A Case of Diabetes Mellitus in Japanese Black Cattle

Takashi HASEGAWA, Kazuyuki UCHIDA, Jun YANASE, Kouhei KITAZAKI, Yasuo UCHINO1, Shigemi NAKAMURA2 and Hirohito SAKIMOTO3
Veterinary Medical Science, Faculty of Agriculture, Miyazaki University, Miyazaki 889–2192, 1Uchino Animal Hospital, Yamada, Kitamorokata, Miyazaki 889–4601, 2Nosai Miyakonojo, Miyakonojo, Miyazaki 885–0093, and 3Kagoshima Central Institute of Animal Health, Kagoshima 891–0116, Japan
(Received 5 June 1998/Accepted 20 April 1999)

ABSTRACT. A 3 year-old female Japanese Black cattle was diagnosed as diabetes mellitus (DM). Hyperglycemia (295 mg/dl), increase of serum fructosamine (487 µmol/l), elevated glycosylated hemoglobin A1 (GHBaA1; 10.9%), low concentration of serum insulin (< 1.0 µU/ml), increased serum glucagon (399 pg/ml), and glucose intolerance (glucose disappearance rate; k=0.53) were noted. On the histopathologic findings in pancreas, insulitis with infiltration of mononuclear cells was found. This case suggests that serum fructosamine and GHBaA1 are available parameters for understanding of pathophysiological conditions of bovine DM.—KEY WORDS: bovine diabetes mellitus, fructosamine, glycosylated hemoglobin.

Diabetes mellitus (DM) is an uncommon disease in ruminants, and most of reports on ruminant DM usually described the clinical and pathological findings [1, 5, 10, 12, 14, 15]. Definitive diagnosis of these cases was based on some laboratory findings such as glycospuria, hyperglycemia, low concentration of plasma insulin, and glucose intolerance [1, 12, 14, 15]. Recently, it has been widely accepted the measurements of fructosamine and glycosylated hemoglobin levels, of which are useful parameters for diagnosis and also for evaluation of pathophysiological conditions in human cases of DM [9, 13]. This report deals with laboratory and pathological findings in a case of Japanese Black cattle with DM, especially measurement of plasma fructosamine, glycosylated hemoglobin A1 (GHBaA1), and 1,5-anhydroglucitol (1,5-AG) levels.

A 3 year-old female Japanese Black cattle weighing 370 kg was admitted with chief complain of anorexia, ketonuria, and glycospuria to the Veterinary Teaching Hospital, Faculty of Agriculture, Miyazaki University. The physical examination revealed elevated rectal temperature (40.4°C), decreased ruminal mobility, and normal ocular fundus. There was no abnormal finding in rumen juice and rumen flora. Abnormal findings included ketonuria (4+), glycosuria (4+), mild neutrophilia (4524/µl), lymphocytopenia (2574/µl), and elevated levels of plasma AST (83 U/l), inorganic phosphorus (iP; 7.0 mg/dl), γGT (51 U/l) and glucose (295 mg/dl). The results of blood gas examination were almost within normal range (pH:7.483, HCO3−: 25.2 mmol/l, BE: -3.1 mmol/l). Immunoreactive insulin (IRI) and glucagon (IRG) concentrations were measured by human radioimmunoassay using porcine antibodies [3, 8]. Fructosamine, GHBaA1, and 1,5-AG were measured by nitroblue tetrazolium (NBT) reduction, high performance liquid chromatography (HPLC), and enzymatic methods, respectively, in the commercial laboratory for human [9, 13, 16]. Abnormal findings were shown in IRI, IRG, fructosamine, and GHBaA1 (Table 1). Intravenous glucose tolerance test was carried out with a single injection of 0.4 g/kg of glucose. Blood glucose levels were measured at 0, 5, 10, 20, 30, 45, 60, 90, and 120 min after injection of glucose. As the glucose disappearance rate (k) and half time (T1/2) were 0.53 and 130 min, respectively, indicating glucose intolerance (age matched clinically healthy control: 1.87 and 37 min, respectively), the cattle was diagnosed to be DM. Neutralizing antibody titer was negative against certain viruses included bovine viral diarrhea-mucosal disease (BVD-MD) virus.

On day 3 after the admission, levels of blood glucose, plasma BUN, CRE, ALT, and AST increased, and plasma electrolytes decreased on day 5. Fluid and insulin therapy with 5% xylitol and regular insulin were started. But severe acidosis (pH:7.212, HCO3−: 5.4 mmol/l, BE: -19.7 mmol/l) was found on day 6, and the cow died.

Necropsy revealed atrophy of the pancreas, abdominal adiponecrosis, and hepatic lipidosis. The pancreas was fixed in 10% neutral buffered formalin or methanol-carnoy solution, and embedded in paraffin. Sections were made using a routine procedure, stained with hematoxylin-eosin, and also stained by the avidin-biotin-peroxidase complex (ABC) method with mouse anti-mammalian MHC (major histocompatibility antigen) class II monoclonal antibody (VMRD, WA, U.S.A.), guinea pig anti-porcine-insulin polyclonal antibody (Miles-Yeda Elkhart, IN, U.S.A.), rabbit anti-porcine-glucagon polyclonal antibody (Dako Japan), and porcine anti-bovine viral diarrhea (BVD) polyclonal antibody for immunohistochemical analysis. On the histopathological examination, insulitis with infiltration of mononuclear cells was found. On the histopathologic findings in pancreas, insulitis with infiltration of mononuclear cells was found. This case suggests that serum fructosamine and GHBaA1 are available parameters for understanding of pathophysiological conditions of bovine DM.—KEY WORDS: bovine diabetes mellitus, fructosamine, glycosylated hemoglobin.

Table 1. Special laboratory findings in the diabetic cattle

<table>
<thead>
<tr>
<th>Case</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin (µU/ml)</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Glucagon (pg/ml)</td>
<td>399</td>
</tr>
<tr>
<td>Fructosamine (µmol/l)</td>
<td>487</td>
</tr>
<tr>
<td>GHBaA1 (%)</td>
<td>10.9</td>
</tr>
<tr>
<td>1,5-AG (µg/ml)</td>
<td>1.0</td>
</tr>
</tbody>
</table>
mononuclear cells and decrease in the number and size of pancreatic islets were observed (Fig. 1). Immunohistochemical analysis revealed an increased number of alpha cells in the pancreatic islets, while the islets contained few beta cells as reported previously [12]. These findings suggested the possible role of virus-induced and/or autoimmunity-mediated DM. The bovine case of autoimmune-mediated DM associated with BVD virus infection has been reported in young cattle in Japan [14]. Taniyama et al. also suggested that persistent infection of BVD virus induced DM in Japanese Black cattle [15]. On the immunohistochemical examination, neither MHC class II positive cells nor BVD virus-antigen positive cells was observed in the pancreas of this case. The autoimmune reactions, however, were not ruled out from these results, because the reactions were usually detected in early phase of the disease [4, 6].

Several new techniques have been applied for diagnosis as well as for evaluation in human cases of DM. Fructosamine and GHbA₁ reflect the long-term previous glycemic conditions for the past 2 to 3 weeks and 4 to 8 weeks, respectively, in DM [9, 13]. Successful treatments induce the decrease of the levels of both parameters. The measurement of 1,5-AG is useful as a diagnostic marker for DM, because it is one of the main sugar alcohols and its plasma concentration decreases specifically in diabetic patients [16]. High levels of GHbA₁ and fructosamine were found in this case, like in diabetic human, canine, and feline cases [9, 11, 13]. The values of GHbA₁ obtained in control cattle were higher than previous data measured by the colorimetric and ion-exchange batch chromatographic methods [2]. These differences might be caused by the assay system used, as reported in GHbA₁ of canine or feline cases [11]. On the other hand, fructosamine level (207.0 ± 10.7 µmol/l) in control cattle observed in this study was similar to that in a previous report [7], indicating that the NBT reduction method is available for the measurement. However, no difference of the serum 1, 5-AG level between the case and control cattle. The enzymatic method used in this study might have low sensitivity for determination of bovine 1, 5-AG, since levels in control cattle were extremely low compared to those in healthy human. From these results, laboratory findings of this case indicate that the measurement of serum fructosamine and GHbA₁ level may be useful for both diagnosis and evaluation of pathophysiological conditions in bovine DM.

ACKNOWLEDGMENTS. The authors thank Dr. Mitsugu Shimizu (Second Laboratory of Virology, Second Research Division, National Institute of Animal Health) for providing porcine anti-BVD antibody, and Dr. Yoshikazu Hirota (Laboratory of Molecular Immunology, Second Research Division, National Institute of Animal Health) for introducing Dr. M. Shimizu.

REFERENCES