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First Description of Partial Atrioventricular Septal Defect in a Rabbit

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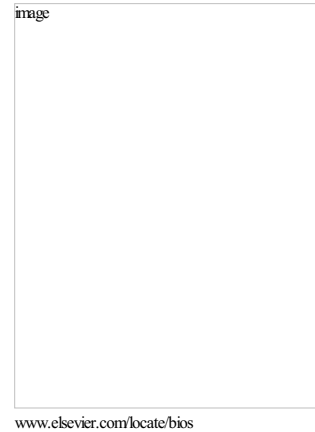
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Nicola Di Girolamo, Chiara Palmieri, Marco Baron  
Toaldo, Annalisa Nicoletti, Giliola Spattini, Ulrich  
Zeyen, Paolo Selleri



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**Brief communication****First description of partial atrioventricular septal defect in a rabbit**

Nicola Di Girolamo, DMV, GPCert(ExAP), MSc(EBHC), PhD, DiplECZM(Herp)<sup>a</sup>

Chiara Palmieri, DMV, DiplECVP<sup>b</sup>

Marco Baron Toaldo, DMV, PhD<sup>d</sup>

Annalisa Nicoletti, DMV<sup>c</sup>

Giliola Spattini, DMV, PhD, DiplECVDI<sup>e</sup>

Ulrich Zeyen, DMV<sup>c</sup>

Paolo Selleri, DMV, PhD, DiplECZM(Herpetology & Small Mammals)<sup>a</sup>

<sup>a</sup>Clinica per Animali Esotici, CVS, Via Sandro Giovannini 53, 00137, Roma, Italy;

<sup>b</sup>School of Veterinary Science, The University of Queensland, Gatton campus, 4343

Gatton, Queensland, Australia; <sup>c</sup>Department of Veterinary Medical Science,

University of Bologna Via Tolara di Sopra 50, 40064 Ozzano Emilia (BO) Italy;

<sup>d</sup>Department of Ultrasonography and Cardiology, CVS, Via Sandro Giovannini 53,

00137, Roma, Italy; <sup>e</sup>Clinica Veterinaria Castellarano, via Fuori Ponte 1/1, 42014,

Castellarano (RE), Italy

Address correspondence to Nicola Di Girolamo, Clinica per Animali Esotici, CVS,

Via Sandro Giovannini 53, Roma, Italy. E-mail: nicoladiggi@gmail.com. Telephone:

(+39)3292003570.

## Partial Atrioventricular Septal Defect in a Rabbit

Nicola Di Girolamo, DMV, GPCert(ExAP), MSc(EBHC), PhD, Dip. ECZM (Herpetology)

Chiara Palmieri, DMV, Dip. ECVF

Marco Baron Toaldo, DMV, PhD

Annalisa Nicoletti, DMV

Giliola Spattini, DMV, PhD, Dip. ECVDI

Ulrich Zeyen, DMV

Paolo Selleri, DMV, PhD, Dip. ECZM (Herpetology & Small Mammals)

From the Clinica per Animali Esotici, 00137, Roma, Italy (Di Girolamo, Selleri), School of Veterinary Science, The University of Queensland, Gatton campus, Queensland, Australia (Palmieri), Department of Veterinary Medical Science, University of Bologna, 40064 Ozzano Emilia (BO) Italy (Nicoletti, Zeyen), Department of Ultrasonography and Cardiology, CVS, 00137, Roma, Italy (Toaldo), Clinica Veterinaria Castellarano, 42014, Castellarano (RE), Italy (Spattini)

Address correspondence to Nicola Di Girolamo, DMV, GPCert(ExAP), MSc(EBHC), PhD, Dip. ECZM (Herpetology), Clinica per Animali Esotici, CVS, Via Sandro Giovannini 53, 00137, Roma, Italy. E-mail: nicoladiggi@gmail.com. Telephone: (+39)3292003570.

### Abstract

**Congenital heart diseases have rarely been described in rabbits. The purpose of the present case report is to describe the clinical, radiological, echocardiographic and pathological features of a partial atrioventricular septal defect in a pet rabbit. A 3-month-old 380-gram male vaccinated pet rabbit was presented for decreased activity, increased respiratory rate and effort, anorexia and decreased fecal output of two days of duration. Total body radiographic images revealed severe cardiomegaly associated with enlarged caudal pulmonary vessels and increased interstitial to alveolar lung pattern. Echocardiographic imaging showed evidence of distended heart chambers, abnormal flow through the atria, and mitral valve**

regurgitation. The rabbit was treated with furosemide and an angiotensin-converting enzyme inhibitor but rapidly deteriorated and died. Necropsy confirmed the dilation of both ventricles and the presence of partial atrioventricular septal defect associated with an *ostium primum* atrial septal defect just over the tricuspid valve and the mitral valve.

**Key words:** atrial septal defect; rabbit; heart; diagnosis

A 3-month-old 380-gram male vaccinated pet rabbit was presented to the Clinica per Animali Esotici for decreased activity, increased respiratory rate and effort, anorexia, and decreased fecal output of two days of duration. The referring veterinarian performed an initial physical examination, vaccination, and administered antiparasitic medication 2 weeks earlier with no abnormalities detected. Upon physical examination the rabbit appeared dull, dehydrated (skin fold 3-4 seconds), hypothermic (37.2°C; reference 38.0-40.0°C)<sup>1</sup>, and tachypneic (approximately 100 breaths per minute). Oral and genital mucous membranes were pale. Cardiac auscultation revealed a heart rate within normal limits (220 bpm), in absence of an appreciable heart murmur.

Total body radiographic images were obtained in the unsedated rabbit while fecal examination was performed using feces found in the inguinal area. Simultaneously, an intravenous 25 g catheter was placed in the cephalic vein while 100% oxygen was delivered at 4 L/min through flow-by. Blood glucose (65 mg/dL; reference range 75-150 mg/dL) was measured by means of a portable blood glucose meter (AccuChek Aviva, Roche, Mannheim, Germany) from a drop of blood obtained during the intravenous catheter placement.

The total body radiographic images were acquired with a digital indirect instrument using 52 kVp, 250 mA and 10 ms (Fig. 1). Adjustment of the window and level were used to study lung parenchyma and reduce the excessive contrast. The cranial mediastinum was difficult to evaluate on the lateral view due to summation with the severely enlarged cardiac silhouette (VHS: 11, reference range 7.17-7.92)<sup>2</sup>, however on the ventro-dorsal view the thickness was within normal limits. The trachea had a consistent diameter and was dorsally elevated throughout its length in the thorax by an increase in the size of the rabbit's heart. The cardiac silhouette showed a straight caudal margin, that extended dorsally along with moderate dorsal and lateral displacement of the left main bronchus. Due to the technique used to obtain the images, the cranial pulmonary artery and veins were not visualized, but the right caudal pulmonary artery was prominent and enlarged. The right pulmonary vein was also prominent. The left caudal pulmonary artery and vein were not visualized due to an increased interstitial to nearly alveolar pattern affecting part of this lung lobe. On the lateral view, the summation of the enlarged pulmonary artery and the interstitial pattern increased the opacity of the caudo-dorsal lung field. The other lung lobes were within normal limits. The poor abdominal detail was considered both age and species related. Granular material was observed in a moderately distended stomach and most of the small and large intestinal loops were filled with ingested material. The cecum was considered within normal size limits and contained a moderate amount of gas and granular material.

The generalized increase in cardiac silhouette size, associated with increased lung vessels and interstitial lung pattern, primarily localized on the

caudo-dorsal lung field, was most likely associated with a volume overload and left sided congestive heart failure. The visible portion of the abdomen was considered within normal limits. Differential disease diagnoses considered in this patient following evaluation of the radiographic images were mitral valve dysplasia, patent-ductus arteriosus, interatrial septal defect, interventricular septal defect and cono-truncal defects. Considering the clinical presentation and the radiographic findings other differential disease diagnosis were considered extremely improbable.

Using thorax ultrasonography, performed with a linear high-frequency ultrasound probe (L8-18i, General Electrics, Fairfield, CT, USA), the authors were able to rule out the presence of masses in the thorax, peritoneal-pericardial herniation, and pericardial or pleural effusion. Color-flow Doppler and B-mode echocardiography performed with a phased array probe (6S-RS, General Electrics, Fairfield, CT, USA) revealed left-to-right, low velocity, blood flow across the interatrial septum (Fig. 2). A regurgitant flow from the left ventricle into the left atrium indicated moderate mitral valve regurgitation. Echocardiography was performed rapidly, as the rabbit showed signs of discomfort along with an increased respiratory effort. An electrocardiogram (ECG) obtained during the echocardiogram did not show any evidence of alterations when compared to reference values.<sup>3</sup> The rabbit's health condition rapidly deteriorated until spontaneous death approximately 1.5 hours after admission.

After obtaining the owner's consent a post-mortem examination was immediately performed on the rabbit. The cecum and the stomach appeared moderately distended. A small volume of clear fluid was present in the

pericardium. The heart appeared generally enlarged when subjectively compared to a similar sized rabbit. The first cardiac incision was performed on the right ventricle parallel to the interventricular septum. A second incision was executed on the midline of the left ventricle from the cardiac apex, including the entire left atrium. All four chambers appeared moderately dilated, compared to hearts from similar size rabbits. The right ventricular wall was considered thin. A large defect in the atrial septum was evident over the mitral and tricuspid valves partially involving the region of the endocardial cushion (Fig. 3), consistent with an AV septal defect associated with an *ostium primum* atrial septal defect. Histopathology revealed mild subendocardial fibrosis and the myocardiocytes were slightly reduced in size characterized by hyperchromatic nuclei and lack of cross-striations (Fig. 3, Inset). Diffuse congestion was observed in the kidney, liver and spleen. The liver was also effaced by multifocal degeneration, mainly centered around the centrilobular veins. The final diagnosis was biventricular congestive heart failure caused by a partial AV septal defect.

## DISCUSSION

Congenital heart diseases (CHDs) remain a leading cause of morbidity and mortality in humans and animals.<sup>4,5</sup> Atrioventricular septal defects occur due to an abnormal and incomplete formation of the endocardial cushion during fetal life. This condition can be either complete or partial. In the former, a common AV valve is present, while partial AV septal defects are associated with 2 separate valves/orifices. Atrioventricular septal defects are usually associated with other malformations of the AV region, such as atrial septal



defects (ASD), ventricular septal defects, persistent left cranial vena cava, and abnormalities of the mitral valve often leading to valvular insufficiency.<sup>6</sup> Atrioventricular septal defects are a rare malformation in dogs, while in cats they represent approximately 2% of all congenital cardiac defects.<sup>7-9</sup>

In rabbits, CHDs are an uncommon finding.<sup>10</sup> Natural occurring ventricular septal defects have been described in three rabbits.<sup>11-13</sup> *Cor triatriatum dexter* had been suspected in a young symptomatic rabbit.<sup>14</sup> A large investigation of a specific laboratory strain of rabbits (III/O/J) revealed a high prevalence (5%) of congenital pulmonary and aortic malformations, often associated with ventricular septal defects.<sup>15</sup> To the best of the authors' knowledge atrial septal defects, including patent foramen ovale, and AV septal defects have not been previously reported in rabbits in the scientific literature.

In recent years there has been more attention focused on rabbit cardiac disease. Relevant diagnostic tests for direct and indirect cardiac evaluation in rabbits<sup>2</sup> have been improved and enhanced thereby increasing the diagnosis of heart disease in these animals.<sup>13</sup> In this report the clinical and pathological changes associated with a partial AV septal defect associated with a large ASD in a clinically ill young rabbit are described. The animal also had mitral valve insufficiency which may have played a significant role in the observed volume overload and increased heart size. The mitral valve insufficiency was likely the consequence of a primary valvular abnormality as this condition is often present in endocardial cushion defects.<sup>6</sup>

In the present case, the interatrial septum was, on the whole, not present. This alteration resembled the *ostium primum* atrial septal defect

diagnosed in humans.<sup>16</sup> An *ostium primum* atrial septal defect is located in the most anterior and inferior aspect of the atrial septum and can be considered the simplest form of AV septal defect.<sup>16</sup> Affected humans and animals may develop clinical signs in childhood, adulthood, or may remain subclinical.<sup>17,18</sup> Given that histopathology of major abdominal organs also revealed pathologic changes, most likely secondary to cardiac disorders, the authors suggest, that in this case, the cardiac malformation was responsible for the congestive heart failure and death of the rabbit. Since histopathology of the lungs was not performed, it is not possible to have a definitive confirmation that the rabbit in this report suffered pulmonary edema. It is not possible to exclude that handling during diagnostic and therapeutic procedures caused stress and tachycardia, thus exacerbating the cardiac insufficiency which subsequently contributed to the death of the patient.

The fact that, in the present case, the ECG showed no evidence of arrhythmias is not completely unexpected since in ASD-affected dogs, ECG alterations are usually observed when ASD is associated with a concomitant heart disease (e.g., aortic stenosis, acquired mitral valve disease).<sup>20</sup> Veterinarians should be aware that AV septal defects may occur in pet rabbits and therefore it should be included in the differential disease diagnoses for early-onset cardiomegaly.

## References

1. Di Girolamo N, Toth G, Selleri P: Prognostic value of rectal temperature at hospital admission in client-owned rabbits. J Am Vet Med Assoc 248:288-297, 2016

2. Onuma M, Ono S, Ishida T, et al: Radiographic measurement of cardiac size in 27 rabbits. *J Vet Med Sci* 72:529-531, 2009
3. Lord B, Boswood A, Petrie A: Electrocardiography of the normal domestic pet rabbit. *Vet Rec* 167:961-965, 2010
4. Buchanan JW: Prevalence of cardiovascular disorders, in Fox PR, Sisson DD, Moise NS (eds): *Textbook of Canine and Feline Cardiology* (ed 2). Philadelphia, PA, WB Saunders Company pp 458–463, 1999
5. Lee K, Khoshnood B, Chen L, et al: Infant mortality from congenital malformations in the United States, 1970-1997. *Obstet Gynecol* 98:620-627, 2001
6. Hari P, Pao RG, Varadarajan P: Echocardiographic evaluation of patent foramen ovale and atrial septal defect. *Echocardiogr* 32:S110-124, 2015
7. Nakayama T, Wakao Y, Uechi M, et al: A case report of surgical treatment of a dog with atrioventricular septal defect (incomplete form of endocardial cushion defect). *J Vet Med Sci* 56: 981-984, 1994
8. Akiyama M, Tanaka R, Maruo K, et al: Surgical correction of a partial atrioventricular septal defect with a ventricular septal defect in a dog. *J Am Anim Hosp Assoc* 41:137-143, 2005
9. Tidholm A, Ljungvall I, Michal J, et al: Congenital heart defects in cats: a retrospective study of 162 cats (1996-2013). *J Vet Cardiol* 17:S215-219, 2015
10. Michaëlsson M, Ho SY (eds): *Congenital Heart Malformations in Mammals*. London, UK, Imperial College Press, 2000
11. Kanemoto I, Chimura S: Congenital heart disease of the rabbit. I. A case of ventricular septal defect [in Japanese, with English summary]. *Adv Anim Electrocard* 16:52-56, 1983

12. Li X, Murphy JC, Lipman NS: Eisenmenger's syndrome in a New Zealand white rabbit. *Lab Anim Sci* 45:618-620, 1995
13. Vörös K, Seehusen F, Hungerbühler S, et al. Ventricular septal defect with aortic valve insufficiency in a New Zealand White rabbit. *J Am Anim Hosp Assoc* 47:e42-49, 2011
14. Varga M (ed): *Textbook of Rabbit Medicine* (ed 2). Oxford, UK, Butterworth Heinemann/Elsevier, 2014
15. Crary DD, Fox RR: Hereditary vestigial pulmonary arterial trunk and related defects in rabbits. *J Hered* 66:50-55, 1975
16. Piccoli GP, Gerlis LM, Wilkinson JL, et al: Morphology and classification of atrioventricular defects. *Br Heart J* 42:621-632, 1979
17. Somerville J: Ostium primum defect: factors causing deterioration in the natural history. *Br Heart J* 27:413-419, 1965
18. Schrope DP: Atrioventricular septal defects: natural history, echocardiographic, electrocardiographic, and radiographic findings in 26 cats. *J Vet Cardiol* 15:233-242, 2013
19. Katsanos K, Mitsos S, Koletsis E, et al: Transauricular embolization of the rabbit coronary artery for experimental myocardial infarction: comparison of a minimally invasive closed-chest model with open-chest surgery. *J Cardiothorac Surg* 7:16, 2012
20. Chetboul V, Charles V, Nicolle A, et al: Retrospective study of 156 atrial septal defects in dogs and cats (2001-2005). *J Vet Med A Physiol Pathol Clin Med* 53:179-184, 2006

## Figures

**Figure 1.** Right lateral and dorso-ventral body radiographs of a 380-grams pet rabbit presented for decreased activity, increased respiratory effort, anorexia, and pale mucous membranes. Despite overall poor positioning consequent to respiratory distress and lack of sedation, there is evidence of a severely enlarged cardiac silhouette (asterisk, arrowheads), associated with enlarged caudal pulmonary vessels and increased interstitial to alveolar lung pattern. This was most likely consistent with congestive left sided heart failure.

**Figure 2.** B-mode and color-flow Doppler echocardiography of a 380-gram rabbit. Apical five-chamber view. The left-to-right flow through a large *ostium primum* ASD is evident.

**Figure 3.** Gross and histopathology specimen of the heart of the rabbit. A. Right ventricle is reflected. B. Left ventricle is sectioned on its midline. Note the large *ostium primum* ASD over the tricuspid and mitral valves (arrowheads). IVS: Interventricular septum; LV: Left ventricle; MV: Mitral valve; RA: Right atrium; RV: Right ventricle; TV: Tricuspid valve. **Inset:** Histology of the heart of the rabbit. Note the reduction in size of myocardiocytes. Haematoxylin & Eosin; Magnification 40x.

