

Case Report

Detailed echocardiographic findings in a newborn foal with tetralogy of Fallot

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Summary

This case report is the first detailed description of the echocardiographic findings in tetralogy of Fallot (TOF) in a newborn foal. In addition to the characteristic elements of TOF, asynchronous wall movement patterns were also evident. Measurements in 2D and M-mode echocardiography revealed marked changes in cardiac dimensions. Haemodynamic studies in both right and left ventricular outflow tracts, as well as haemodynamic studies of the shunt flow situation, were performed. Shunting flows through the ventricular septal defect in both directions, and also from the right ventricle into the aorta, were present. A mild to moderate stenosis of the pulmonary valve, as the determining factor in long-term prognosis, could be found by echocardiography.

Introduction

Congenital diseases of the heart are uncommon in foals. With an occurrence of 0.16%, congenital cardiac disorders occur rarely related to the number of births (Gumbrell 1970). Ventricular septal defect (VSD) is found most frequently, followed by atrial septal defect (ASD), persisting *ductus arteriosus* (PDA), tricuspid atresia and other rarer occurring malformations (Reef 1998). Complex cardiac disorders are extremely rare, although among these, tetralogy of Fallot (TOF) is regarded to be the most frequent (Reef 1991). Tetralogy of Fallot is defined as a combination of: subaortic ventricular septal defect, dextropositioning of the aorta, obstruction of the pulmonary outflow and hypertrophy of the right ventricular myocardium.

Only 10 cases have been described and addressed as TOF in the horse in the last 50 years (Wensvoort 1959; Prickett *et al.* 1973; Greene *et al.* 1975; Borst 1978; Reynolds and Nicholl 1978; Keith 1981; Cargile *et al.* 1991; Houe *et al.* 1996; Gesell and Brandes 2006). From 10 cases, 2 should have

better been termed as pentalogy of Fallot, because of an existing PDA (Borst 1978; Reynolds 1978). Another single case of pentalogy of Fallot is described by Bayly *et al.* (1982). Also, 3 cases of complete atresia of the pulmonary artery with VSD, overriding aorta and right ventricular hypertrophy are described, but this is regarded as an independent heart disease (Vitums and Bayly 1982). In only 3 cases of the mentioned 14 was the *ante mortem* diagnosis supported by sonographic investigations and able to be identified clearly as TOF (Cargile *et al.* 1991; Houe *et al.* 1996; Gesell and Brandes 2006). Limited investigative possibilities were responsible for the difficulties in the diagnosis before ultrasound became a routine diagnostic tool. To date, detailed investigations with sonographic methods, above all with Doppler echocardiography, have not been conducted in cases of TOF of the newborn foal.

This case report describes all distinctive echocardiographic findings, including blood flow patterns and wall movement characteristics, in a newborn foal with TOF.

Case details

History

A 3-day-old Quarter Horse foal was referred to the Clinic for Horses of the Free University of Berlin with the clinical signs of respiratory disease. The symptoms had become obvious 12 h after birth. All therapeutic efforts such as infusion therapy, antibiotics, anti-inflammatory therapy and plasma transfusion remained without visible success.

Clinical findings

The clinical picture covered weakness, dyspnoea, increased respiratory rate (40 breaths/min) and bluish mucous membranes. A harsh bronchial sound could be heard over the entire auscultation field of the lung. Auscultation revealed a heart rate of 86 beats/min, a pansystolic murmur *grade 5/6* with the point of maximal intensity over the aortic valve and a pansystolic murmur *grade 5/6* with the point of maximal

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intensity over the tricuspid valve on the right hemithorax. Laboratory findings consisted of moderate hypoxaemia (Pa 75.7 mmHg) and hypercapnia (Pa 55.8 mmHg) of the arterial blood, hyperfibrinogenaemia (5.38 g/l), dehydration and mild metabolic acidosis (base excess = -6.0). Radiological examination indicated bronchopneumonia.

Echocardiographic examination

Echocardiographic examination was performed using a 5.0 MHz sector scanner (System FiVe)¹.

Two-dimensional echocardiography

B-mode echocardiography is the basic method used for investigation of morphological structures such as size and shape of the heart and heart cavities. Almost all congenital defects can be visualised with this method. The overview evaluation in the right parasternal long-axis 4-chamber reference view revealed a hypertrophy of the right ventricular wall and dilatation of the right ventricle, particularly in the apex region. Hypertrophy of the left ventricular myocardium could

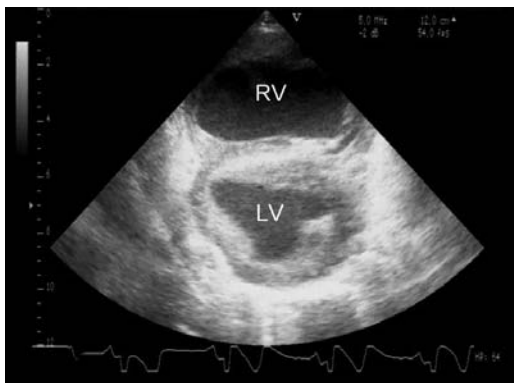


Fig 1: Right parasternal short-axis view at the level of the papillary muscles at end diastole. Dilatation of the right ventricle (RV) and hypertrophy of the right ventricular wall. Note the flattened septum interventriculare, showing pressure overload of the right ventricle. LV = left ventricle.

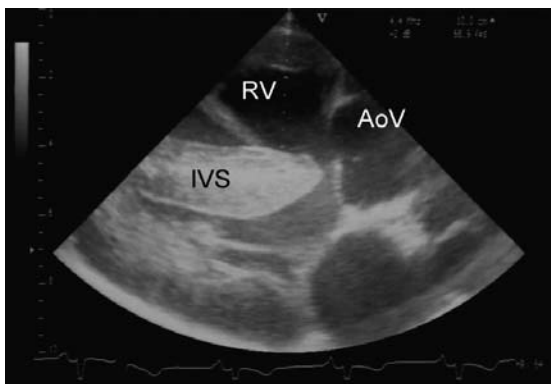


Fig 2: Right parasternal long-axis view at end systole. Dextropositioning of the aorta and ventricular septal defect. AoV = aortic valve; RV = right ventricle; IVS = interventricular septum.

be assumed. This could be shown in the right short-axis view (**Fig 1**) and left long-axis view. In addition, a thickening of the septomarginal trabeculum of the right ventricle (**Fig 2**) could be observed. During the overview evaluation of the heart action, increased ejection fraction of the left ventricle and reduced ejection fraction of the right ventricle were seen. In human cardiology the ejection fraction (EF) is the most important parameter of global systolic function of the left ventricle. It is calculated by the formula: $EF = (EDV - ESV)/EDV$, where EDV and ESV are the end-diastolic and end-systolic volumes, respectively. There are several methods to obtain the EF. The method of discs (Simpson's rule) for the calculation of the left ventricular volume is very accurate even for ventricular cavities with distorted shape. This method summates volumes of multiple cylinders of equal height along the long axis of the left ventricle (Flachskampf 2002; Gottdiener *et al.* 2004). An EF of 0.82 resulted from the measurements for the left ventricle.

During the representation of the aortic valve from the right long-axis aortic view the dextropositioning of the aorta could be proven (**Fig 2**). The malalignment of the aorta produced an 'overriding' on the interventricular septum. The ventricular septal defect measured 21 mm in its maximum expansion at end diastole. Another clear statement of the dextropositioning of the aorta is the fact that the aortic and pulmonary roots could be represented in the same plane next to each other, whereby the pulmonary root is cut lengthwise and the aortic root is cut slightly obliquely (**Fig 3**).

The interpretation of 2D cardiac measurements is problematic, because to our knowledge there are no data published about 2D echocardiographic measurements in the newborn foal. Cardiac measurements revealed approximately the same thickness of the right ventricular wall (RVW 10.1 mm), interventricular septum (IVS 11.5 mm) and left ventricular free wall (LVW 9.7 mm) at end diastole. The diameter of the right ventricle (RVD) with 41.5 mm was larger than the diameter of the left ventricle with 38.9 mm at end diastole. The leaflets of the pulmonary valve were difficult to represent, both in the right long-axis view of the right ventricular outflow tract as well as in the right short-axis view. They also appeared hypoplastic (**Fig 3**). Comparing the

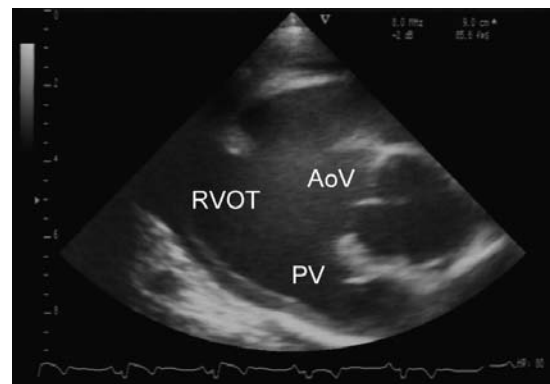


Fig 3: Representation of aortic and pulmonary root from the right long-axis view of the right ventricular outflow tract (RVOT) at end diastole. Stenosis at the level of the pulmonary valve (PV). AoV = aortic valve.

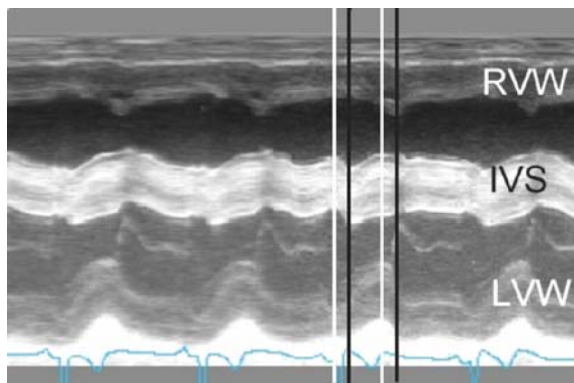


Fig 4: M-Mode from the right parasternal long-axis view. Asynchronous contraction of left ventricular free wall (LVW), interventricular septum (IVS) and right ventricular wall (RVW). Note the time delay between left ventricular mechanical systole (white bars) and right ventricular mechanical systole (black bars).

obtained 2D measurement data of this foal with measurement values of two 6-week-old sound Warmblood foals (R.R. Schmitz, unpublished data), dilatation of the aortic root (32.1 mm vs. 27.9 mm in healthy foals), stenosis of the pulmonary valve (12.7 mm vs. 20.5 mm in healthy foals), hypertrophy of right (10.1 mm vs. 5.5 mm in healthy foals) and left (9.7 mm vs. 8.3 mm in healthy foals) ventricular myocardia, and an elevated ejection fraction (0.82 vs. 0.69 in healthy foals) can be assumed. When comparing the aortic to the pulmonary valve, a moderate stenosis can be assumed at the level of the pulmonary valve.

M-mode

Because of its high temporal resolution, this method is superior in describing time related patterns of moving structures in the heart. Asynchronous movement patterns of

TABLE 1: M-Mode measurement values out of the right parasternal long-axis view in a 3-day-old foal with tetralogy of Fallot (TOF) in comparison to the data of Stewart *et al.* (1984)

	TOF		Unit
	Present case	Stewart <i>et al.</i> (1984)	
IVSd	16.0	13.1 ± 2.1	mm
IVSs	18.2	-	mm
LVWd	8.9	6.1 ± 0.4	mm
LVWs	17.2	-	mm
LVDd	35.7	61.9 ± 7.4	mm
LVDs	17.9	54.4 ± 8.4	mm
RVDd	46.1	24.6 ± 8.8	mm
RVWd	10.2	-	mm
AoD	38.1	35.7 ± 3.10	mm
FS	48.21	18.61 ± 3.76	%
LVEF	0.86	-	-

RVW = right ventricular wall; RAD = right atrial diameter; RVD = right ventricular diameter; IVS = interventricular septum; LVW = left ventricular wall; LVD = left ventricular diameter; LAD = left atrial diameter; LVEF = left ventricular ejection fraction; AoD = aortic root diameter; d = diastolic; s = systolic.

the right ventricular wall, of the interventricular septum, and of the left ventricular free wall could be noted in respect to each other (Fig 4). Measurement of the time from Q in the ECG to onset in systolic shortening of the myocardium revealed a decreased value at the left ventricular free wall with 0.02 s in respect to the right ventricular wall with 0.09 s.

The measurement data of the M-mode analysis are shown in Table 1. Measurements in the M-mode revealed hypertrophy of left and right ventricles, increased fractional shortening (FS) of 48% and elevated EF of 0.86. Comparing these values with data obtained by Stewart *et al.* (1984), the huge differences of left and right ventricular dimensions and FS are to be noted.

Colour Doppler

The benefit of this method in cases of TOF is the visualisation of blood flow directions, depiction of shunting situation and demonstration of turbulent blood flow. Best representation of the common bloodstream from the right ventricle and from the left ventricular outflow tract into the aorta can be made in the right long-axis aortic view (Fig 5). Turbulences showed up only in early systole. The diastolic left to right shunt could be observed both in right (Fig 6) and left long-axis views. In the

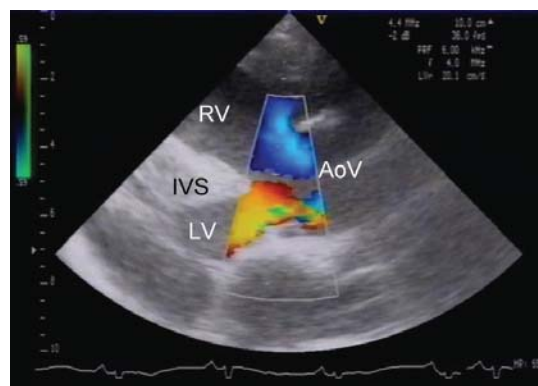


Fig 5: Bloodstream at the aortic valve from both left ventricle (LV) (red) and right ventricle (RV) (blue) during systole in the right long-axis view. IVS = interventricular septum; AoV = aortic valve.

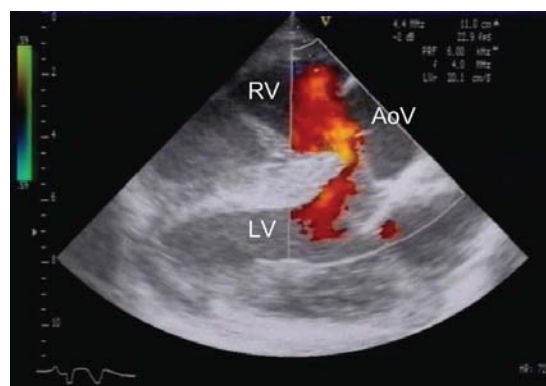


Fig 6: Right parasternal long axis-view. Diastolic left to right shunt (red) through the ventricular septal defect between the 2 heart chambers. LV = left ventricle; RV = right ventricle; AoV = aortic valve.

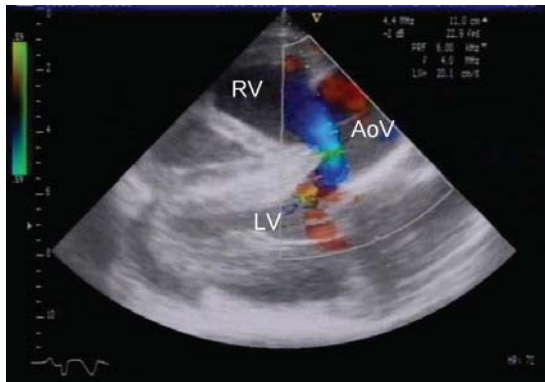


Fig 7: Right parasternal long-axis view - early diastolic right to left shunt (blue) through the ventricular septal defect between the 2 heart chambers. LV = left ventricle; RV = right ventricle; AoV = aortic valve.

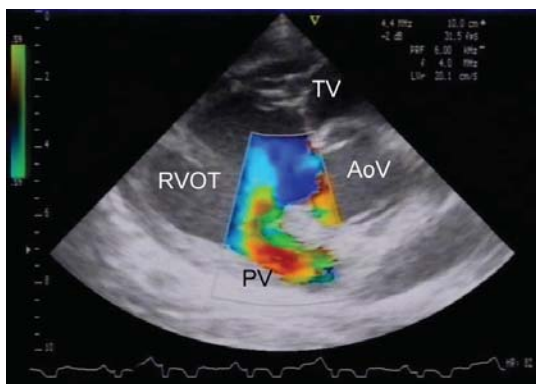


Fig 8: Turbulent stenotic flow at the pulmonary valve (PV) in the right long-axis view of the right ventricular outflow tract (RVOT). Note the common outflow from the RVOT (blue) in both aorta (AoV) and pulmonary artery. TV = tricuspid valve.

TABLE 2: Measurement data of spectral Doppler analysis in the left ventricular outflow tract (LVOT) just before the aortic valve (AoV), of the systolic shunt flow from the right ventricle into the aorta, at the pulmonary valve (PV) in the sinus of the pulmonary artery (PA) and in the aorta ascendens (AoAs)

	LVOT (AoV)	Shunt flow from right ventricle into the aorta	AoAs	PV (RVOT)	PA (Sinus)	Unit
V_{max}	1.70	1.93	1.46	2.29	1.87	m/s
V_{mean}	0.96	1.10	0.98	1.22	0.99	m/s
P_{max}	11.56	14.82	8.56	20.89	13.60	mmHg
P_{mean}	4.41	6.51	4.39	7.29	4.85	mmHg
VTI	26.05	23.85	26.52	36.73	26.59	cm
PEP	0.02	-	-	0.08	-	s
dt	0.09	0.10	0.076	0.11	0.12	s
dv/dt	18.21	18.81	18.4	20.81	16.44	m/s ²
HR	82.17	77.86	64.86	75.17	78.84	bpm
θ	38	20	58	35	35	°

V_{max} = maximal velocity; V_{mean} = mean velocity; P_{max} = maximal pressure; P_{mean} = mean pressure; VTI = velocity time integra; PEP = pre-ejection period; dt = time of systolic flow; dv/dt = acceleration; HR = heart rate; θ = insonation angle; bpm = beats/min.

right long-axis view early diastolic right to left shunt of very short duration from the right into the left ventricle could be visualised with colour Doppler (Fig 7). The systolic blood flow from the left ventricle into the aorta and from the right ventricle into the pulmonary artery is seen best in a single plane in the right long-axis view of the right ventricular outflow tract. A turbulent systolic blood flow could be recognised at the stenotic pulmonary valve (Fig 8).

Spectral Doppler

Spectral Doppler analysis is very useful in the quantitative description of the magnitude, direction and time duration of blood flow. Additionally, pressure gradients across a stenosis can be derived, important estimation of the degree of obstruction in the right ventricular outflow tract in patients with a TOF. The evaluation of the spectral Doppler traces revealed high maximum velocities of systolic blood flow. The measurements of the left and right ventricular blood flow into the aorta just before the aortic valve, as well as the flow measurements in the right ventricular outflow tract at the level of the pulmonary valve, in the pulmonary sinus, and into the aorta ascendens in the sinus valsalvae are shown in Table 2. Blood flow velocities were recorded with angle correction. A pressure drop across the pulmonary valve could be found, despite the fact that the post valvular sample volume was set in the sinus of the pulmonary artery. Placing the measurement site further from the pulmonary valve probably would have shown a greater difference in pre- and post valvular pressure.

The blood flow characteristics, especially the shunting flows found with colour Doppler, could be confirmed with spectral Doppler. Depending on the point of the measurement, spectral analysis yielded a holodiastolic left to right shunt and transient early diastolic right to left shunt from the right into the left ventricle (Fig 9), and a systolic right to left shunt from the right

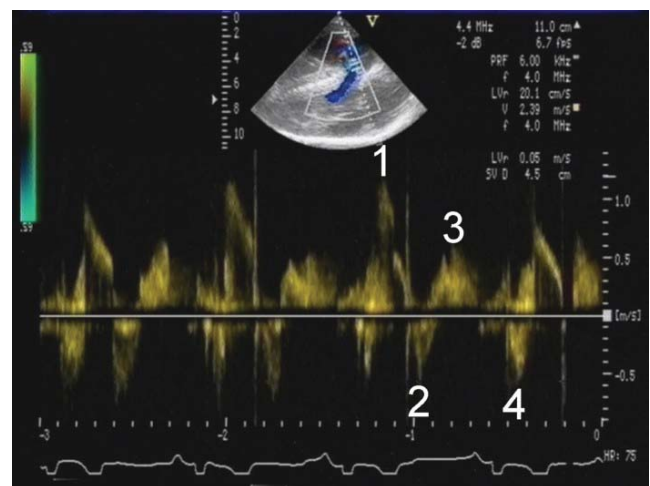


Fig 9: Right parasternal long-axis view. Spectral Doppler representation of the flow and shunting situation at the site of the VSD below the aortic valve. No angle correction used. 1 = systolic outflow, 2 = early diastolic right to left shunt (represented also in the small 2D-image), 3 = diastolic left to right shunt, 4 = turbulent early systolic flow.

ventricle into the aorta. The pre-ejection period (PEP) measured with spectral Doppler in the right and left ventricular outflow tracts confirmed the time delay in systolic function between left and right ventricles.

Discussion

The available literature is based largely on gross sectional findings. Vitums and Bayly (1982) obtained data by conducting a *post mortem* examination of a 10-day-old foal with TOF. With exception of the size of the VSD in foals with this complex malformation, no sonographic data are available. To our knowledge, only Stewart *et al.* (1984) and Lombard *et al.* (1984) compiled sonographic reference values for newborn foals in the unguided M-mode. Tetralogy of Fallot is a developmental aberration of the *truncus arteriosus*. Through abnormal growth of endocardial cushions and underdevelopment of the *bulbus cordis*, the spiral development of the *septum aortico-pulmonale* and *truncobulbare* does not take place. This leads to the transposition of the aortic root, missing conclusion of the interventricular septum, and stenosis of the pulmonary root (Rüsse and Sinowatz 1991). The right ventricular hypertrophy is the consequence of the volume and pressure overload caused by the other 3 factors described earlier.

The findings of 2D echocardiography in the present case are characteristic and correspond exactly to the specification of the diagnosis of TOF: subaortic ventricular septal defect (Fig 2), dextropositioning of the aorta (Figs 2 and 3), stenosis at the level of the pulmonary valve (Fig 3) and hypertrophy of the right ventricular myocardium (Fig 1). It could be shown that on the third day *post partum*, a hypertrophy of the musculature of the right ventricle was already present. Borst (1978) found similar results in a necropsy of a one-day-old foal. This proves that the hypertrophy of the right ventricle develops *in utero*, apart from the physiological intrauterine hypertrophy of the right fetal heart. The absolute values of the M-mode measurements confirm the existing hypertrophy of the right and the left ventricular wall (Table 1). The presence of right ventricular hypertrophy is found to be influenced by the degree of right ventricular outflow obstruction. Despite the fact that fetal circulation has its own characteristics, it seems that the changes in heart dimensions due to the manner of altered haemodynamic conditions in the heart with TOF are already present *in utero*.

The different flow directions through the VSD can be explained by the slight pressure differences existing in different phases of the cardiac cycle between both ventricles. Apparently there is a passive pressure equilibration through the left to right shunt in the diastole. A transient right to left shunt could be recorded during early diastole. This would not necessarily contradict the investigations of Prickett *et al.* (1973), where approximately identical pressure ratios could be found throughout heart catheterisation in the right and left ventricle. To some extent, shunt flows through the VSD as in the present case are seen also in human TOF (Reef 1998). In summary, there was a major holodiastolic left to right shunt

and a considerable volume is shunted from the right ventricle into the aorta systolically. However, an insignificant volume is shunted through the VSD from the right into the left ventricle.

Mild cyanosis of the mucous membranes is explained not only by the high share in venous blood that leaves the *aorta ascendens*, but is also a consequence of a minor perfusion of the lung.

The increased maximum velocity of blood flow in the LVOT at the aortic valve is an indirect sequel of the pronounced hypertrophy of the left ventricle. Systolic time intervals depend on contractility, afterload and preload of the ventricle. Change in preload is considered by many authors to be the principal cause of alteration in left ventricular PEP; the PEP is behaving inversely to the preload (Weissler 1977; Atkins and Snyder 1992). In the present case we should expect an increased PEP in the left ventricle because of decreased preload, and a decreased PEP in the right ventricle because of increased preload. The PEPs measured were opposite to this, indicating that preload on the PEP was of little importance in this special case. Asynchronous onset of contraction and different PEP in the left and right ventricular myocardia are a result of increased contractility of the left and decreased contractility of the right myocardia. Delayed right ventricular wall shortening is also documented in human patients with a repaired TOF and is considered to be an infundibular dysfunction rather than a global dysfunction of the right ventricle (Uebing *et al.* 2007). PEP was also assessed as a marker of peripheral and central sympathetic activation (Schächinger *et al.* 2001). Sympathetic nerve stimulation as a result of hypoxaemia and hypercapnia is very likely to be one of the reasons for the elevated FS, high velocities of blood flow, and decreased PEP of the left ventricle. In the interpretation of the left ventricular parameters the lung affection must also be considered. Its emergence is favoured partially by the minor perfusion of lung tissue. Dehydration and hypovolaemia must also be considered because of their influence on functional measurements. In the right ventricle, both pressure and volume overload are present. Moderate stenosis of the pulmonary valve primarily leads to a pressure overload in the right ventricle. The increased afterload and the left to right shunt in the diastole cause a volume overload. This is also the reason for eccentric rather than concentric hypertrophy, as it is described in case of exclusive presence of a pulmonary stenosis in man.

In children, a pressure gradient at the stenotic pulmonary valve of 30–50 mmHg is consistent with the diagnosis of mild to moderate pulmonary stenosis. A stenotic pulmonary valve with this pressure gradient is subject to surgical intervention. Obstruction of the outflow tract with a pressure gradient <20 mmHg does not need a surgical correction (Houston *et al.* 1985). In the absence of data about the normal variations of pressure gradients at the pulmonary valve in the newborn foal and taking into account the 2D measurements in the present case, we consider the stenosis as mild to moderate. Another problem in establishing the severity of pulmonary stenosis by means of spectral Doppler and flow measurements is the high ambiguity range depending on correct ultrasound beam alignment, angle correction and position of the sample volume.

The present case of TOF demonstrates that not only severe obstructions of right ventricular outflow, but also a mild to moderate stenosis can lead to a marked enlargement of the right ventricle and hypertrophy of the intrauterine myocardium.

A more detailed analysis of the echocardiographic values was not possible, because of the absence of basic echocardiographic data in the newborn foal, with exception of the M-mode values compiled by Stewart *et al.* (1984). Nevertheless, broad data about cardiac congenital disease in the horse are needed to create a basis for understanding cardiac malformations and for the development of operative techniques in the future. In foals there are only few reports on surgical interventions in cardiovascular disturbances (Bauer *et al.* 2006), but none in the case of TOF.

Despite intensive care medicine the condition of the foal deteriorated rapidly. Because of the unfavourable prognosis also in reference to the neonatal respiratory distress syndrome, the animal was subjected to euthanasia. Necropsy confirmed the clinical diagnosis and revealed no further congenital abnormalities.

Many horses apparently survive with this malformation for months and even years (Houe *et al.* 1996; Gesell and Kristin 2006). However, long-term prognosis is to be classified as unfavourable. For the final estimate of the prognosis in such extremely rare congenital cardiac disorders and for the assessment of possible therapy worthiness in the future, similar to human therapy, further information is needed on normal newborn foals, to allow better determination of the extent of pulmonary outflow obstruction and its influence on the outcome of the patient.

Manufacturer's address

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