Mitral atresia *Morphological details*

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SUMMARY The morphological characteristics of mitral atresia were studied in 30 hearts to determine the presence or absence of a morphological rudiment of the atretic valve and the relation of this rudiment, if found, to any chamber in the ventricular mass. All the hearts showed atrial situs solitus and no ventricular inversion; consequently all had left atrioventricular atresia. In all instances dense fibrous tissue connected the floor of the left atrium to the left ventricle. This connective tissue is considered to be the morphological rudiment of the atretic mitral valve. In several hearts the intervening fibrous tissue varied from a thick fibrous membrane to a tiny fibrous cord; it is impossible to detect these variations clinically. It is, therefore, more practical to classify those hearts which have a detectable fibrous membrane macroscopically as having an "imperforate membrane" and those with a fibrous strand detectable only microscopically as having an "absent atrioventricular connection."

In the present study we examined certain morphological characteristics of mitral atresia.¹⁻³ For hearts with atresia of one atrioventricular orifice a new positional nomenclature has been advocated,⁴⁻⁸ which is considered to be of particular value for clinical use.⁹⁻¹¹ Thus both mitral and tricuspid atresia are classified as atresia of either the left or the right atrioventricular orifice. This is because in hearts with different ventricular arrangement both the right sided and the left sided valves may be of mitral or tricuspid morphology. While it is important to know which side a given valve occupies, it is equally important to know if it is of mitral or tricuspid morphology.¹²

In most hearts the anatomy allows the ventricular mass to be described in terms of morphological leftness or rightness. The same applies to the morphological left and right atrioventricular orifice—that is, the mitral and tricuspid orifices respectively. Since we intended to describe the anatomical characteristics of atresia of the morphologically left atrioventricular valve (mitral valve) we could not solely use the positional nomenclature.

Hearts showing atresia of one atrioventricular orifice form a complicated group.^{4,7,8,11} As a first step in solving the problem of mitral rather than tricuspid atresia, we selected those hearts which undoubtedly had an atretic mitral orifice. Hearts with left sided tricuspid atresia, as well as the rare instances in which the indeterminate ventricular morphology did not indicate tricuspid or mitral atresia, were excluded from the study.

We studied the morphological characteristics of an atretic mitral valve both macroscopically and microscopically to determine (a) whether a morphological rudiment of the atretic mitral valve was present; and (b) whether this rudiment, if found, might be related to any other ventricular cavity than the left ventricle. We have further differentiated mitral atresia into "absent atrioventricular connection" and "imperforate membrane"^{5,7,8,10,11} in the light of our results.

Materials and methods

Thirty hearts were examined by the segmental approach.¹³ All the hearts showed left sided mitral atresia, on the basis of the morphological characteristics in the ventricular part of the heart, which are described in our results.

Macroscopically a thin imperforate membrane was evident in four hearts; in the remaining 26 we could not easily decide whether there was a very small com-

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pect membrane or no mitral valve.^{58 10 11}

To determine the anatomical characteristics of mitral atresia in more detail we examined complete serial sections of 11 hearts. The central fibrous body, the conducting system, the region of the atretic mitral valve, and a part of the ventricles were included in the sections.

Results

The specimens were divided into two subgroups depending on whether the dominant ventricle had a right ventricular (26 hearts) or left ventricular (four hearts) morphology.

DOMINANT RIGHT VENTRICLE

Macroscopical appearance

All 26 hearts showed atrial situs solitus. The right atrium was large and connected through a patent foramen ovale to a much smaller left atrium. The valvula foraminis ovalis bulged more or less extensively

Fig. 1 Macroscopic morphological appearance of the heart showing the small left ventricle (LV) with the lateral wall (LW) pulled upward. Part of the endocardium covering the septum is artificially loosened. The atretic mitral valve (AM) consists of a large fibrous membrane which bulges into the left ventricle. LAA, left atrial appendage; LAD, left anterior descending coronary artery.

Fig. 2 Macroscopic morphological appearance of the heart showing left atrial cavity (LA) with a dimple (D) in the floor indicating the possible site of the atretic mitral valve. The small left ventricle (LV) is located directly underneath the dimple. (See also Fig. 3.) FO, patent foramen ovale; PV, pulmonary veins; LAA, left atrial appendage.

into the lumen of the right atrium. The right atrium connected through a patent tricuspid orifice to the dominant right ventricle. The diagnosis of right ventricular morphology was based on the finding of coarse apical trabeculations and a more or less clearly marked trabecula septomarginalis. The septum reached the crux posteriorly.

Two hearts showed a small perimembranous septal defect, through which a small cavity in the left posterior position was reached. As these two hearts also had a double outlet connection from the right ventricle the ventricular septal defect provided the sole connection to the small cavity.

Macroscopic inspection of the left atrium showed a fibrous membrane of 3 mm or more in diameter in three hearts. Underneath this membrane was a small ventricular cavity (Fig. 1). In the remaining 23 hearts a dimple was evident in the floor of the left atrium, indicating the possible location of the atretic mitral valve (Fig. 2). Guided by the site of the dimple, the external coronary arterial pattern—and by a ventricu-

Fig. 3 Macroscopic morphological appearance of the heart showing the small left ventricle (LV) found directly underneath the dimple in the left atrium shown in Fig 2. The endocardium is normal, as is to be expected in mitral atresia. Clearly visible is the left anterior descending coronary artery (LAD) which does not closely relate to the cavity of the left ventricle. RV, right ventricle; P, pulmonary trunk; LA, left atrium.

lar septal defect in two hearts—a small ventricular cavity, sometimes containing a blood clot, was detected macroscopically in 16 hearts (Fig. 3). In the remaining seven we did not search extensively as these hearts were to be used for histological examination.

Macroscopic detection of an outflow tract to the aortic orifice was often difficult. In 21 hearts there was aortic atresia; in three the aortic orifice was patent. As has been mentioned already, the remaining two hearts with a ventricular septal defect had a patent aortic orifice originating from the right ventricular chamber.

Microscopical appearance

Complete serial sections were made in seven hearts without a ventricular septal defect. Fig. 4 shows the histological findings. A small ventricular cavity was always present. In some hearts it was so small that it could not have been detected macroscopically. In its

apical extension the cavity could resemble a coronary arterial system (Fig. 4c). In all seven hearts there was dense connective tissue between the floor of the left atrium and the ventricular cavity, with no intervening sulcus tissue or myocardium. This fibrous connection varied from a thick membrane (Fig. 5) to a thin fibrous cord (Fig. 6). It was continuous with the fibrous tissue of the central fibrous body, which in several hearts partly surrounded the small left ventricle (Figs. 5 and 6). All hearts had a normal distribution of the conducting system, with a left bundle branch relating to the small ventricular cavity. The left bundle branch sometimes extended beyond the cavity towards the apex of the heart.

The eighth heart studied histologically showed a ventricular septal defect and double outlet from the right ventricle. Histological examination showed a continuous fibrous connection between the left atrium and the central fibrous body leading to the small left posterior cavity (Fig. 4d).

DOMINANT LEFT VENTRICLE

In four hearts there was atrial situs solitus and a right sided anterior outlet chamber with a right ventricular trabecular pattern. On the posterior wall of the left ventricle a muscle ridge was evident, which we considered to be the posteromedial muscle found in hearts with a double inlet left ventricle.¹⁴

In two hearts there was an inlet septal defect, through which the tricuspid valve straddled more than 50% into the large left ventricle. The septum did not run to the crux, being deviated posteriorly to the right of a muscle ridge on the posterior wall of the left ventricle. This morphology is typical of a straddling tricuspid valve.¹⁵ The tricuspid valve connected to the right atrium. In the left atrium there was no atrioventricular orifice. Probing of the floor of the left atrium at the possible site of the atretic mitral valve indicated that it was located in the roof of the ventricle to the left of the posteromedial muscle (Fig. 7).

Microscopical examination of the two hearts with a straddling tricuspid valve showed a fibrous cord connecting the floor of the left atrium to the main chamber of left ventricular type in one and a small compact fibrous membrane in the other (Fig. 4e).

In the remaining two hearts the right atrium connected to the left ventricle by way of the tricuspid valve which was completely committed to this chamber. Again there was no orifice in the floor of the left atrium. In one heart a translucent membrane was found at the site of the atretic mitral valve, being located in the main chamber at the expected site to the left of the posteromedial muscle. The second heart was examined histologically; again the floor of the left atrium was connected by a continuous fibrous membrane to the underlying left ventricle (Fig. 4f).

Fig. 4 Schematic representation of mitral atresia in 11 hearts examined histologically. (a) At the site of the atretic mitral valve a fibrous cord connects the left atrium (LA) to the small left ventricle (LV) via the central fibrous body (black crescent) (three hearts) (see also Fig. 6). (b) This is identical to (a) but here the atretic mitral valve is a small compact membrane (two hearts) (see also Fig. 5). (c) This is identical to (a) but the LV is vestigial and may only be identified histologically (two hearts). (The hearts represented in (a), (b), and (c) all showed aortic atresia and are generally described as hypoplastic left hearts.) (d) This heart showed a small ventricular septal defect, a double outlet RV, and a fibrous cord at the site of the atretic mitral valve. (e) Two hearts showed a tricuspid valve straddling into the "LV"; one had a fibrous membrane at the site of the atretic mitral orifice (depicted) the other a fibrous cord. The central fibrous body is indicated by the black area. (f) One heart showed a complete commitment of the tricuspid valve to the "LV" and a fibrous cord at the site of the atretic mitral valve. The outlet chamber ("RV") is opposite the atretic valve.

Fig. 5 Histological sagittal section of a hypoplastic left heart. The atretic mitral valve is a compact fibrous membrane (see arrow) interposed between the left atrium (LA) and the left ventricle (LV). The latter is partially enclosed by the central fibrous body (CFB). The common bundle (CB) of the conducting system almost reaches the top of the ventricular septum between the right ventricle (RV) and the small LV. TV, septal tricuspid valve leaflet; CS, coronary sinus; S, sulcus tissue (see also Fig. 4b). Van Gieson elastic tissue stain $\times 10$ final magnification.

Fig. 6 Histological sagittal section of a hypoplastic left heart. At the site of the atretic mitral valve there is a fibrous cord (see arrow) connecting the left atrium (LA) and the small left ventricle (LV). There is no intervening sulcus tissue (S) or myocardium. The LV is enclosed by the central fibrous body (CFB), but in more apical sections the LV lies in the myocardium. The CFB is interrupted by the common bundle (CB) of the conducting system. RV, right ventricle; RA, right atrium; TV, septal leaflet of tricuspid valve (see also Fig. 4a). Haematoxylin and eosin tissue stain $\times 10$ final magnification.

Fig. 7 Macroscopic morphological appearance of the left ventricle of a heart in which the tricuspid valve (TV) straddles through the posterior part of a large ventricular septal defect. The straddling valve is almost completely committed to the "LV." The site (arrow) of the atretic mitral orifice (which proved histologically to be a fibrous cord) is next to the posteromedial muscle (PMM). One semilunar valve of the aortic orifice (Ao) is seen. VS, ventricular septum; LW, lateral wall of "LV."

Discussion

In all the hearts examined the site of the connection between the floor of the left atrium and the underlying left ventricle was indicated by dense fibrous tissue, which was sometimes only detectable microscopically. This fibrous tissue is thought to be the morphological rudiment of what in normal development should have been the region of the mitral orifice and valve. This positive histological evidence of a morphological rudiment of the atretic mitral valve allows the relation of this rudiment to the cavities in the ventricular mass to be determined.

In all hearts with a large cavity with right ventricular morphology, the fibrous connection was found between the floor of the left atrium and a small slit like cavity in the left posterior position. This finding, together with the normal distribution of the conducting system and an extension of the ventricular septum to the crux, led us to the conclusion that this second small cavity was indeed a rudimentary left ventricle.

In the hearts with a large left ventricle, the morphological rudiment of the atretic mitral valve was found above this chamber. In all the hearts, therefore, there was a fibrous connection with a left ventricular chamber, whether rudimentary or not.

In our material we found no evidence for a relation between an atretic mitral valve and a right ventricle. Such a finding would represent the morphologically left counterpart of the more common form of right sided tricuspid atresia, in which the atretic orifice is above a left ventricular chamber; this produces an architecture similar to that of hearts with a double inlet connection to a left ventricle.^{5 14 16} We would, of course, be interested to know if an atretic mitral

orifice placed above a right ventricle would still have retained its morphologically left characteristics and therefore still be different from an atretic tricuspid orifice above a left ventricle. Previously, we described such a difference between straddling tricuspid and mitral valves¹⁵ and have shown that a straddling mitral valve is found in hearts with an infundibular septal defect, usually subpulmonary, in the setting of a double outlet right ventricle. This is a typical pathway for the mitral valve to reach the right ventricle. It is, therefore, interesting that recently Ando *et al* found three instances of membranous mitral atresia in which the imperforate membrane was above the right ventricle.¹⁷ All three hearts had a double outlet right ventricle with a subpulmonary ventricular septal defect. We consider that these findings indicate that a mitral valve retains its own characteristic feature when it is above a right ventricle, even when it is atretic.

Further published evidence concentrates on three areas. A first point concerns the presence or absence of a rudimentary left ventricle in hearts with mitral atresia. In general, published reports confirm that a left ventricular cavity is found in close relation to the atretic mitral orifice¹³; sometimes the left ventricle is so small that it resembles only a blood clot in the annulus fibrosus.² This agrees with our findings, which showed, because of the small dimensions, a close relation between the fibrous tissue of the atretic mitral valve, the central fibrous body, and the rudimentary left ventricle. If occasionally a small left ventricle is not found, this is probably due to the inadequacy of the technique.^{3,7} In this respect we are interested in the histological findings of the two hearts with mitral atresia described by Ando *et al* in which the left ventricle was said to be absent.¹⁷

A second point concerns the consistent finding in our material of a morphological rudiment of the mitral valve which varied histologically from a fibrous membrane to a thin fibrous cord. In a study¹⁸ of several hearts with univentricular atrioventricular connection with atresia of one atrioventricular orifice to investigate the distribution of the conduction system, one appeared to have an indeterminate ventricular morphology. Histological examination, however, showed a rudimentary left ventricle and a normal distribution of the conduction system, which is similar to our finding.¹⁸ In this report the legend to the macroscopical figure indicates that there was no evidence of a left ventricular-atrioventricular connection. The accompanying figure of a histological section, which does not show a fibrous connection, cannot be accepted as decisive since the level of the section was not selected for the problem we are analysing. It is, therefore, uncertain whether a fibrous connection was really absent or simply not acknowledged as a morphologi-

cal rudiment of an atretic mitral valve.

Finally, a third point relates to nomenclature and morphology. Anderson and coworkers introduced a nomenclature which is relevant for hearts with atresia of an atrioventricular orifice, whether it is left sided or right sided.^{5,8,10,19} In this positional nomenclature an additional distinction is possible in hearts with an "imperforate membrane" and an "absent atrioventricular connection."^{7,8,11,19} Clinically, it is relevant to distinguish between an "imperforate membrane" and an "absent atrioventricular connection," since valve replacement may be considered in rare cases.⁹ We know that the differentiation can be made with cross sectional echocardiography.^{11,20} Using both macroscopic and histological techniques, in our material we found a range of fibrous tissue varying from a fibrous membrane to a thin fibrous strand. It seems, therefore, that those hearts that have a macroscopically detectable fibrous membrane should be classified as having an "imperforate membrane." Those hearts with a fibrous connection only at the microscopic level should then be considered as cases with an "absent atrioventricular connection." The same applies to the distinction between "membranous atresia" and "muscular atresia",^{16,21} which we believe covers "imperforate membrane" and "absent connection" respectively.

Those hearts that show an imperforate membrane relating to a ventricle with either right or left ventricular morphology may easily be classified as having mitral or tricuspid atresia. Hearts that show an absent atrioventricular connection are more difficult to classify. If an absent atrioventricular connection is found in combination with a large right ventricle, a rudimentary left ventricle, and a septum running to the crux the atretic orifice is most likely to be the mitral orifice, whether it is right sided or left sided. The latter finding is the most common. If there is an absent atrioventricular connection in combination with a large left ventricle the defect is most likely to be tricuspid atresia, in which the position of the atretic orifice is close to the posterior part of the deviated septum and thus to the outlet chamber. In rare cases the atresia is mitral if the outlet chamber is opposite the atretic orifice.

In most hearts with atresia of an atrioventricular orifice we were, therefore, able to decide whether the atresia was mitral or tricuspid. This is also true of most cases that have been reported in sufficient morphological detail.^{4,8,17} In a recent report by Restivo *et al* four illustrative cases are described with left sided atrioventricular atresia.⁸ As these workers have suggested already, two hearts had left sided tricuspid atresia (cases 2 and 4) and one left sided mitral atresia (case 1). In view of our results we are not surprised that the atretic orifice was found to be opposite the

outlet chamber in the latter case. In mitral atresia the patent tricuspid valve may not be characteristic in its appearance.⁸ This should not be used as an argument against it being the morphological right atrioventricular valve. Valve leaflet formation occurs late in development.²² In those hearts showing a straddling tricuspid valve or complete commitment of this valve to a left ventricular cavity there is an underlying abnormal development of the ventricular septum resulting in an abnormal tricuspid valve leaflet pattern.

In a few cases the distinction between a morphological left and right atrioventricular valve cannot be made because of indeterminate ventricular morphology, as in the report (case 3) of Restivo *et al.*⁸ We hope that with increasing knowledge of cardiac development some characteristic morphological details may be identified in these cases also.

In summary, to describe fully the morphological nature of valve atresia not only is it necessary to know the sidedness and nature of the atresia but also whether the morphology is tricuspid or mitral.

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