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Effect of Dexamethasone on Porcine Enterovirus Infections in Pigs

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仔豚의 Enterovirus 感染症에 Dexamethasone이 미치는 影響

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抄 錄 : Enterovirus 感染症時 dexamethasone이 미치는 影響을 알아보기 위하여 初乳를 먹지 않은 1日齡 仔豚에 enterovirus를 經口感染시키고 dexamethasone을 筋肉注射한 후 臨床 및 病理組織學的으로 觀察하였던 바 다음과 같은 結果를 얻었다.

臨床的으로는 dexamethasone을 投與한 仔豚에서 感染後 3日째 體溫의 上昇, 4日째 步行失調 그리고 8日째 橫臥한 反面 enterovirus만을 感染시킨 對照群은 感染後 7日째 體溫의 上昇, 14日째 步行失調가 認定되었다.

病理組織學的 所見으로는 中樞神經系 全般에 걸쳐 髓膜下 圓形細胞의 侵潤, 血管周圍 圓形細胞의 侵潤, 彌漫性 또는 限局性 gliosis, 神經細胞의 退行性 變化가 觀察되었고, 특히 大腦 第3腦室部와 中腦水道, 第4腦室 및 脊髓의 中心管 周邊部에서 glia 細胞의 侵潤이 顯著하였으며, 病變의 程度는 enterovirus만을 感染시킨 對照群에 비해 dexamethasone을 投與한 仔豚에서 훨씬 심하게 나타난 점으로 보아 dexamethasone 投與는 仔豚의 enterovirus 感染症을 促進시킬 수 있는 한 誘因으로 看做된다.

Introduction

Porcine enterovirus has been reported to be involved in various clinical conditions including polioencephalomyelitis, female reproductive disorders, enteric disease, pneumonia, pericarditis and myocarditis (Leman *et al*, 1981). The susceptibility of porcine enterovirus infections was varied by the age of pig, older pigs being appeared to be less susceptible to infection and a great number of enterovirus infections occurred when colostral immunity presumably was low(Stewart *et al.*, 1974).

In Korea, some pathogenic porcine enteroviruses were isolated from swine and reproduced porcine polioencephalomyelitis in SPF pigs(Kwon *et al.*, 1978). Shin and Lee(1985) suggested that usual outbreak of porcine enterovirus infections be associated with hog cholera vaccination in addition to reprodution of identical polioencephalomyelitis by porcine enterovirus isolated in this country.

Corticosteroids stabilize lysosomes in damaged tissue, thereby preventing lysosomal proteolytic enzymes and long term therapy causes a decrease of lymphocytes and interference of host response to infection(Gilman *et al.*, 1980). Increased susceptibility of adult mice to enterovirus(Cox B3) has been

reported after pretreatment with cortisone(Kilbourne and Horsfall, 1951).

To provide further information on porcine enterovirus infections, authors have examined the results of immunosuppression with dexamethasone on porcine enterovirus infections in colostrum-deprived pigs.

Materials and Methods

Virus : The porcine enterovirus(PEV) was originally isolated from the lung of a diseased pig and its pathogenicity was proved to be in the previous report(Shin and Lee, 1985). The virus titer of the inoculum was $10^{6.7}TCID_{50}$/ml.

Experimental pigs : One litter of 4 colostrum-deprived pigs(1-day-old) was divided into 2 experimental groups. Each group was housed separately in cage and bottle feeding was performed.

Treatment : An experimental group of pigs was orally infected with PEV tissue culture suspension, followed by an intramuscular injection of dexamethasone(5mg/kg/day) for 3 days. A control group of pigs was infected with PEV only.

Clinical and histopathological examination : Rectal temperature and clinical signs were recorded daily. Each pig which showed neural disorder was necropsied. Organs were prepared for histopathological examination by fixation with formol saline. Tissue specimens were collected from brain and spinal cord for viral isolation and kept under storage at −40°C.

Results

Control group : Two infected pigs received no additional treatment developed a rise in rectal temperature and diarrhea at 7 post-infection days (PID) and gradually followed incordination and ataxia at 14 PID.

Histopathologically there was non-purulent polioencephalomyelitis consisting of neuronal degeneration, meningeal infiltration, focal gliosis and perivascular cuffing in the spinal cord, medulla oblongata, cerebrum(Fig. 1) and cerebellum(Fig. 2). The lesions were present in both grey and white matter at all levels of CNS, though usually more severe in the grey matter.

Treated group : Two infected pigs treated with dexamethasone had a febrile response at 3 PID, ataxia at 4 PID, convulsion and severe dyspnea at 8 PID. There were no significant gross lesions in one pig, but the other necropsied at 8 PID had pericarditis. Histopathological examination revealed a non-purulent polioencephalomyelitis in samples of tissues from 2 treated pigs. Lesions were present in the spinal cord (Fig. 3, 4), medulla oblongata(Fig. 5), cerebellum and cerebral hemispheres. In these areas, there were marked perivascular cuffing, meningeal infiltration(Fig. 6) and focal and diffuse accumulations of glia cells. The more severe changes were present in the ventral horns of the spinal cord(Fig. 4) and in the grey matter of the CNS. There were also a few diffuse and focal accumulations of mononuclear cells in close proximity to the ependyma of the lateral ventricle, cerebral aquiduct and spinal cord.

Recovery of virus : The cytopathogenic PEV was reisolated from the collected brain and spinal cord in both control and experimental group.

Discussion

The neural disorder, including ataxia, incordination and recumbency, in the dexamethasone-treated pigs developed at 8 PID when was approximately 1 week earlier than that of the controls. The present findings particularly correspond with the observations of the identical polioencephalomyelitis which are neuronal degeneration, neuronophagia, meningeal infiltration, perivascular cuffing, diffuse and focal gliosis (Harding *et al.*, 1957; Long *et al.*, 1966; Richard *et al.*, 1973; Shin and Lee, 1985). However the severity of the histopathological findings varied more or less owing to the area outbroken. The histological difference between the treated pigs and the controls was not recognized although the severity of the lesions in the treated pigs was more prominent than that of the controls. It was demonstrated that the susceptibility of colostrum-deprived pigs to oral infection with PEV could be greatly increased by administration of dexamethasone, clinically and histopathologically.

Corticosteroids stabilize lysosomes in damaged tissue, thereby preventing lysosomal proteolytic enzymes from escaping to damage surrounding cells. This suppression of tissue response obviously interferes with host

response to infection. Glucocorticoids cause a marked reduction in circulating eosinophils. Prolonged therapy results in lympholysis, decrease of circulating lymphocytes and involution of lymph nodes, thymus and spleen. The immunosuppressive effects of corticoids would also enhance the entry of infectious agents(Gilman *et al.*, 1980).

Derbyshire(1983) confirmed that humoral immune response played a significant role in the defense mechanism against porcine enterovirus infection in piglets. Experiments on an enterovirus infection in mice(Rager-Zisman and Allison, 1973) indicated that in this species also, circulating antibody, rather than cell mediated immunity, played the major defensive role.

As PEV was reisolated from the brains and spinal cords of both dexamethasone-treated and control pigs, it could be supposed that the orally administered virus multiplied considerably in the intestinal epithelium, lymphatic tissue, or both and then reached the brain in overwhelming quantity.

The PEV of our isolates in this country was capable of producing polioencephalomyelitis in colostrum-deprived pigs when infected with PEV orally in this study, intracerebrally(Shin and Lee, 1985) and in conventional pigs intramuscularly(Shin and Lee, 1985).

The susceptibility of PEV was particularly increased in the pigs inoculated with hog cholera vaccine(Shin and Lee, 1985), cyclophosphamide(Derbyshire, 1983) and dexamethasone in this present study.

The higher susceptibility of the dexamethasone-treated pigs might be associated with increased virus replication and pathological changes in CNS.

Conclusions

Four colostrum-deprived, 1 day old pigs were orally infected with the porcine enterovirus isolated in Korea. Two of the pigs were treated with dexamethasone(5mg/kg/day) for 3 days. The others as control were infected with porcine enterovirus only.

The treated, infected pigs developed ataxia at 3 postinoculation days, neural disorders at 8 postinoculation days, 1 week earlier than those of the controls.

Histopathological examination of both the treated and the control pigs revealed non-purulent polioencephalomyelitis consisting of neuronal degeneration, perivascular cuffing, meningeal infiltration, focal and diffuse gliosis. The severity of the histopathological lesions in the treated pigs was more prominent than those of the controls.

It was demonstrated that the susceptibility of colostrum-deprived pigs to oral infection with porcine enterovirus could be greatly increased by administration of dexamethasone clinically and histopathologically.

Legends for Figures

Fig. 1. Cerebrum of a control pig infected with porcine enterovirus only. Perivascular cuffing and gliosis are seen in the subependymal layer of lateral ventricle. H-E stain. ×112.

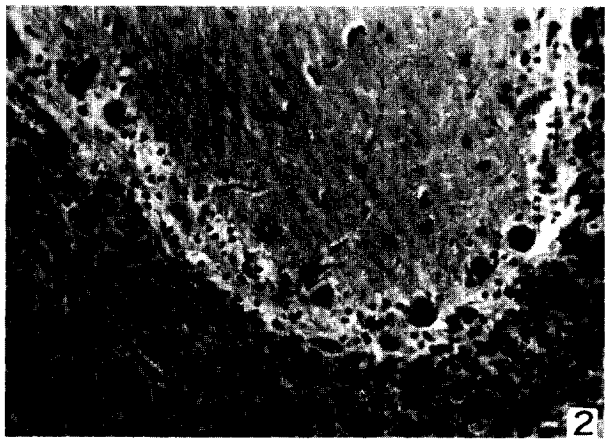
Fig. 2. Cerebellum of a control pig. Degeneration of Purkinje cells and diffuse gliosis of Purkinje cell layer are recognized. H-E stain. ×56.

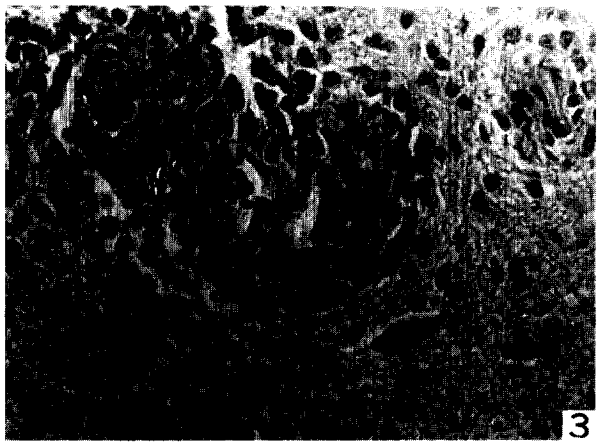
Fig. 3. Spinal cord of a dexamethasone-treated pig infected with porcine enterovirus. Severe perivascular cuffing is seen in the grey matter. H-E stain. ×112.

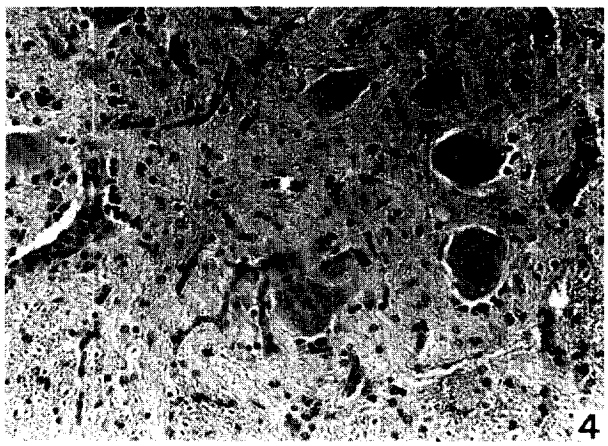
Fig. 4. Spinal cord of a treated pig. Diffuse and focal gliosis, neuronophagia, and perivascular cuffing are seen. H-E stain. ×56.

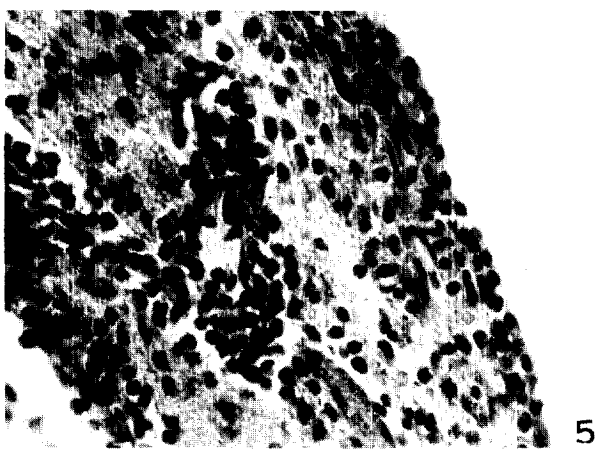
Fig 5. Medulla oblongata of a treated pig. Perivascular cuffing and diffuse gliosis are seen in the close proximity of ependymal layer. H-E stain. ×112.

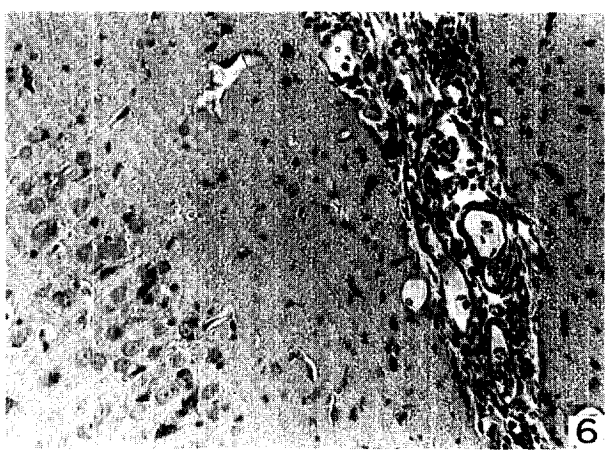
Fig. 6. Cerebrum of a treated pig. Meningeal infiltration of mononuclear cells is conspicious. H-E stain. ×56.











Reference

Derbyshire, J.B. (1983) The effect of immunosuppression with cyclophosphamide on an exprimental porcine enterovirus infection in piglets. Can. J. Comp. Med., 47:235~237.

Gilman, A.G., Goodman, L.S. and Goodman, A. (1980) The pharmacological basis of therapeutics. 6th ed., Macmillan Publishing Co., New York, pp. 1470~1493.

Harding, J.D.J., Done, J.T. and Kershaw, G.F. (1957) A transmissible polioencephalomyelitis of pigs(Talfan disease). Vet. Rec., 69:824~831.

Kilbourne, E.D. and Horsfall, F.L. (1951) Lethal infection with Coxsackie virus in adult mice given cortisone. Proc. Soc. Exp. Biol. Med., 77:135~138.

Kwon, H.J., Lim, Y.M., Cha, Y.H. and Lee, C.K. (1978) Epidemiology and identification of porcine enterovirus. Annual Research Report. Institute of Veterinary Research, Office of Rural Development, An Yang, pp. 105~124.

Leman, A.D., Glock, R.D., Mengeling, W.L., Penny, R.H.C., Scholl, E. and Straw, B. (1981) Disease of swine. 5th ed., Iowa State University Press, Ames, Iowa, pp. 265~270.

Long, J.F., Koestner, A. and Kasza, L. (1966) Infectivity of three porcine polioencephalomyelitis viruses for germfree and pathogen-free pigs. Am. J. Vet. Res., 27:274~279.

Rager-Zisman, B. and Allison, A.C. (1973) Effects of immunosuppression on Coxsackie B-3 virus infection in mice and passive protection by circulating antibody. J. Gen. Virol., 19:339~351.

Richard, Y., Toma, B. and Goret, P. (1973) Experimental study of Talfan disease in France. Isolation and identification of the virus. Bulletin de l'Academie Veterinaire de France, 46:73~81.

Shin, T.K. and Lee, C.S. (1985) Polioencephalomyelitis in pigs experimentally infected with porcine enterovirus isolated in Korea: I. Histopathological observations. Korean J. Vet. Res., 25:103~112.

Stewart, W.C., Carbrey, E.A., Kresse, J.I. and Snyder, M.L. (1974) Infections of swine with pseudorabies virus and enteroviruses: Laboratory confirmation, clinical and epizootiological features. J. Am. Vet. Med. Assoc., 165:440~442.