Systemic embolic hepatitis and pneumonia caused by subacute ruminal acidosis in Korean indigenous cattle: A case report

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SUMMARY

A 44-month-old Korean indigenous cow was found in the lateral recumbency in a pasture while grazing. Decreased heart sound and rate, hypothermia, scleral injection, subcutaneous petechial hemorrhage, and moderate dehydration were observed upon inspection. Complete blood count showed significant neutropenia. Serum biochemical analysis revealed azotemia, increased globulin, decreased albumin/globulin ratio, and increased aspartate transaminase, creatinine kinase, phosphorus, and magnesium. Blood gas analysis indicated hypokalemia and high anion gap metabolic acidosis. Ultrasonography of the right abdomen and chest showed hyperechoic nodules in the liver and cranial lung fields. Based on clinical status, late state sepsis was diagnosed, and necropsy was performed after euthanasia. Embolic inflammation was found in the liver, lung, and spleen, rumenitis and ruminal parakeratosis were observed, and the pH of the recovered ruminal fluid was 5.5. Based on necropsy findings, death for sepsis, systemic embolic hepatitis and pneumonia caused by subacute ruminal acidosis (SARA) was assessed. While SARA is thought to be prevalent in Korean indigenous cattle raised with concentrated feed, few studies or case reports that would confirm this have been published to date.

KEY WORDS

Embolic inflammation; Korean indigenous cow; subacute ruminal acidosis ultrasonography.

INTRODUCTION

Ruminal acidosis can be clinically divided into acute and subacute acidosis (SARA)[1]. Both forms can be attributed to the excessive supply of concentrated feed and low-quality roughage[1-4]. While acute forms can be caused by sudden oversupply, subacute forms differ inasmuch as they arise from chronic oversupply[1-4]. Therefore, the acute type is considered an individual disease, but the subacute type can be considered a herd disease[5].

Acute ruminal acidosis has to be considered an emergency. Moderate dehydration is observed and, unless properly treated, mortality rate can reach 90%[3]. With SARA, in contrast, there are no obvious clinical signs of dehydration or overt symptoms, but the disease affects other organs, such as liver, also causing a decrease in productivity[2-4].

A prerequisite for acute and subacute ruminal acidosis is a decrease of ruminal pH. During acute rumen acidosis, excessive lactic acid production by microflora increases osmotic pressure and fluid loss, resulting in systemic severe dehydration and systemic lactic acidosis[1]. The primary cause of SARA is an increase in volatile fatty acids (VFAs) that decrease ruminal pH[6]. Under an acidic environment, ruminal epithelium unprotected by the mucus develops secondary ruminitis[7]. The acidic environment in the rumen causes the death of Gram-negative bacteria, release of Lipopolysaccharide (LPS) and leads to a systemic inflammatory response[8,9]. Liver abscesses, pneumonia, endocarditis, pyelonephritis, and arthritis can also be caused by the migration of bacteria into the rumen through blood vessels, and caudal vena cava thrombosis can also occur[2-5].

Based on the results of previous studies in which a sensor was inserted a sensor in the rumen, Korean indigenous cattle seem not to be resistant to SARA[10]. Since Korean indigenous cattle are raised on concentrated feed, SARA may be prevalent, and this is potentially major factor for decreased productivity of livestock farms in Korea. To the best of our knowledge, this is the first report of SARA with embolic hepatitis and pneumonia detected by ultrasonography in Korean indigenous cattle.

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CASE PRESENTATION

A 44-month-old Korean indigenous cow was observed in lateral recumbency in a pasture while grazing. Physical examination showed hypothermia (38°), a respiratory rate of 20 beats/min, and a lowered heart rate of 37 beats/min with dampened heart sounds. Moreover, scleral injection and petechial hemorrhage on the pinna were found. Based on this information, the animal was clinically diagnosed to be in later stages of sepsis. After hematological analysis and ultrasonography, this animal was necropsied because of extremely severe condition. A complete blood cell (CBC) test using a Procyte DX hematologic analyzer (IDEXX Laboratories, Westbrook, ME, USA) revealed increased hematocrit (Hct, 49.5%) and a decrease in white blood cells count, especially neutropenia (0.02 x 10^3/μL). Blood gas analysis (i-STAT 1 analyzer, Abbott, USA) showed high anion gap metabolic acidosis. Serum biochemistry analysis (Drychem 4000i, Fujifilm, Japan) revealed a decrease in the albumin/globulin ratio (0.53) and an increase in globulin (5.1 g/dL), suggesting chronic inflammation. Moreover, creatinine was 2.7 mg/dL, and blood urea nitrogen (BUN) was 103.4 mg/dL, indicating azotemia. Aspartate aminotransferase (AST) was also increased to 328 U/L, and indirect bilirubin was 1.2 mg/dL with a total bilirubin of 1.3 mg/dL, indicating hepatic-predominant hyper-bilirubinemia. Lactate level was very high at 11.08 mmol/L (Table 1).

An ultrasound examination (LOGIQ e R8, GE Healthcare, USA) using a 5 MHz linear probe revealed many hyperechoic nodules in the right 9th, 10th, and 11th intercostal space (Figure 1a). In the right third intercostal space, consolidation was found in the right cranial ventral lobe of the lung and multiple hyperechoic nodules with a mean diameter of 0.46 cm (Figure 1b). The echogenicity of the pancreas observed in the right 13th intercostal space was significantly more hyperechoic than nor-

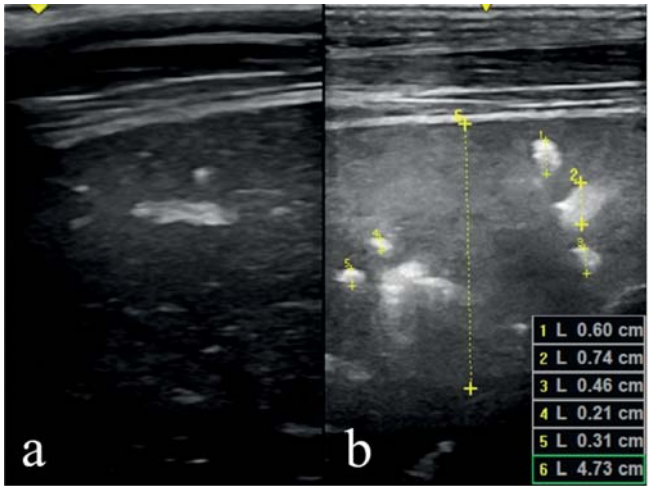

Figure 1 - Ultrasonogram of right abdomen and chest. (a) hyperechoic nodules were found in the parenchyma of the liver at the right 9th and 10th intercostal spaces. (b) At the right third intercostal space, consolidation and a hyperechoic nodule were found in the lung parenchyma. The depth of the consolidation in lung was 4.73 cm and the mean diameter of the nodules was 0.46 cm.

Table 1 - Findings on serum chemistry and blood gas analysis in a Korean indigenous cow with systemic embolic inflammation caused by SARA.

Assay		Result	Reference limits
Serum Biochemistry	Total protein (mg/dL)	7.8	6.7-7.5
	Albumin (mg/dL)	2.7	3.0-3.6
	Globulin (mg/dL)	5.1	3.0-3.5
	Total bilirubin (mg/dL)	1.3	0.01-0.5
	Direct bilirubin (mg/dL)	0.1	0.0-0.2
	γ-glutamyl transferase (U/L)	24	15-39
	Asparate transaminase (U/L)	328	78-132
	Alkaline phosphatase (U/L)	81	0-488
	Creatinine kinase (U/L)	981	44-211
	Blood urea nitrogen (mg/dL)	103.4	20-30
	Creatinine (mg/dL)	2.7	1.0-2.0
	Magnesium (mg/dL)	3.5	1.8-2.3
	Calcium (mg/dL)	7.7	9.7-12.4
	Phosphorus (mg/dL)	14.1	5.6-6.5
	Lactate (U/L)	11.1	0.56-2.22
Blood Gas Analysis	Sodium (mmol/L)	140	132-152
	Potassium (mmol/L)	2.9	3.9-5.8
	Chloride (mmol/L)	99	97-111
	Total CO_2 (mmol/L)	19	21-32
	pH	7.27	7.31-7.53
	pCO_2 (mmHg)	39.5	35-44
	Bicarbonate (mmol/L)	18.2	17-29
	Anion gap (mmol/L)	26	14-20

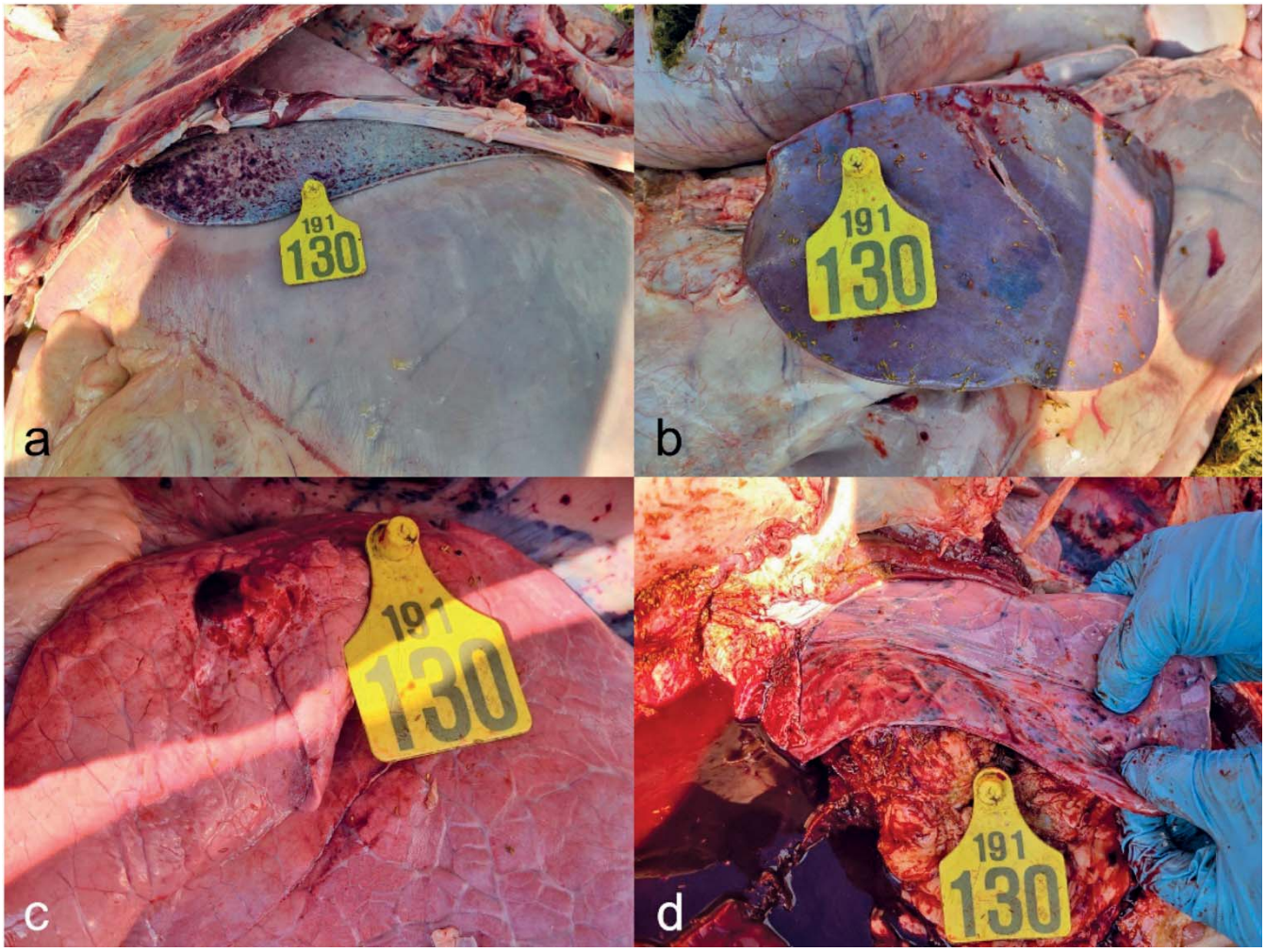

Figure 2 - Gross findings after euthanasia. (a) Embolic inflammation with splenomegaly. (b) Embolic hepatitis in the posterior lobe of the liver, but no liver abscess was found. (c and d) Although embolic pneumonia was found throughout the lung field, the overall lung color was normal.

mal. However, the diameter of the caudal vena cava was normal.

Consequently, decreased heart rate and sound on auscultation, hypothermia, scleral injection, and marked neutropenia on the CBC test, and high anion gap metabolic acidosis accompanied by a rapid increase in lactate on blood gas analysis were observed. This was assumed to be the end stage of septic shock, and euthanasia followed by necropsy was performed for the animal's welfare.

Necropsy revealed marked jugular vein dilation, and embolism with splenomegaly (Figure 2a). In consistent with ultrasound findings, embolic hepatitis without abscess was observed (Figure 2b). Although lungs were diffusely bright red, some congestion was found in the cranial lobe of the lung, indicating embolic pneumonia (Figures 2c and 2d). Moreover, erosion and parakeratosis due to inflammation were observed in the rumen wall (Figure 3), and the pH of the ruminal fluid collected through the necropsy was acidified to 5.5. Therefore, embolic systemic inflammation in the liver, lungs, and spleen, as well as sepsis, was caused by chronic SARA.

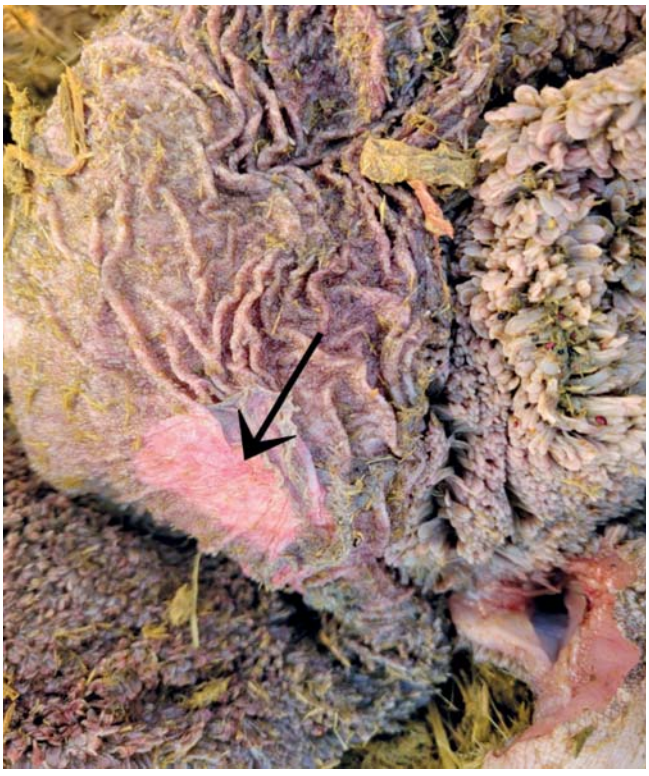

Figure 3 - A number of erosive findings (arrow) in rumen were found due to ruminal acidosis.

DISCUSSION

Studies in grazing cattle in Ireland and New Zealand[11,12] have shown that SARA is caused by a diet with high fermentable and

low fiber grass[12, 13]. In our case, beef cattle used for breeding in four month of grazing and in the fourth month of pregnancy, 6 months after parturition, were examined. It is not clear what caused SARA; some factors might have been the increase in their feed intake in the one month immediately post-calving, the intake of grasses that were lush and low fiber in improperly managed pastures, or some combination of these factors.

A diagnosis of SARA is usually confirmed by a ruminal pH of 5.5 or less[14, 15]. In this case, the pH was 5.5. The average pH of cattle fed mainly concentrated diet is 5.5-6.5, while the average pH of cattle fed with forage is 6.0-7.2[3, 16]. Thus, while a pH of 5.5 corresponded to the baseline, the result was considered particularly meaningful considering that forage represented the main feed in grazing pasture. In addition, one report mentioned that the risk of SARA exists when the ruminal pH is 5.5-5.8[17]. Perhaps a new diagnostic criterion for ruminal pH in cattle reared with concentrated feed and roughage should be established. In addition to the evaluation of ruminal fluid by oral probe or rumenocentesis, the evaluation of SARA by measuring rumen wall thickness using transabdominal ultrasonography is have been studied, which is likely to be utilized in the future[18].

Unlike the abomasum, ruminal mucosa protective factors do not exist; so it can be chemically damaged by acidic ruminal fluid[7]. These factors directly cause rumenitis and reduce the integrity of rumen epithelial cells[19]. Gram-negative bacteria sensitive to low pH die, releasing LPS, which are introduced (along with ruminal bacteria) into systemic circulation through the portal vein. These can then cause inflammation in organs such as liver, lungs, and kidneys[2-5, 8, 9]. However, in this case, no liver abscess, which is commonly found in cases of SARA, and no caudal vena cava syndrome, were observed.

Moreover, rumenitis and ruminal parakeratosis were observed in this case which is caused by hyperproliferation of the ruminal epithelial cells due to increased VFAs such as butyric acid and propionic acid[20]. Ruminal parakeratosis has also been reported to further accelerate rumenitis by interfering with the absorption of VFAs[21].

Ultrasonography to evaluate liver disease in cattle has been previously reported, specifically for liver abscess and fatty liver[22-24]. In the case of liver abscesses, nodules can vary from nonechoic to hyperechoic, and from homogeneously to heterogeneously[25]. Ultrasound evaluation of pulmonary lesions, such as the presence of pulmonary abscess through measurement of diameter of mass or nodule, and the presence of pulmonary consolidation through identification of Broncho-aerogram and fluid bronchogram with evaluation of echogenicity of lung parenchyma, have been reported[26, 27]. Several hyperechoic nodules, similar to those found in the liver were also found in the lungs (the right 9th, 10th, and 11th intercostal spaces). These findings suggest that embolic inflammation should be considered as a differential diagnosis when there are multiple nodules in various organs on ultrasonography.

In cases of septic shock, heart rate and heart sound increase in the early stage (Hyper-dynamic phase), whereas heart rate and heart sound decrease is seen in the late stage when blood flow to tissues drops off (Hypo-dynamic phase)[3]. Our case showed a decreased respiratory rate (20 beats/min) and heart rate (37 beats/min) with dampened heart sound. Multiple scleral injections and petechial hemorrhages were also observed. These findings indicated the late stages of septic shock.

We note, however, that a definition of septic shock applicable to cattle has not yet been established. Fecteau G *et al*. defined the condition with any two criteria of the following: blood culture growth within 48 h, bacteria cultured as pathogens, white blood cell increase/decrease in CBC, fibrinogen of 500 mg/dL, and more than 2% of band neutrophils were observed[28]. As sepsis is an emergency, considering the significant time it would take to perform all these tests, we suggest that methods for rapid diagnosis of sepsis in cattle should be developed. In this case, the lactate level had increased to 11.08 mmol/L. As tissue hypoxia caused by sepsis can increase lactate levels[3], this may prove valuable as a diagnostic tool for sepsis.

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Conflict of Interest

The authors declare that there were no conflicts of interest.

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