Japanese Black Cattle with Orotic Aciduria Detected by Gas-Chromatography/Mass-Spectrometry

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Orotic aciduria is a condition in which orotic acid is excreted into urine. In humans, slight to moderate increases have been observed in pregnancy and premature births and in patients with heart failure, hypertension, diabetes, malignancy, trauma, liver damage, and so on [14]. High urinary excretions of orotic acid were found in conditions that induce hyperammonemia and an accumulation of intramitochondrial carbomoyl phosphate [8]. Moreover, most cases of orotic aciduria arise from inherited defects of enzymes involved in the urea cycle after the synthesis of intramitochondrial carbamoyl phosphate. Such defects include ornithine transcarbamylase (OTC) deficiency [2], arginemia, lysinuric protein intolerance [6], and argininosuccinic acid synthetase deficiency [9], as well as a deficiency of uridine monophosphate synthase (UMPS) [13]. In veterinary medicine, the hereditary orotic aciduria in Holstein and Red Holstein cattle has been made famous in cattle as the DUMPS (deficiency of UMP synthase) [1, 7]. In a normal calf the peak of orotic acid was ambiguous (Fig. 2A). In the affected cattle, the peak was sprung (Fig. 2B). The normal calf is No.6 (Fig. 1). In the other 11 cattle as well as No. 6 the peak of orotic acid was ambiguous.

In addition, the calf’s serum specimen showed an obvious peak of orotic acid (data not shown).

The affected calf showed growth retardation and emaciation with consistently body weight, very low, i.e., 60 kg and 42 kg at 4.0 and 5.5 months of age, respectively. His rectal temperature was 39.0 centigrade, heart rate 78 beats/min, and respiratory rate 18 respirations/min. From birth to death, the calf suffered repeated aqueous diarrhea that showed no response to antibiotics or sulfa drugs. His appetite ranged from normal to sub-normal.

As shown in Table 1, the RBC, WBC and mean corpuscular volumes were normal, and the hematocrit was slightly low. Microcytes and acanthocytes were observed in blood smears, but megaloblasts could not be detected. The calf had slightly high serum AST activity, and somewhat low concentrations of serum urea nitrogen, creatinine, total protein, albumin, and glucose. At 5.5 months of age, the calf had hypoglycemia and hyper-ammoniemia. Serum insulin-like growth factor-1, insulin, total tri-iodothyronine, total thyroxine, and cortisol concentrations were low. In urinalysis, ketone body and protein showed positive with a dipstick test paper. The pH (8.5) and specific gravity (1.038) were normal. In urine sediments, needle-shaped crystals of orotic acid were observed in urinary sediments. Sequence homologous analysis with cattle uridine monophosphate synthase DNA indicated silent mutation in the affected calf.

KEY WORDS: gas chromatography/mass spectrometry, Japanese black cattle, orotic aciduria.
of UMPS of the 13 cattle was amplified by PCR using the data (Schoeber and others 1993) [10] and were sequenced by the dideoxy chain termination method with GeneRapid automated DNA sequencer (Amersham Biosciences, Piscataway, U.S.A.). Sequence homologous analysis with cattle UMPS DNA [10, 11] indicated silent mutation (ACT to

Fig. 1. Pedigree network of the family of calf with orotic aciduria. ■ Affected calf, □ male, ◦ female. Circles and squares with the number indicate 12 consanguineous cattle examined. Squares with capital letter indicate sire.

Fig. 2. Chromatograms in urine of normal calf (A) and the affected calf (B). The arrow indicates high peak of orotic acid. The normal calf is No. 6 (Fig. 1). In the other 11 cattle as well as No. 6 the peak of orotic acid was ambiguous.
liver. Histiocytes and fibrinoblasts were observed around the hepatocytes surrounding them were vacuolated in the Histopathologically, the central veins were hemostatic, and the right lung, cranial and middle lobes were hepatized. Enlarged lymph nodes 3 to 4 cm in size were observed. In pneum, mesentery, and pericardium. In the mesentery, some were edematous. Dropsy was noted in the pleura, peritoneum, and cecum were thin and fragile, and their chorions were edematous. Mucous membranes of the duodenum, jejunum, and the trabeculae were clear. Using a hemosiderin-like dye, many macrophages were observed in the splenic sinus. Glisson’s capsule. In the spleen, the red pulp was atrophied because the specimen contains numerous organic acids and other chemical groups of compounds at a variety of concentrations [4, 5, 15]. Support of a diagnosis of inherited errors of metabolism, orotic aciduria is rare in humans [8]. In any event, this may be the first report of orotic aciduria in Japanese black cattle. GC/MS analysis of urine and serum can provide data in support of a diagnosis of inherited errors of metabolism, because the specimen contains numerous organic acids and other chemical groups of compounds at a variety of concentrations [4, 5, 15]. Screenings for metabolic defects using GC/MS can detect diseases also in cattle early enough to devise adequate countermeasures.

**REFERENCES**