Filamin A gene pathogenic variant and fetal cardiac valvular dysplasia

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Objective
We aimed to present a case of prenatal diagnosis of Filamin A (FLNA) gene variant in a fetus presenting with severe cardiac polyvalvular dysfunction and no previous family history of heart anomalies. Filamin A is an actin-binding protein involved in cardiac development, particularly in valvular morphogenesis.

Methods
This is a case report.

Results
26-year-old healthy patient, with no medical history of interest and gravida 1, was referred to our centre at 22.6 weeks for a complex cardiac defect identified in the second trimester routine ultrasound. The echocardiography showed a severe cardiomegaly, with a cardiothoracic ratio > 45% associated with polyvalvular insufficiency, more severe at the level of the mitral valve. The mitral leaflets motion was severely restricted which conditioned a massive mitral regurgitation from the apex of the left ventricle (Ebstein’s-like physiology). The aortic arch was also hypoplastic and its flow was reverted from the ductus arteriosus. Additional extracardiac malformations and intrauterine infections were excluded. After confirming a normal molecular karyotype, a targeted clinical exome was performed based on the described cardiac phenotypic abnormalities. It revealed a new variant in hemizygosis in the FLNA gene (c.6401_6404del) classified as a probably pathogenic. The carrier status of the mother was also confirmed, who showed a normal echocardiography. Prenatal follow-up every two weeks revealed an unfavourable progression of cardiomegaly (cardiothoracic ratio >60%) with worsening of mitral valve regurgitation and abnormal ductus venosus Doppler. A labour induction was indicated at 38.6 weeks. Early neonatal echocardiography confirmed the prenatal findings. After a period of clinical stability, the patient developed pulmonary hypertension that led to multiple cardiac decompensations and cardiac insufficiency. Currently, the patient is 5 months old and is awaiting repair surgery of the mitral valve.

Conclusion
We present new FLNA gen variant classified as a probably pathogenic in a fetus with severe cardiac polyvalvular dysfunction. As described in our case, other FLNA gen pathogenic variants have been reported in the context of the cardiac valvular dysplasia X-linked syndrome, which is associated with hypermobility and myxomatous degeneration of the atrioventricular valves; with more severe hemodynamic consequences in male patients.

![Images](a.png)  ![Images](b.png)  ![Images](c.png)