Congenital heart defects in two Italian Simmental (Pezzata Rossa Italiana) calves

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SUMMARY

Congenital heart diseases (CHDs) are the consequence of anomalies during the embryonic development of the heart and they are defined as rare in cattle with scarce reports in the literature. The ventricular septal defects (VSDs) and the atrial septal defects (ASDs) are reported to be the most common, followed by other malformations such as patent ductus arteriosus (PDA).
The aetiology of the CHDs has not been fully explained yet, but is commonly considered linked to either inherited or non-inherited causes. Although uncommonly reported, the inherited congenital anomalies could affect different breeds of cattle with a potential significant economic impact. In addition, the wide use of the *in vitro* fertilization could be associated with a potential reduction of genetic variability in bovine population, therefore favouring the development of congenital defects such as CHDs. Among the non-inherited causes, foetal viral infections (*e.g.* Schmallenberg virus, Bovine diarrhea virus, Blue Tongue virus), nutritional deficiencies of the dam and toxic agents may play a key role in the development of CHDs.
The two cases herein described report the occurrence of cardiac congenital malformations in Italian Simmental breed (Pezzata Rossa Italiana, PRI) calves. In the first case, the ASD was accompanied by concurrent anomalies in other organs (liver and brain); in the second case, the calf presented both PDA and ASD. Based on the anamnestic data and the laboratory results, a possible role of viral agents seems to be unlikely. The investigation and determination of the possible causes of CHDs is challenging both for veterinary practitioners and laboratory diagnosticians due to the wide range in the severity of clinical signs, to the lacking of pathognomonic signs and to the possible absence of clinical signs until adulthood. The description of congenital malformations aimed to focus on these rare pathologies in order to collect information and to monitor their presence and diffusion in the bovines, especially in the PRI breed where these CHDs were not previously reported.

KEY WORDS

Congenital heart diseases; Pezzata Rossa Italiana (PRI); calf.

INTRODUCTION

Congenital heart diseases (CHDs) in cattle are rare, accounting for approximately 0.17 % up to less than 3% of all congenital abnormalities. They represent a challenge both for the diagnosis and for the treatment (1- 4). Based on the type of malformation and the condition, the prognosis can vary from guarded to poor, since no specific treatment is available (1) and frequently euthanasia is required (2). Moreover, they can also affect adversely the zootechnical performance (5-6).
In general, congenital anomalies may have a genetic origin, due to the selection of a specific trait, propagating the defect or may be non-inherited defects. Among these latter, viral, toxicological, nutritional and hormonal causes are encountered (4, 5). Pathogenesis includes defective formation of the septa and of the cardiac chambers during the different phases of the embryonic development (3). Ventricular septal defects (VSDs) and atrial septal defects (ASDs) are reported to be the most common, followed by other different malformations such as double outlet right ventricle, aortic stenosis, and patent ductus arteriosus (PDA) (2, 3, 7-8). The aetiology is poorly understood, and the genetic basis of these conditions have not been fully elucidated yet (2).
CHDs cases are reported in different breeds, but only few are described in Simmental breed (9-14). In this report, we describe the *post mortem* findings in two cases of cardiac congenital anomalies affecting two Italian Simmental breed (Pezzata Rossa Italiana, PRI) calves. In the first case, the calf had congenital abnormalities of the heart and large vessels, associated with concurrent anomalies in the liver and in the brain, while the other calf presented congenital malformation of the heart only.

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CASE PRESENTATION

Case 1. A one-day-old male PRI was necropsied at the diagnostic laboratory in Udine (Istituto Zooprofilattico Sperimentale delle Venezie). Anamnestic data referred the birth was laborious, the calf (56 kg of weight) was depressed, reluctant to stand up and with an increased respiratory rate.

Pericardium was thin, shiny and bright red and contained a large clot obscuring the left heart. This clot originated from a solution of continuity, surrounded by a moderate hematoma, located at the base of the pulmonary artery (Fig. 1). The heart was pale, rounded in shape and, on the cross section, the left and right ventricular free walls, as well as the interventricular septum, were markedly thickened with almost complete obliteration of ventricular lumina (bilateral concentric hypertrophy). Moreover, ASD was observed. Finally, rare haemocysts on the margins of the atrioventricular valves (AV) were also noted. There was a mild increase of the cerebrospinal fluid within the lateral ventricles. The liver appeared smaller in size, with rounded margins and increased consistency. The diaphragmatic surface of the organ was multinodular with prominent and irregular white bands on the right lobe (Fig 2). Samples from heart, liver, brain, and spleen, were fixed in 10% neutral buffered formalin and routinely processed for histopathological examination. Histologically, the pulmonary trunk is characterized by focally extensive disruption and haemorrhage affecting the outer portion of the tunica media, the adventitia and the lining epicardium (Fig. 3). The haemorrhage extends to the epicardial adipose tissue surrounding the arterial root. Disrupted adventitial collagen fibers are multifocally necrotic and thin fibrin strands cover the epicardial surface. Scattered through the lesion are small colonies of coccobacillary bacteria. The liver is characterized by alteration of lobular architecture, with closer and irregular spacing of portal triads (lobular atrophy) and centrilobular veins. Mild fibrosis, ductular and arteriolar hyperplasia are also noted (Fig. 4). In the brain, the ependymal epithelium lining the lateral ventricles is multifocally flattened and occasionally lost, with microspongiosis and rare haemorrhages of the contiguous neuropil. Disseminated microhaemorrhages are observed in the splenic parenchyma.

Case 2. A fifteen-day-old female PRI calf was presented for the necropsy. Anamnestic data referred the animal suffered of en-

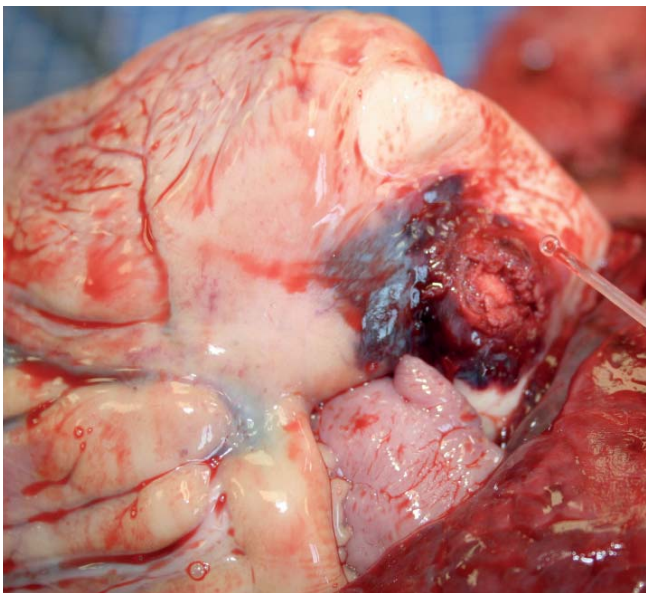

Figure 1 - Case 1. Pulmonary trunk partial rupture and haemorrhage of heart base adipose tissue.

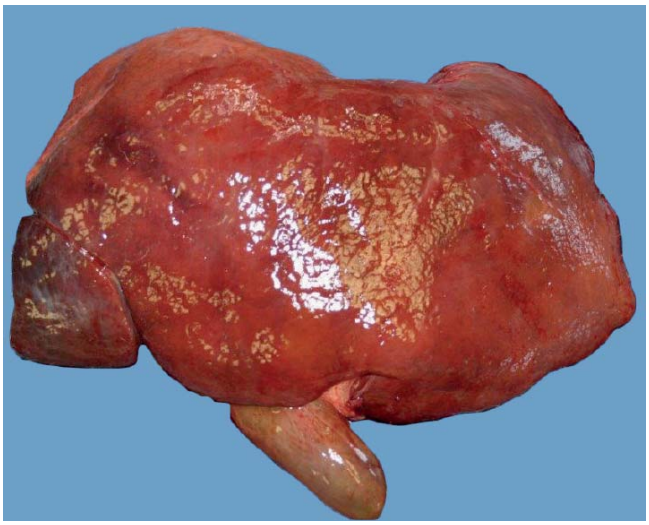

Figure 2 - Case 1. The liver appeared smaller, with rounded margins and irregular surface, with white bands on the right lobe.

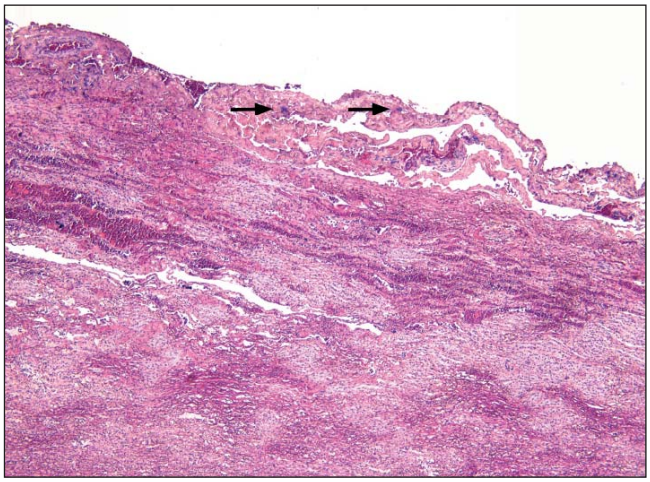

Figure 3 - Case 1. Histological aspect of the pulmonary trunk, with disrupted tunica media and adventitia. Haemorrhages, mild fibrinous exudation and necrosis of collagen fibers are seen, along with scattered coccobacillary colonies (arrows).

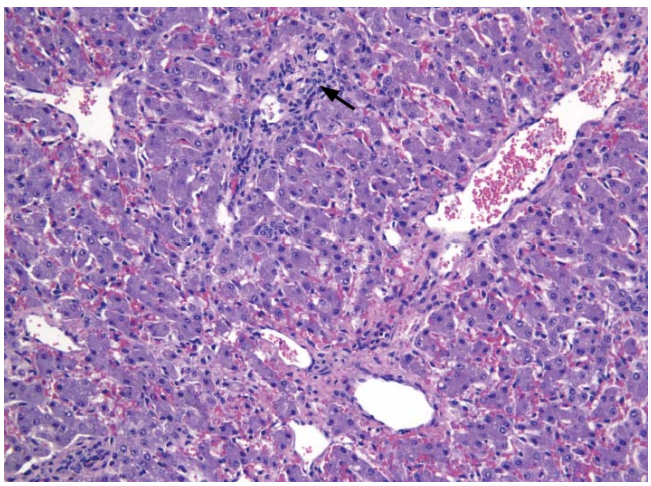

Figure 4 - Case 1. Histological aspect of the liver, characterized by severe alteration of lobular architecture, mild fibrosis and ductular hyperplasia (arrow).

teritis since the second week of life. Despite antibiotic treatment, the enteritis has worsened until the death. The animal was in moderate body condition. Main findings were observed in the cardiovascular system and in the digestive tract. The heart showed a mild right ventricular dilation, PDA, ASD (approximately 0.4 cm in diameter, in the lower part of the interatrial septum). Moreover, the septal cusp of the right AV valves was thickened and rare haemocysts were present. The base of the pulmonary trunk appeared moderately dilated. The small intestine presented a segmental catarrhal enteritis. Moreover, mild hepatomegaly was observed.

Samples from liver (case 1) and from liver, intestine and pericardium of the case 2 were submitted to bacteriological examination, following routine bacteriological procedure. Moreover, analyses for *Listeria* spp. from the medulla oblongata and for *Salmonella* spp. from the intestine were performed from case 1 and 2, respectively (15-16). Finally, molecular investigations for Schmallenberg virus (SBV), *Neospora caninum*, and *Toxoplasma gondii* were performed from brain samples and for Bovine Viral Diarrhea virus (BVDV) from spleen samples in case 1, following procedures previously reported in the literature (17-19).

Bacteriological cultures revealed *Escherichia coli* from intestine and liver of the case 2, while molecular tests were negative.

DISCUSSION

In this case report we describe 2 cases of CHDs in PRI calves. Case 1 pertains to a concurrent ASD and a bilateral cardiac concentric hypertrophy accompanied by partial rupture of the pulmonary trunk, and multiple organs malformations. In case 2, PDA and ASD were seen.

Reports of CHDs in Simmental calves are scarce and include a case of a combination of defects (*i.e.* ASD, VSD and PDA) and a case of *ectopia cordis* (20-21). A rare congenital syndrome, identified as pentalogy of Cantrell, characterized by different cardiac abnormalities (vessels displacement, PDA, VSD and increased thickness of the atrial septum) associated with anomalies in different organs, is also described by Floeck *et al.* The authors stated that the proposed pathogenesis in humans is a defect in embryogenesis between 14 and 18 days of gestation (22). In PRI, no previous cases of CHDs are described. With this regard, a previous case of dextroposition of the aorta has been previously observed (Cocchi, personnel information). In general, CHDs are described in different bovine breeds (1, 9-13, 20-23) with a low incidence (1- 4). VSD alone or in combination with other malformations, whether cardiac or in other organs, represents the main cardiac defect (2, 17, 24). While the connections between atria, ventricles and great vessels is physiologic during the foetal life, lacking of their closure in the perinatal period causes the development of ASD, VSD and PDA, respectively. These pathological conditions have different macroscopic findings and determine alterations of the blood flow, as well (25). In case 1, we may suppose that the hepatic alterations including atrophy and fibrosis, could have likely resulted in a vascular bed of increased resistance in this organ. This in turn, could have led to a redistribution of a significant amount of blood flow/pressure towards the *foramen ovale* into the left atrium and ventricle possibly explaining the development of myocardial hypertrophy. Moreover, it is not excluded that also the damage to the pulmonary trunk could have been caused by an increased resistance to the outflow towards the ductus arteriosus in the ascending aorta (25-26). In case 2, the persistence of ASD associated with PDA have caused alteration in the blood flow. In fact, PDA physiologically closes few hours or days after the birth. Its persistence causes different sequelae depending on degree of patency and the relationship between the pulmonary and systemic vascular resistance (25). In our case, the thickening of the septal cusp of the right AV and the mild dilation of pulmonary trunk may have led to an increased pressure, likely causing a mild flaccid right ventricle. CHDs can be hidden by compensatory mechanisms for months or even years. In this regard, VSD or, more rarely, the tetralogy of Fallot may go unnoticed until adulthood in cattle (1). In our cases, calf 2 ages 15 days and calf 1, affected by multiple defects, was 1 day-old.

Even if CHDs are uncommon in the bovine and the aetiology is not fully elucidated yet, some CHDs are genetically determined (2, 22). Heritability has been documented in Limousine with VSD (27), and in Grey Alpine with Ellis-van Creveld syndrome, which is characterized by concurrent ASD and left atrioventricular valvular dysplasia (28). Moreover, a case of hypospadias associated with VSD and caused by a chromosomal aberration, was described in a Holstein calf (29).

Other factors involved in the development of CHDs include viruses, nutritional deficiencies, and toxic plants (4, 30). BVDV, SBV, Blue Tongue virus (BTV) can lead to a wide range of congenital malformations. The most severe lesions involve the central nervous system, especially the brain, and the musculoskeletal system (30). In SBV infection, a small percentage of cases shows also VSDs (4). In our cases, no skeletal abnormalities were present and, in case 1, rRT-PCR for SBV resulted negative. In addition, in these farms the ongoing surveillance plans for BVDV and BTV tested negative.

CONCLUSION

This report highlights two CHDs in PRI. The description of congenital malformations aims to draw the attention of both, practitioners and farmers. In fact, collecting information is important not only because they are poorly described, but also because they could be connected to the reduction of genetic variability, due to the widespread use of *in vitro* fertilization (21).

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