mellitus (FT1D) through the complete and rapid destruction of pancreatic beta cells [4]. Studies have reported a variety of enteroviral infections, including Coxsackie virus B1, B3, B4, A4, A5, and A6, to be involved in the development of Fulminant Type 1 Diabetes Mellitus (FT1D) [5]. Of these human enteropathogens, Coxsackie Virus B (CV-B) constitutes one of the most clinically significant groups [6]. Coxsackie viruses are small viruses with a single stranded, positive-sense RNA genome belonging to the Picornaviridae family. Coxsackie viral infection has been detected in islets of 50% of the pancreatic tissue recovered from recent-onset Type 1 Diabetes (T1D) patients [7]. It has also been demonstrated that Type 1 Diabetes (T1D) patients harbour Coxsackie Virus B (CV-B) RNA in their Peripheral Blood Mononuclear Cells (PBMC) [8,9]. The possible involvement of enteroviruses in Type 1 Diabetes (T1D) was pointed out for the first time in the year 1969 when in the case it was observed that anti-CV antibodies were found more frequently in patients with Type 1 Diabetes (T1D) than in control subjects [10]. In the year 1979, another study described the isolation of Coxsackie Virus B (CV-B4) from the pancreas of a ten year old boy who died of diabetic ketoacidosis [11,12]. It has further been postulated by some authors that the increase in the incidence of Type 1 Diabetes (T1D) could be related to changes in the epidemiology of Coxsackie viral infections [13,14]. This case report presents a very unique story of Coxsackie virus B (CV-B) induced fulminant diabetes in a young woman from eastern India.

CASE REPORT

A 25-year-old woman was admitted to our hospital with symptoms of acute thirst and polyuria. The patient developed fever and fatigue about one week before the date of admission. Few days later, she developed thirst along with polyuria and was treated with a general cold drug at a local health centre. However, her symptoms worsened, and she visited our hospital the after two days. During admission, she was perfectly alert, her body temperature was normal but she had complains of fatigue, thirst, and polyuria but did not complain of headache, sore throat, myalgia, or respiratory or abdominal symptoms. There was no visible edema, exanthema on the skin, swelling of the superficial lymph nodes or symptoms of muscle weakness. Her blood pressure and pulse rate both were quite low. Her oral cavity was dry, but no redness or white patches were observed on the pharynx and no vesicular rash or ulcers were observed on the oral mucous membrane. Here heart and abdominal conditions were observed to be perfectly normal. An arterial blood gas analysis revealed metabolic acidosis. The laboratory findings showed a high white blood cell count, ketonemia, anaemia and severe hyperglycemia with normal HbA1c and a high serum glycoalbumin level. In addition, the patient's serum levels of creatinine, urea nitrogen, C-Reactive Protein (CRP), and amylase, lipase, elastase-1, and phospholipase A2, were high. Serum Glutamic Pyruvic Transaminase (SGPT), Serum Glutamic Oxaloacetic Transaminase (SGOT) and Gamma Glutamyl Transferase (GGT) values were normal. Chest and abdominal computed tomography detected fatty deposition in the liver, but no abnormalities were found in the lungs, pancreas, spleen, or kidneys. Blood and urine cultures were negative. She was diagnosed with acute renal failure and Diabetic Ketoacidosis (DKA). Treatment resided on intravenous saline and regular insulin. Antibodies titers were measured in serum samples at the time of admission to test for various pathogens like rotavirus, adenovirus, echovirus 6 and 9, Coxsackie virus type A and B, parainfluenza virus, influenza virus A and B, Epstein-Barr virus, human herpes virus 6 and 7, cytomegalovirus, simple herpes virus, hepatitis A, B, and C viruses, mumps, and parvovirus B19. Of these, a significantly elevated antibody titer was only detected against Coxsackie Virus B (CV-B) by a neutralization test. Qualitative RT-PCR for Coxsackie Virus B (CV-B) gave positive results. By day 7 after admission, the patient's thirst and polyuria had resolved, and her temperature, blood pressure and pulse rate had normalized. Her plasma glucose level and electrolytes were normal. Subcutaneous insulin injection

therapy was initiated from that day. After three weeks of admission, the patient's blood chemical profile showed significant improvements (white blood cells, 4,756/ μL; serum C-reactive protein, 0.32 mg/ dL) and renal function (serum creatinine, 0.81 mg/ dL; urea nitrogen, 11.1 mg/ dL). Her fasting serum C-peptide was undetectable (< 0.1 ng/ mL) before and 5 minutes after intravenous glucagon loading, indicating Fulminant Type 1 Diabetes (FT1D). She tested negative for islet-related autoantibodies. She was also negative for other organ-specific autoantibodies, such as pituitary cell antibody, thyroid peroxidase antibody, thyroglobulin antibody, thyroid-stimulating hormone receptor antibody, gastric parietal cell antibody, intrinsic factor antibody, and the adrenal cortex antibody. The patient was discharged after a month completing a diabetes mellitus self-management education program. Her serum levels of amylase, lipase, elastase-1, and phospholipase A2 remained high till 3 months after discharge and then normalized gradually within 6 months. The patient continued to undergo treatment with multiple daily insulin injection therapy (a total of 30 U/day) as an outpatient. After 12 months of treatment, she weighed 56 kg, and laboratory examinations showed the following results: HbA1c (NGSP) 9.3%, casual plasma glucose 7.7 mmol/ L, and undetectable serum C peptide. Her subsequent clinical course has been uneventful. The titer for CV-B remained high till 1 year after admission.

DISCUSSION

Fulminant Type 1 Diabetes (FT1D) is considered to be a new form or subtype of Type 1 Diabetes (T1D). It is a mostly characterized by an almost complete destruction of the β-cells in pancreas and identified by a rapid onset. Several studies have suggested that both genetic and environmental factors like viral infections can equally contribute to the development of this disease [15]. Viral involvement has been proposed in the pathogenesis Fulminant Type 1 Diabetes (FT1D) by many studies worldwide.

Sekine et al. [16] reported that the pancreatic β-cells are destroyed within just a few days in case of Fulminant Type 1 Diabetes (FT1D). Studies presenting reports on nationwide surveys have revealed that flu-like symptoms were observed in about 71.2% of patients with Fulminant Type 1 Diabetes (FT1D). This suggests that viral infection was definitely critical in the development of Fulminant Type 1 Diabetes (FT1D). Among the other symptoms, fever was the most frequent and was observed in 60.0% of patients, followed by sore throat (25.2%), cough (12.0%), headache (11.5%) and nasal discharge (7.9%). Symptoms associated with gastrointestinal infection, such as diarrhoea (5.5%) or lower abdominal pain (11.0%), were also reported in other studies [17].

Our patient developed severe hyperglycemia and Diabetic Ketoacidosis (DKA) with normal HbA1c and undetectable C-peptide levels after 2 days of exhibiting hyperglycemic symptoms. These findings are very consistent with the diagnosis of Fulminant Type 1 Diabetes (FT1D) [18]. In our case, the presence of elevated serum pancreatic enzymes, negativity for verifiable islet-related autoantibodies, fever and pre-existing flulike symptoms support this diagnosis. Coxsackie Virus B Virus (CV-B) infection was ascertained as the main trigger inducing this condition, verified with molecular diagnostic methods. Our patient presented with fever and fatigue without any other symptoms before developing Type 1 Diabetes (FT1D), and the Coxsackie Virus B virus (CV-B) infection was confirmed serologically.

CONCLUSION

As per our knowledge this is the first reported case of Fulminant Type 1 Diabetes (FT1D) to be associated with Coxsackie Virus B virus (CV-B4) infection from eastern India and this case supports the etiological role of common viral infections in the development of Fulminant Type 1 Diabetes (FT1D). This case therefore presents the medical practitioners with a new insight and highlights the need to assess individuals with both common colds and acute hyperglycemic symptoms for the presence of Fulminant Type 1 Diabetes (FTID) and coxsackie viral infections.

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