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Original Article

Fistulous communications with the coronary arteries in the setting of hypoplastic ventricles

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Abstract Neonates born with hypoplastic left heart syndrome now have a remarkably improved prognosis compared with the situation existing before the development of the Norwood sequence of operative procedures. Some of those born with hypoplastic right ventricles in the setting of pulmonary atresia with an intact ventricular septum, however, still have a relatively poor prognosis. In part this reflects the presence of fistulous communication between the cavity of the right hypoplastic right ventricle and the coronary arterial tree. Such fistulous communications are now increasingly recognised as being important in the setting of hypoplastic left heart syndrome. In this brief review, we describe the anatomy of the communications. Those found with hypoplastic right ventricles are seen most frequently when the cavity of the ventricle effectively represents only the inlet, this in turn reflecting mural overgrowth of the apical trabecular and outlet components during foetal development. This almost certainly reflects an earlier appearance of the pulmonary valvar lesion that promotes the cavitary hypoplasia. In those with hypoplastic left ventricles, the key feature differentiating those with fistulous communications is the presence of a patent mitral valve, since the left ventricle is typically no more than a virtual slit in postero-inferior ventricular wall in the setting of mitral valvar atresia or absence of the left atrioventricular connection.

Keywords: Coronary arterial anomalies; pulmonary atresia with intact ventricular septum; hypoplastic left heart syndrome

THE ADVANCES MADE OVER THE LATTER HALF OF the 20th century in the treatment of infants and neonates with congenitally malformed hearts have been truly spectacular. Perhaps the most noteworthy advance, and arguably the greatest paradigmatic change, came with the appreciation that it was possible to offer surgical treatment for those born with hypoplastic left heart syndrome.[1] At the time, it was also accepted that, although the prognosis was not as dismal for those born with hypoplasia of the right ventricle in the setting of an intact ventricular septum as for those with hypoplastic left ventricles, results of surgical treatment were far from universally successful. It is perhaps paradoxical, therefore, that results should now be so encouraging for those with hypoplastic left hearts, but still somewhat depressing for those born with hypoplasia of the right ventricle and intact ventricular septum.[2] Not all patients, nonetheless, with hypoplastic right ventricles have a bad prognosis. The differentiating feature, as we will show, lies in the morphology at the pulmonary ventriculo-arterial junction,[3] but this anatomical finding is closely associated with the presence of fistulous communications between the cavity of the right ventricle and the coronary arterial circulation. It is these latter communications that underscore the so-called "right ventricular-dependent circulation",[4]

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which has long been known to carry a grave prognostic significance.[5] Fistulous communications between the ventricular cavity and the coronary arterial circulation are also known to exist in the setting of hypoplastic left heart syndrome, albeit not being nearly as obvious during gross anatomical investigations,[5,6] but now observed on occasion during foetal echocardiography.[7] In this review, we discuss the morphological features of the fistulous communications when seen in the setting of hypoplastic right and left ventricles with intact ventricular septum.

Pulmonary atresia with intact ventricular septum

The very fact that the ventricular septum is intact in this entity points to its pathogenesis as acquired disease during foetal life, a conclusion further endorsed by the close morphological similarities between hearts having pulmonary atresia with an intact ventricular septum and those with critical pulmonary stenosis. Even within patients born with pulmonary atresia and an intact ventricular septum, however, there is a marked variability in the morphological features. This variability depends, in the first instance, on whether the right ventricular cavity is hypoplastic or dilated. Cases with right ventricular dilation form a particular subset of patients, with the most florid examples presenting with so-called "wall-to-wall" hearts (Fig 1).[2] These patients have perhaps the worst prognosis of those within this group, the poor outcome reflecting the fact that the size of the heart squeezes out the lungs, so that although the lungs are morphologically normal, they are grossly hypoplastic, and unable to perform their normal function. The huge size of the right atrium and ventricle reflects the gross tricuspid incompetence occurring during foetal life.[9] Patients with dilated right ventricles, however, constitute but a small subset of those with pulmonary atresia and intact ventricular septum, and are never, to the best of our knowledge, associated with fistulous communications between the right ventricular cavity and the coronary arterial circulation.

The fistulous communications are found in a subset of patients with hypoplastic right ventricular cavities. In this subset, accounting for the majority of cases, the degree of hypoplasia of the ventricular cavity can still vary markedly. The fistulous communications, broadly speaking, are found in those with the smallest right ventricular cavities. The size of the ventricular cavities is dependent on the degree of right ventricular mural hypertrophy, with this almost certainly being related to the time during gestation when the pulmonary valve becomes atretic. Within the overall spectrum of

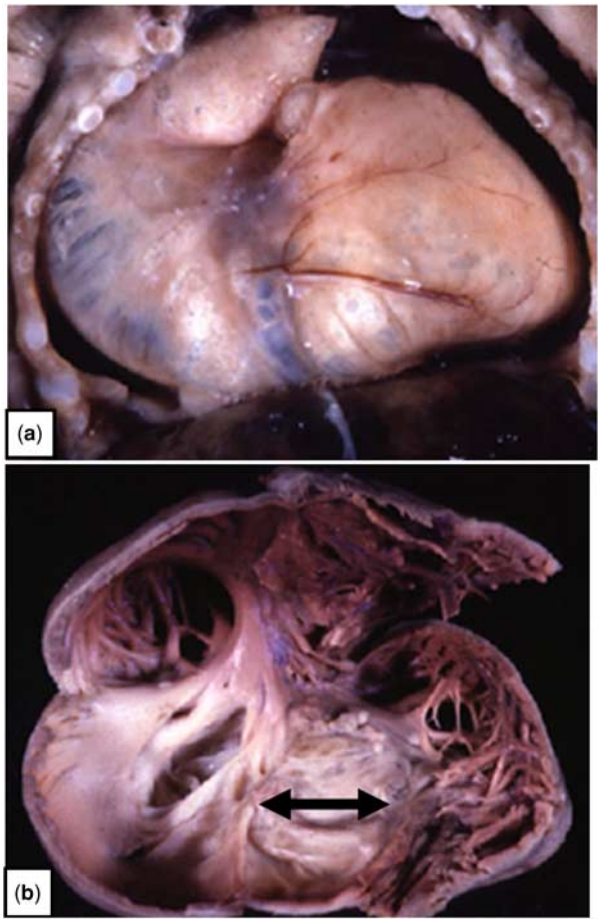

Figure 1.
*The upper panel (**a**) shows a so-called "wall-to-wall" heart produced by pulmonary atresia with intact ventricular septum. The size of the heart has squeezed out the lungs. The lower panel (**b**) shows the heart itself, the tricuspid valve exhibiting Ebstein's malformation (double-headed arrow), and the gross incompetence during foetal life producing the marked dilation of both the right ventricle and the right atrium.*

mural hypertrophy, it is possible to recognise three major anatomical subsets (Fig 2). In the worst subset, the mural hypertrophy is so extreme as to obliterate entirely the right ventricular outflow tract, such that a muscular plate interposes between the cavity of the ventricle and that of the pulmonary trunk. The hypertrophy is also sufficient to effectively exclude the apical trabecular cavity (Fig 2a). In the least afflicted subset, the pulmonary valve is recognisable as an imperforate fibrous plate (Fig 2c). Between these extremes is the subset in which the mural hypertrophy reduces the extent of the apical trabecular ventricular component, and narrows the infundibulum, albeit that the infundibulum remains recognisable as a tract leading towards the ventriculo-arterial junction (Fig 2b). The changes are well understood on the basis of the tripartite structure of the right ventricle. In the

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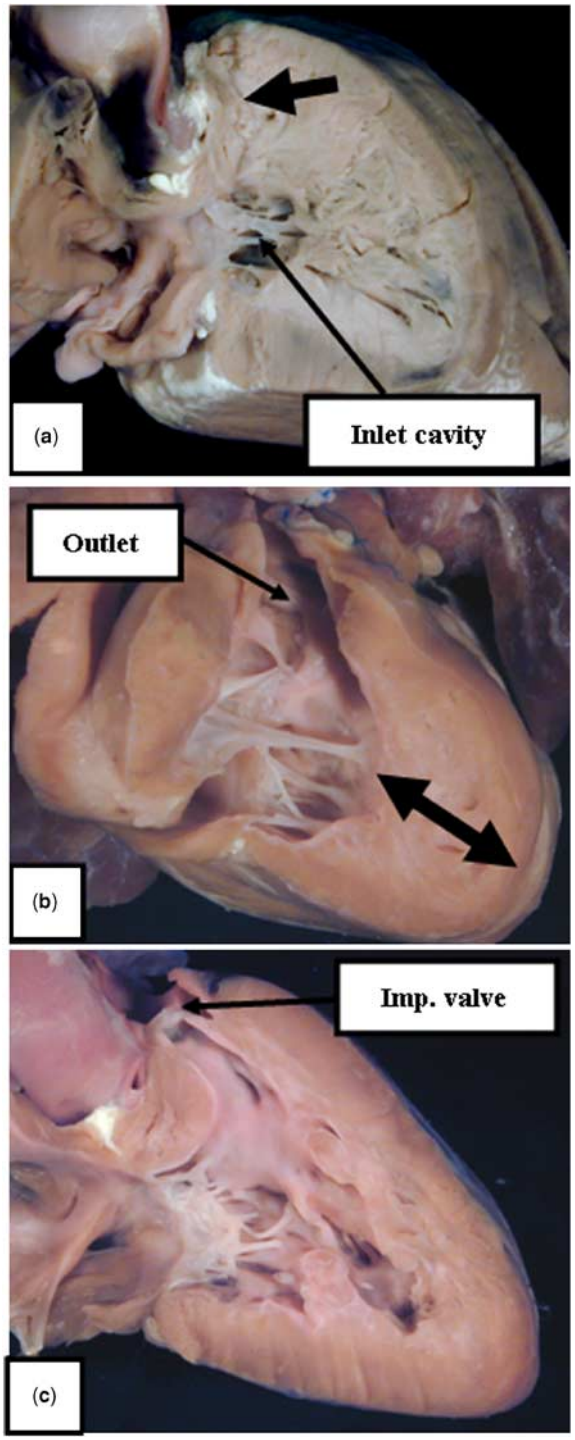

Figure 2.
*The hearts show the spectrum of decreasing cavity size with increasing mural hypertrophy in the setting of pulmonary atresia with intact ventricular septum. The upper panel (**a**) shows the situation in which the hypertrophy has obliterated both the outlet and the best part of the apical trabecular component. In the middle panel (**b**), the hypertrophy (double-headed arrow) obliterates the apical component, but spares the outlet and inlet components. The lower panel (**c**) shows the anatomy associated with an imperforate (Imp.) pulmonary valve. All three components of the ventricular cavity are relatively well formed.*

patients with the largest ventricular cavities, the mural hypertrophy overall is minimal, and all three ventricular components are well seen. In the intermediate subset, the mural hypertrophy has effectively obliterated the ventricular outlet component, so that the cavity is represented by the apical trabecular and inlet components. In the worst examples, as discussed, the hypertrophy has obliterated also the larger part of the apical trabecular component, so that the ventricular cavity, in essence, is represented only by the inlet component. All hearts still possess all three ventricular components, but with increasing obliteration of their cavities according to the extent of mural hypertrophy.[10]

In general terms, it is in those patients with the ventricular cavity represented only by the inlet component, and with muscular atresia at the ventriculo-arterial junction, that it is most frequent to find fistulous communications with the coronary arterial tree. The association between fistulous communications and grossly hypoplastic right ventricular cavities is found in autopsy series examined from specimens obtained in both foetal[11] and postnatal[3] life. The communications have long been recognised, albeit initially described in terms of "sinusoids", or "spongy myocardium".[12] The investigation of Gittenberger-de Groot et al[13] did the most to clarify the relationship between the intertrabecular spaces within the hypertrophied ventricular walls and the epicardial arteries themselves, although an important investigation had also been published by the group from Auckland, New Zealand,[14] with this group recently updating their experience to emphasise the clinical significance of the communications.[15]

The critical feature is the communications between the right ventricular cavity and the epicardial coronary arteries. These fistulous communications are present in the setting of systemic right ventricular pressure, usually with a competent tricuspid valve, so the flow of blood in the presence of significant communications is typically from the right ventricle to the coronary arterial tree, underscoring the so-called right ventricular-dependent circulation.[4,5] The fistulous communications are readily revealed by angiographic investigations,[16] and by echocardiographic interrogation, again in both foetal and postnatal life.[11,16] The abnormal coronary arteries are obvious at autopsy examination (Fig 3), with the flow of blood into the coronary arterial tree producing significant disease of the proximal segments of the coronary arteries themselves (Fig 4). The changes in the walls of the coronary arteries were initially considered to be inflammatory in origin. We now know that this is not the case.[5] Instead, the changes are the consequence of myointimal hyperplasia.[5] In the most severe cases, the proximal coronary arteries can show severe stenosis, or even complete occlusion

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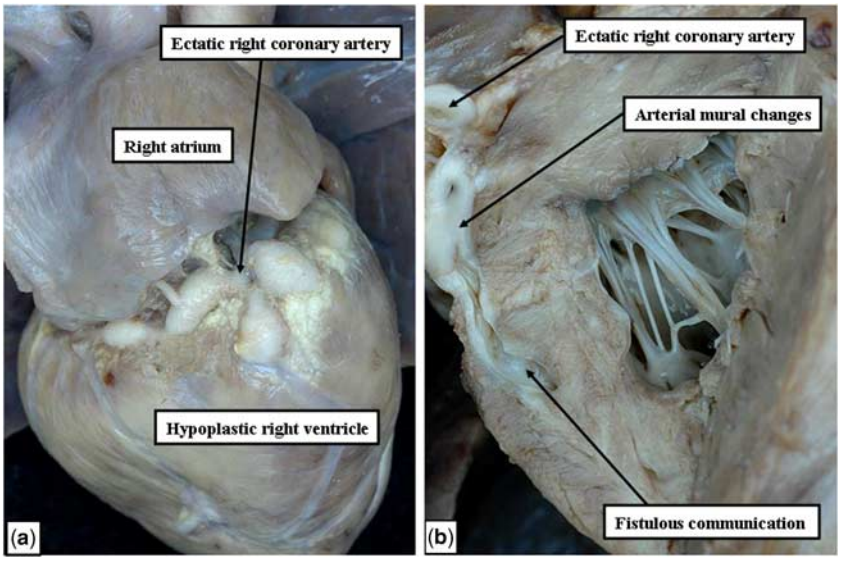

Figure 3.
*The panels (**a**–**b**) show the ectatic right coronary artery in a patient with pulmonary atresia and intact ventricular septum (**a**), with dissection revealing the fistulous communication between the hypoplastic ventricular cavity and the abnormal right coronary artery (**b**).*

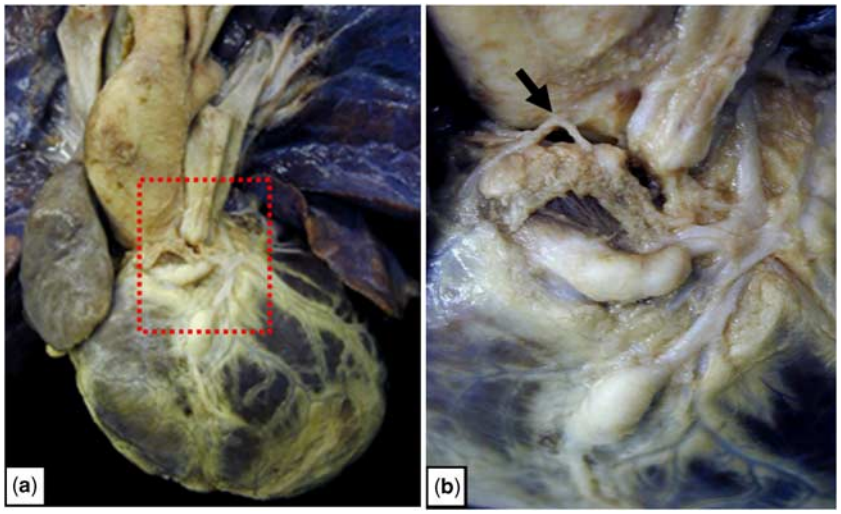

Figure 4.
*The panels (**a**–**b**) show the consequence of fistulous communications with the coronary arteries in the heart from a patient with pulmonary atresia and intact ventricular septum. Panel **a** shows the overview, with the boxed area enlarged in panel **b**. The right coronary artery (arrow) is atretic at its aortic origin, and the anterior interventricular artery is thickened and abnormal.*

of the lumens (Fig 5). Indeed, in rare cases both right and left coronary arteries lose their connections with the aortic root.[17] It is the obstructive lesions in the proximal coronary arteries that underscore the myocardial ischaemia known to be associated with the presence of the fistulous communications. Myocardial rupture, secondary to acute myocardial infarction, has been reported in the occasional patient.[18] It is the fistulous communications, therefore, that indicate the likelihood of a poor prognosis in neonates born with pulmonary atresia with intact ventricular septum, these lesions being a feature of the subset of patients having muscular rather than valvar atresia, and typically being found in those with the most hypoplastic right ventricular cavities.[3,5]

Hypoplastic left heart syndrome

Like pulmonary atresia with intact ventricular septum, hypoplastic left heart syndrome represents cardiac disease acquired during foetal life. In addition, as with the right-sided malformations, there is also marked

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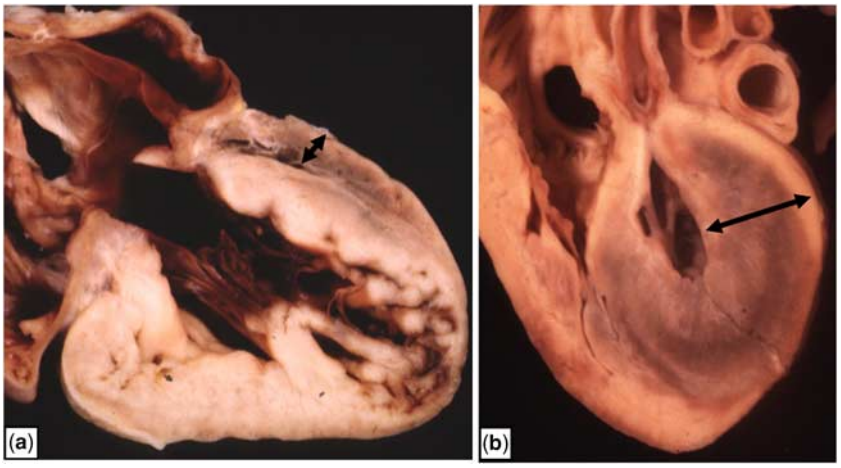

Figure 5.
*The panels (**a**–**b**) show the fundamental difference in the architecture of the left ventricular wall when there is absence of the left atrioventricular connection (**a**) as opposed to mitral stenosis (**b**) in the setting of hypoplastic left heart syndrome. The left ventricular wall is appreciably thicker, and "blighted" (double-headed arrows) when there is flow of blood into the left ventricle in the presence of mitral stenosis (**b**).*

anatomical heterogeneity to be found among those patients falling within the definition of the syndrome. In those with hypoplastic left ventricles, the major difference reflects the formation of the left atrioventricular junction, which in turn has significance for the architecture of the left ventricular walls. In a minority of patients, there is complete absence of the left atrioventricular connection, and in another small subset, the mitral valve is formed but imperforate (Fig 5a). In these patients, there has never been flow of blood into the left ventricle, which in consequence has a grossly hypoplastic cavity, in some instances only being discovered following careful dissection guided by the location of the anterior and inferior interventricular arteries. In these instances, although the ventricular cavity is grossly hypoplastic, its walls are relatively thin, and the endocardial lining is normal. In the larger subset of patients, the mitral valve is patent, with either aortic atresia or critical aortic stenosis (Fig 5b). In these latter cases, there has been flow of blood into the hypoplastic ventricle during foetal life, and the ventricular walls are hypertrophied, typically with formation of a thick layer of gross endocardial fibroelastosis. It is these patients with hypertrophied ventricular walls and fibroelastosis that the late Robert Freedom considered to have "blighted myocardium". He had opined that such patients might have a poorer outcome after surgical treatment than those with mitral atresia, albeit that initially little evidence was forthcoming to support his prognostications. It had also been shown, however, that the patients with mitral stenosis rather than atresia also had microscopic fistulous communications with the coronary arterial circulation.[6,7] The presence of the fibroelastosis likely prevents the development of

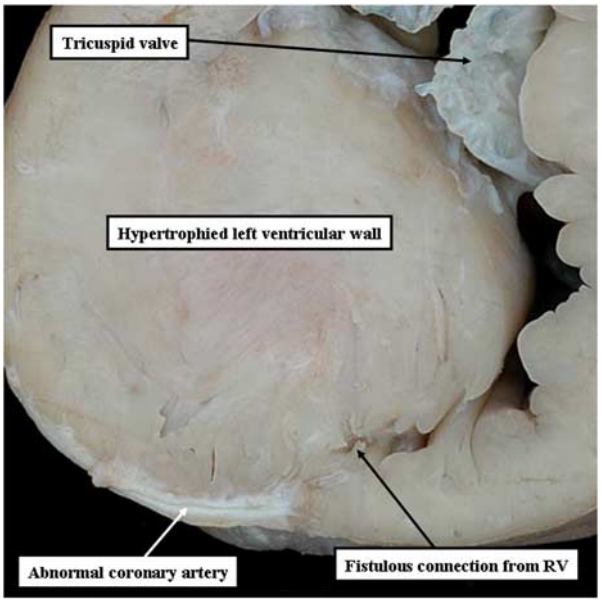

Figure 6.
The image shows a section through the ventricular septum in an explanted heart from the patient with hypoplastic left heart syndrome. There is an overt fistulous communication from the cavity of the right ventricle to the diseased inferior interventricular artery.

large connections with the epicardial coronary arteries, as is seen in pulmonary atresia with intact ventricular septum; but increasing experience shows that, on occasion, such overt communications can be found.[8] We have recently encountered such connections in an explanted heart from a patient with hypoplastic left heart syndrome. It proved possible to probe a fistulous communication to the inferior interventricular artery from the cavity of the right ventricle, and sectioning

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the heart revealed a diseased artery (Fig 6). The left ventricular myocardium was grossly hypertrophied, albeit that overt fistulous connections were not identified from the cavity of the left ventricle, which was very restricted. It may well be, nonetheless, that as predicted by Robert Freedom, the myocardium can be "blighted" in the setting of hypoplastic left heart syndrome, and that such findings could indicate a poorer prognosis.

Conclusions

Fistulous communications between the ventricular cavities and the coronary arterial tree can be found in the presence of hypoplasia of both the right and left ventricle when the ventricular septum is intact. The communications are obvious in the setting of pulmonary atresia with intact ventricular septum, and are well-known to carry a poor prognostic significance. Fistulous communications may prove to be equally important in the setting of hypoplastic left heart syndrome, albeit not as easy to define morphologically.

References

1. Norwood WI, Lang P, Hansen DD. Physiologic repair of aortic atresia-hypoplastic left heart syndrome. N Engl J Med 1983; 308: 23–26.
2. Freedom RM, Jaeggi E, Perrin D, Yoo SJ, Anderson RH. The "wall-to-wall" heart in the patient with pulmonary atresia and intact ventricular septum. Cardiol Young 2006; 16: 18–29.
3. Anderson RH, Anderson C, Zuberbuhler JR. Further morphologic studies on hearts with pulmonary atresia and intact ventricular septum. Cardiol Young 1991; 1: 105–114.
4. Freedom RM, Harrington DP. Contribution of intramyocardial sinusoids in pulmonary atresia and intact ventricular septum to a right-sided circular shunt. Br Heart J 1974; 36: 1061–1065.
5. Freedom RM, Anderson RH, Perrin D. The significance of ventriculo-coronary arterial connections in the setting of pulmonary atresia with an intact ventricular septum. Cardiol Young 2005; 15: 447–468.
6. O'Connor WN, Cash JB, Cottrell CM, Johnson GL, Noonan JA. Ventriculocoronary connections in hypoplastic left hearts. An autopsy microscopic study. Circulation 1982; 66: 1078–1086.
7. Sauer U, Gittenberger-de Groot AC, Geishauser M, et al. Coronary arteries in the hypoplastic left heart syndrome. Histopathologic and histometrical studies and implications for surgery. Circulation 1989; 80: I168–I176.
8. Roberson DA, Cui W, Cuneo BF, Van Bergen AH, Javois AJ, Bharati S. Extensive left ventricular to coronary artery connections in hypoplastic left heart syndrome. Echocardiography 2008; 25: 529–533.
9. Oberhoffer R, Cook AC, Lang D, et al. Correlation between echocardiographic and morphological investigations of lesions of the tricuspid valve diagnosed during fetal life. Br Heart J 1992; 68: 580–585.
10. De Leval M, Bull C, Stark J, Anderson RH, Taylor JFN, Macartney FJ. Pulmonary atresia and intact ventricular septum: surgical management based on a revised classification. Circulation 1982; 66: 272–280.
11. Sandor GGS, Cook AC, Sharland GK, Ho SY, Potts JE, Anderson RH. Coronary arterial abnormalities in pulmonary atresia with intact ventricular septum diagnosed during fetal life. Cardiol Young 2002; 12: 436–444.
12. Dusek J, Ostadal B, Duskova M. Postnatal persistence of spongy myocardium with embryonic blood supply. Arch Pathol 1975; 99: 312–317.
13. Gittenberger-de Groot AC, Sauer U, Bindl L, Babic R, Essed CE, Buhlmeyer K. Competition of coronary arteries and ventriculo-coronary arterial communications in pulmonary atresia with intact ventricular septum. Int J Cardiol 1988; 18: 243–258.
14. Calder AL, Co EE, Sage MD. Coronary arterial abnormalities in pulmonary atresia with intact ventricular septum. Am J Cardiol 1987; 59: 437–442.
15. Calder AL, Peebles CR, Occleshaw CJ. The prevalence of coronary arterial abnormalities in pulmonary atresia with intact ventricular septum and their influence on surgical results. Cardiol Young 2007; 17: 387–396.
16. Dyamenahalli U, McCrindle BW, McDonald CM, et al. Pulmonary atresia with intact ventricular septum: management and outcomes of 210 consecutive patients. Cardiol Young 2004; 14: 299–308.
17. Lenox CC, Briner J. Absent proximal coronary arteries associated with pulmonic atresia. Am J Cardiol 1972; 30: 666–669.
18. Hubbard JF, Girod DA, Caldwell RA, Hurwitz RA, Mahoney LA, Waller BF. Right ventricular infarction with cardiac rupture in an infant with pulmonary atresia with intact ventricular septum. JACC 1983; 2: 363–368.

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