

## Clinical, ophthalmological, and pathological findings of hypovitaminosis A in cattle

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**Abstract:** From February to September in 1996, a lot of blind cattle were reported in Dangjin Area of Chungnam Province. Blindness were observed in the 143 calves of the 1,496 calves from 79 farms. Blind cattle were found only in the farms where green pasture was not fed. After administration of vitamin A as the type of feed additives and parenteral injection, the blindness cases were not occurred in those farms. Both pupils were totally dilated with the absence of pupillary light reflex in all blind cattle. In the ophthalmoscopic examination, the fundus revealed multifocal linear white mottling which was more severe in nontapetal fundus than tapetal fundus. Serum vitamin A concentration was as low as 4.1  $\mu\text{g}/\text{dl}$  in the calves of the affected farms. Narrowing of optic foramen, retinal degeneration and optic disc atrophy were shown in pathological findings.

*Key words:* cattle, clinical, hypovitaminosis A, ophthalmologic, pathologic

### Introduction

Hypovitaminosis A can be occurred in several animal species including mice, sheep, and cattle, even though in humans.<sup>1</sup> But it is well described in cattle. In calves, various clinical signs such as night blindness, reduced appetite, ataxia, papilledema, dilatated pupil, and exophthalmos have been reported.<sup>2</sup> In more mature cattle, night blindness, neurologic signs, degeneration of nontapetal region have been reported.<sup>2</sup> It is necessary to add vitamin A (V-A) in feed in the farm which cereal meal is the main feed, because V-A is absent in cereal meal except yellow corn.<sup>3</sup> V-A is present in most leafy-green plants as carotene. In cattle, carotene is converted to V-A in the intestinal epithelium and hepatocytes of liver, which is then stored in the liver.<sup>4</sup>

There are two types of hypovitaminosis A.<sup>4</sup> Primary deficiency occurs as a result of inadequate dietary intake. Secondary deficiency occurs usually due to maldigestion, malabsorption or metabolic disorder in the case of chronic liver disease. High temperature and humidity, exposure to light, mineral mixes, presence of oxygen and long duration of storage are known hasten destruction of V-A.<sup>2,4</sup>

Occurrence of hypovitaminosis A has been supposed in Korea because most cattle are fed a ration composed of few green grass, a lot of cereal diet and dry rice straw. From February to September in 1996, many blind cattle were observed in Dangjin Area of Chungnam Province. In this report, ophthalmoscopic findings of fundus, serum vitamin A concentration and pathological findings on the affected calves were described.

### Materials and Methods

#### Survey

Korean native cattle and Holstein cattle reared in Dangjin Area of Chungnam Province were surveyed for blindness. A, B and C farm fed only cereal diet and dry rice straw to cattle, but D farm fed the green grass frequently to them. A and C farm offered the vitamin A as feed supplement for about one month recently.

#### Physical and eye examination

Cattle were examined by general methods focused on dilatation of pupil and pupillary light reflex with pen light.<sup>5</sup>

The eyes were examined using indirect ophthalmoscope (Vantage<sup>®</sup>, Keeler, UK), focal illuminator and fundus camera (Genesis<sup>®</sup>, Kowa, Japan).

#### **Clinical pathology (Complete blood count and determination of serum vitamin A concentration)**

Thirteen blood samples were collected from cattle with blindness from three farm (A, B and C farm) and two blood samples were collected from healthy two cattle from one farm (D farm). All calves examined were Korean native cattle. Automatic blood counter, System 9018, (Serono<sup>®</sup>, S.A., USA) was used for measurement of blood parameters and serum vitamin A concentration was measured by high performance liquid chromatography.

#### **Necropsy**

Necropsies were performed on two Korean native calves from one farm. One calf was female, five months old and blind congenitally, the another calf was male, three months old and became blind on one month old.

#### **Histopathology**

All the tissues were fixed in 10% phosphate buffered neutral formalin. All the tissues were processed routinely and stained with hematoxyline-eosin for histopathology. Optic nerve was stained with Masson's trichrome method for connective tissue.

## **Results**

#### **Survey**

Blindness were founded in the 143 calves of the 1,496 calves from 79 farms surveyed. The age of occurrence of blindness calves was variable from neonatal to 7 months old. However, there were no blind calves over 7 month old in this survey. Male (98 heads) was more frequent in occurrence than female. Both of the Korean native cattle and Holstein cattle were equally susceptible to vitamin A deficiency.

Blindness cases were not occurred in the farm in which green pasture was fed. Even though the other rations were same with farms not affected, it was occurred in the farm where grass was not fed. Blind calves were not observed after supplementation of vitamin A as additives in those

affected farms.

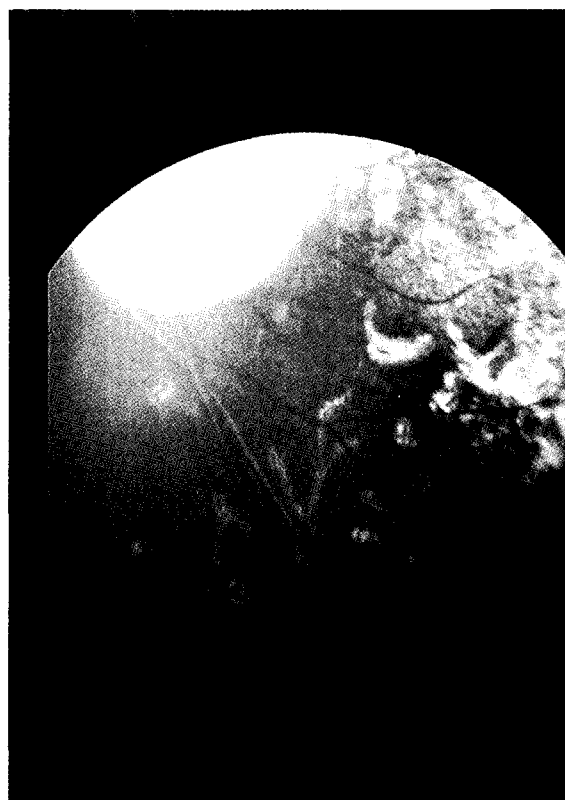
#### **Physical examination**

In all blind calves, both pupils were severely dilated and the pupillary light reflex was completely absent. The eyes of blind calves were bluish and glittering in the dark places but the corneal reflex was normal. There were no inflammatory lesions in the eyelids.

No significant gross abnormalities were not found on other parenchymal organs examined.

#### **Ophthalmoscopic finding of optic fundus**

The fundus revealed multifocal linear white mottling which was more severe in nontapetal fundus than tapetal fundus (Fig. 1). Optic disc atrophy was observed in all calves examined although there was some variation in severity.



**Fig 1.** Eye; cow. Photograph of the fundus of the cow with hypovitaminosis A. Notice the multifocal linear white mottling of the nontapetal fundus.

#### **Clinical pathology (Complete Blood count and determination of serum vitamin A concentration)**

**Table 1.** Concentrations of blood parameters and serum vitamin A level

Farm	Concentrations of blood parameters				Vitamin A concentration ( $\mu\text{g}/\text{dl}$ )
	WBC ( $\times 10^3/\text{ml}$ )	RBC ( $\times 10^6/\text{ml}$ )	Hb (g/dl)	HCT (%)	
A* (n=7)	9.4 $\pm$ 0.4**	6.0 $\pm$ 0.1	11.4 $\pm$ 0.1	20.6 $\pm$ 0.1	26.1 $\pm$ 1.9
B (n=4)	15.5 $\pm$ 2.3	6.2 $\pm$ 0.4	10.1 $\pm$ 0.0	23.2 $\pm$ 1.6	4.1 $\pm$ 1.6
C (n=2)	12.0 $\pm$ 3.1	6.1 $\pm$ 0.6	10.6 $\pm$ 0.7	22.9 $\pm$ 3.0	23.6 $\pm$ 5.1
D (n=2)	12.8 $\pm$ 1.9	5.4 $\pm$ 1.1	13.5 $\pm$ 1.2	22.8 $\pm$ 0.5	5.6 $\pm$ 1.9
Normal range	4~12	5~10	8~15	24~46	5~60 이상

\* Farms A and C : V-A fed on one month, recently.

Farms A, B, C : blindness occurred, Farm D : blindness not occurred.

\*\* mean $\pm$ SD.

On hematology, there was no significant difference in values of WBC, RBC, Hb and HCT among 4 farms. Vitamin A concentration was as low as 4.1  $\mu\text{g}/\text{dl}$  in farm B in which blind calf was occur, but vitamin A concentration of farm D was higher than farm B and shows 5.6  $\mu\text{g}/\text{dl}$ .

### Gross pathology

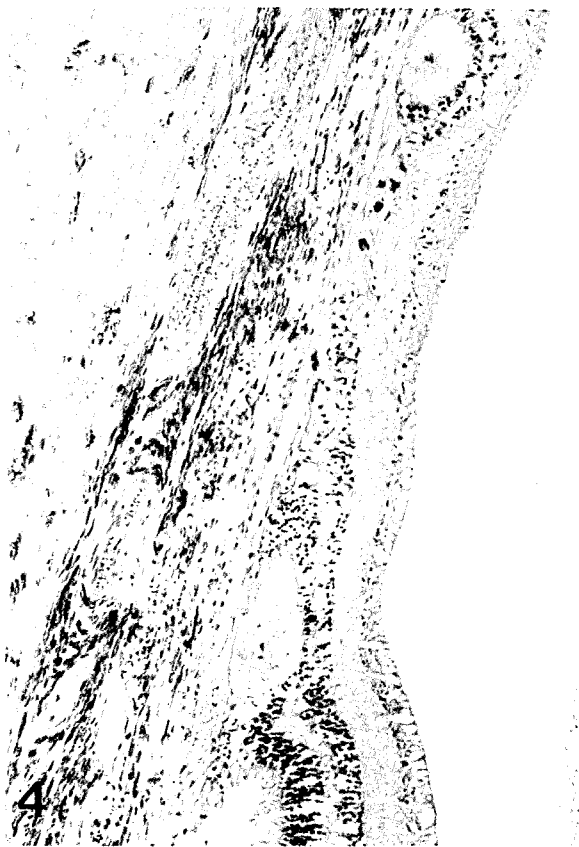
Optic foramina were bilaterally narrowed with dorsoventral position in size in both calves. And optic nerves were severely compressed (Fig. 2). Cerebellum was compressed with slight prolapse of the caudal portion of vermis.



**Fig 2.** Eye; cow. Photograph of the optic foramen of the cow with hypovitaminosis A. Notice the optic nerve bundle around the foramen are narrowed dorsoventrally. Bar=0.75 cm.



**Fig 3.** Eye; cow. Photomicrograph of the optic nerve of the cow with hypovitaminosis A. Notice the atrophied optic nerve bundle around optic foramen and thickened fibrous tissue of the optic nerve. H&E, Bar=400  $\mu\text{m}$ .



**Fig 4.** Eye; cow. Photomicrograph of the retina of the cow with hypovitaminosis A. Notice the retinal degeneration and focal loss of retinal layer, especially outer nuclear layer and photoreceptor layer. H&E, Bar=100  $\mu$ m.

### Histopathological findings

Optic nerve bundle around optic foramen was atrophic. There was severe fibrous thickening of dura matter (Fig. 3) and partial loss of optic nerve. There was atrophy of retina and loss of retina layer, especially nuclear layer and photoreceptor layer (Fig. 4). By Masson's trichrome stain to optic nerve, thickened fibrous tissue was positive for connective tissue.

### Discussions

It has been suggested that blindness due to hypovitaminosis A is occurred only in male cattle because vitamin A is made in corpus luteum of female.<sup>6</sup> But in our survey, blindness has been occurred in female cattle also even though male is more susceptible than female. This result was similar to other report.<sup>7</sup>

Hypovitaminosis A is easily caused by failure of colos-

trum because carotene is not transported through placenta to fetus during pregnancy.

Differential diagnosis of blindness with neurologic signs in cattle also includes polyencephalomalacia and lead poisoning.<sup>2,7</sup> In the case of hypovitaminosis A, nervous signs are milder than other two types. The absence of pupillary light response and presence of pupillary dilatation in hypovitaminosis A are different findings compared to other two types. In this case, pupillary light response are absent and also pupillary dilatation are present bilaterally. Thus we have tentatively diagnosed this cases as a hypovitaminosis A.

Fundic examination revealed extensive depigmentation (mottled) and retinal degeneration in the nontapetal region of the retina. It was similar to previous results.<sup>3,6,8</sup> Papilledema is a very consistent finding in hypovitaminosis A of all ages.<sup>4</sup> But it is the first detectable change and usually occurs before the onset of other clinical signs including blindness. Atrophy of optic disc occurs and results in irreversible blindness especially in calves. Therefore in this complete blindness case, papilledema was not detected, but atrophy of optic disc was easily observed.

Grossly, main lesions were confined in the optic canals. The optic canals were bilaterally narrowed dorsoventrally than normal size. In the portion of optic nerves located within the optic canals, severe constriction was present. It was same anatomical change with other reports.<sup>1,9</sup> There is replacement with osteoblast at sites where osteolytic osteoclast are normally found.<sup>10</sup> The result are induced from the abnormal growth of bone with excess formation of cancellous bone termed bone overgrowth in growing young cattle. Lumen of optic foramen is narrowed by this abnormal bone overgrowth. Thus optic nerve is damaged by pressure. In this case, recovery is very hard.<sup>10</sup> Thus an experiment in mature cow fed on a hypovitaminosis A ration for a long term was failed to develop blindness due to constricture of optic nerve like this case, but developed nyctalopia, incoordination and an edema of the leg.<sup>8</sup>

Histopathologically, dura matters in optic canals were moderately thickened by fibrous tissues. There are also multifocal retinal dysplasia. Outer nuclear layer and photoreceptor layer were absent, and inner nuclear layer was slightly distorted. This findings were similar to other reports.<sup>1,9,11</sup> Anderson et al<sup>7</sup> reported that the number of photoreceptor, especially rod cells seemed to be decreased. Night blindness was due to the decrease of rod cells which

function to react with brightness.<sup>11</sup> Neural tissue was completely replaced by dense sheet of mature collagen. Optic nerves were covered by marked thickened meninges. In the case of polioencephalomalacia and lead poisoning, cerebrocortical necrosis was prominent changes in the brain.<sup>11</sup> In the case of serum V-A concentration below 4  $\mu\text{g}/\text{dl}$ , squamous metaplasia of parotid ducts is prominent. Decrease of mucin production resulted from squamous metaplasia of parotid ducts.<sup>1</sup>

There were many reports on limit concentration of V-A in serum of cattle. The diagnostic values of hypovitaminosis were variable according to the researchers as follows: below 4  $\mu\text{g}/\text{dl}$ , 5  $\mu\text{g}/\text{dl}$ , 11  $\mu\text{g}/\text{dl}$  and 20  $\mu\text{g}/\text{dl}$ .<sup>1,4,12-14,20</sup> In our study, average concentration of serum V-A of the farm outbreaked hypovitaminosis A was as low as 4.1  $\mu\text{g}/\text{dl}$ .

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