Ostium secundum type of atrial septal defect in a rabbit

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Running head: ATRIAL SEPTAL DEFECT IN A RABBIT
A 14-month-old, female mini rex was referred for a detailed examination because of exercise intolerance with associated dyspnea. The thoracic radiograph demonstrated severe cardiac enlargement and elevation of the trachea. The echocardiography revealed dilatations of the right-side heart and pulmonary artery, and the color flow Doppler echocardiography demonstrated an atrial septum defect with left to right shunt, resulting in a disturbed flow. The rabbit died 19 days after the initial presentation, and a necropsy was performed. At the necropsy, a defect, 5 mm in diameter, was detected in the atrial septum. Based on the location of the defect, an ostium secundum type atrial septal defect was diagnosed. This is the first clinical report of atrial septal defect in rabbits.

KEYWORDS: atrial septal defect, congenital heart disease, rabbit
Atrial septal defect (ASD) is a common congenital heart disease in human, but believed to be rare in dogs and cats [1, 2]. However, Chetboul et al. were reported that ASD was represented approximately 40% of all canine and feline congenital heart diseases, and the incidence of canine and feline ASD is much higher than previously supposed [3]. ASD is characterized by communication between the two atria owing to a defect in the interatrial septum [3]. There are 3 types (ostium secundum, ostium primum, and sinus venosus) of ASD, which are classified according to the location of the septal defect [1, 3, 9], although this classification is considered controversial [15]. Ostium secundum type ASD is localized in the region of the fossa ovalis, and is the most common type in dogs and cats [3, 9]. On the other hand, there is a report that says ostium primum type ASD is more common than ostium secundum type in cats, and few cases had no apparent atrium septum [1], which was similar to single atrium case in human [11].

In rabbits, experimentally induced cardiovascular disorders have been reported, but reports of spontaneous cardiac diseases are rare. There have been a few reports of other congenital cardiac diseases, such as ventricular septal defects, in rabbits [6, 10, 12, 13, 16, 17]. However, to the author’s knowledge, there is no description of clinical findings of ASD in rabbits in the literature. The purpose of the present report is to describe the clinical and pathological findings of ASD in a rabbit.

A 14-month-old, female mini rex weighing 1.2 kg was referred to our animal hospital for a detailed examination because of exercise intolerance and associated dyspnea. Several months earlier, the rabbit had been diagnosed with heart failure at another clinic, for
which an ACE-inhibitor had been prescribed. The rabbit did not show any problems with activity and appetite, but mild emaciation was observed during the physical examination. The clinical examination revealed normal mucosal membranes, and didn’t present with obvious systemic edema. The respiratory rate was 100 breaths/min (reference values, 30-60 breaths/min), and the heart rate was 200-240 beats/min (reference values, 180-250 beats/min) [14]. The rabbit showed exophthalmos in response to restrain such as palpation. Cardiac systolic murmur (Levine III/VI) was detected on auscultation. Moderate hyperkalemia (7.3 mM) (reference values, 3.3-5.7mM) [8] was detected in the blood serum biochemistry analysis, although there were no significant changes in the other serum biochemistry results nor the complete blood cell count. Severe cardiac enlargement was observed on the thoracic radiograph (Figure 1). However, because the condition of the rabbit was unstable, radiograph was taken without anesthetizing the rabbit and thus radius and ulna overlapped the thorax and the rabbit’s back was curved on the radiograph. The echocardiogram (10MHz probe; GE Health care UK Ltd., Buckinghamshire, U.K.) revealed dilatations of the right-side heart and pulmonary artery on the left ventricular short-axis view, and the color flow Doppler echocardiogram demonstrated an ASD with a left-to-right shunt and a disturbed flow on the right ventricular outflow tract view (Fig. 2A and 2B). A detailed evaluation of the cardiac function and the tricuspid flow was not possible. Based on these echocardiographic findings, a presumptive diagnosis of ASD with left to right shunting was suspected.

The rabbit was treated with a regimen of enalapril (Enacard; Nippon Zenyaku Kogyo Co., Ltd., Fukushima, Japan) 0.5 mg/kg, oral, q 24 hr, furosemide (Lasix; Sanofi K.K.,
Tokyo, Japan), 1.5 mg/kg, oral, q 12 hr, isosorbide dinitrate (Kalliant SR; Pfizer, Tokyo, Japan)
0.5 mg/kg, oral, q 12 hr, theophylline (Theodur; Mitsubishi Tanabe Pharma Co., Osaka, Japan)
10 mg/kg, oral, q 12 hr, and metoclopramide hydrochloride (Primperan; Astellas Pharma Inc.,
Tokyo, Japan) 0.5 mg/kg, oral, q 12 hr. The dose of furosemide was gradually decreased
because the rabbit’s potassium levels were improved after five days (5.3 mM). The rabbit died
at home, 19 days after the initial presentation. According to the owner, the general condition
and appetite were normal until the day before the rabbit died, and there were no abnormal
symptoms other than a slight decrease of activity in the morning. The necropsy was performed
on that day.

At the necropsy, the right atrium was significantly enlarged, occupying almost half of
the thoracic cavity (Fig. 3A). The lungs were compressed by the enlarged heart and showed
moderate edema and emphysema. The liver was severely congested and enlarged. The heart and
other organs were removed and then infused with 10% neutral buffered formalin for fixation. On
gross examination of the heart after fixation, the right atrium, right ventricle, and pulmonary artery
were severely dilated (Fig. 3B). On opening the right atrium, a defect of 5 mm in diameter was
observed in the atrial septum (Fig. 3C). Based on the location of the defect, an ASD of the ostium
secundum type was diagnosed. On histopathological examination, myocardial degeneration and
fibrosis were observed. The atrioventricular valves were myxcedematous and thickened. Other
visceral organs, including the lungs, liver, kidneys, and adrenal glands, were congested. In the
lungs, alveolar walls were diffusely thick due to congestion and mild fibrosis. Mild alveolar
hemorrhage and heart failure cells were observed. Also, tunica media of the arterial walls were occasionally thickened. In the liver, severe congestion and mild fibrosis were observed.

The clinical signs of ASD depend on the size and location of the defect, direction and speed of the blood flow in the shunt, concurrence of other valve diseases, and residual cardiac function [1, 3]. Furthermore, each type of ASD has different hemodynamic implications [5]. Even if the entire atrium is missing (i.e., single atrium), it may develop clinical signs or may remain asymptomatic. Therefore, it should be considered that clinical symptoms may develop after the animal has aged (over 1 year old) as in the present case of a rabbit with ASD. Although evidence on the hemodynamic effect of ASD in rabbit is currently lacking, the pathophysiology caused by the different hemodynamic effect should be considered in each case of ASD in rabbit.

In general, the clinical signs include exercise intolerance, dyspnea, and coughing in dogs and cats. Moreover, cyanosis and syncope may be caused if the blood flow in the shunt changes direction. In this case, the clinical signs were exercise intolerance and dyspnea, similar to those in dogs and cats, except for the exophthalmos in response to restraint. In rabbits, exophthalmos can be caused by the presence of a precordial mass, such as a thymoma or mediastinal lymphoma [13]. This sign is consistent with a diagnosis of cranial vena caval syndrome caused by the space-occupying mass compressing the vessels of the anterior thorax and impeding vascular return to the heart [4]. In the present case, exophthalmos was likely to be caused by severe cardiac enlargement.

The chronic left-to-right shunt results in an increased pulmonary blood flow and
diastolic overload of the right ventricle, and can alter the pulmonary vascular resistance, leading to pulmonary arterial hypertension, and even a reversal of the shunt (Eisenmenger syndrome) at a terminal stage [1]. Rabbits are susceptible to pulmonary arterial hypertension due to the developed pulmonary artery smooth muscle [7]. In the present case, it was difficult to measure the blood flow velocity of the pulmonary artery, tricuspid valve, and mitral valve, so the pressure gradient between the left and right atrium could not be evaluated accurately. However, gross and histopathological findings of the lung and other visceral organs indicated chronic pulmonary circulatory disturbance and systemic congestion. And the findings of the echocardiogram with the severe dilations of the right-side heart and pulmonary artery suggested pulmonary arterial hypertension which may have been the cause of death in the present case.

In conclusion, this is the first clinical report of ASD in rabbits. In this case, it was difficult to evaluate a long-term therapeutic response or prognosis. Therefore, additional cases and data are necessary to evaluate the diagnostic examinations and the efficacy of different therapeutic strategies in rabbits with congenital cardiac disease.
REFERENCES


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FIGURE LEGENDS:

Fig. 1: Thoracic radiography
Thoracic radiography revealed severe cardiac enlargement and elevation of the trachea. Because the rabbit was unstable, radius and ulna overlapped the thorax and rabbit’s back was curved under unanesthetization in lateral view. (A) Ventral-dorsal view. (B) Lateral view.

Fig. 2: B-mode and color flow Doppler echocardiography
Echocardiography revealed severe dilatation of the right-side heart and pulmonary artery (A), and color flow Doppler echocardiography demonstrated an atrial septum defect (arrow) with left to right shunt (B). RA, right atrium; RV, right ventricle; LA, left atrium; PA, pulmonary artery; AO, aorta.

Fig. 3: Gross pathology
(A) Gross picture of the thoracic cavity at necropsy. The right atrium is significantly enlarged, occupying almost half of the thoracic cavity. (B) Gross picture of the heart after fixation. The right atrium, right ventricle, and pulmonary artery were severely dilated. (C) Gross picture of the heart, after opening the right atrium. The right atrium was cut opened at the white line and viewed from the direction of the arrow indicated in figure 3B. A defect of 5 mm in diameter was observed in the atrial septum (pinpoint). RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle; PA, pulmonary artery.
Figure 2