Tetralogy of Fallot with aortic stenosis and common arterial trunk: Is there a morphological overlap?

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ABSTRACT

Tetralogy of Fallot with aortic stenosis is an extremely rare entity which bears some morphological similarities with the common arterial trunk. Through two illustrative cases of TOF with aortic stenosis we describe the shared anatomical peculiarities of the two anomalies with a review of the possible genetic and developmental factors responsible for the association.

Keywords: Aortic stenosis, common arterial trunk, doubly committed ventricular septal defect, tetralogy of Fallot

INTRODUCTION

Cardiac morphologists have speculated on the similarities of some variants of tetralogy of Fallot (TOF) and the common arterial trunk.[1] The connection between the two entities seem more evident when TOF is associated with aortic valve involvement. We describe the morphological characteristics of two patients with TOF and severe aortic stenosis and explore the semblance to the common arterial trunk.

CASE REPORT

Case 1

A term newborn girl was referred to us with a history of respiratory distress and cyanosis soon after birth. She was born to a diabetic mother and she was antenatally diagnosed to have a common arterial trunk (Edward-Collett Type I). At presentation on postnatal day 1, her oxygen saturation was 50%. She was in heart failure with prolonged capillary filling time. An electrocardiogram showed normal QRS axis with biventricular forces. There was mild cardiomegaly with concave pulmonary bay and oligemic lung fields. The child had severe biventricular dysfunction with N-terminal probrain natriuretic peptide of 29,200 pg/ml at admission. Echocardiography revealed large doubly committed ventricular septal defect (VSD) with 60% of aortic override, severe valvar pulmonary, and aortic stenosis. The right ventricular infundibulum was absent giving the impression of aortopulmonary continuity. The pulmonary annulus and main pulmonary artery and the branch pulmonary arteries were hypoplastic[Figure 1a and b)]. The branch pulmonary arteries gave a crossed appearance, with the left pulmonary artery seemingly arising from the right. The aortic valve was bicuspid and there was significant biventricular hypertrophy. The arterial duct was absent, although the baby was only a few hours old. The baby deteriorated rapidly and was taken up for interventional aortic and pulmonary valvotomy as she was deemed high risk for surgery. Cardiac catheterization showed

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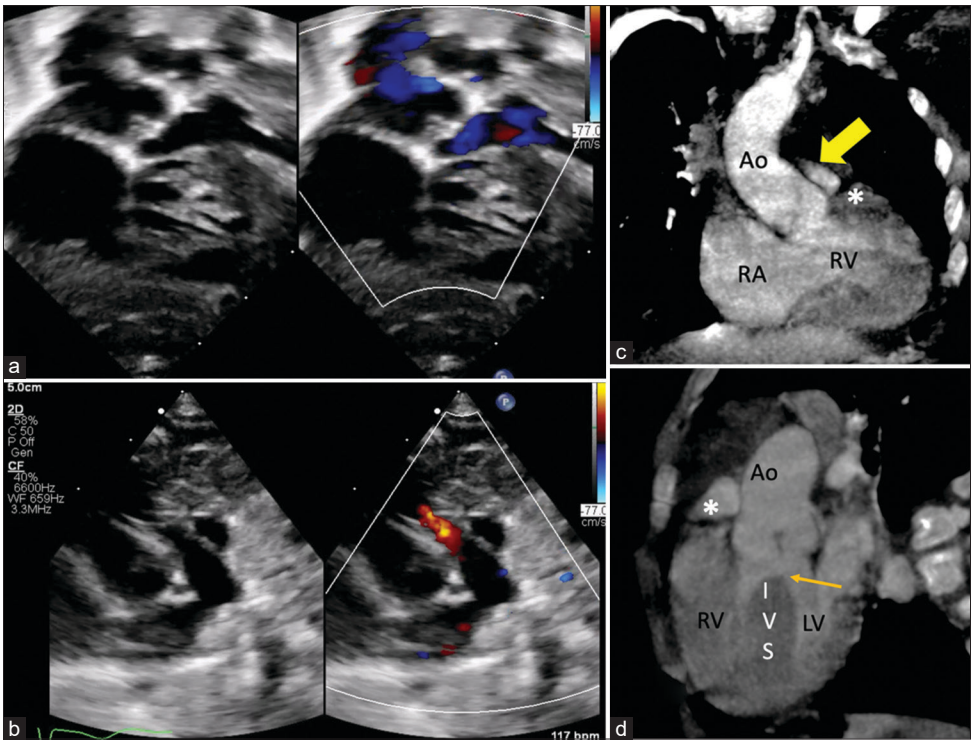

Figure 1: (a) Subcostal long-axis images showing the aorta with no separate outflow noted from the ventricles in this view, easily mistaken as a common arterial trunk (yellow solid arrow). (b) Parasternal short axis frozen image at the level of outflow tracts showing the bicuspid aortic valve and separate pulmonary arterial origin with pulmonary regurgitation and bicuspid aortic valve and absent outflow septum (yellow solid arrow). (c) Two-chamber view of right atrium and ventricle shows the absence of an infundibular portion of RV (asterisk) and opacified proximal main pulmonary artery (yellow solid arrow) is seen. (d) Outflow view of both ventricles showing hypertrophied interventricular septum and both ventricular walls and a doubly committed VSD (orange arrow) with 50% override of the aorta over interventricular septum. Ao: Aorta, PA: Pulmonary artery, LV: Left ventricle, RV: Right ventricle, VSD: Ventricular septal defect

LV and RV pressures of 138 mmHg and transvalvular aortic gradient of 68 mmHg. Although balloon aortic valvotomy was done, the baby developed recurrent ventricular tachycardia which degenerated to ventricular fibrillation and she could not be salvaged. The parents did not consent to an autopsy.

Case 2

A 1-year-old boy diagnosed to have large doubly committed VSD with long-segment pulmonary atresia had undergone modified Blalock–Thomas–Taussig shunt at 3 months of age. He was noted to have mild valvar aortic stenosis with bicuspid aortic valve. On follow-up, the aortic stenosis progressed to moderate severity and a cardiac computed tomography (CT) was done to delineate anatomy before planning intracardiac repair. The cardiac CT showed large doubly committed VSD, with absent membranous interventricular septum [Figure 1c and d]. There was aortic-tricuspid discontinuity. The right-ventricular infundibulum was absent. The orientation of the left pulmonary artery over the right pulmonary artery suggested the appearance of crossed pulmonary arteries. The aortic valve was bicuspid and the coronary arteries originated from the facing sinuses close to the aortic commissure.

DISCUSSION

The morphological characteristics of TOF comprise a large malaligned VSD with anterior and cephalad deviation of the interventricular septum. The deviated outlet septum along with the septoparietal trabeculations leads to the outflow obstruction in TOF. It is of interest to note that subpulmonary infundibulum is present in most cases of TOF with pulmonary stenosis and even pulmonary atresia where the most common VSD is the perimembranous type. However, in TOF with doubly committed VSD, the outlet septum is fibrous rather than muscular with a free-standing infundibular sleeve. The absence of the subpulmonary infundibulum gives it a close resemblance to the outflow tract of the common arterial trunk. The absence of infundibular septum has been noted in previous reports of TOF with valvar aortic stenosis also.[2-4] The developmental anomaly leading to the common arterial trunk has been attributed to the abnormalities of neural crest cell migration which causes improper development of endocardial cushions of the outflow tract [Figure 2]. The same neural crest anomaly can also result in doubly committed VSD with two outflow tracts and two valve orifices in some cases. This has been substantiated in embryological studies as well, where the deficiency of the sox4 gene has been found to result

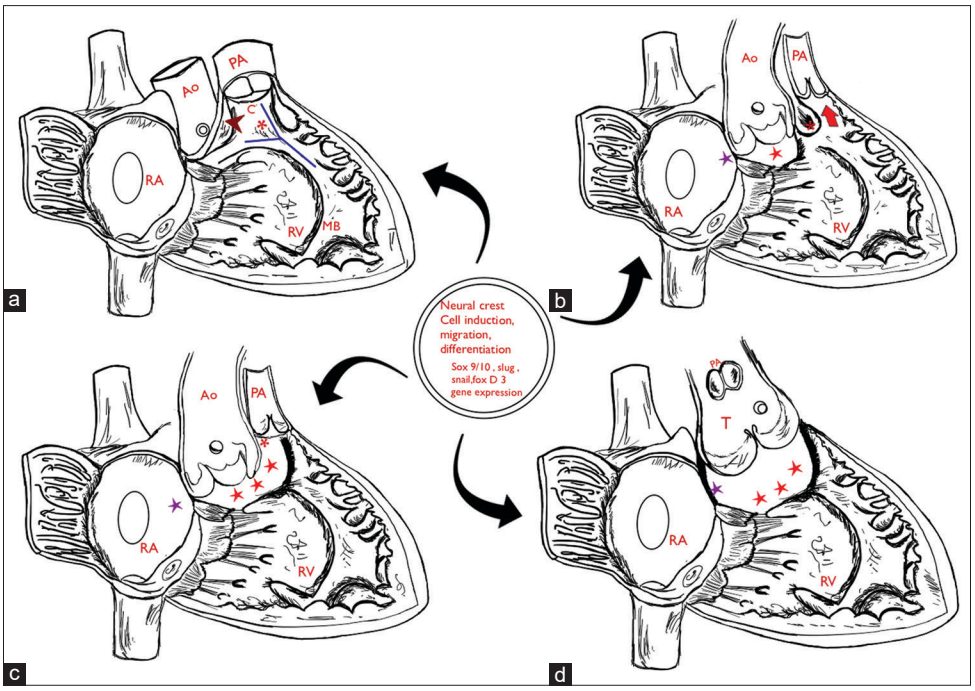

Figure 2: Pictorial illustration of the spectrum of anomalies involving the outlet septum. Neural crest cell induction, migration, and differentiation with the expression of various genes play a major role in the formation of the outlet septum. (a) The right ventricular aspect of the ventricular septum in a normal heart showing a PB; subpulmonary conus (C), MB, supraventricular crest (arrow head), septal papillary muscle outflow septum (*) enclosed by septomarginal trabecula with its two limbs anterosuperior and posteroinferior (blue colored "Y". (b) Cartoon of tetralogy of Fallot showing subaortic VSD (red star) with aortic override, subpulmonary infundibular septum (*), causing the subpulmonary obstruction (arrow), Aorto tricuspid continuity (purple star) seen. (c) Cartoon of the doubly committed VSD (red star); with aortic override; absent infundibular septum (*), aortotricuspid continuity (purple star). (d) Cartoon of truncus arteriosus showing the sub truncal VSD (red star), absent infundibulum and truncal tricuspid discontinuity (purple star). Truncus valve (T), PA absent and both branch PA's are directly originating from the truncus. MB: Moderator band, PB: Parietal band, VSD: Ventricular septal defect, PA: Pulmonary artery

in either common arterial trunk or doubly committed VSD. Association with 22q11 deletion has been well described in the common arterial trunk (~30%) and in doubly committed VSD.

Involvement of left-sided heart structures is uncommon in the TOF. The presence of aortic stenosis is very rarely described in the TOF, with less than 15 cases reported in literature.[1,3-7] Truncal valve abnormalities, however, occur in one-third of patients with the common arterial trunk, the most frequent anomaly being the bicuspid aortic valve. Although truncal valves are more commonly regurgitant than stenotic, outflow stenosis is more commonly observed with common arterial trunk than TOF (11% vs. 1%) [Table 1].[1] Abnormalities of coronary origins, such as high sinusoidal origin and origin close to the commissures, are also more in the common arterial trunk.[1,2] In our patients, coronary arteries originated close to the commissures in the first patient and the other had a high sinusoidal origin of coronaries. The presence of crossed pulmonary arteries (the right pulmonary artery originating to the left of the pulmonary confluence) is described in some patients with common arterial trunk (type I of Collett Edwards).[2] Both our patients also had crossed pulmonary arteries. The arterial duct was absent in the patient with severe valvar pulmonary stenosis, which is an unusual finding. While the absence of arterial duct is unusual in TOF, patients with common arterial trunk and normal arch rarely have patent arterial duct (2% in previous studies).[2] This interesting fact has been hypothesized to be due to the prominent development of the fourth arch with regression of the sixth arch in common arterial trunk.[2] Neural crest migration abnormalities have also been implicated in the absence of arterial duct in this condition.[1,2]

Although morphological similarities exist between our two illustrative cases and patients with common arterial trunk, their management is vastly different. The presence of obstruction of both outflow tracts puts the patient with TOF with aortic stenosis at high risk of mortality. These patients are often significantly symptomatic in early neonatal life particularly if the stenosis at the aortic valve level is critical. The optimum treatment strategy for a combination of critical aortic and pulmonary stenosis has not been described. Relief of both outflow tract obstructions is imperative for survival. High risk of mortality has been reported for surgical and interventional management in this subset. The absence of infundibulum in this subset makes them

Table 1: Comparison of index cases with classic TOF, doubly committed VSD, common arterial trunk

	Classical TOF	Doubly committed VSD	Case 1	Case 2	Common arterial trunk
Aorto-tricuspid discontinuity	66%	74%	Present	Present	Absent (98%)
Subpulmonary infundibulum	Present	Absent	Absent	Absent	Absent
Aortic valve abnormalities	Uncommon (aortic stenosis 1%)	Uncommon	Bicuspid aortic valve, AS	Bicuspid aortic valve, AS	Common (truncal stenosis 11%)
Aortopulmonary continuity	Absent	Present	Present	Present	Common truncal valve
Coronary artery abnormalities	5%–7%	Uncommon	Normal	High sinus origin	Common (~45%)
Patent arterial duct	Present	Present	Absent	Present	Absent
Crossed pulmonary arteries	Uncommon	Uncommon	Present	Present	Common in common arterial trunk type I
22q11 deletion	~15%	Common	Not done	Not done	35%

TOF: Tetralogy of Fallot, VSD: Ventricular septal defect, AS: Aortic stenosis

unsuitable for right ventricular outflow tract stenting. The absence of the arterial duct in some cases rules out ductal stenting as a means to provide pulmonary blood flow. Although balloon aortic and pulmonary valvotomy can be attempted as an immediate life-saving measure, this strategy also is associated with high mortality due to the risk of arrhythmias and perforation during the procedure. In the unstable newborn, an aortopulmonary shunt with surgical or balloon aortic valvotomy may serve as a temporizing measure till the patient becomes a suitable candidate for intracardiac repair. Early neonatal intracardiac repair can be an option in stable patients.[4] Overall, prognosis seems better in patients with less severe aortic stenosis[2,3] as indicated by our second case who had mild aortic stenosis in the newborn period and had a stable course in infancy.

CONCLUSION

The rare entity of TOF with doubly committed VSD and aortic valve involvement shares many morphological similarities with the common arterial trunk. The recognition of a common genetic mechanism for both could have diagnostic and prognostic implications in management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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