How normal is a “normal” heart in fetuses with Down syndrome?


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Introduction: Congenital heart disease is present in 44-56% of fetuses with Down syndrome (DS). There are, however, signs that hearts in DS without apparent structural heart defects, also differ from the normal population. Sonic hedgehog signaling may be involved in the pathogenesis of AVSD in DS, although currently data is limited.

We aimed to compare the atrioventricular septum and valves in 3 groups: DS without atrioventricular septal defect (‘DS no-AVSD’), DS with AVSD (‘DS AVSD’) and control hearts.

Methods: The ventricular septum, the atrioventricular (white arrow) and interventricular (black arrow) -membranous septum and AV valves were examined and measured in histological sections of 15 ‘DS no-AVSD’, 8 ‘DS AVSD’ and 34 ‘control’ hearts (Gestational age 10-22 weeks) In addition, the ventricular septum length was measured on ultrasound images of fetal (6 ‘DS AVSD’, 9 ‘controls’) and infant (10 ‘DS no-AVSD’, 10 ‘DS AVSD’, 10 ‘controls’) hearts.

Results: The membranous septum volume was 3 times larger in ‘DS no-AVSD’ fetuses compared to control foetuses (panel A-B) and valve dysplasia (panel D asterisk) was frequently (64%) observed. In the DS fetuses with a (complete) AVSD, fibrous tissue was observed at the top of the ventricular septum in 3 cases. The ventricular septum was shorter in patients with DS both with (0.7 times the length of controls, p=0.001) and without AVSD (0.78 times the sizes of the control, p<0.001). In contrast to controls, in ‘DS no-AVSD’ fetuses, clear expression of Gli1, an effector of sonic hedgehog signaling, was present in the dysplastic plump AV valves and membranous septum in 2 out of 4 cases.

Conclusions: DS no-AVSD hearts are not normal as they have a larger membranous septum, shorter ventricular septum and dysplasia of the AV valves as compared to control hearts. Findings indicate that a careful cardiac follow-up may be warranted in these patients.

Figure: RA = right atrium, RV = right ventricle, LA = left atrium, LV, left ventricle, white arrow atrioventricular membranous septum, black arrow interventricular membranous septum, * = atrioventricular valves.