## A Case of Natural Mycoplasmosis in Spontaneously Hypertensive Rats

In-Soon Roh, Seung Hyun Oh, Ji Young Park, Kyung-Chul Choi<sup>1</sup>, Jeong-Hee Han<sup>2</sup>, Hee-Kyung Jin<sup>2</sup>, Seon Gil Do<sup>3</sup>, Jun Gyo Suh<sup>3</sup>, Yang Seok Oh<sup>3</sup>, Seong-Jun Park<sup>4</sup>, and Je-Kyung Seong\*

Department of Laboratory Animal Medicine, Yonsei University College of Medicine, Seoul, 120-749, Korea

<sup>1</sup>Department of Biomedical Science, College of Veterinary Medicine, Cornell University, Ithaca, NY14853, USA

<sup>2</sup>Department of Veterinary Medicine, Kangwon National University, Chunchon, 200-701, Korea

<sup>3</sup>Experimental Animal Center, College of Medicine, Hallym University, Chunchon, 200-702, Korea

<sup>4</sup>Department of Veterinary Internal Medicine, Tokyo University of Agriculture and Technology, 3-5-8,

Saiwai-cho, Fuchu, Tokyo 183-8509, Japan

(Accepted October 28, 2001)

Twenty one Spontaneously Hypertensive Rats(SHR) that were 4- to 21-month-old were examined histopathologically and serologically during a routine health monitoring of the rat colony. The results of the enzyme linked immunosorbent assay(ELISA) for murine pathogens demonstrated that 14 of 21 SHR rats had antibodies to *Mycoplasma pulmonis*. Histopathologically, the mycoplasma positive SHR rats were observed to have the typical pulmonary lesions which are characterized by the hyperplasia of the lymphoid tissue around the bronchi, bronchioles and vessels. Based on the histopathological findings and serological results, this case was diagnosed as a murine mycoplasmosis of SHR rats.

Key word: SHR, M. pulmonis, Mycoplasmosis

Mycoplasma pulmonis which is the etiologic agent of murine respiratory mycoplasmosis (MRM), is member of the order Mycoplasmatales, which is a small bacteria devoid of cell walls[2] and regarded to be a member of a group of wide-spread murine pathogens that are present in conventional rodent colonies. The microorganism may be acquired by aerosol transmission. This infection is increasing the number of conventionally housed breeding and research colonies as being potential reservoirs[1]. MRM is often clinically silent, has a slow, cumulative mortality, and is a slowly progressive respiratory disease that may persist for life[1,3]. A strain of spontaneously hypertensive rats (SHR), which has been established as an animal model for the essential hypertension in humans[4], undergoes a progressive decline of T cell functions with age[8]. This strain has also been found to produce a natural thymocytotoxic autoantibody (NTA) early in life[6] as well as arterial lesions that resemble human polyarteritis nodosa when the rats are 6 months of age[5].

We presently report naturally infected Mycoplasmosis in SHR rats that were reared in a conventional environment. The SHR rats were maintained under conventional conditions that

included a semibarrier filtered air system at an educational institution. The diet and water was fed on libitium. 21 SHR rats were randomly selected for routine health monitoring of the animal colony. Blood was collected from the abdominal aorta under anesthesia by I.V. injection of pentobarbital sodium. The animals were sacrificed after blood collection by an overdose injection of pentobarbital sodium. Internal tissues were removed and then fixed in 10% neutral buffered formalin. Samples were processed for routine paraffin section and stained with hematoxylin and eosin by routin histopathologic techniques. The ELISA test was performed using the sera of the animals in order to detect the antigen of Mycoplasma pulmonis, MHV (mouse hepatitis virus), the Sendai virus, and Tyzzer's disease using a commercial ELISA kit (CIEA, Japan). Also Helicobacter infection was monitored from feces of animals by using PCR methods.

Microscopic changes in the lungs of SHR showed a bronchiole associated lymphoid tissue (BALT) hyperplasia, perivasculitis and chronic alveolitis. We observed chronic inflammatory cell infiltration into the submucosa of the trachea (Fig 1). A peribronchial and perivascular infiltration that has

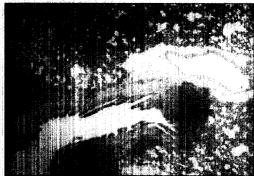
<sup>\*</sup>Corresponding author: Tel: 02-361-8395 Fax: 02-363-7984 E-mail: yslabanim@yumc.yonsei.ac.kr

lymphocytes and plasma cells is a prominent feature at 4- to 21-months of age of the rats (Fig 2). Bronchial epithelial cells in the affected areas showed a local hyperplasia or flattening caused by bronchiectasis. The alveolar changes were focal to segmental in distribution. The alveolar wall was thickened by a distinctive infiltration by alveolar macrophages and PMNs in the adjacent area of the lesions. There were variable degrees of alveolar emphysema. In a potion of the rats, there was presented pulmonary abscess present that was caused by a chronic suppurative process(Fig 3). The ELISA test for IgG antibodies to M. pulmonis was strongly positive in 14 of 21 the SHR rats. There was no relationship between age and infections. This case illustrates SHR in 4- to 11-month-old rats were infected with M. pulmonis using histopathology and serology examinations. Characteristic features were BALT hyperplasia in the lung and the presence of antibody to M. pulmonis by ELISA.

MRM represents a disease of major importance in the rat. The disease may seriously compromise the usefulness of affected animals in research, particularly those animals that are to be used for chronic studies[2]. Subclinical infections with *M. pulmonis* have been shown to impair other functions, including the humoral immune response. The organism is an important potential contaminant of cell cultures and is a potential complication in vitro immunological assays[1].

A strain of SHR has been known to cause various abnormalities of the immune systems as the animal ages[8]. Also SHR have the susceptibility to natural infection by several murine pathogenic microorganisms such as MHV, Sendai virus and M. pulmonis[7]. Takeichi etc[8] observed the depression of T cell functions and the production of NTA in SHR that were reared in a conventional environment. SHR have a high incidence of lethal infection by viruses and bacteria in their life. SHRs need to be maintained under a SPF-like conditions[8]. In the present routine monitoring, the other strain of rat, Sprague Dawley in the same animal room was not show positive for murine pathogens by the ELISA test(Data not shown). Although these rats were harbored under a semi-barrier system, we assumed that they were infected M. pulmonis before they were 4 months of age. This is the first report in Korea about the natural infection of Mycoplasmosis in SHR in conventional conditions.





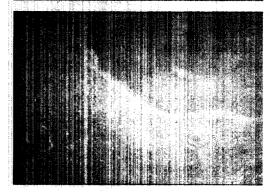


Fig 3. Lung. Large abscess(★) in parenchyma. HE, ×132.

## References

- Cassell, G.H., and M.B. Brown. Enzyme linked immunosorbent assay(ELISA) for the detection of antimycoplasmal antibody. Methods Mycoplasmol. 1983, 1, 457-469.
- Dean, H.P., and Stephan, W.B. Pathology of Laboratory Rodents and Rabbits, pp.80-84. 1st ed. Iowa State University Press, Ames, 1993.
- Lindsey, J.R., H.J. Baker, R.G. Overcash, G.H. Cassell, and C.E. Hunt. Murine chronic respiratory disease. Significance as a research complication and experimental production with *Mycoplasma pulmonis*. Am. J. Pathol. 1971, 64, 675-716.
- Okamoto, K., and Aoki, K. Development of a strain of spontaneously hypertensive rats. Jpn. Circ. J. 1963, 27, 282-293.

- Suzuki, T., Motoyama, T., and Sato, R. Periarteritis nodosa in spontaneously hypertensive rats. Acta Pathol. Jpn. 1980, 30, 907-912.
- Takeichi, N., Ba, D., and Kohayashi, H. Natural cytotoxic autoantibody against thymocytes in spontaneously hypertensive rats. Cell. Immunol. 1981, 60, 181-190.
- Takeichi, N., Hamada, J., Takimoto, M., Fujiwara, K., and Kobayashi, H. Depression of T cell-mediated immunity and enhancement of autoantibody production by natural infection with microorganisms in Spontaneously Hypertensive Rats(SHR). Microbiol. Immunol. 1988, 32, 1235-1244.
- Takeichi, N., Suzuki, K., and Kobayashi, H. Characterization of immunological depression in spontaneously hypertensive rats. Eur. J. Immunol. 1981, 11, 483-487.

## Mycoplasm pulmonis에 자연 감염된 SHR 랫드

노인순·오승현·박지영·최경철¹·한정회²·진회경²·도선길³·서준교³·오양석³·박성준⁴·성제경\* 연세대학교 의과대학 임상의학연구센터 실험동물부

<sup>1</sup>코넬대학교 수의과대학 생물의학과 <sup>2</sup>강원대학교 동물자원대학 수의학과 <sup>3</sup>한림대학교 의과대학 실험동물부 <sup>4</sup>동경 농공대학교 농학부 (2001년 10월 28일 게재승인)

국문초록: SHR 랜드 4-21 개월령 colony에서 혈청 및 조직학적으로 정기적인 health monitoring을 실시하던 중 ELISA test에서 21 개체 중 12 개체에서 Mycoplasma pulmonis에 대한 항체가 검출되었다. Mycoplasma 양성 개체군의 부검 소견에서 기관지, 세기관지 주변 림프절의 중식과 전형적인 폐 기관지의 병변 소견을 보였다. 혈청학적 검사와 조직학적 소견에서 SHR 랜드 군의 자연적인 Mycoplasm 감염 예로 진단되어 보고하는 바이다.

중심어 : SHR 랫드, M. pulmonis, Mycoplasm