Aortic dilatation and miscarriages as a main presentation of FLNA mutation in a Croatian family – case report, part two

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Introduction: FLNA gene provides instructions for producing protein filamin A. It plays a role in regulating skeletal and brain development, formation of heart tissue and blood vessels, maintenance of lung tissue, function of digestive system, etc. It is found on the X chromosome and has X linked dominant inheritance (**Table 1**). Pregnancy with aortic aneurysm is rare but potentially fatal. Aortic dissection in pregnancy accounts for 0,1-0,4% of all dissections. Maternal mortality is high.[1-4] Currently there are no guidelines for the management of vascular, cardiac, and connective tissue problems during pregnancy with FLNA mutation.

Case report: We present a family (**Figure 1**) with heterozygous pathogenic variant of FLNA (c.2191-2192insGT (p.Tyr731Cysfs *12)) and aortic aneurism.

Mother: double miscarriages (16th week), two deliveries (vaginal), died at age 60, due to aortic dissection. Last known size of ascendent aorta was 43-45mm. She had mild/moderate aortic regurgitation, mild mitral and tricuspid regurgitation, coronary artery disease and underwent percutaneous coronary intervention at the age of 56.

Sister: one miscarriage (8th week), moderate aortic regurgitation, dilatation of ascending aorta (42mm), pulmonary artery dilatation (40mm), mild pulmonary regurgitation, bilateral periventricular heterotopia, hypoplastic body of corpus calosum. In 2021. gave birth (C-section) to a baby girl GA 34+4 weeks. Baby girl is FLNA mutation positive and has subependymal heterotopia, echocardiography is normal.

Sister: double miscarriage (13th, 8th week), mild mitral and aortic regurgitation, aortic dilatation (2020/2022. 46mm/48mm), joint hyperlaxity, hypoplastic back third of corpus callosum, and bilateral periventricular heterotopia. In 2022 she gave birth (C-section) to a healthy boy GA 34+3 weeks (genetic results pending).

Grandmother: one delivery, three miscarriages, died at the age of 64. We don't have genetic confirmation of mutation. She had sister who has a healthy son, further details are unknown.

Father has dilatation of ascending aorta (41mm), he is not a carrier of FLNA mutation.

TABLE 1. Clinical findings in patients with FLNA mutation.

CARDIOVASCULAR	CENTRAL NERVOUS SYSTEM	GASTROINTESTINAL	OTHER
-Aortic dilatation	-Periventricular nodular hyperplasia	-Intestinal malrotation	-Joint hypermobility
-Outflow tract malformation	-Seizures	-Congenital short small intestine	-Thrombocytopenia
-Patent ductus arteriosus	-Mental retardation	-Pseudo-obstruction/ severe chronic constipation	-Dysmorphic facies
-Atrial/ventricular septal defect	-Cerebellar hypoplasia	-Anal stenosis	-Respiratory infections
-Vascular malformation	-Early hypotonia		-Hypospadias
	-Spasticity		
	-Polymicrogyria		

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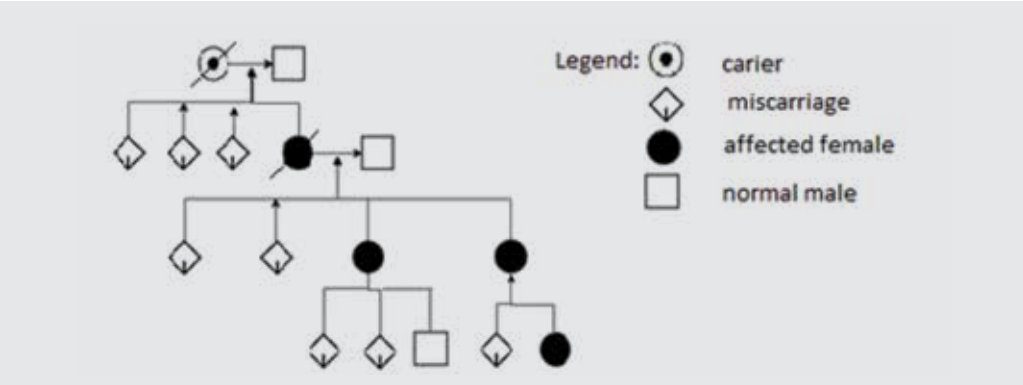

FIGURE 1. Genetic tree.

Conclusion: Both sisters were advised against pregnancy, because there is still no exact data on this mutation and its influence on aneurism progression and childbirth. The pregnancies were high-risk and required team approach - frequent monitoring by cardiologist and gynecologist (during pregnancy and 6 months after delivery).

Patient consent: Obtained from family.

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