

## Head Tilt Associated with Encephalitozoonosis in Four Pet Rabbits

Jin-Cheol Shin, Sang-Hun Kim\*, Suk Kim\*\* and Kun-Ho Song<sup>1</sup>

College of Veterinary Medicine, Chungnam National University, Daejeon 305-764, Korea

\*Hanaro Veterinary Clinic, Daejeon 300-070, Korea

\*\* College of Veterinary Medicine, Gyeongsang National University, Jinju 660-701, Korea

(Accepted: April 10, 2015)

**Abstract :** *Encephalitozoon cuniculi* is an obligate intracellular microsporidian parasite commonly found in rabbits, causing encephalitozoonosis. This organism can also infect a wide range of hosts including humans, which is known to cause opportunistic infections in immunocompromised individuals. In this case, four rabbits presented with head tilt and nystagmus were diagnosed for *E. cuniculi* infection using ELISA. The rabbits were treated with fenbendazole for 4 weeks and therapeutic success was evaluated by assessing the neurological symptoms. Three out of 4 rabbits showed improved health condition 3 to 5 days after treatment, but one rabbit showed persistent anorexia and head tilt after treatment and then died after 10 days. This report is the first to investigate the therapeutic response of fenbendazole for rabbit encephalitozoonosis in Korea, and suggests that pet rabbits may serve as potential *E. cuniculi* reservoirs for both pet animals and humans.

**Key words :** *Encephalitozoon cuniculi*, fenbendazole, rabbit.

### Introduction

Encephalitozoonosis in rabbits is caused by an obligate, intracellular protozoan *Encephalitozoon cuniculi*, which is a member of the phylum Microspora. *E. cuniculi* is a zoonotic and opportunistic pathogen in humans, predominantly in patients with acquired immunodeficiency syndrome (AIDS) or immunocompromised (2,5). Infection of most mammalian hosts with *E. cuniculi* occurs by ingestion or inhalation of spores from contaminated urine shed by infected hosts. Clinical signs may include renal failure, hepatic failure, ocular disease, head tilt, hemiparesis, inability to right itself, rolling, seizure, ataxia and paralysis. Diagnosis of *E. cuniculi* is usually done through physical examination, hematology and serology. Albendazole and fenbendazole are generally used to minimize the inflammatory response associated with the infection (2,5).

There has been no published reports on rabbit encephalitozoonosis in Korea. Here, the authors reported 4 cases with encephalitozoonosis which showed a favorable therapeutic response with fenbendazole treatment in pet rabbits.

### Case

Four rabbits (3 to 49 months old, 0.6 to 1.8 kg, two males and two females) were presented with chief complaints of head tilt and nystagmus (Table 1) (Fig 1). Otoscopy and skull radiography were not specific. In blood test, renal function and hepatic function were normal. However, all rabbits had leukocytosis, eosinophilia and globulinemia. Serological exam-

ination was carried out using ELISA (Medicago, Uppsala, Sweden) according to the manufacturer's instruction. Briefly, serum samples and conjugate were diluted 1:40 and 1:1000 using phosphate buffer saline (PBS), respectively, prior to dispensing into the antigen-coated plates and absorbances (A) were read at 450 nm using a microplate reader (BioRad, St. Louis, MO, USA). The results were expressed with the formula suggested by manufacturer's protocol: (Sample A<sub>450</sub> *E. cuniculi* coated - Sample A<sub>450</sub> control antigen coated)/(A<sub>450</sub> negative control *E. cuniculi* coated - A<sub>450</sub> negative control antigen coated). The samples were classified as positive for *E. cuniculi* antibodies if the value exceeded 3, whereas negative if the value was < 3. All of the samples tested showed positive results. The rabbits were then treated with oral fenbendazole 20 mg/kg (Panacur<sup>®</sup>, Intervet international B.V., Austria) for 3 weeks daily and one shot of dexamethasone 2 mg/kg (Dexamethasone inj<sup>®</sup>, Jeil pharm co., LTD., Korea). Three out of four rabbits showed improved condition 3 to 5 days after treatment. There were no head tilt and nystagmus observed in the rabbits. The rabbits were treated successfully without adverse reactions. One rabbit showed persistent anor-

**Table 1.** Signalments and clinical findings of the tested rabbits

Case No.	Gender	Age (Months)	Clinical findings
1	Female	3	Head tilt, Rolling, Horizontal nystagmus, Positional nystagmus
2	Male	6	Head tilt, Falling, Horizontal nystagmus
3	Female	30	Head tilt, Horizontal nystagmus
4	Male	49	Head tilt, Rolling, Positional nystagmus

<sup>1</sup>Corresponding author.  
E-mail : songkh@cnu.ac.kr



**Fig 1.** Head tilt manifested by the rabbits with encephalitozoonosis.

exia and head tilt after treatment and then died after 10 days.

### Discussion

*E. cuniculi* is an obligate, intracellular, microsporidian parasite that can infect a wide range of vertebrate hosts including rabbits, mice, dogs, cats, goats, pigs, horses and humans. Although clinical signs in many rabbits infected with *E. cuniculi* are asymptomatic, other neurologic signs may include renal failure, hepatic failure, ocular disease, head tilt, hemiparesis, rolling, seizure, ataxia and paralysis (2,5).

Worldwide surveys have shown high rates (43-100%) of *E. cuniculi* infection in rabbits with neurological signs, vestibular disease or ocular lesions. Asymptomatic rabbits also have

shown high rates (37-68%) of infection in various countries including UK, Austria, Italy, Taiwan and Japan (1,3,4,6).

Fenbendazole is, at present, the drug of choice in rabbits as it has been shown to be effective in reducing clinical signs in an already established infection and to prevent it in exposed animals, when administered at 20 mg/kg once daily for 28 days (5).

In this case report, the rabbits were treated daily with oral fenbendazole 20 mg/kg for 3 weeks and one shot of dexamethasone 2 mg/kg. Three rabbits responded successfully to the medication and the clinical signs disappeared 3 to 5 days after treatment. However, one rabbit showed persistent anorexia and head tilt and then died after 10 days. Possibly due to stage of *E. cuniculi* infection in this animal which can be too severe to be resolved.

In conclusion, this case report suggests that fenbendazole is effective for the treatment of encephalitozoonosis in pet rabbits.

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## 애완 토끼에서 뇌포자육충에 의한 사경

신진철 · 김상훈\* · 김석\*\* · 송근호<sup>1</sup>

충남대학교 수의과대학, \*하나로동물병원, \*\*경상대학교 수의과대학

**요 약** : 토끼에서 뇌포자육충증은 *Encephalitozoon(E.) cuniculi*에 의해 유발되는 전염성 질환이다. *E.cuniculi*는 숙주 영역이 상당히 넓으며, 특히 면역능이 저하된 사람에서 기회 감염을 유발하기도 한다. 본 증례 보고에서 4 마리의 토끼가 사경과 안구진탕 증상으로 내원하였으며, 각 개체의 채혈을 통해 ELISA 검사를 수행하여 *E.cuniculi*에 양성임을 확인하였다. 토끼들은 fenbendazole로 4 주간 치료를 실시하였고, 치료효과는 신경증상의 발현정도에 따라 평가하였다. 치료한 네 마리 토끼 중 세 마리의 토끼에서 치료 3-5일 후부터 증상이 상당히 개선되었으나, 한 마리는 식욕부진과 사경증상이 개선되지 않고 치료 후 10일째 폐사하였다. 본 증례보고는 뇌포자육충 감염 애완토끼에 대한 fenbendazole의 치료효과를 규명한 최초의 보고이며, 본 증례를 통하여 애완토끼가 사람과 동물에 있어서 잠재적 *E. cuniculi* 보균 동물로 인식되므로 이에 대한 주의를 필요로 한다.

**주요어** : *Encephalitozoon cuniculi*, fenbendazole, 토끼