









Major cardiac defects in cattle in southern Brazil: retrospective study of necropsies over 20 years (2000-2019)

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ABSTRACT: Cardiac malformations are reported to be relatively rare in bovine species, with ventricular septal defects being the most common abnormality observed predominantly in young calves. This report aims to describe the cardiac malformations observed in bovinds and review the literature related to those malformations in this species. The necropsy reports of 1,783 bovinds were reviewed, and 0.4% were diagnosed with a cardiac congenital defect. The most common cardiac congenital malformation detected in this study was ventricular septal defect, observed alone or associated with other anomalies (in one case, as part of tetralogy of Fallot); followed by atrial septal defect, also alone or with other cardiac malformations. Secondary findings in the lungs and liver were observed in 75% of all cases. Histologic cardiac lesions were identified in 25% of all cases, characterized mainly by fibrosis. Other congenital malformations in different organs were observed in 25% of the cases. Considering the importance of cardiac congenital malformations observed in this study, these conditions should be considered as a differential diagnosis for calves who died with no specific clinical signs. Furthermore, macroscopic evaluation is crucial for the diagnosis of cardiac congenital malformations.

Key words: congenital malformations, ventricular septal defect, atrial septal defect, bovine.

Principais defeitos cardíacos em bovinos no sul do Brasil: estudo retrospectivo de necropsias em 20 anos (2000-2019)

RESUMO: Malformações cardíacas são descritas como relativamente raras para bovinos, e defeitos do septo interventricular são as anomalias mais observadas em bezerros. O objetivo deste artigo é descrever os casos de malformações cardíacas observadas em bovinos e uma revisão de literatura sobre estas malformações nesta espécie. Os relatórios de necropsia de 1.783 bovinos foram revisados, e 0,4% destes foram diagnosticados com defeitos cardíacos congênitos. A malformação cardíaca congênita mais diagnosticada neste estudo foi defeito do septo interventricular, observado sozinho ou associado a outras anomalias (em um caso de tetralogia de Fallot); seguida de defeito no septo interatrial, também observado sozinho ou juntamente com outras malformações cardíacas. Lesões secundárias nos pulmões e fígado foram observadas em 75% dos casos. As alterações histológicas no coração, visualizadas em 25% dos casos, foram caracterizadas principalmente por fibrose. Outras malformações congênitas em diferentes órgãos foram identificadas em 25% dos casos. Considerando a importância de malformações cardíacas congênitas observadas neste estudo, estas condições devem ser consideradas como diagnósticos diferenciais para bezerros que morrem sem sinais clínicos específicos. Adicionalmente, a avaliação macroscópica é fundamental para o diagnóstico de malformações cardíacas congênitas.

Palavras-chave: malformações congênitas, defeito do septo interventricular, defeito do septo interatrial, bezerros.

INTRODUCTION

Congenital malformations have been reported in all animal species throughout many years. The first published reports in bovinds date from 1934, when a review on congenital defects in animals was published and in which cattle were overrepresented (LILLENGEN, 1934). Congenital malformations can occur in any organ and can result from genetic defects or an insult or agent associated with the fetal environment or their interaction (LEIPOLD

& DENNIS, 1986). Malformations can affect only one system, for example, the cardiovascular, or multiple systems concurrently, such as cases of multiple malformations involving the central nervous system and musculoskeletal system (WHITLOCK et al., 2008; WHITLOCK & COFFMAN, 2015). Cardiac malformations are among the most important malformations diagnosed in bovinds in several retrospective studies, although they are still rare, being involved in 1 to 5% of all congenital anomalies for this species (DANTAS et al., 2010;

MARCOLONGO-PEREIRA et al., 2010; MACÊDO et al., 2011; OLIVEIRA et al., 2011; ROBINSON & ROBINSON 2016, DIAS-MOREIRA et al., 2019).

Substantial adjustments occur in the cardiovascular system during fetal and neonatal life, including changes in pressures from cardiac chambers and great vessels, in addition to modifications in blood volume and flow (ROBINSON & ROBINSON 2016). For this reason, retention of fetal structures, such as fetal vasculature and communications between the cardiac chambers, can lead to cardiac overload in the postnatal period or beyond, with growth and development of the bovine (ROBINSON & ROBINSON 2016). Prominent cardiac malformations can be recognized during a clinical examination and confirmed through necropsy, depending on the organ or system affected, although the cause is usually difficult to determine (RADOSTITS et al., 2007; MACÊDO et al., 2011). This study aims to describe cardiac malformations diagnosed in the bovine species between 2000 and 2019 in the state of Rio Grande do Sul, Brazil.

MATERIALS AND METHODS

A retrospective study of cardiac congenital defects of bovines necropsied in the metropolitan region of Porto Alegre was performed. Necropsy

reports from 2000 to 2019 were retrieved and reviewed, searching for necropsies of cattle based on a combination of keywords such as “bovine”, “congenital heart defect”, “cardiac malformation”, “patent foramen ovale”, “septal defect”, “interatrial” and “interventricular”. Selected cases included necropsies of bovines from the state of Rio Grande do Sul, Brazil. Necropsy reports, photographs, and histologic slides were reviewed.

The reports of the selected cases were evaluated, and information regarding age, breed, sex, clinical signs, as well as gross and histologic alterations in the heart and other systemic organs, were obtained. Additionally, when available, information regarding additional molecular tests, such as RT-PCR for bovine viral diarrhoea virus (BVDV), were retrieved.

RESULTS

During the studied period, 1,783 necropsies were performed in the bovine species, and eight of them (0.4%) were diagnosed with cardiac congenital defects. Information regarding sex, age, breed, primary cardiac abnormalities, compensatory cardiac alterations, and other systemic lesions are described in table 1. Males and females were equally affected, and age ranged from stillborn to 7-months-old, with

Table 1 - Cardiac congenital defects diagnosed in the bovine species and concomitant extracardiac alterations.

Case	Sex	Age	Breed	Primary cardiac alteration	Compensatory cardiac alteration	Concomitant alterations
1	F	50 days	Red Angus	Ventricular septal defect	Bilateral eccentric ventricular hypertrophy	Hydrothorax, pulmonary edema, liver congestion
2	F	Stillborn	Mixed Angus	Ventricular septal defect	None	Pulmonary edema
3	F	7 months	Holstein	Ventricular septal defect	Bilateral eccentric ventricular hypertrophy	Hydrocephalus, pulmonary edema, complete tracheal rings
4	M	3 days	Angus	Ventricular septal defect	None	Pulmonary edema
5	F	45 days	Braford	Tetralogy of Fallot, patent ductus arteriosus, atrial septal defect	Right eccentric ventricular hypertrophy	Pulmonary edema, liver congestion
6	M	2 months	NI	Ventricular septal defect	Left eccentric ventricular hypertrophy	Bacterial pneumonia, enterocolitis
7	M	2 months	Braford	Atrial septal defect, endocardial fibrosis	Bilateral eccentric ventricular hypertrophy	Pulmonary edema, liver congestion
8	M	6 days	Mixed breed	Atrial septal defect	Right eccentric ventricular hypertrophy	Bilateral thoracic hemimelia, unilateral renal agenesis

F – female; M – male; NI – not informed.

calves being the most affected. European breeds (Angus and Holstein), or crossbred with European (Braford and mixed Angus), were predominant in this study.

Clinical signs were mainly characterized by apathy and dyspnea, and on clinical examination, the calves occasionally presented with a heart murmur. Additionally, bovinds frequently were born weak and small and, with development, showed a decreased growth rate. For two cases, death occurred with no previous clinical signs, followed by an episode of intense physical exercise (such as movement between pastures).

Among the cardiac defects diagnosed, ventricular septal defects were the main alterations in this study (75%; 6/8), observed alone in five cases (Figure 1A and 1B), and associated with other anomalies, as in the case of tetralogy of Fallot (Figure 1C) (Table 1). The second most important alteration in this study was atrial septal defects (37.5%; 3/8) (Figure 1D). Cardiomegaly and ventricular eccentric hypertrophy were the most common compensatory findings, observed in 87.5% of cases (7/8).

Extracardiac alterations related to the cardiac defects were frequently observed in the lungs and liver. Pulmonary lesions were seen in 75% of cases (7/8) and were characterized by wet, heavy, and non-collapsed lungs, with variable amount of

fluid oozing on cut surface (pulmonary edema). Hepatic lesions were less common, observed in 37.5% of cases (3/8), and were characterized grossly by rounded hepatic edges and a pronounced lobular pattern on cut surface, with multiple dark red areas surrounded by pink to gray areas (liver congestion). Other malformations were not frequently seen, with presentation in only 25% of cases (2/8). In one case the bovine also presented with hydrocephalus and complete tracheal rings (case 3) and one case displayed bilateral thoracic hemimelia and unilateral renal hypoplasia (case 8).

Histologically, lesions were observed in the heart for only two cases. The first one was characterized by mild vacuolization and atrophy of cardiomyocytes in the case of tetralogy of Fallot (case 5). The second one was a case of patent foramen ovale (case 7), which presented abundant fibrosis surrounding the septal defect associated with mild lymphocytic infiltrate.

Pulmonary histologic lesions were seen in all cases, mainly characterized by variable amounts of pale eosinophilic and amorphous material inside the alveolar spaces (pulmonary edema), associated with alveolar macrophages and variable deposition of eosinophilic fibrillar material (fibrin) in chronic cases. In a case of secondary bacterial infection

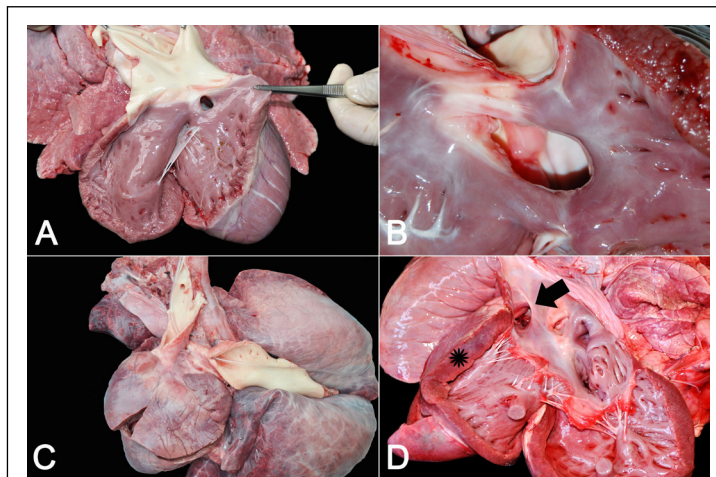


Figure 1 - Cardiac malformation in cattle. A - Ventricular septal defect (Case 6) in a high location in the ventricular septum and measuring 1.0 cm in diameter. Also note the eccentric hypertrophy of the left ventriculus. B - Higher magnification of a ventricular septal defect with severe connective tissue proliferation surrounding the defect (Case 7). C - A case of tetralogy of Fallot, with the evidence of the persistence of the arterial duct (Case 5). D - Persistency of the foramen ovale (arrow) with hypertrophy of the right ventricle (asterisk) (Case 7).

(case 6), multiple areas of necrosis associated with deposition of fibrin and a mixed inflammatory infiltrate were observed, sometimes surrounded by a capsule of fibrous connective tissue forming multiple abscesses. Hepatic lesions were seen in five cases, characterized by mild to marked centrilobular congestion associated with variable degeneration and necrosis of hepatocytes, in addition to mild to moderate proliferation of fibrous connective tissue around periportal areas in a few cases.

None of the samples were positive for BVDV, based on molecular testing. No additional suspected causes were noted by the pathologists who evaluated the cases.

DISCUSSION

The diagnosis of cardiac congenital malformations in all bovids from this study was based predominantly on macroscopic changes and represented 0.44% of all causes of death of animals necropsied for 20 years. In Brazil, the frequency of congenital anomalies in cattle is estimated to be 0.2 to 3%, ranging according to the region and epidemiological factors such as exposure to toxic plants, infectious agents, and inherited traits (DANTAS et al., 2010; MARCOLONGO-PEREIRA et al., 2010; MACÊDO et al., 2011; OLIVEIRA et al., 2011). For cardiac malformation alone, the number is lower; different studies of congenital malformations of cattle performed in Brazil found cardiac abnormalities accounted for 0.07% (MACÊDO et al., 2011) and 0.27% (MARCOLONGO-PEREIRA et al., 2010). In this study, cardiac malformations showed greater frequency for cattle in the coverage area than in those studies.

Heart conditions in bovids can be a challenge to diagnose clinically. Some animals can exhibit exercise intolerance, poor growth, dyspnea, or even episodes of syncope, and at clinical examination distention of the jugular vein, ventral edema, and heart and lung murmurs can be observed. However, most commonly, the animals are just found dead, as seen in some of the cases described here (JACKSON & SLATER, 1997; MCKENNA et al., 2003; BUCZINSKI et al., 2010). The severity and age at onset of clinical signs vary with the severity of the lesion. Large septal defects usually result in obvious clinical signs and death at an early age (JACKSON & SLATER, 1997). The prognosis of affected bovids is usually poor, since surgery is the recommended treatment, but is not economically viable (BUCZINSKI et al., 2010). Other concomitant conditions can be associated

with cardiac malformations. These include chronic unresponsive pneumonia, as seen in one of the cases in this study, and bacterial endocarditis (BUCZINSKI et al., 2006).

The main cardiac congenital malformation diagnosed in this research was ventricular septal defect (VSD), and this is considered the most common cardiac defect observed in domestic animals (BUCZINSKI et al., 2006; ROBINSON & ROBINSON, 2016). In bovids, this defect can be hereditary in some breeds such as Hereford or Limousin, although a hereditary cause was not investigated thoroughly in these cases since other animals from the same farms did not show similar lesions (JACKSON & SLATER, 1997). The left-to-right shunt, related to the incomplete development of the embryonic heart, overloads the right ventricle and pulmonary vascular tree after birth, inducing pulmonary hypertension and decreased peripheral perfusion, leading to cyanosis and death (JACKSON & SLATER, 1997; ROBINSON & ROBINSON, 2016). Both ventricles undergo hypertrophy with the left showing more obvious eccentricity (ROBINSON & ROBINSON, 2016).

The second most important cardiac congenital malformation were atrial septal defects, diagnosed in three calves. This malformation is often associated with patent *foramen ovale*, which is a result of non-closure of the communication between the right and left atrium, and which exists in the fetal life to allow blood to bypass the lungs. Atrial septal defects can alternately be a result of a true interseptal defect due to failure in the development of the interatrial septum (MACÊDO et al., 2011; ROBINSON & ROBINSON, 2016). Physiologically, the *foramen ovale* closes after birth; however, failure in closing this structure can result in excessive blood flow from the left to the right atrium, resulting in right ventricular overload and, consequently, right ventricular dilation and high central venous pressure (ROBINSON & ROBINSON 2016).

Finally, one bovine was diagnosed with tetralogy of Fallot. This condition is characterized by a primary obstruction of the right ventricular outflow due to the narrowing of the right ventricular infundibulum by pulmonic stenosis or infundibular stenosis. The defect results in inability of the septum to participate in closure of the interventricular foramen, consequently leading to ventricular septal defect, overriding aorta, and compensatory right ventricular hypertrophy (JACKSON & SLATER, 1997; MCKENNA et al., 2003; ROBINSON & ROBINSON, 2016). The bovids from this study

presented mild clinical signs, characterized by apathy and fever. Tetralogy of Fallot is one of the congenital heart conditions that resulted in more significant clinical signs, such as exercise intolerance, cyanosis, and deficient growth rate in addition to the milder signs most of the animals from this study showed (ROBINSON & ROBINSON, 2016).

Congenital malformations can occur as isolated defects or accompanied by malformations in several other organs (LEIPOLD & DENNIS, 1986; MICHAELSSON & HO, 2000; WHITLOCK et al., 2008). A study evaluating these abnormalities in the bovine species showed multiple congenital malformations are involved in approximately 0.17% of all causes of death; however, when evaluating them on a case-by-case basis, 38.7% of all cattle with these abnormalities showed involvement of multiple organs (MACÊDO et al., 2011). Considering animals of young age, the number of calves with multiple malformations can reach 1.8% (BELLOWS et al., 1987). In this study, the number of bovines with multiple congenital malformations is lower when compared with the literature.

The etiologies of congenital malformations in the bovine species can be divided into heritable, toxic, nutritional, and infectious, the latter represented mainly by viruses (MARCOLONGO-PEREIRA et al., 2010; AGERHOLM et al., 2015). Additionally, many congenital malformations are sporadic and not associated with any specific cause (RADOSTITS et al., 2007; SCHILD 2007; MARCOLONGO-PEREIRA et al., 2010). As a nutritional etiology, hypovitaminosis A in cattle is listed as a possible cause of ocular and cardiac malformation (MILLEMAN et al., 2007). Several viruses can be related to congenital malformations, among them: bovine viral diarrhoea virus (BVDV), Bluetongue virus (BTV), Akabane virus (AKAV), and Schmallenberg virus (SBV) (AGERHOLM et al., 2015). In southern Brazil, the most common etiology related to congenital defects is BVDV, and it is usually associated with central nervous system lesions like cerebellar hypoplasia and porencephaly (SCHILD, 2007; PAVARINI et al., 2008). In this study, however, none of the cases had a confirmed etiology.

In conclusion, considering the clinical significance of these lesions in the studied region, cardiac congenital malformations should be included as an important differential diagnosis of causes of death in bovine species, mainly in cases of calves who died with no specific clinical signs. In this study, the main cardiac congenital malformations diagnosed were ventricular and atrial septal defects,

and cardiomegaly associated with myocardial hypertrophy were common compensatory findings. Pulmonary and hepatic congestion were frequent secondary lesions. Our findings suggest that a thorough macroscopic evaluation is imperative for the diagnosis of these cardiac abnormalities since they rarely cause histologic lesions in the heart. In addition, they are most commonly the only alterations seen at necropsy, although secondary lesions in the lungs and liver can be seen. Finally, multiple congenital malformations can occur. Thus, a complete necropsy is essential for an accurate diagnosis.

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DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

AUTHORS' CONTRIBUTIONS

All authors contributed equally for the conception and writing of the manuscript. All authors critically revised the manuscript and approved of the final version.

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