

Diabetes mellitus in cattle infected with bovine viral diarrhoea mucosal disease virus

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Introduction

Diabetes in cattle has various etiologies¹. In humans, virus-induced insulin dependent diabetes mellitus (IDDM) has been reported. It has also been reported that cattle infected with foot-and-mouth disease contracted diabetes mellitus². Craighead and coworkers observed experimental diabetes in mice after inoculation of encephalomyocarditis virus³. Other viruses suspected of inducing diabetes are coxsackie, mumps, rubella and cytomegalo virus⁴.

Bovine viral diarrhoea mucosal disease (BVD-MD) is a frequently fatal infectious disease of cattle. There is no concrete evidence to date that BVD-MD virus induces diabetes. In this report, the clinicopathological characteristics of diabetes mellitus in cattle were described, and the relationship between BVD-MD and diabetes mellitus was discussed.

Materials and Methods

Animals : Four Japanese black cattle (0.5 to 4 years old) and four Holstein-Friesian cows (0.5 to 3 years old) were diagnosed diabetes. These cattle had no genetic relationship, and their place of origin was different.

Clinical examination : Physical examination, complete blood counts, serum biochemical analysis and urinary analysis were performed. Complete blood counts included packed cell volume, hemoglobin concentration, and erythrocyte and leukocyte counts.

Serum total protein, fibrinogen, serum albumin-globulin ratio, sodium, potassium, free fatty acid, blood urinary nitrogen, creatinine, glucose, insulin, amylase and lipase were measured. Urinalysis was performed using N-Multistix (Miles-Sankyou Co., Ltd., Tokyo).

Glucose tolerance test : Glucose tolerance tests (GTT) were performed on the second day of hospitalization. Glucose solution (50% w/v concentration) was administered intravenously at a dosage of 0.5 g/kg of body weight within a 5-minute period. Blood samples were collected before administration, and at 0, 15, 30, 60, 90, 120, 180 and 240 minutes after administration of glucose. Plasma glucose concentration and serum insulin were measured by enzymatic determination (Iatron-Chrom Glu-Lq, Iatron Labs., Tokyo) and radioimmunoassay, respectively.

Virological examination : Leukocytes and serum of affected cattle were used for virological examination. Isolation of BVD-MD virus and measurement of antibody titer for neutralization were performed in the Laboratory of Ishikari Livestock Hygiene Center.

Results

A noncytopathogenic strain of BVD-MD virus was isolated from both the leukocytes and the sera of all cases. Also a cytopathogenic strain was detected in two Japanese Black cattle and all Holstein cows. The antibody titer against BVD-MD virus was low in all cases.

Anorexia, dehydration, diarrhoea

Table 1. Clinical details of affected cattle

Strain* ¹	Age (Year)	Sex	Glucose* ² (mg/dl)	Insulin* ³ (μ U/ml)	Urine		
					PH	Glucose	Ketonebody
JB	0.5	Male	356	6.3	5	+	-
JB	0.5	Male	350	8.1	6	+	-
JB	1	Female	136	9.5	6	+	-
JB	4	Female	221	6.4	6	+	-
HF	3	Female	782	4.6	6	+	+
HF	0.5	Female	115	4.7	6	+	-
HF	0.7	Female	450	9.1	6	+	\pm
HF	0.8	Female	363	2.3	6.5	+	-

*1. JB;Japanese Black, HF;Holstein-Friesian.

*2. Plasma glucose concentration.

*3. Serum insulin concentration.

and mucosal ulcers were recognized in all cases. Fever was recognized in three cases. In some cases, pneumonia, dermatitis and lameness due to interdigital ulcers were observed.

All cases were hyperglycemic and hypoproteinemic (Table 1). Plasma glucose concentrations were over 100mg/dl in all cases. Insulin concentrations were low compared with healthy cattle. Anti-insulin antibody titer of these cases did not differ significantly from that of normal cattle. Hypoproteinemia was linked to the levels of γ -globulin. Packed cell volume and erythrocyte and leukocyte counts were high in all cases. Other hematologic results were normal. Urinalysis revealed aciduria and glycosuria. In two cases, ketonuria was recognized.

GTT results indicated a slow return of plasma glucose concentration to baseline. Plasma concentration did not return to normal until 4 hours after glucose administration (Fig.1). The half value period of plasma glucose in all cases was prolonged compared with normal cattle. Insulin response to increased plasma glucose was low in all cases.

Necropsy findings revealed pathognomonic lesions for BVD-MD,

including mucosal ulcer, and erosions from the mouth to rectum. In the exocrine pancreas of all cases, fatty degeneration, decrease of secretory granules and infiltration of lymphocytes into connective tissue were recognized. There were no marked changes of numbers and constitution of the islets of Langerhans. The insulinitis by the infiltration of lymphocytes to the islets and vacuolar degeneration of islet cells were recognized in the islets.

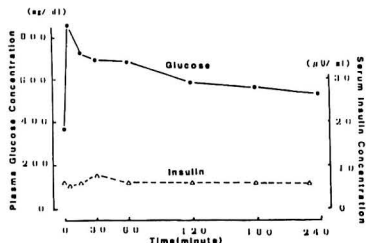


FIGURE 1. Result of glucose tolerance test in a Japanese Black cattlewith hyperglycemia (365 mg/dl). The serum insulin concentration did not increase after administration of glucose. Glucose (0.5g/ml) was administered intravenously.

Discussion

All cattle in this paper were diagnosed with BVD-MD based on physical, pathological and virological examination. Moreover, all cases had hyperglycemia and glycosuria. GTT showed the half value period of plasma glucose concentration was at least double that of healthy cattle. The serum insulin concentrations of patients were low, and were almost constant even after administration of glucose. Therefore, these cattle were diagnosed as having IDDM based on the criterion for diagnosis of human patients.

There are few reports of bovine diabetes mellitus (DM)⁵⁻⁹. Almost all reports described clinical signs, treatment and pathological changes. In previous papers, the type of DM was not distinguished, and the causes were not clearly indicated. Kitchen et al. reported IDDM in a bull¹⁰. The results of the GTT in this paper were the same as those in the report by Kitchen & Roussel.

Pathological examination of the pancreas of affected cattle revealed lymphocyte infiltration around the islets. This morphological change is a feature of insulinitis. In human IDDM patient, insulinitis has been a characteristic pathological change¹¹. Coxsackie, mumps, Epstein-Barr, rubella, encephalomyocarditis, lymphocytic choriomeningitis and foot-and-mouth disease virus may induce DM in humans, mice and cattle^{2-4,12}. Persechino et al. reported DM in a Friesian cow associated with viral diarrhoea-mucosal disease¹³. There is however, no evidence of a direct correlation between DM and virus infection. In human IDDM induced viral infection, epidemiological features regarding viral and environmental factors were reported¹¹. As shown in Materials and Methods, there was no genetic correlation between the current

cases, and the feeding place was different. The only common finding in these cattle was the infection with BVD-MD virus. In our clinic, 65 cattle infected with BVD-MD have been hospitalized from 1986 to present. The incidence of DM is 12.3%. This is higher than the incidence in human patients¹¹. Thus, it is strongly suggested that BVD-MD virus induced IDDM in cattle.

Cattle infected with BVD-MD suffer immunosuppression or immunotolerance¹⁴. Noncytopathogenic BVD-MD virus was isolated from all cases in this paper and the antibody titers against BVD-MD virus were low. These results indicate an immunotolerance status. In human patients, it is suspected that autoimmunity is connected with the occurrence of IDDM. This autoimmunity includes anti-insulin antibody or islet cell antibody (ICA)¹⁵. Shown in Results, anti-insulin antibody titers in these cases were not high compared with normal cattle. We now plan to examine bovine ICA of the cattle reported in this paper.

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Summary

Four Japanese black cattle and four Holstein-Friesian cows were diagnosed with diabetes mellitus. Based on the results of an intravenous glucose tolerance test, all of these cases were insulin dependent diabetes mellitus. Moreover, bovine viral diarrhoea mucosal disease (BVD-MD) virus was isolated, and mucosal lesions and diarrhoea were recognized in all cases. There was no genetic

relationship between the affected cattle, and all eight cattle were bred at different places. It is therefore, strongly suggested that BVD-MD virus induced the diabetes mellitus in these cattle.

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