Journal of Veterinary Cardiology (2019) **21**, 28—33

Journal of Veterinary Cardiology ESVC

www.elsevier.com/locate/jvc

Case Report

Tricuspid valve dysplasia and a patent foramen ovale resulting in severe tricuspid regurgitation and right-heart dilation in a Red Angus calf☆

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Received 24 March 2018; received in revised form 12 October 2018; accepted 26 October 2018

KEYWORDS
Bovine;
Congenital heart defect;
Echocardiography

Abstract A two-month-old Red Angus heifer calf presented to the University of Wisconsin Veterinary Care for evaluation of suspected severe bronchopneumonia. Pertinent physical exam findings included tachycardia, tachypnea, dyspnea with a significant abdominal component, and cyanotic mucous membranes. On thoracic auscultation, wheezes were present bilaterally, as well as a grade 2/6 right apical systolic murmur. Thoracic radiographs revealed cardiomegaly, most severely affecting the right side. Echocardiography showed tricuspid valve dysplasia, resulting in severe tricuspid regurgitation and right-heart dilation, as well as a patent foramen ovale. A postmortem examination confirmed the presence of the aforementioned cardiac abnormalities and revealed only mild pulmonary changes. This

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https://doi.org/10.1016/j.jvc.2018.10.005

case report is the first to describe tricuspid dysplasia in the absence of multiple, complex congenital cardiac abnormalities in a calf, and it highlights the value of echocardiography for an antemortem diagnosis.

A two-month-old Red Angus heifer twin calf was presented to the University of Wisconsin for evaluation of suspected severe bronchopneumonia. The calf had been maintained on pasture with its dam since birth and had been apparently healthy until three days before presentation, when the owner first noticed an increased respiratory rate and effort. Bronchopneumonia was suspected and the heifer was treated with danofloxacin and sulfadimethoxine. The calf was also vaccinated against *Clostridium perfringens* types C and D and received tetanus toxoid at that time. Over the following 48 h, the clinical signs progressed to dyspnea, recumbency, and cyanosis on the morning of presentation. Before referral, the primary care veterinarian examined the animal and administered dexamethasone and tripelennamine.

On presentation at the University of Wisconsin Veterinary Care Large Animal Hospital, the calf weighed 55 kg, was recumbent, depressed, and dyspneic, with a significant abdominal component to the breathing pattern. The initial physical examination revealed a temperature of 38.1 °C, heart rate of 120 beats per minute, respiratory rate of 40 breaths per minute, and cyanotic mucous membranes. On thoracic auscultation, wheezes were present bilaterally and a grade 2/6 right-sided apical systolic murmur. The heart rhythm was regular. No other abnormalities were identified. Supplemental oxygen via a nasal cannula at 5 L/min was initiated.

A complete blood count showed polycythemia, with anisocytosis, poikilocytosis, red cell crenation and some smudge cells, with an otherwise normal leukogram (Supplementary Table A, data available in Supplemental Material online). A serum biochemistry profile revealed mild hypokalemia, hypocalcemia, decreased total CO_2, slight hyperphosphatemia, hypermagnesemia, hyperglycemia, hyperproteinemia due to hyperalbuminemia, and increased urea nitrogen, creatine kinase, aspartate aminotransferase, glutamate dehydrogenase, and gamma glutamyl transferase (Supplementary Table B, data available in Supplemental Material online). Clinically significant findings were consistent with dehydration and prerenal azotemia, stress, and myopathy associated with prolonged recumbency and poor peripheral perfusion. An arterial blood gas test, obtained from the auricular artery with a 25G, 5/8 inch needle and a 1 mL preheparinized syringe while on supplemental nasal oxygen, revealed respiratory acidosis (Supplementary Table C, data available in Supplemental Material online).

Thoracic radiographs showed marked enlargement of the cardiac silhouette on all views, most severely affecting the right side, with a globoid shape on the ventrodorsal view (Fig. 1), in which the cardiac width spanned four intercostal spaces and occupied approximately 100% of the width of the thoracic cavity on the ventrodorsal projection. The trachea was dorsally displaced cranial to the carina, consistent with right atrial enlargement. In addition, an alveolar pattern was present over the cranioventral lung fields, and a moderate bronchointerstitial pattern could be identified over the caudodorsal lung fields. Atelectasis, due to cardiomegaly, and mild bronchopneumonia were both

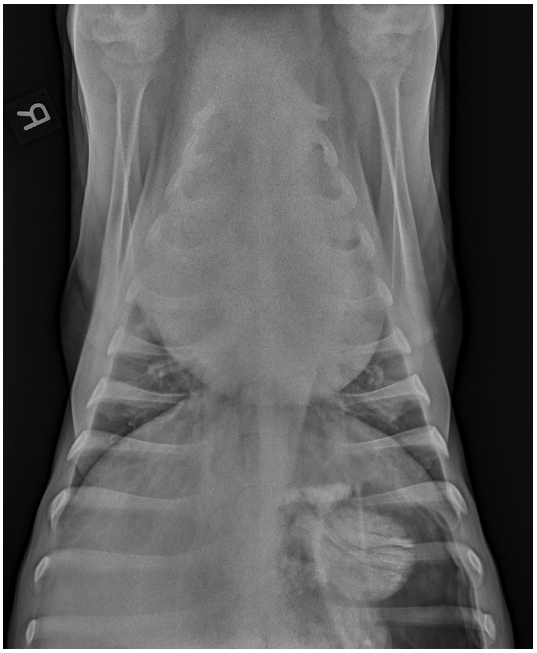

Fig. 1 Ventrodorsal radiograph of the thorax. Marked enlargement of the cardiac silhouette, most severely affecting the right side. Note the globoid shape of the heart, which occupies approximately 100% of the width of the thoracic cavity. The margins of the cardiac silhouette are crisp and well delineated.

considered, with atelectasis being more likely given the normal leukogram and globulin values.

The clinical and radiographic findings prompted an echocardiogram, which confirmed the presence of a severely enlarged right atrium. The coronary sinus also appeared dilated, and there was a small amount of flow across the interatrial septum, indicative of a patent foramen ovale. The right ventricle was also markedly enlarged, but overall normal systolic function was present. The tricuspid valve appeared malformed, with thickened, tethered leaflets, and incomplete coaptation, leading to severe tricuspid regurgitation (Fig. 2). The peak velocity of the tricuspid regurgitation jet was 3.86 m/s. The diameter of the pulmonary artery in the short axis was increased (37 mm) compared with the aortic cross-sectional diameter in the same view (28 mm), with a pulmonary artery-to-aorta ratio of 1.3. The pulmonic valve was normal; however, moderate regurgitation was present (2.95 m/s). The left atrium and mitral valve were normal, with trivial mitral regurgitation identified. The left ventricular diameter in diastole was decreased at 37.59 mm (reference interval 50.1—54.3 mm), with a normal left ventricular posterior wall thickness at the end diastole of 11.38 mm (reference interval 10.4—11.4 mm), normal left ventricular systolic function and a thickened interventricular septum (16.55 mm in systole, reference interval 18.0—19.4 mm; 13.97 mm in diastole, reference interval 12.4-13.6 mm) as per weight-based ranges[d]. There was marked septal flattening, particularly during diastole, suggestive of increased volume loading of the right ventricle. The aortic valve was normal, with expected outflow velocity, but mild aortic regurgitation was also present (5.19 m/s). Finally, the coronary sinus appeared dilated, potentially secondary to an increased right atrial pressure (Supplementary Table D, data available in Supplemental Material online). Based on the severity of the clinical signs, echocardiographic findings, and prognosis, humane euthanasia was recommended and elected by the owners.

On postmortem gross examination, the heart weighed 0.71 kg (1.3% body weight, reference 0.48%[e]) and the right ventricular wall, left ventricular wall, and the ventricular septum measured 1, 2, and 1.8 cm in thickness, respectively (Supplementary Table E, data available in Supplemental Material online). Gross measurements of both ventricular walls demonstrated a normal ratio of 1:2. The right atrium and ventricle were markedly dilated, and the tricuspid valve was dysplastic, with the septal leaflet tethered to the interventricular wall (Fig. 3), confirming the

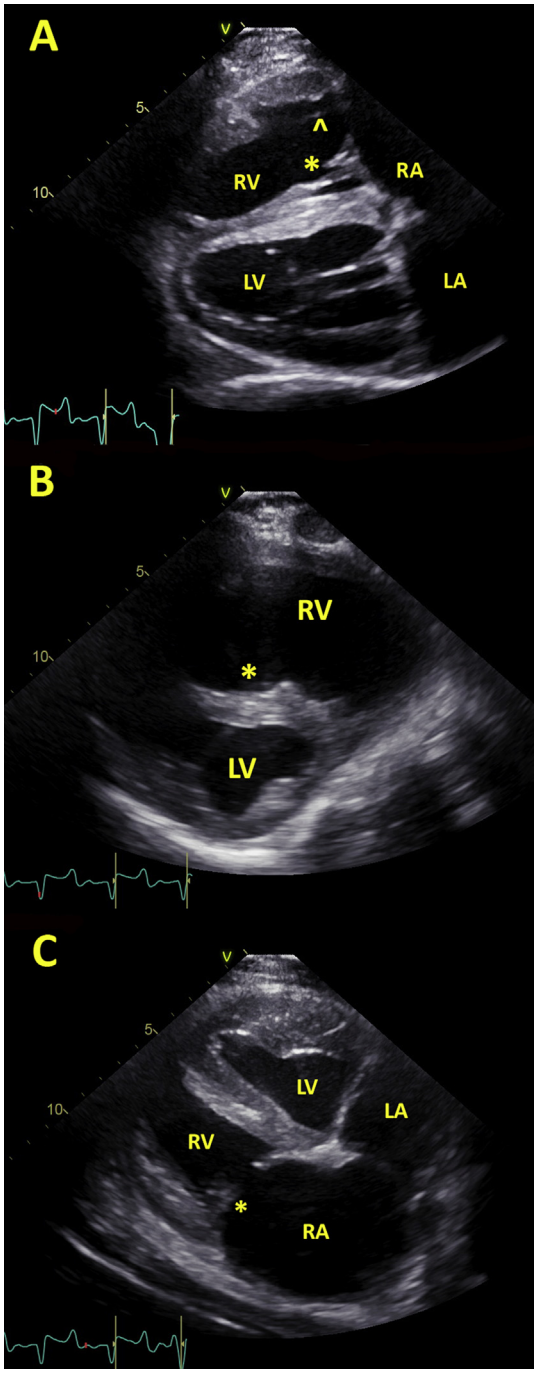

Fig. 2 Echocardiography of dysplastic tricuspid valve and secondary cardiac changes.2-D transthoracic echocardiography. (A) Right parasternal, long-axis, four-chamber view demonstrating the thickened and tethered septal tricuspid valve leaflet (asterisk) and tethered mural leaflet (arrowhead). (B) Right parasternal, short-axis, apical view showing the severe right ventricular dilation. Asterisk denotes the moderate-to-severe diastolic flattening indicative of volume overload. (C) Left parasternal, long-axis, four-chamber view displaying the right atrial and ventricular dilation with an asterisk indicating the thickening of the mural tricuspid valve leaflet.

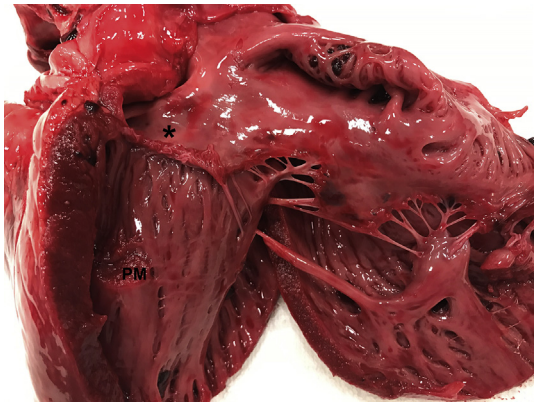

Fig. 3 Postmortem image of dysplastic tricuspid valve. Marked tricuspid valve dysplasia. Asterisk denotes the septal leaflet of the tricuspid valve adhered to the interventricular wall. Note the detached chordae tendineae present at the septal leaflet. PM, area of attachment of a papillary muscle (sectioned during necropsy).

echocardiographic findings. There was a 5 mm opening between the right and left atrium, consistent with a patent foramen ovale. A 3 mm-by-4.5 mm, oblong-shaped, soft, well-demarcated, dark red hematocyst was also identified on the posterior leaflet of the mitral valve and considered a normal variant. At the level of the pulmonary valve, there was a single, firm, thin pink band, approximately 1 cm cranial to the leaflets, which extended across the width of the pulmonary artery. Bilaterally the cranial lung lobes were dark red and atelectatic.

Histologic lesions corresponded with the gross findings and included multifocal cardiomyocyte hypertrophy, multifocal cardiomyocyte degeneration with fibrosis, focal subintimal and tunica media fibrosis of the main pulmonary artery, and multifocal atelectasis, more severely affecting the right cranial lung lobe, with minimal bronchitis. No changes associated with pulmonary hypertension were seen histologically.

Discussion

Tricuspid valve malformation is a rare congenital heart disease (CHD) that has been reported in both humans and animals, including dogs, cats, goats, and horses [1—6]. The only report of tricuspid valve dysplasia (TVD) that the authors could find in the literature was as a coincident finding in a calf with multiple severe congenital defects, including a double outlet right ventricle and a hypoplastic left ventricle [5]. Tricuspid valve malformations can present in conjunction with other cardiac anomalies in other species [1—8]. As a broad term, tricuspid valve malformation encompasses two distinct types of defects involving the tricuspid valve, namely Ebstein's anomaly and TVD. In the case of Ebstein's anomaly, there is apical displacement of the valve toward the right ventricular outflow tract, with incomplete delamination of the septal and inferior leaflets. In addition, the right ventricle rarely has normal morphology and function [1]. In TVD, there is leaflet deformation without valve displacement from the level of the true tricuspid annulus. The leaflets are thickened and may have flail segments with broken chordae, which prevents complete coaptation and leads to significant tricuspid regurgitation. However, the myocardium of the right ventricle is usually normal [1]. Although morphologically different, these malformations lead to an identical hemodynamic consequence—tricuspid regurgitation, progressive right atrial enlargement, right ventricular dilation with eventual reduction in systolic function, and right-to-left shunting at the level of the atrial septum [1].

In cattle, the incidence of CHD is approximately 0.7%, with ventricular septal defect being the most common anomaly [9—11]. Other multiple congenital defects such as atrial septal defect, double outlet right ventricle, aortic stenosis, patent ductus arteriosus, and tetralogy of Fallot have been described in this species [9,10]. The cause of CHD in animals is yet to be established. Heritability has been documented in Limousine cattle with ventricular septal defects [12]. Other factors may contribute to the development of CHD including maternal infection, age and nutritional status, fetal anoxia from placental insufficiency, fetal infection, or metabolic dysfunction [13]. In dogs, TVD represents 2%—5% of CHD and is more prevalent in Labrador retrievers, Golden retrievers, German shepherds, and English bulldogs [2,8,14]. It is a heritable condition in Labrador retrievers and suspected to be heritable in other large dog breeds as well [14].

To the authors' knowledge, this is the first report describing TVD as the main congenital abnormality in a calf. The clinical signs of tachypnea, weakness, and the presence of a right-sided systolic murmur presented by this particular calf are in accordance with what has been previously described in several forms of heart disease in cattle [10,13]. Multiple parallels can also be established between the clinical presentation of TVD in this calf and human neonates with tricuspid valve malformations. Human neonates with severe Ebstein's anomaly or TVD may exhibit cyanosis due to right-to-left shunting across a patent foramen

ovale. In this case, the patent foramen ovale confirmed in the postmortem examination was likely a persistent congenital defect rather than purely secondary to increased blood flow and pressure within the right atrium as a result of TVD. Atrial septal defects, and more specifically patent foramen ovale, are relatively common in calves [5,12,13]. Human neonates may also present with increased pulmonary vascular resistance and massive cardiomegaly leading to pulmonary hypoplasia [1]. The cardiomegaly, initially diagnosed radiographically in this patient, was significant, with a vertebral heart score of approximately 10—10.25 vertebrae (reference interval 8.0—9.0 vertebrae) that is predictive of CHD in calves [15]. This likely led to atelectasis, which may have contributed to cyanosis by inducing ventilation perfusion mismatch and pulmonary shunting. The respiratory acidosis, hypercapnia, and sub-optimal oxygen saturation on oxygen insufflation noted in the antemortem examination were considered most likely reflective of the significant atelectasis and poor lung function confirmed at the postmortem examination. Based on the analysis of the tricuspid regurgitation, jet velocity—determined pressure gradient obtained echocardiographically, and by comparing it to canine models, pulmonary hypertension was also suspected [16]. However, this was not corroborated by histologic findings, because of the lack of changes to the pulmonary arteriolar tree. On the other hand, the significance of the fibrosis of the main pulmonary artery and the presence of a thin band at the level of the pulmonary valve are unknown. We cautiously speculate that this may have represented an additional congenital abnormality, although it did not likely contribute significantly to cardiac dysfunction because measured pulmonary arterial outflow velocities were not elevated.

In cattle, CHD has a guarded to poor long-term prognosis and can be associated with sudden death, stunted growth, and poor reproductive performance, often leading to euthanasia or early culling, given the lack of specific treatments available for this species [10,15]. This calf originated from a commercial beef farm; thus, humane euthanasia was elected by the owners.

In species in which this anomaly is more frequently identified, medical and surgical treatment options are available. Bioprosthetic valve replacement has been successfully performed in dogs [14]. In humans, the overall perinatal mortality in fetuses with Ebstein's anomaly or TVD is 45%, and fetuses with pulmonary regurgitation are at increased risk for mortality [17]. Valve repair, bioprosthetic valve replacement, interventional catheterization, and cardiac transplantation are some of the available surgical procedures [1,17].

Echocardiography has been considered the gold standard for the diagnostic evaluation of patients with Ebstein's anomaly [1]. In the calf of this report, it revealed itself to be an accurate, non-invasive diagnostic imaging technique, allowing the definitive diagnosis of TVD in a calf. It can be performed in a farm setting as well as in hospital, and it should be considered in calves displaying clinical signs consistent with heart disease [18], although more complicated functional cardiac assessment will likely remain the province of specialist cardiologists and large animal internists for the near future. Extra attention while performing necropsy and more frequent use of echocardiography is recommended to confirm the diagnosis and provide better insight on the prevalence of TVD.

Conflicts of Interest Statement

The authors do not have any conflicts of interest to disclose.

Acknowledgments

None to report.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvc.2018.10.005.

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