Complex congenital heart defects in three Holstein Friesian calves

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SUMMARY

Congenital heart defects are uncommon in cattle, being reported a prevalence < 0.2% in two large necropsy studies, and the most frequently encountered anomalies are represented by ventricular and atrial septal defects. The aim of this article is to describe clinical, ultrasonographic and pathological findings of complex congenital heart defects in three calves of Italian dairy farms. The calves were examined for respiratory distress, stunted growth, or cardiac murmur. Clinical examination and echocardiography allowed to perform a diagnosis of ventricular septal defect associated to other congenital cardiac anomalies in all three calves. In case 1, a diagnosis of ventricular septal defect and complete transposition of the aorta and pulmonary artery was made. In case 2, an atrioventricular canal defect associated to persistent ductus arteriosus were diagnosed. A ventricular septal defect associated to atrial septal defect, dextroposition of the aorta and right ventricular hypertrophy were diagnosed in case 3. Echocardiographic findings were confirmed by *post-mortem* examination in all calves. Complex congenital cardiac defects represent a diagnostic challenge for veterinarians, but an accurate clinical and echocardiographic examination can be useful for an *ante-mortem* diagnosis and prognosis. Clinical signs as weakness, respiratory distress and heart murmur associated to a history of failure to thrive or respiratory disease unresponsive to appropriate therapy, are common in calves with congenital heart defects. Echocardiography is a readily available diagnostic tool and can be performed in veterinary hospitals as well as in farms. An *ante-mortem* diagnosis of congenital heart defects can be useful to discriminate between isolated anomalies, frequently characterized by a favourable prognosis, and complex anomalies, characterized by a guarded to poor prognosis. Finally, our case series can be important to update current knowledge of the complex congenital heart defects in cattle: atrioventricular canal defect and aneurismal dilation of Valsalva sinus associated to ventricular septal defect have been never reported in cattle.

KEY WORDS

Cattle; ventricular septal defect; great vessels transposition; atrioventricular canal defect; echocardiography.

INTRODUCTION

Congenital heart defects (CHD) are relatively rare in cattle, being reported a prevalence of 0.17% in two large necropsy studies[1,2]. Most frequently encountered CHD are represented by ventricular (VSD) and atrial (ASD) septal defects[1-4]. Complex CHD, such as tetralogy of Fallot, transposition of the great vessels (TGV) and double outlet right ventricle, are occasionally reported in this species[3,5-7].

Congenital heart defects have been described in cattle of Italian farms in few reports[7-9], and these mainly provided pathological findings with very limited details about clinical presentation and ultrasonographic findings of affected animals. The aim of the present report was to describe the clinical, ultrasonographic and pathological findings of complex CHD in three calves of Italian dairy farms.

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CASES PRESENTATION

Case n. 1

An 8-week-old female Holstein Friesian calf was examined for respiratory distress and stunted growth at the Veterinary Teaching Hospital of Perugia University. On presentation, the calf showed a temperature of 38.8° C, tachycardia with regular heart rate (130 beats per minute), dyspnea with respiratory rate of 45 breaths per minute, and cyanotic mucous membranes, especially evident when she was coaxed to move for a short distance. On thoracic auscultation, increased and harsh respiratory sounds were present bilaterally and a grade 4/6 systolic murmur was clearly audible over the left and right hemithoraces (point of maximal intensity over the tricuspid valve area and over the great vessels area). No other abnormalities were identified. Echocardiographic exam revealed enlargement of the right ventricle, hypertrophy of the right ventricular wall and a subvalvular VSD of approximately 1-1.5 cm in diameter (Figure 1A). Right parasternal long axis view of the left ventricular outflow tract displayed a great vessel arising from the left ventricle and, in parallel alignment, a second great vessel leaving

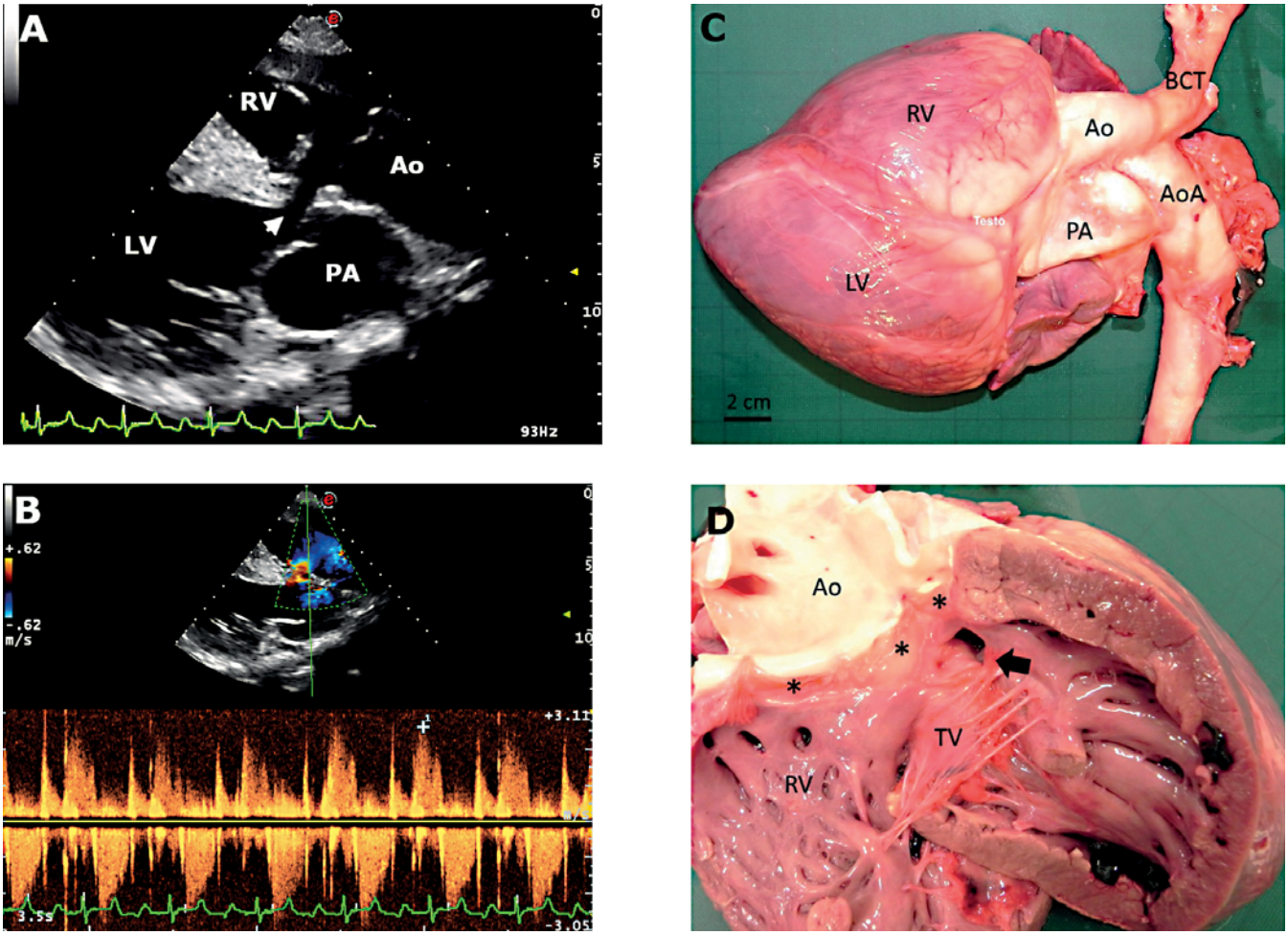

Figure 1 - Echocardiographic and gross findings in case n. 1. (**A**) Right parasternal long axis view of the left ventricular outflow tract displaying a subvalvular ventricular septal defect (arrowhead). Note the great vessels (Ao - aorta and PA - pulmonary artery) arising from ventricles in parallel alignment, suggesting an anomaly of the right ventricular outlet position. (**B**) Bi-directional, turbulent flow through the ventricular septal defect is recorded by spectral Doppler. Direction of flow is left to right during diastole and right to left during systole. (**C**) Gross appearance of the heart showing enlarged right ventricle (RV) and two parallel vessels arising from the heart base, the aorta (Ao) and Pulmonary Artery (PA). (**D**): Open right ventricle (RV), with large outlet ventricular septal defect (arrow) just below semilunar valves (asterisk) near the tricuspid valve (TV). BCT, brachiocephalic trunk; AoA, aortic arch; LV, left ventricle.

the right ventricle, suggesting an anomaly of the right ventricular outlet position (Figure 1A). The two great vessels were differentiated by identifying the coronary arteries arising from the aorta (the great vessel that leaved the right ventricle) and the left and right pulmonary arteries arising from the main pulmonary artery (the great vessel that leaved the left ventricle). Colour and spectral Doppler revealed bi-directional, turbulent flow through the VSD (Figure 1B). A diagnosis of subvalvular VSD with bidirectional blood flow and complete transposition of the aorta and pulmonary artery was made. Based on the severity of the clinical signs, echocardiographic findings, and prognosis, humane euthanasia was elected by the calf's owner.

On post-mortem gross examination, the heart was moderately enlarged mostly in right ventricular silhouette; two large vessels emerged from the base running parallel; the anterior emerged from right ventricle and about 10 cm from the origin branched in a large brachiocephalic trunk. The arterial trunk arising from left ventricle suddenly branched into two main (left and right) pulmonary arteries (Figure 1C). The coronaries arose from the aortic sinus in front of the pulmonary trunk. The atria were moderately enlarged as were the ventricular lumina, with thickening of the right ventricular wall (eccentric hypertrophy due to volume overload); the communication between right and left circulations was allowed by a patent *foramen ovale* and a large outlet muscular VSD (Figure 1D). The ductus arteriosus was regularly regressed with complete anatomic closure.

Case n. 2

An 8-week-old male Holstein Friesian calf was examined for a cardiac murmur in a dairy farm of Umbria (Central Italy). At physical examination, the calf showed a temperature of 38.7° C, regular heart rate (110 beats per minute), normal breathing (40 breaths per minute) and pale mucous membranes. On thoracic auscultation, increased respiratory sounds were present bilaterally. Cardiac auscultation revealed a grade 4/6 continuous murmur in the left axillary region and a grade 4/6 systolic murmur over the tricuspid valve area. No other abnormalities were identified. Echocardiographic examination showed dilation of all 4 cardiac chambers with a ventricular communication (1.5 cm) below the atrioventricular valves and an atrial communication (1.5 cm) adjacent to the atrioventricular valves (Figure 2A). Atrioventricular valves were abnormal with shortened septal leaflets anchored to the dorsal portion of the ventricular septum by short chordae tendineae.

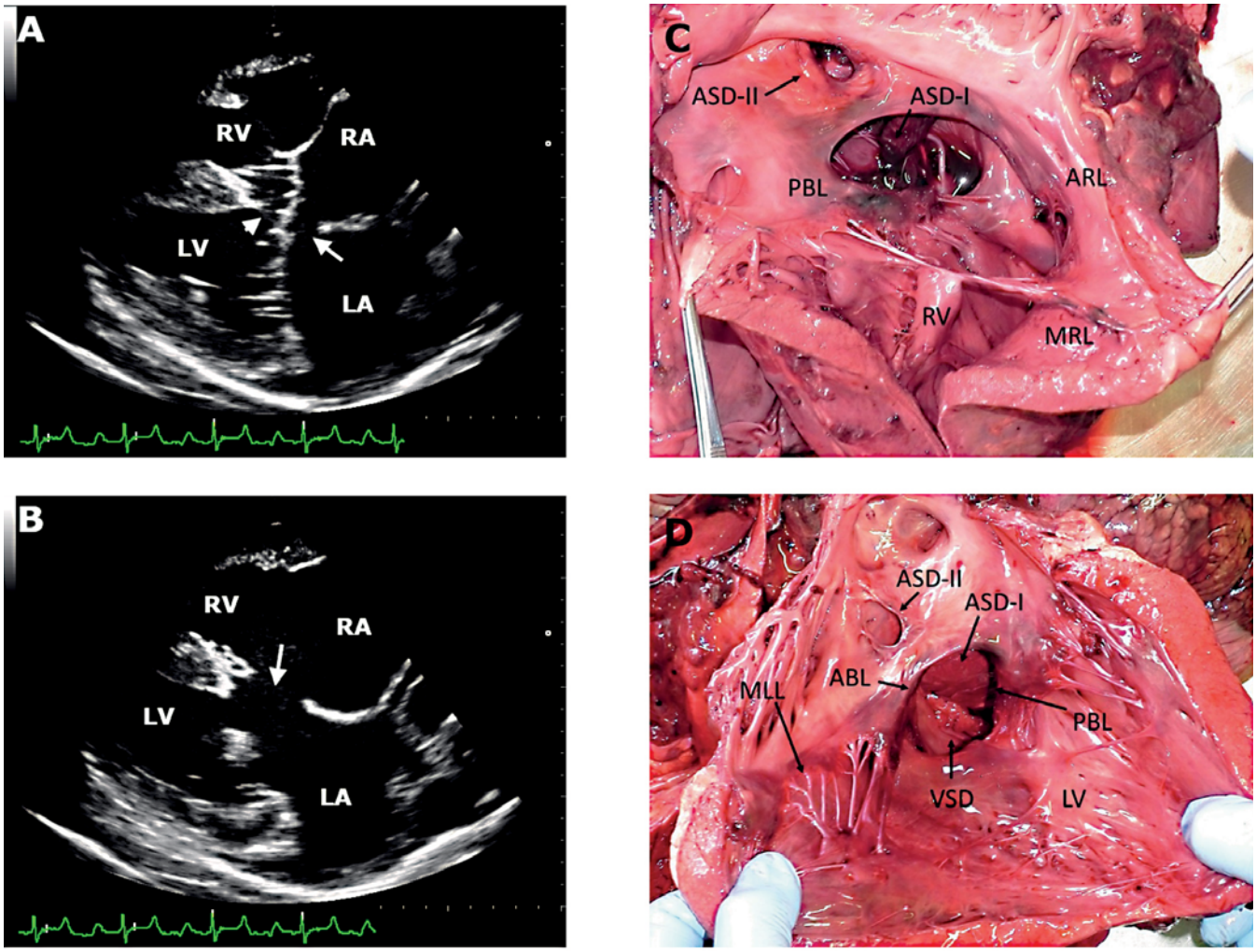

Figure 2 - Echocardiographic and gross findings in case n. 2. (**A**) Right parasternal long axis four chamber view showing a ventricular communication below the atrioventricular valves (arrowhead) and an atrial communication adjacent to the atrioventricular valves (arrow). Note the shortened septal leaflets anchored to the dorsal portion of the ventricular septum by short chordae tendineae. (**B**) Right parasternal long axis four chamber view with opened atrioventricular valves showing an evident anomaly (arrow) occurring at the site of the atrioventricular septum. (**C**) Right and (**D**) left views showing a large ostium primum-type ASD (ASD-I), a smaller upper ostium secundum-type ASD (ASD-II) and a large ventricular septal defect (VSD); single valvular orifice is present, bordered by posterior bridging leaflet (PBL), mural right leaflet (MRL), anterosuperior right leaflet (ARL), mural left leaflet (MLL) and anterior bringing leaflet (ABL). RV, right ventricle; RA, right atrium; LV, left ventricle; LA, left atrium.

At the level of the heart base, the diameter of the pulmonary artery was increased compared with the aortic cross-sectional diameter with normal pulmonic valve. A jet of regurgitation across the mitral and tricuspidal valves and left-to-right turbulent flow through VSD was observed by colour and spectral Doppler (Figure 2B). Turbulent and retrograde flow in the main pulmonary artery compatible with persistent ductus arteriosus (left-to-right shunt) was also observed by Doppler. Based on clinical and echocardiographic findings, a diagnosis of atrioventricular canal defect associated with persistent ductus arteriosus was made. The calf remained in the farm until 7 months of age when he suddenly died. Necroscopy was performed.

On post-mortem gross examination, there was moderate amount of serous effusion in the abdominal cavity, and the liver showed moderate enlargement with bump, irregular, from yellowish to dark red in color appearance, that on cut surface corresponded to pale areas admixed with the brownish ones ("Nutmeg liver"). Lungs were pale and glistening with widened interlobular septa. The heart showed a predominantly right-sided ventricular enlargement due to lumen dilation with moderate thickening of the right ventricle's free wall (eccentric hypertrophy). Both atrial lumens appeared dilated. Inside the heart a large inlet VSD including both membranous and muscular component of interventricular septum and a large ASD in the lower part of the interatrial septum (ostium primum-type), together with a smaller ostium secundum-type ASD in the upper part of the septum, were present (Figure 2C). The former two defects were across a large, unique atrioventricular orifice bordered by a common atrioventricular valve formed by two bridging leaflets, posterior (or inferior) and anterior (or superior), that overridden the ventricular septum, a left mural leaflet, a right anterosuperior mural and a right mural one. The chordae tendineae were shortened and thinned, several of them attaching the superior bridging leaflet to the papillary muscles of each ventricle, while others connecting the posterior bridging leaflet both to the crest of the ventricular septum and to the posterior papillary muscles of each ventricle (Figure 2D). The ductus arteriosus was patent. The gross findings suggested a complete (Rastelli A type) atrioventricular canal defect.

Case n. 3

A 40-week-old female Holstein Friesian calf was examined for stunted growth in a dairy farm of Umbria (Central Italy). At physical examination, the calf showed a temperature of 38.5° C, regular heart rate (70 beats per minute) and normal breathing (30 breaths per minute). On cardiac auscultation, a grade 3/6 systolic murmur was clearly audible over the right hemithorax and a grade 3/6 diastolic murmur was audible over the left hemithorax at the heart base. No other abnormalities were identified. Echocardiographic examination documented a large VSD (3.7 cm) localized in the dorsal part of the septum and an ASD (3 cm) localized in the dorsal portion of the interatrial septum. The aorta was dextrally located, beyond VSD, and right-sided cardiac chambers were enlarged with thickened right ventricular free wall (Figure 3A).

A jet of aortic regurgitation and left-to-right turbulent flow through VSD was observed by colour and spectral Doppler (Figure 3B). No morphological anomalies and turbulent flow were detected in the right ventricle outflow tract and pulmonary artery. Given the severity of the cardiac abnormalities, the calf was slaughtered and only the heart was submitted to *post-mortem* examination.

Before cutting the heart, a dorsal view through the aortic orifice allowed to see the ventricular muscular edge of VSD and both tricuspid and mitral valve, suggestive of dextroposition of aorta (overriding aorta) (Figure 3C). Then, examination of formalin-fixed heart was performed with a four-chamber cut; right ventricular free wall appeared severely thickened, being equal in thickness to left ventricular free wall, and the lumen was restricted (concentric hypertrophy); an apical, inlet VSD of about 2 cm in width was also evident; a smaller, ostium secundum-type ASD was also present, even if less easily to detect due to coartation of formalin-fixed tissues (Figure 3D). The left coronary Valsalva sinus of the aortic valve was dilated (aneurysm) with irregular surface. The right ventricular outlet tract was apparently normal.

DISCUSSION

Ventricular septal defects, either as isolated malformations or in connection with other anomalies characterizing a complex malformation, are the most commonly reported CHD in cattle [1,4-6,10-13]. Calves of this report showed complex CHD in which VSD was associated with other cardiac anomalies. Some of these anomalies have been never reported in cattle.

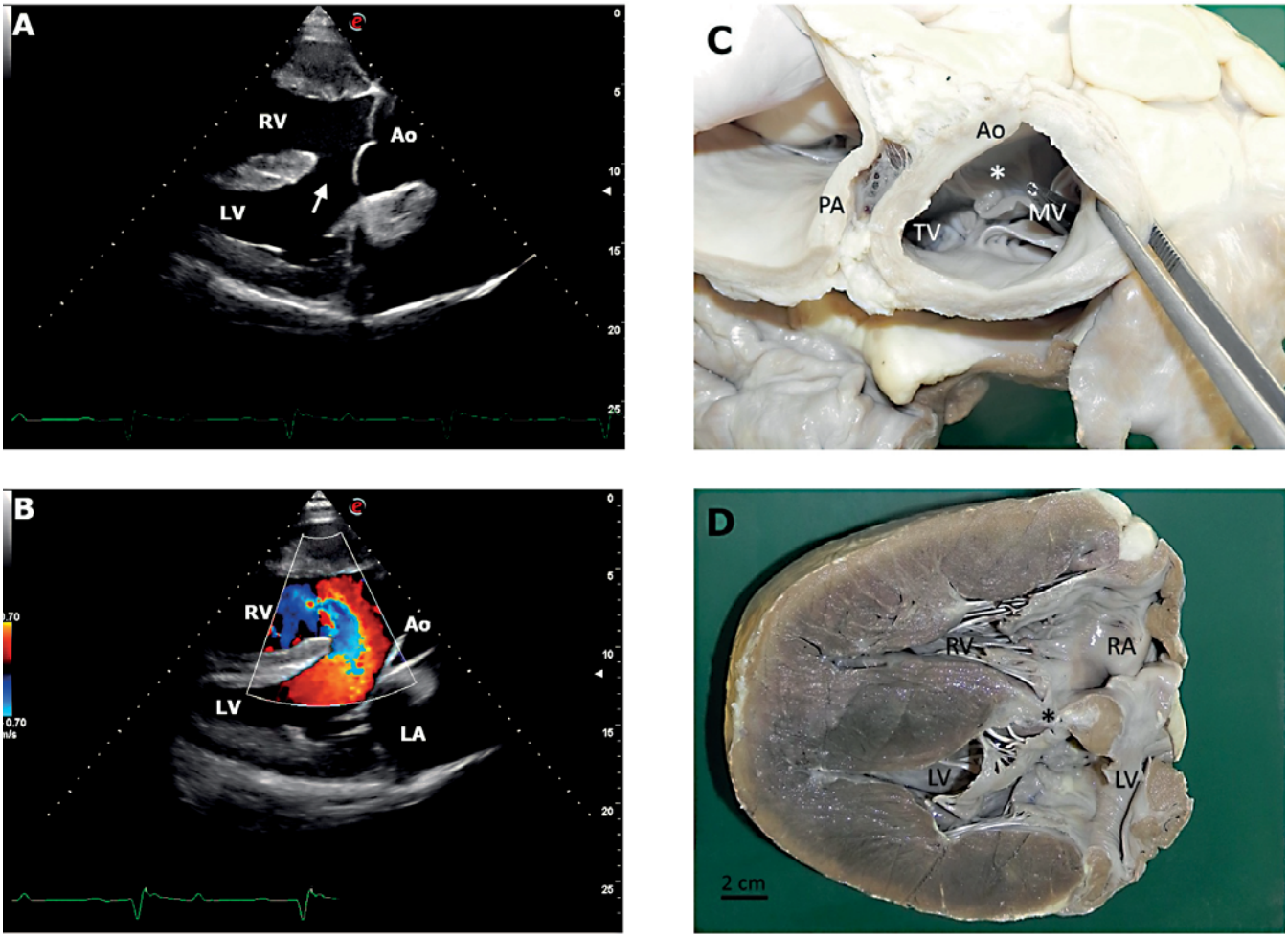

Figure 3 - Echocardiographic and gross findings in case n. 3. (**A**) Right parasternal long axis view of the left ventricular outflow tract showing large ventricular septal defect, dextrally located aorta (Ao), enlarged right ventricle (RV) and thickened right ventricular free wall. (**B**) Colour flow mapping indicates end-systolic flow across the defect. (**C**) Dorsal view through overriding aorta (Ao) showing both mitral (MV) and tricuspid (TV) valves, with enlarged Valsalva sinus (asterisk). (**D**) Four chamber view showing a ventricular septal defect (asterisk). LV, left ventricle; LA, left atrium; PA, pulmonary artery.

In case 1, VSD was associated to TGV. This complex CHD is characterized by atrioventricular concordance and ventriculoarterial discordance, that is to say that the aorta arises from the right ventricle and the pulmonary artery from the left ventricle, due to absence of the normal 180° rotation of the great vessels during development. The double close parallel circulation that follows, is incompatible with life without associated left to right shunting, that can result most commonly via VSD, but also via ASD or Patent Ductus Arteriosus (PDA)[14]. Transposition of the great vessels has been previously described in cattle and VSD was identified as connection between systemic and pulmonary circulation[6,15]. In our case, interatrial communication via a patent *foramen ovale* was also identified as connection between systemic and pulmonary circulation.

In case 2, VSD was part of a complex anomaly occurring at the site of the atrioventricular septum and commonly described as atrioventricular canal defects or endocardial cushion defects. This complex anomaly can present 4 types: complete, partial, intermediate and transitional, according to the location of ASD and VSD and to the morphology of atrioventricular valve (number of orifices and site of insertion of chordae tendineae)[16]. In the reported calf, the anomalies observed (ostium primum ASD, large VSD and common atrioventricular valve with single orifice) were compatible with a complete atrioventricular canal defect. Atrioventricular canal defects have been reported in humans, cats, dogs and horses, but never in cattle[16-19].

In case 3, VSD was associated to ASD, dextroposition of the aorta and right ventricular hypertrophy. During embryonal life, the conotruncal septum forms the dorsal portion of the interventricular septum, but if this does not occur, a VSD results [10-11]. Ventricular septal defect, overriding aorta and right ventricular hypertrophy are component of the tetralogy of Fallot[20], that also include stenosis of the right ventricular outflow tract; this latter malformation was not present in the case 3. The aneurismal dilation of sinus of Valsalva is a rare anomaly that is frequently associated in human patients with VSD and can be cause of anomalous heart murmur[21] and possibly to aortic regurgitation due to prolapse of enlarged leaflet into VSD[22]; in this case no other cause of aortic regurgitation has been identified, but this association remains speculative.

In all the three cases a moderate to marked right ventricular hypertrophy was present; it was of the eccentric type in cases 1 and 2, while it was concentric in case 3. In cases with left to right shunting, the right ventricle undergoes eccentric hypertrophy induced by volume overload, as occurred in case 2; with time, arterial pressure increases in pulmonary circulation, also due to remodelling of pulmonary arterioles, and this pressure overload induces right ventricle concentric hypertrophy, as seen in case 3, that was the only calf to survive enough time to allow this hemodynamic adaptation; unfortunately, in that case, lungs were not submitted to examination to confirm this hypothesis.

The aetiology of CHD is still under investigation in humans and animals: heritability, maternal or fetal infection, fetal anoxia secondary to placental insufficiency and metabolic dysfunction have been reported as factors that can contribute to the development of CHD[3,23]. Heritability has been reported in the Limousine and Herford breed affected by VSD[3,10]. Genetic predisposition is also reported in Jersey cattle[24], while in other dairy breeds, no information is currently available on possible genetic implications. In the present report, the cause of CHD described in the three calves is unknown.

Clinical signs reported in the three calves of this report were different among themselves: in the first case, respiratory distress and cyanosis were predominant because of mixing of deoxygenated with oxygenated blood via the VSD/patent *foramen ovale* and enabling adequate oxygenated blood to reach the body via the transposed aorta; in the second case, increased respiratory sounds at thoracic auscultation were a result of pulmonary volume overload from left-to-right shunting; in the third case, stunted growth was only observed. In all 3 calves, heart murmurs were clearly audible. The clinical findings observed in calves of this report are in accordance with those described from other authors: indeed, a diagnosis of CHD in cattle is suspected when clinical signs as weakness, respiratory distress and heart murmur are present[3,10,25,26]; a history of failure to thrive and/or respiratory disease unresponsive to appropriate therapy is also reported[6,26,27].

Echocardiography is a safe and non-invasive imaging technique that can be useful to confirm or rule out the presence of CHD in cattle[25-27]. Moreover, this diagnostic tool is readily available and can be performed in veterinary hospitals as well as in farms. In calves of this report, echocardiography allowed to obtain the definitive diagnosis of CHD, although calves were affected by complex CHD. All echocardiographic findings were confirmed by *post-mortem* examination. An accurate diagnosis and assessment of CHD severity can be useful in calves affected by isolated defects, which can be associated with a favourable prognosis. Conversely, complex CHD have a guarded to poor prognosis, frequently associated with stunted growth and poor productive performance, and often leading to sudden death[25,28].

In conclusion, this case series described clinical, ultrasonographic and pathological findings of complex CHD in calves of Italian dairy farms. Complex CHD can be a diagnostic challenge for veterinarians and imaging tools, as ultrasonography, can be useful for the diagnosis and prognosis. Finally, our report can be important to update current knowledge of the complex CHD in cattle.

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Conflict of Interest

The authors declare that there were no conflicts of interest.

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