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Elevated pancreatic enzymes, IgM, soluble interleukin-2 receptor in anti-GADab(+) type 1 diabetes

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Abstract

Type 1 diabetes can be classified into immune-mediated diabetes (type 1A) and idiopathic diabetes, which lacks immunological evidence for beta cell autoimmunity (type 1B). Type 1A diabetes is characterized by the presence of the anti-glutamic acid decarboxylase antibody (anti-GADab). Fulminant type 1 diabetes is classified as type 1B diabetes, and characterized by the absence of anti-GADab, flu-like symptoms, and elevated serum exocrine pancreatic enzymes. We report a type 1 diabetic patient who showed flu-like symptoms, elevated serum exocrine pancreatic enzymes, and an extremely high-titer of anti-GADab, manifesting the characteristics of both type 1A and fulminant type 1 diabetes.

Key words: Anti-glutamic acid decarboxylase antibody; Exocrine pancreatic enzymes; Type 1 diabetes; Soluble interleukin-2 receptor

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TO THE EDITOR

According to the guidelines of the American Diabetes Association, type 1 diabetes can be classified into immune-mediated diabetes (type 1A) and idiopathic diabetes, which lacks immunological evidence for beta cell autoimmunity (type 1B)[1]. Type 1A diabetes is characterized by the presence of an islet-related autoantibody, such as anti-glutamic acid decarboxylase antibody (anti-GADab). Fulminant type 1 diabetes, which is basically classified into type 1B diabetes, is characterized by a remarkably abrupt onset, the absence of autoantibodies, flu-like symptoms, and elevated serum exocrine pancreatic enzymes[2].

Here, we report a type 1 diabetic patient who showed an extremely high-titer of anti-GADab, flu-like symptoms, and elevated serum levels of exocrine pancreatic enzymes, immunoglobulin M (IgM) and the soluble interleukin-2 receptor (sIL-2R).

A 37-year-old woman was referred to our hospital on April 30, 2010, suffering from fever of unknown origin. She was relatively healthy, and had suffered flu-like symptoms for 1 mo. To reveal the cause of the fever, we measured serum C-reactive protein (CRP), IgM and sIL-2R levels. Laboratory data showed normal serum CRP level (0.25 RR < 0.3 mg/dL), and increased levels of serum IgM (22 428 < RR < 196 mg/dL) and sIL-2R (588 145 < RR < 519 units/mL). The patient was admitted to our

department with diabetic ketoacidosis (pH, 7.019; serum ketone bodies, 9352 mol/L) on July 9. She had suffered from low-grade fever for 2 mo, and had lost 8 kg in weight in the last month before admission. Serum glucose and HbA1c levels promptly increased before the admission (95, 239, and 572 mg/dL; 6.8%, 7.0%, 10.4%, on May 12, June 7, and July 9, respectively). On admission, her body weight was 55.0 kg (BMI 23.5 kg/m^2). Serum CRP (0.93 mg/dL), amylase (14 937 < RR < 125 units/L), lipase (16 511 < RR < 53 units/L), trypsin (900 110 < RR < 460 ng/mL), and elastase Ⅰ (590 100 < RR < 400 ng/dL) levels were elevated. Chest and abdominal computed tomography did not show any evidences of pancreatitis and/or lymphoma. The titer of anti-GADab was extremely high (99 800 RR < 1.5 units/mL). After treatment with intensive insulin therapy, her symptoms and plasma glucose levels rapidly improved. However, serum lipase (90 units/L), trypsin (600 ng/mL), and elastase Ⅰ (720 ng/dL) levels were still high 2 wk after admission, and IgM (220 mg/dL) and sIL-2R (583 units/mL) levels were also still high at 3 wk after admission. The urine C-peptide level was 7.1 g/d.

An extremely high-titer of anti-GADab in this patient supports the diagnosis as type 1A diabetes[3]. However, she also showed flu-like symptoms and elevated serum exocrine pancreatic enzymes, manifesting the characteristics of fulminant type 1 diabetes, which is classified into type 1B diabetes[4]. This patient does seem to have relatively acute-onset type 1 diabetes; however, this case does not fulfil the criteria for fulminate type 1 diabetes as defined by Hanafusa *et al*[4]. Our patient showed the characteristics of both type 1A and fulminant type 1 diabetes. To our knowledge, three type 1 diabetic patients who showed positive for anti-GADab and elevated serum exocrine pancreatic enzymes have been reported in the literature[5,6,7]. However, the titers of anti-GADab in these patients were very low (116.0, 13.1 and 14.0 units/mL) when compared with the titer in our patient.

Hanafusa *et al* studied pancreatic tissues immunohistologically in patients with type 1A and fulminant type 1 diabetes[8]. Lymphocytic infiltration to the exocrine pancreatic tissue was observed only in fulminant type 1 diabetes, whereas immunologically abnormal findings in islet cells were detected only in type 1A diabetes. They concluded that in type 1A diabetes, beta cells may be destroyed through a long-standing autoimmune process, whereas in fulminant type 1 diabetes, beta cells may be destroyed by a destructive process triggered by viral infection. Coxsackie B virus, mumps virus, adenovirus, cytomegalovirus infection have all been associated with beta cell destruction[3]. Coxsackie B virus, herpes simplex virus, human herpes 6 virus, enterovirus infection have also been reported to be implicated in the onset of fulminant type 1 diabetes[9]. Although we could not detect causative viruses, neither did we use anti-viral therapy, the flu-like symptoms, elevated serum exocrine pancreatic enzymes, IgM and sIL-2R levels in our patient suggest that a sudden aggressive viral infection may accelerate pancreatic injury.

We have to mention that, in retrospect, we should have determined anti-GADab titers in blood collected at the earlier dates (May 12 and June 7), rather than the eventual development of diabetic ketoacidosis in order to have understood the precise pathogenesis of this patient's diabetic state.

In conclusion, although type 1 diabetes is a complex, heterogeneous disease, our patient shows characteristics which have never been reported. An accumulation of similar cases may prompt us to understand the pathogenesis for type 1A and fulminant type 1 diabetes.

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