Virchows Arch. A Path. Anat. and Histol. 379, 313–320 (1978)

Virchows Archiv A
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Double Outlet Right Ventricle in a Human Embryo

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Summary. A human embryo of 14 mm crown-rump length is described to exemplify the anomaly of double outlet right ventricle with subaortic defect. The configuration of endocardial swellings in the outflow portion of the heart are compatible with the general architecture of full-grown examples of the anomaly. This configuration differs considerably from normal embryonic anatomy, but is still supported by the architecture of the myoepicardial mantle. It is concluded that endocardial swellings play a secondary role in the determination of fullgrown cardiac anatomy.

Key words: Cardiac embryology – Double outlet right ventricle – Bulbar ridges – Bulboventricular fold.

Introduction

Explanation of congenital cardiac malformations has to be based largely upon the knowledge provided by normal embryonic hearts from all relevant stages and by collections of fully developed malformed hearts. Reported examples of embryonic stages of such malformations are scarce. Here a description is given of a case of double outlet right ventricle in a human embryo of 14 mm crown-rump length. This one case cannot provide full explanation of the pathogenesis of double outlet right ventricle, but the observed morphology is thought to be relevant for cardiac maldevelopment in general.

Material and Methods

The embryo under discussion had been obtained from an extrauterine pregnancy of unknown duration. It had a crown-rump length of 14 mm. According to the criteria laid down by Streeter (1948), its developmental stage belonged in Horizon XVII. Serial sections (10 μm) were made in an oblique frontal direction, and stained with hematoxylin and eosin.

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0340-1227/78/0379/0313/$01.60

Reconstructions of the heart were made both in cardboard and by a direct graphic method. In the illustrations only the graphic reconstructions are shown.

Description of the Heart

At first sight, the heart had an abnormally long, stretched form (Figs. 1 and 5). The venous side of the heart was normal. The atrioventricular endocardial cushions were close together so as completely to separate left and right atrioventricular orifices (Fig. 6).

However, the outflow tract did not show normal morphology; the aortic orifice was posterior to and below the pulmonary orifice, and both arterial orifices were above the right ventricle.

The configuration of endocardial swellings below the arterial orifices was remarkable. Most distally, a left and right bulbar ridge could be distinguished, which had fused into a bulbar septum (Fig. 2). Although this fusion would have been expected to have proceeded more proximally in the present developmental stage, no gross abnormality was noted. More proximally, however, it was difficult to distinguish normal left and right bulbar ridges. The endocardial swelling, which distally could be identified as the right bulbar ridge, was seen to taper off in an apical direction (Fig. 3). It never reached its normal position relative to the tricuspid orifice.

The left bulbar ridge also showed abnormalities in its more proximal part. It did not extend along the anterior border of the interventricular foramen, but remained posterior to the latter and thinned out to the right of an abnormal rightward expansion of the bulboventricular fold (Figs. 3 and 5). This expansion was very close to the right bulbar wall, just proximal to the site where the right bulbar ridge was seen to diminish. Here, continuous with the thin strand of endocardium, which was the proximal end of the left bulbar ridge, a new thick endocardial swelling was present (Fig. 4). This swelling was seen to be continuous with the most proximal end of the incomplete right bulbar ridge. Its position relative to the right atrioventricular orifice was as would have been expected with a normal right bulbar ridge. Its relationships with the upper atrioventricular cushion and the right lateral cushion were reminiscent of a normal right bulbar ridge (Figs. 5 and 6).

The connection between the two bulbar ridges, that is the elevation connecting the bulboventricular fold to the right bulbar wall, formed a threshold between the left ventricular outflow tract and the aortic orifice (Figs. 4 and 7). The elevation was, itself, to the right of the plane of the ventricular septum, so, at the same time, it formed a threshold between the right atrioventricular orifice and the aortic orifice (Fig. 6).

The important features of this heart may be summarized as follows:

– both arterial orifices were above the right ventricle (Fig. 8);

– accentuation of the bulboventricular fold caused the aortic orifice to be distant from both atrioventricular orifices (Fig. 8);

– an additional endocardial swelling was apposed to the bulboventricular fold; it formed a second, proximal connection between the left and right bulbar ridges in addition to the bulbar septum (Fig. 6).

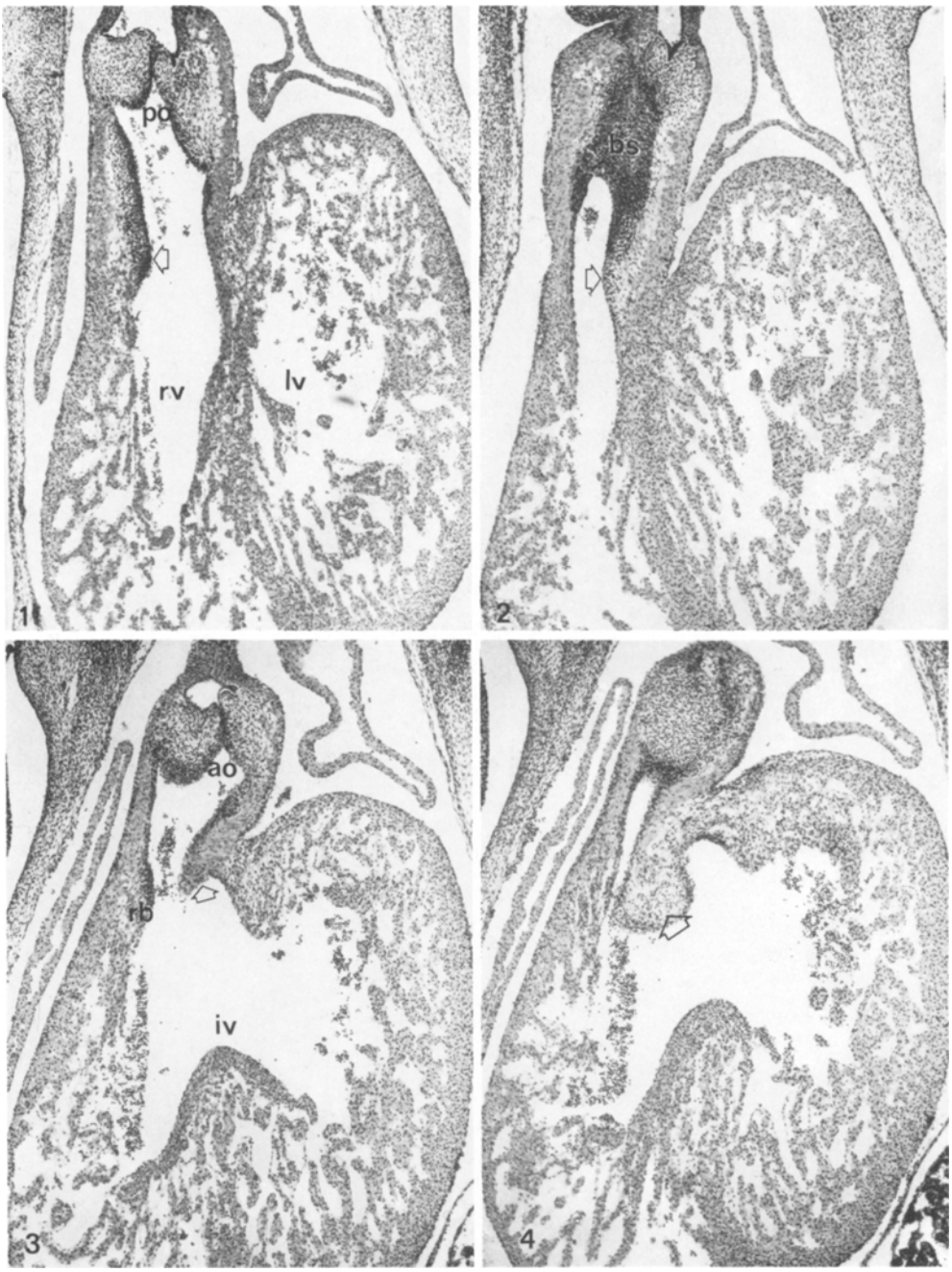
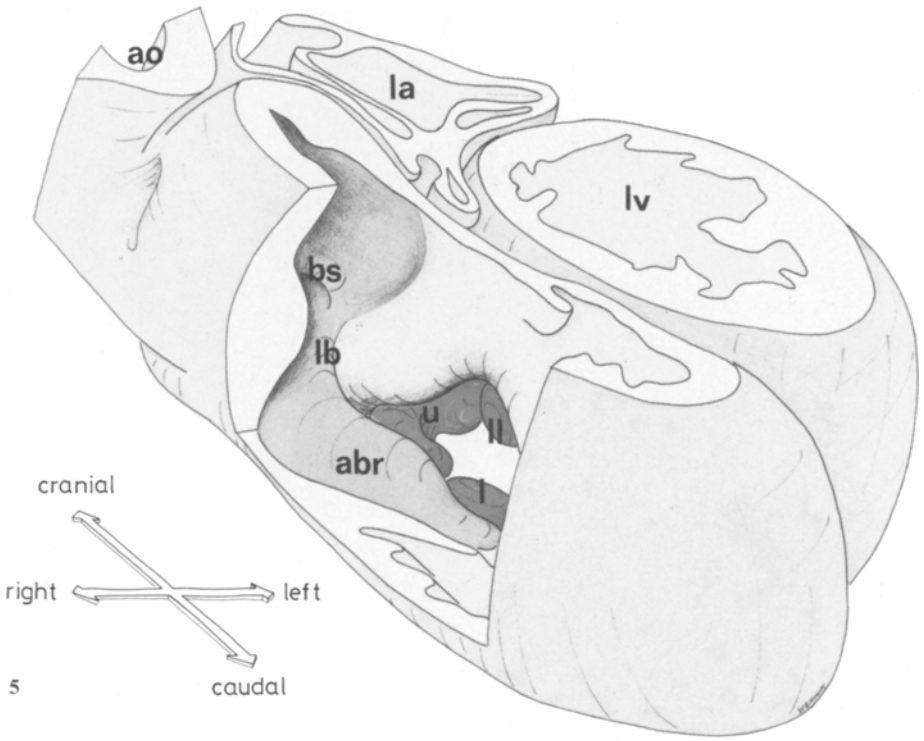


Fig. 1. Oblique frontal section of the heart. Note its stretched appearance. *lv* left ventricle, *rv* right ventricle, *po* pulmonary orifice. The right bulbar ridge is arrowed (× 52)

Fig. 2. Slightly more posterior and inferior section, showing the compact bulbar septum (*bs*). The left bulbar ridge is arrowed (× 52)

Fig. 3. Section at the level of the interventricular foramen (*iv*), showing the left bulbar ridge to thin out along the strong bulboventricular fold (*arrow*). Note the tiny right bulbar ridge (*rb*). *ao* aortic orifice (× 52)

Fig. 4. Section to show the additional bulbar ridge (*arrow*), very close to the right bulbar wall (× 52)



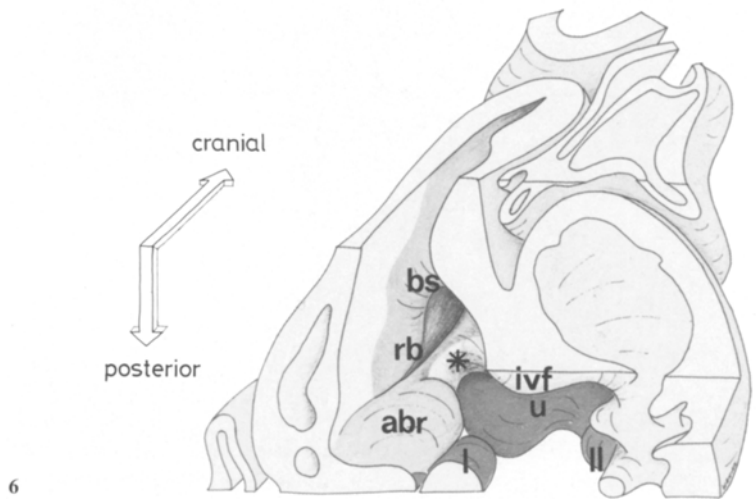


Fig. 5. Reconstruction of the heart. Note its stretched appearance. The additional bulbar ridge (*abr*) is continuous with the thin left bulbar ridge (*lb*). Its relations with the upper (*u*) and lower (*l*) atrioventricular cushions remind of those of the right bulbar ridge in normal hearts. Through the interventricular foramen, the left lateral atrioventricular cushion (*ll*) is visible as well. *lv* left ventricle, *la* left auricle, *ao* ascending aorta, *bs* bulbar septum

Fig. 6. Part of the same reconstruction, antero-inferior view. The tricuspid orifice is surrounded by the upper (*u*) and lower (*l*) atrioventricular cushions, and the additional bulbar ridge (*abr*). The bulboventricular fold (*asterisk*) forms a threshold between the ventricles and the aortic orifice (see also Fig. 7). *rb* right bulbar ridge, *bs* bulbar septum, *ll* left lateral cushion, *ivf* roof of the interventricular foramen

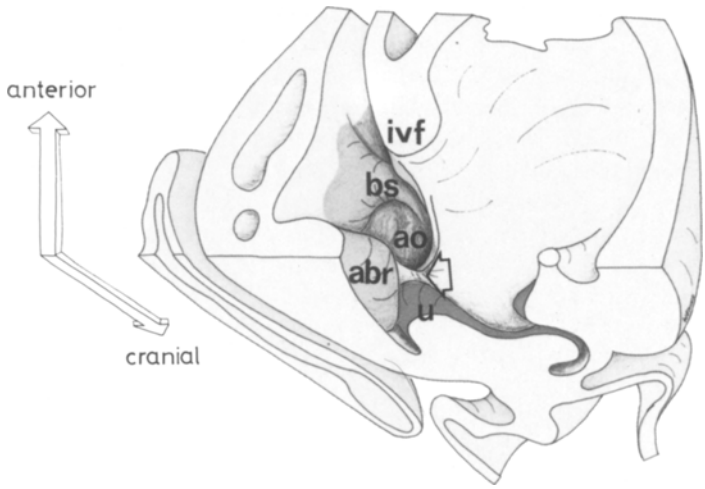


Fig. 7. The same part viewed from a postero-inferior direction. The bulboventricular fold (*arrow*) forms a threshold to the entrance to the aortic orifice (*ao*). *bs* bulbar septum, *abr* additional bulbar ridge, *u* upper atrioventricular cushion, *ivf* roof of the interventricular foramen

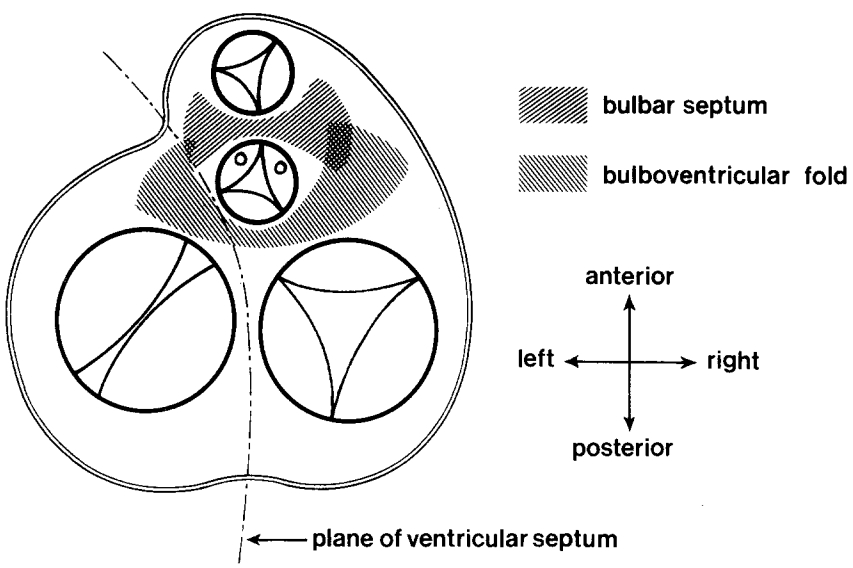


Fig. 8. Schematic representation of the condition of the present heart. Both great arteries are shown to be above the right ventricle. The aortic orifice is separated from both atrioventricular orifices by the bulboventricular fold. Note that the double outlet condition causes two separate bands to be present in the roof of the right ventricle, which is indeed the case in adult specimens with this malformation

Discussion

In early developmental stages neither of the great arteries is above the future left ventricle, but the present embryo shows a cardiac morphology not en-

countered in normal embryonic stages. The malformation can be described as double outlet right ventricle with subaortic defect. It must be added that an interventricular communication is not a surprising phenomenon in a 14 mm embryo, but since the anomaly described is much more common when associated with a ventricular septal defect, it can be suggested that the communication would not have closed in subsequent development. As to the relative positions of the arterial orifices, it is known that in the majority of cases with this malformation the aortic orifice is to the right of the pulmonary orifice and in approximately the same horizontal plane (Hollman, 1968; Edwards, 1968; Lev et al., 1972; Anderson et al., 1974). In the present embryo, atypically the aortic orifice was in a posterior position possibly connected with the abnormally long, stretched form of the heart itself. In addition, during subsequent development the relative positions of the orifices might have changed.

The next point of discussion is the question of aortic-mitral fibrous continuity. According to Lev et al. (1972), the present heart fulfills the criteria for double outlet right ventricle. If, however, the anomaly is also required to lack aortic-mitral continuity (e.g. Sridaromont et al., 1976), no definite statement can be made. In the 14 mm embryo there was a conspicuous elevation between aortic and mitral orifices, which contained myocardium. The anomaly is, therefore, localized in what has been called the conflict zone (Doerr, 1952). It cannot be predicted what the fate of this elevation would have been in further development and its persistence has been described in a case that exhibited normal ventriculoarterial connections (Bersch et al., 1975). Be this as it may, the elevation in this case is felt to be more pronounced than is normal in developmental stages. This elevation is deliberately described as an abnormal expansion of the bulboventricular fold to suggest that it is possible that the muscular band between aortic and atrioventricular orifices in double outlet right ventricle is not merely the effect of persistence of the bulboventricular fold (Anderson et al., 1974), but of its abnormal accentuation. This reminds us of Grant's (1962) statement, that no resorption of the bulbus would be necessary to explain the proximity of the aorta to the mitral orifice in normal adult hearts. He suggested that the change in distance seen during normal development is only a relative one.

It is important to note that in the present embryo an abnormal endocardial swelling added to the accentuation. Interestingly, this same embryonic heart has been described before by Los (1972) who did not publish histological sections, and whose drawings of his reconstruction do not show the relationships of the endocardial swellings in much detail. Although Los (1972) did mention the endocardial ridge between the aorta and the left ventricle, he came to no conclusions on the abnormality of the heart. However, the configuration of the endocardial swellings in this embryo may explain the morphology of the myocardial bands surrounding the orifices in most cases of double outlet right ventricle. This configuration is not directly comparable to that of the bulbar ridges in normal embryonic hearts (Wenink, 1971). This makes the endocardial swellings less reliable points of reference in the explanation of cardiac maldevelopment in general.

The present embryo may be a good illustration of the importance of the

bulboventricular fold (bulboauricular flange) in cardiac development (Bersch, 1971). Moreover, the abnormal additional bulbar ridge, that was so close to the bulboventricular fold, bears some resemblance to the bulboauricular ridge, as described by Bersch (1971). However, the present author is not inclined to overestimate the importance of endocardial swellings in cardiac morphogenesis. It has been stated (Wenink, 1977) that the embryonic endocardial swellings indicate the site of elevations in the myoepicardial mantle. This may be considered a paraphrase of Goerttler's (1955) conclusion, that formation of endocardial swellings is a (secondary) effect of the form of the heart tube. They could be considered only as fleeting structures which do not determine final gross morphology. Their susceptibility to hemodynamic influences (Pexieder, 1975), and their very minor role in valve formation (van Gils, 1978) are in favour of this hypothesis.

Whatever the precise role of endocardial swellings in valve formation, there is general agreement about the right bulbar ridge being the predecessor of the anterior tricuspid valve, or part of it. If it is accepted that in double outlet right ventricle and in Fallot's tetralogy the infundibular septum (which originates from the embryonic bulbar septum) is displaced anteriorly (Anderson et al., 1974; Becker et al., 1975), then the right bulbar ridge would not be able to take part in the formation of an anterior tricuspid leaflet in these malformations. Nevertheless, in most cases of double outlet right ventricle and Fallot's tetralogy, the anterior tricuspid leaflet does not show major abnormalities (Wenink, unpublished observation). This means that the bulboventricular fold, which is interposed between the aortic and atrioventricular orifices, must be able to provide enough material to ensure the formation of a well-shaped anterior leaflet. The "additional bulbar ridge" of the present embryo fits very well with this hypothesis.

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Received April 26, 1978