NOTE *Internal Medicine*

Three cases of idiopathic eosinophilic enteritis with chronic obstinate diarrhea in Japanese Black fattening cattle

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ABSTRACT. Eosinophilic enteritis (EOE) is a type of inflammatory bowel disease and is characterized clinically by chronic obstinate diarrhea. Three Japanese Black (JB) fattening cattle (2 males and 1 female) on different cattle farms presented with chronic episodic diarrhea without fever or dehydration. Soft reddish spherical carneous tissues (1−3 cm) were occasionally excreted within the diarrheic feces. Administration of antibiotics, antidiarrheal drugs and vermicides had no therapeutic effect, but dexamethasone improved the fecal characteristics. The symptoms persisted until the animals were slaughtered at 27–30 months of age. Histopathological examination of the intestines revealed marked eosinophilic infiltration in the lamina propria and submucosa. From these findings, we diagnosed these cattle as the first cases of EOE in JB cattle.

KEY WORDS: eosinophilic enteritis, inflammatory bowel disease, Japanese Black cattle

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Inflammatory bowel disease (IBD) refers to a group of idiopathic, chronic gastrointestinal tract disorders characterized by infiltration of the gastrointestinal tract by inflammatory cells that are generally confined to the mucosa, such as lymphocytes, plasma cells, neutrophils and eosinophils [6]. IBD is a common disease characterized by persistent or recurrent gastrointestinal signs, such as diarrhea and weight loss, in certain animal species and humans [6, 7]. Eosinophilic enteritis (EOE) is part of the IBD complex and is a morphological diagnosis characterized by inflammation in which eosinophilic leucocytes predominate [1], with clinical signs typified by chronic obstinate diarrhea. It is a minor cause of IBD in humans [6, 11], dogs [10], cats [4, 5] and horses [1, 8, 9]; however, few cases of EOE in cattle have been reported [2]. This research group previously reported 4 cases of idiopathic EOE in cattle, aged 1 (Angus heifer), 5 (Simmental bull), 7 (Holstein cow) and 11 (Holstein cow) years old, diagnosed on the basis of clinical and histopathological findings and exclusion of other differential diagnoses for cattle with chronic diarrhea and weight loss. However, to the best of our knowledge, neither the occurrence of EOE in Japanese Black (JB) cattle nor the associated clinical symptoms from the first appearance of their symptoms after purchase or birth to completion of their fattening periods (approximately 30 months of age) have been reported thus far.

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Herein, we describe 3 JB fattening cattle that showed chronic diarrhea with excretion of "spherical tissue" in their feces and improved fecal characteristics for several days with only dexamethasone administration. Thus, we made a preliminary diagnosis of EOE on the basis of a combination of clinical findings and exclusion of other diseases by biochemical analysis before slaughter at completion of the normal fattening period and confirmed the diagnosis by histopathological examination of intestinal tissues. Predictive diagnostic criteria of bovine EOE are proposed from the clinical and histopathological findings.

Our clinical records from 2010 to 2013 include 3 such cases: 3 JB animals (2 steers and 1 heifer) reared for fattening purposes on different cattle farms. The detailed information/histories and clinical signs of these 3 animals are summarized in Table 1. All 3 animals displayed similar characteristic clinical symptoms: chronic episodic diarrhea without fever or dehydration starting at an early stage after purchase (Cases 1 and 2) or birth (Case 3), with occasional excretion within the diarrheic feces of a small number of soft reddish spherical carneous tissues (1−3 cm in diameter) of unknown origin (Fig. 1). In all cases, although therapeutic interventions consisting mainly of antibiotics, antidiarrheal drugs and vermicides administered when the diarrhea was observed had no therapeutic effect, the administration of dexamethasone (3−5 mg/head mixed with ampicillin and administered by intramuscular injection daily for 3 days) temporarily improved the fecal characteristics for a period of several days. The chronic diarrhea and excretion of the "spherical tissue" persisted until the cattle were slaughtered at 27–30 months of age; however, all 3 animals had normal appetites, growth rates and body weights when compared to other cattle without diarrhea that were housed on the same farm.

Table 1. Summarized clinical histories of the 3 Japanese Black animals

	Case 1	Case 2	Case 3
Sex	Male (castrated)	Male (castrated)	Female
Birth date	Sep. 26, 2010	Apr. 11, 2011	June 24, 2011
Slaughter date (Age)	Dec. 15, 2012 (27 months)	Oct. 21, 2013 (30 months)	Dec. 17, 2013 (30 months)
History	Purchased at 10 months of age by the involved farm	Purchased at 9 months of age by the involved farm	Born on the involved farm
Age at first appearance of the symptoms	13 months	9 months	2 months
Main treatment for the symptoms	Antibiotics, antidiarrheal drugs, vermicides and corticosteroid	Antibiotics, antidiarrheal drugs, vermicides and corticosteroid	Antibiotics, antidiarrheal drugs, vermicides and corticosteroid
Number of treatments	30 (from 13 to 27 months of age)	18 (from 9 to 30 months of age)	31 (from 2 to 17 months of age)
Chronic diarrhea and carneous tissue excretion	Continued till slaughter	Continued till slaughter	Continued till slaughter
General condition during administration	Good body condition, good appetite, no dehydration	Good body condition, good appetite, no dehydration	Good body condition, good appetite, no dehydration

For exclusion of differential disease diagnoses, antemortem fecal examinations of these 3 animals were performed to determine the presence of pathogenic bacteria (*Escherichia coli,* culture on DHL agar and detection of 99K antigen with TETRASTRIPS [Bio-X Diagnostics, Sprl]; *Salmonella* spp., culture on DHL agar; *Clostridium perfringens*, culture on DHL agar; and *C. difficile* [C. Diff Quick Check Complete; Techlab®]), viruses (coronavirus [Tetrastrips; Bio-X Diagnostics, Sprl]) and rotavirus [Tetrastrips]), protozoa (*Eimeria* spp. and *Cryptosporidium* spp.) and parasites. A complete blood count and serum biochemical profile were performed in 2 of the animals (Cases 2 and 3). Additionally, PCR and ELISA (Johne's screening ELISA kit; Institute of Microbial Chemistry) assays were performed to exclude bovine viral diarrhea (BVD) and Johne's disease, respectively. Overall, pathogenic microorganisms that may cause long-term chronic diarrhea were not detected in the feces of the 3 animals. Additionally, the test results for BVD and Johne's disease were negative.

For final diagnosis of the affected animals, tissue samples of the intestinal tracts were collected immediately after slaughter at completion (27 and 30 months of age) of the fattening period and were evaluated histopathologically, along with the excreted spherical tissues, which were collected at first appearance of the symptoms and fixed in 10% neutral buffered formalin. The fixed intestinal and spherical tissues were embedded in paraffin wax, sectioned at 4-μm thickness, stained with hematoxylin and eosin, and examined histopathologically. Macroscopic observation of the intestinal tract revealed areas of severe hemorrhage, particularly in the colonic mucosa, in all 3 cases (Fig. 2). However, macroscopic observation revealed no pathological abnormalities in other organs in any of the 3 cases. Histological examination revealed marked eosinophilic, lymphocytic and plasmacytic inflammatory-cell infiltration in the lamina propria of the jejunum, cecum, colon and rectum, which partially extended to the submucosa (Fig. 3). Microscopic examination of the spherical tissues in the diarrheic feces revealed that they consisted mainly of a fibrin clot, including mucosal epithelial cells, red blood cells and eosinophils, which were speculated to have derived from the persistently inflamed tissues in the intestinal tract of the affected cattle (Fig. 4).

The white blood cell (WBC) counts were 8,800 and 10,500 cells/μl, and the percentages of eosinophils were 3% and 1%, respectively, which indicated no elevation of eosinophils in the peripheral blood. Parameters reflecting hydration status were all within the normal range. Additionally, although the levels of certain serum biochemical parameters were outside the reference range (e.g., in Case 3, the high GGT concentration [37.0 U/*l*] was considered to reflect cholangitis diagnosed when the animal was slaughtered), no abnormalities in the biochemical profile of the parameters reflecting albumin and electrolyte levels affected by enteritis were observed. Overall, the results of hematological and biochemical analyses prior to slaughter indicated no signs of inflammatory reaction in 2 of the animals with EOE.

EOE has previously been diagnosed in cattle [2] on the basis of a combination of clinical and histopathological findings and exclusion of other diseases. Additionally, we made a preliminary diagnosis of EOE in our 3 animals by consid-

Fig. 1. Soft reddish spherical carneous tissues (1−3 cm in diameter) in the diarrheic feces of the 3 cattle cases (a, Case 1; b, Case 2; c, Case 3).

Fig. 2. Gross appearance of the colon of the 3 cattle cases. Note the severe hemorrhage, particularly in the colonic mucosa, observed in all 3 cases (a, Case 1; b, Case 2; c, Case 3).

Fig. 3. Microscopic appearance of the colon of the animal in Case 1 as a representative case (a; ×100). There is marked eosinophilic, lymphocytic and plasmacytic infiltration in the lamina propria of the colon (b; × 400). Eosinophils are indicated with arrows.

Fig. 4. Microscopic appearance of the spherical tissues in the diarrheic feces obtained from the affected cattle (a; ×10). The tissues are predominantly composed of a fibrin clot, including mucosal epithelial cells, red blood cells and inflammatory cells, speculated to have originated from the persistently inflamed tissues in the intestinal tract of the affected cattle (b; × 400). Epithelial cells are indicated with arrows and eosinophils with arrowheads.

Fig.1

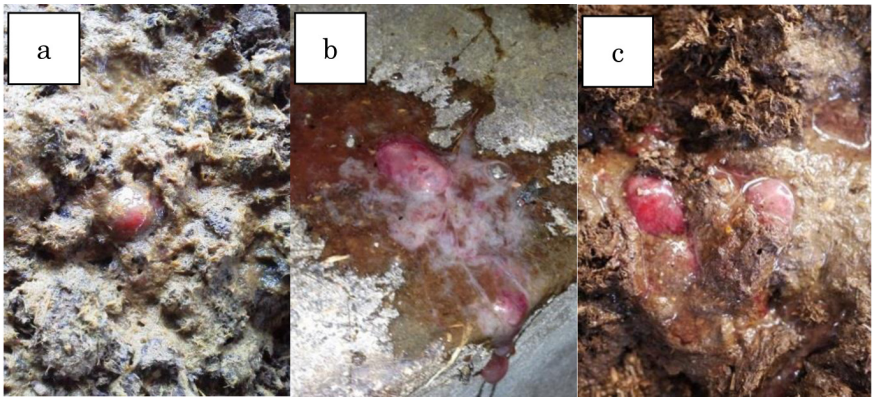


Fig.2

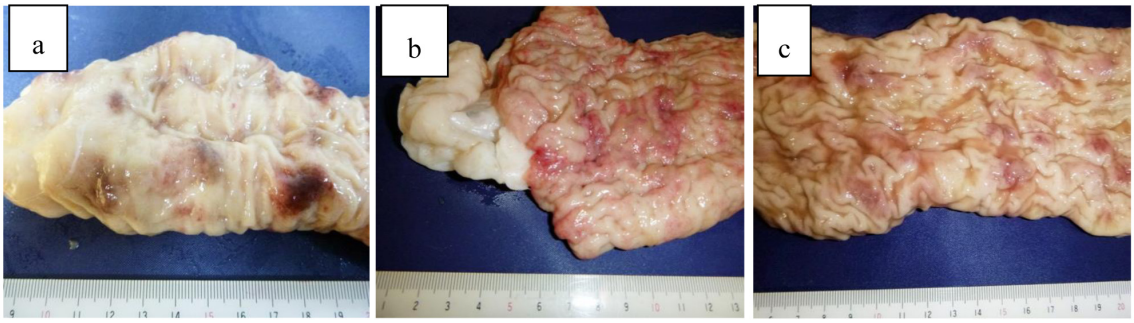


Fig.3

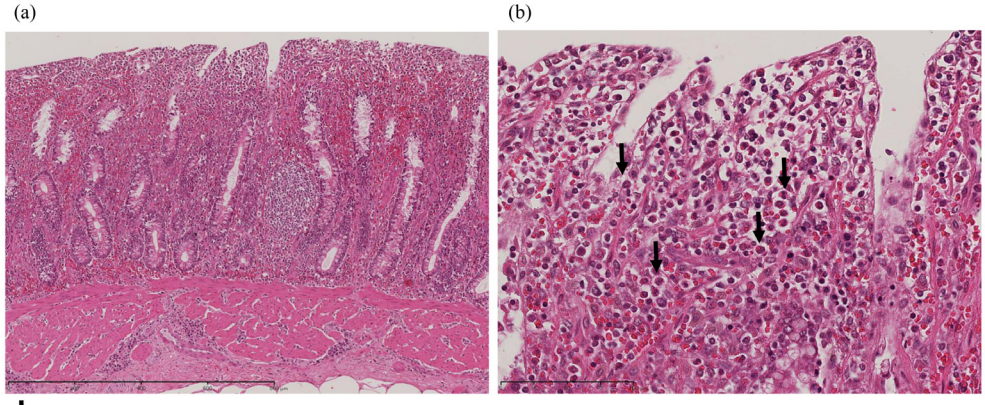
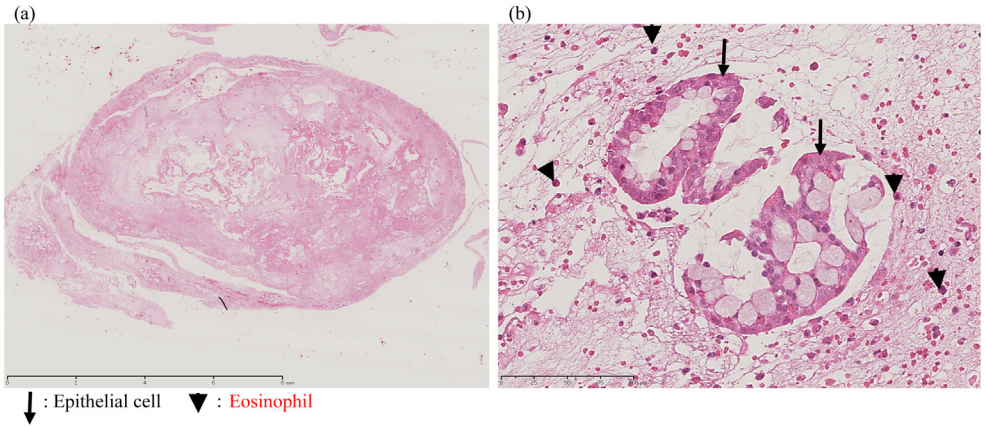


Fig.4



ering the clinical symptoms, including the response to corticosteroids and the results of clinical examinations of blood and fecal samples to exclude differential disease diagnoses. The diagnosis of EOE was confirmed by histopathological examination of intestinal tissues obtained at slaughter after completion (27 and 30 months of age) of fattening.

On the basis of clinical and examination results of the 3 affected cattle in the present study, the following antemortem predictive diagnostic criteria and/or clinical characteristics of bovine EOE are proposed: (1) chronic obstinate diarrhea persisting until 27−30 months of age; (2) maintenance of good growth rates; (3) excretion of spherical tissues including eosinophils in feces; (4) normal WBC, eosinophil counts, total protein and A/G ratio; and (5) good therapeutic response to corticosteroids. Eosinophilia, hypoalbuminemia and hyperglobulinemia have been suggested as useful parameters in the diagnosis of EOE based on hematological and biochemical examination results [3, 7, 9]. Additionally, it has been suggested that there is a strong relationship between the clinical and biochemical findings and the degree of eosinophilic infiltration of intestinal layers in EOE-affected animals [7]. In the present study, the results of hematological and serum biochemical examinations in our 3 cattle cases were within normal ranges, which was in agreement with a previous report in cattle by Cebra *et al*. [2]. Although the reasons for the discrepancies between the results of hematological and serum biochemical examinations and the chronic symptoms exhibited by the affected cattle are obscure, this finding suggests the possible pathophysiology in EOE-affected cattle. Additionally, histopathological examination of the intestinal tissues from the 3 animals indicated marked infiltration of eosinophils, lymphocytes and plasma cells in the lamina propria of the mucosa, with occasional extension of the infiltration of lymphocytes and plasma cells into the submucosa or muscular layer of the jejunum, ileum and large intestine, which might be in line with the previous report by Cebra *et al*. [2]. However, the clinical symptoms of our patients differed from those in the report by Cebra *et al*. [2] regarding 2 parameters: (1) maintenance of good growth rates and (2) excretion of carneous tissue. Cebra *et al*. [2] suggested that there is a wide spectrum of clinical symptoms in EOE in cattle; this might explain these differences. Cebra *et al*. [2] diagnosed EOE in 2 out of 4 affected cattle during the antemortem period by examining excisional biopsy samples obtained during exploratory laparotomy via a right-flank incision, and administration of corticosteroids was initiated on the basis of an objective diagnosis. Allowing for evidence-based medicine and animal-welfare issues in cattle with chronic illness, endoscopic observation and biopsy of the large intestine after a preliminary diagnosis of EOE has been made may enable timely confirmation and appropriate treatment of EOE in JB cattle.

The underlying cause and pathophysiologic mechanism of EOE have not been determined in humans and animals [1, 2, 7]; possible proposed causes include food allergies and endoparasitism. Interestingly, the typical symptoms of chronic diarrhea continued in the heifer in Case 3 from the lactation period to slaughter, indicating that food allergies are a possible cause of EOE from birth to maturity in cattle. Expansion of the clinical database of bovine EOE is needed to clarify the etiology of this disease.

Administration of corticosteroids has been reported to be effective for the relief of clinical symptoms of EOE in humans [7] and certain animal species [2], and may be useful for the elimination of certain differential disease diagnoses in cattle practice. In our study, dexamethasone administration was initiated in one case in the lactation period, and the series of treatments were repeated when the diarrhea returned. Cebra *et al*. [2] reported that long-term administration of corticosteroid with gradually diminishing doses was effective for resolving diarrhea and maintaining growth rates. Therefore, we assumed that administration of dexamethasone on recurrence of diarrhea would have positive effects regarding the growth rate of the EOE cattle.

In conclusion, to our knowledge, these cases are the first JB cattle cases of idiopathic EOE. The excretion of spherical tissues in the feces may serve as an important and identifiable clinical sign in affected cattle. Idiopathic EOE should be considered a differential diagnosis in cases of chronic obstinate diarrhea in JB cattle.

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