X-linked FLNA mutation with valvular dysplasia

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Introduction: *FLNA* gene codes the protein filamin A that builds the cell cytoskeleton and plays the role in regulating skeletal and brain development, formation of heart tissue and blood vessels, blood clotting, skin elasticity, etc.[1,2] It is found on the *X chromosome* and has X linked inheritance. Cardiovascular abnormalities include dilatation and rupture of the thoracic aorta, outflow tract malformations, valvular dysplasia, patent ductus arteriosus (PDA), atrial and ventricular septal defects, etc[3,4]. Individuals diagnosed with FLNA mutation are usually females because this condition is prenatal/neonatal lethal in most males.[3]

Case report: 19-year-old young man was referred for further follow up due to FLNA mutation (c.4240T>Ap.Tyr1414Asn) and worsening of the left ventricular (LV) function. He was under pediatric cardiologist's surveillance since birth due to PDA, that was percutaneously closed at the age of 3 years. Regular echocardiography exams revealed myxomatous valves and dilation of the left ventricle. On the CMR dilated LV (EDV 147/ml/m^2) with EF of 52% was described, as well as morphological changes of the mitral valve, but no mitral regurgitation (MR). Cardiac CT showed no dilation of the aorta. Genome sequencing was performed and FLNA mutation was found. Afterwards, the same mutation was found in his mother (heterozygotic), whose echocardiogram was normal except mild mitral and tricuspid regurgitation. Our patient was born from mother's third pregnancy. The first pregnancy ended with a miscarriage, while from the second pregnancy apparently healthy female was born (genetic testing pending). Echocardiography revealed severely dilated left ventricle with reduced ejection fraction (EDV 114ml/m^2, LVEF 40%), dilation of the right ventricle (46mm in the apical 4-chamber view) and severe MR (**Figures 1-4**). All heart valves were severely myxomatous with prolapse of the cusps, but with no other significant valvular heart disease. After the new CMR, he will be referred for cardiac surgery.

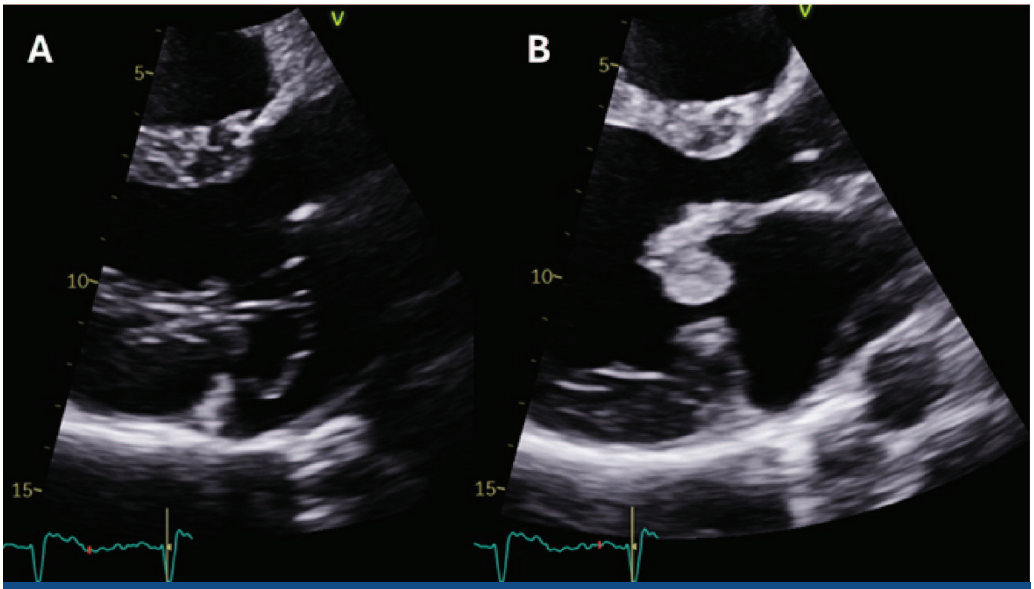

FIGURE 1. Parasternal long axis view in systole (A) and diastole (B) showing prolapse of an extremely myxomatous and thickened anterior mitral leaflet.

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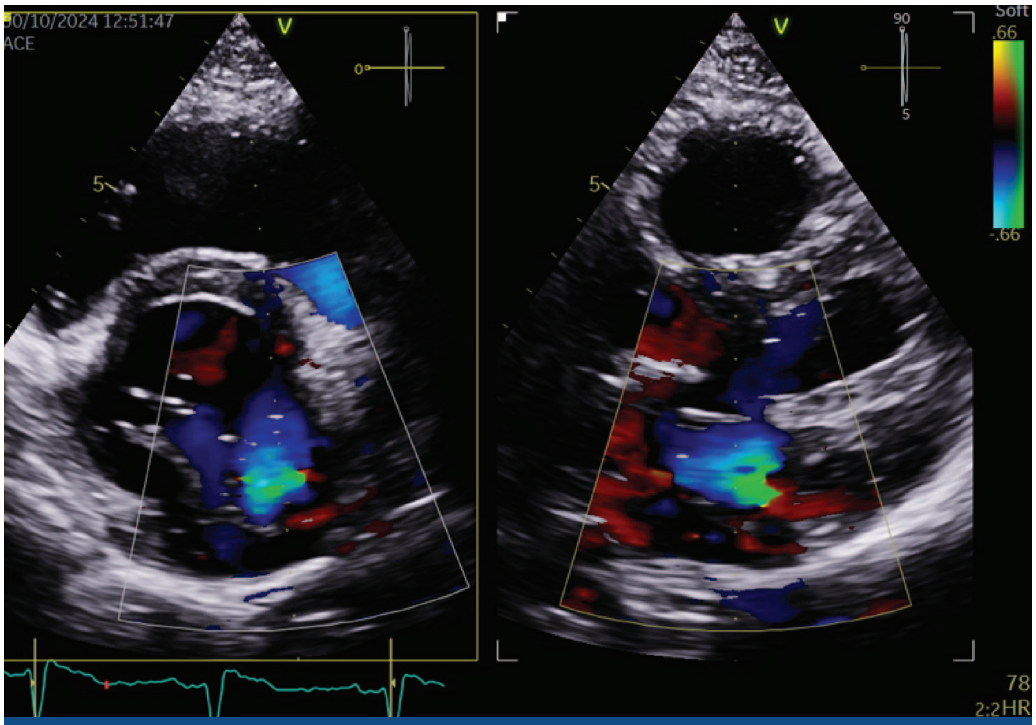

FIGURE 2. Parasternal biplane short axis views showing an extremely eccentric mitral regurgitation jet.

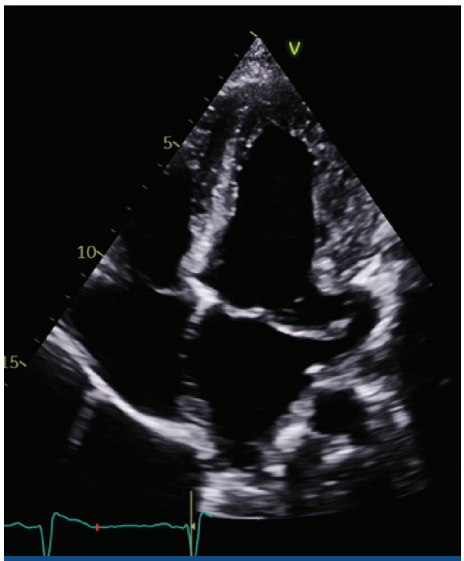

FIGURE 3. Apical 4-chamber view, showing both mitral and tricuspid valve prolapse and pronounced mitral annular disjunction.

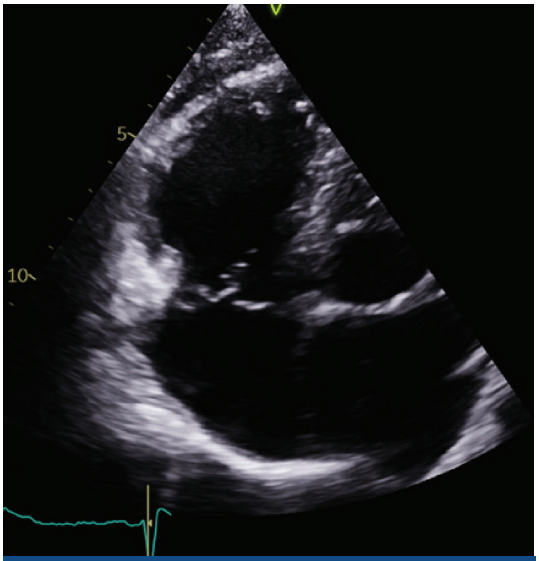

FIGURE 4. Focused apical 4-chamber view showing the dilated right ventricle and prolapse of the tricuspid valve.

Conclusion: Spectrum of FLNA mutation phenotype is wide. The most common phenotype in males is valvular dysplasia. Due to complex changes in the structure and morphology of the mitral valve, diagnosis of MR is challenging.

LITERATURE

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