Central Nervous System Lesions Due to *Escherichia coli* Infection in Neonatal Calves

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*Escherichia coli* infection is one of the major causes of economic loss in neonatal calves. The infection has been divided into 3 forms: septicemic, enteric-toxemic, and enteric [2]. The septicemic form is virtually limited to calves less than 2 weeks of age [3], and usually results in death with a rapid course of the disease [2]. Invasion of the organisms into the central nervous system is usually preceded by septicemia in neonatal calves [8], and the lesions are characterized by fibrinopurulent inflammation of the leptomeninges, choroid plexus, and ventricular wall with rare involvement of the underlining parenchyma [1]. There are no reports on the changes in the brain parenchyma [1]. This paper describes the presence of cerebral infarct in 5 neonatal calves with meningoventriculitis associated with *E. coli* infection.

Five calves, aged between 9 and 21 days at death (Nos. 1 and 3) or euthanasia (Nos. 2, 4 and 5), were used in the present study. Clinically, three cases (Nos. 2–4) made a little or no attempt to suck colostrum from their dams. The other two animals took colostrum by themselves. Affected animals initially exhibited anorexia, depression, and pyrexia of about 40°C. Nervous signs such as opisthotonus, nystagmus, and paddling movements were observed after administration with antibiotics once (Nos. 2–4) or more than twice (Nos. 1 and 5) within three days. Corneal cloudiness in the left eye (No. 3) and moderate diarrhea (Nos. 1, 2 and 5) were associated. After 2 to 5 days of the disease onset, the animals died, or were euthanized assuming an unfavorable prognosis.

Macroscopically, there was an increase in amount of cloudy cerebrospinal fluid. In the leptomeninges, congestion, petechiae, and cloudy areas were seen. Fibrinous exudate adhered to the ependymal surface of the dilated ventricles, especially the lateral ventricles. Scattered necrotic foci ranging from 2 to 15 mm in diameter were found in frontal sections of the cerebrum (No. 5), corpus striatum (Nos. 2 and 3), thalamus (Nos. 2, 3 and 5), and mesencephalon (No. 5). Other findings were fibrinous exudate on the peritoneal surface (No. 3), dark reddish lesions in the lungs (Nos. 2 and 3), and atrophic thymus (Nos. 3 and 4). Omphalitis was not observed in any case.

Histologically, all the cases had marked leptomeningitis in the cerebrum. This change was more prominent in the two cases that had undergone antibiotic therapy (Nos. 1 and 5), in which the meninx of the brain stem and spinal cord was also affected. The leptomeningitis consisted of congestion, mild perivascular hemorrhages, fibrinous exudate, and infiltration of neutrophils, macrophages, and lymphocytes. The choroid plexuses in various sites were affected in all the cases; mild in No. 2 and marked in No. 5 (Fig. 1). The subpial and subependymal parenchyma and the ventricles were less involved.

The parenchymal necrosis was observed in the cerebrum (Nos. 2, 3 and 5), corpus striatum (Nos. 2, 3 and 5), thalamus of all cases, mesencephalon (Nos. 2 and 5), and cerebellar white matter (No. 5). The size of lesions was larger in the corpus striatum and thalamus. Most of them were located in the cortico-medullary junction of the cerebrum, at some distance from the ventricles in the corpus striatum and thalamus, and around the aqueduct in the mesencephalon. The necrotic lesions consisted of loosening of neuropli and degeneration of neurons, associated with hemorrhage, perivascular sero-fibrinous exudate, and neutrophil infiltration. Vascular changes such as loosening of the wall and fibrinous thrombi were frequently observed in these lesions (Fig. 2). Furthermore, capillarization and an increased number of macrophages concurrently occurred in some necrotic lesions. Loosening of vascular walls or fibrinous thrombi were only the features in other lesions. Laminar and focal loosenings of neuropli were recognized in the deeper cerebral gray matter (Nos. 3 and 5).

Infiltration of neutrophils and macrophages was also recognized in the subleptomeningeal space of the optic nerve (No. 4), and the cornea and anterior chamber of the left eye (No. 3). Fibrinous or fibrinopurulent peritonitis was seen in 4 (Nos. 2–5) and epiraditis in 2 cases (Nos. 1 and 3). There were fibrinous thrombus formation and vascular degeneration in the walls of the digestive tracts (Nos. 2–5) and endovascularitis in the gallbladder (No. 4). Foci of neutrophils were present in the cardiac interstitial tissues (Nos. 1 and 4) and the adreno-cortical stroma (No. 4). Catarrh bronchopneumonia was found in Nos. 2 and 3 and colitis in Nos. 1 and 3.

By the avidin-biotin-complex immunoperoxidase technique (ABCTT) [4–6], a large amount of *E. coli* antigens, being distributed diffusely, was detected in the affected leptomeninges and ventricles, and the necrotic lesions of the cerebral parenchyma. The antigens were also found in the subependymal zone with marked inflammatory changes (No. 5). Droplet-like or small rod-shaped antigens were present in the cytoplasm of many macrophages and several neutrophils and in the extra-cellular space in the involved areas. No *Haemophilus somnus* antigen was detected in the brain and spinal cord.

*E. coli* was isolated from the brain and cerebrospinal fluid of all the cases and from one (No. 4) or more (Nos. 2–5).
1–3 and 5) of the other organs.

The lesions observed in the brain of the present cases consisted of fibrinopurulent meningoventriculitis and scattered necrosis predominant in the corpus striatum and thalamus. Most of the necrosis appeared to be an infarct, since the lesions were located at some distance from the ventricles that were inflamed and frequently associated with vascular degeneration and thrombosis.

Cordy [1] has described that only 5 out of 26 neonatal ungulates with fibrinopurulent meningoventriculitis possessed discrete foci of necrosis or malacia in the basal ganglia or thalamus, and that those lesions were often clearly associated with nearby thrombi. Occurrence of the cerebral necrotic lesions was more frequent in our calves than that in the cases reported by Cordy [1]. Our results suggest that meningoventriculitis due to E. coli infection was frequently associated with cerebral infarcts and that the latter might be of importance in the development of E. coli septicemia of neonatal calves.

It has been known that several cell wall components of the causal bacteria, which contribute to further injury to the affected leptomeninges, were produced by antibiotics administered [9], and that pathophysiologic conditions including vasogenic, cytotoxic, and interstitial brain edema, which can precipitate neuronal injury, were not unaffected by antibiotic therapy [7]. It is therefore conceivable that, in the present cases, antibiotic therapy may have resulted in surviving the initial septic stage of the disease, though the repeated treatment promoted a more severe inflammation in the meningoventricular lesions.

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REFERENCES