Aortic and Pulmonary Artery Dilation Due to a Novel Frameshift Mutation in *FLNA*

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Background

Filamin A (encoded by *FLNA*) is an actin-binding phosphoroprotein involved in cytoskeletal organization. Mutations in *FLNA* are associated with cardiac anomalies, cerebral migratory disorders, interstitial lung disease, pulmonary hypertension and less commonly aortic aneurysms. Pulmonary artery (PA) dilation has only been reported twice previously, once in a male and once ina female.

Case Introduction

A 53-year-old woman undergoing genetic evaluation for vasculopathy was found to have a previously unreported pathogenic *FLNA* mutation (c.5619delC(p.Asn1873Lysfs*55).

Physical Exam

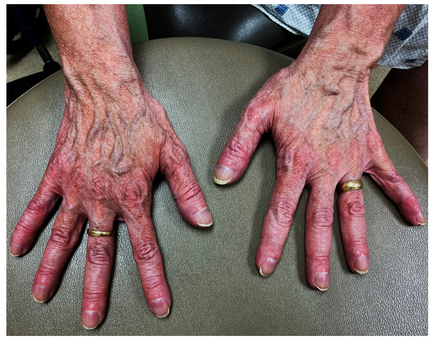

Figure 1: Patient's hands showing acrogeria and the extent of her varicosities

- Cyanotic at baseline
- Normal heart rate and regular rhythm with I/VI systolic flow murmur
- Pectus excavatum
- Hands with acrogeria, increased skin translucency and clubbing
- Diffuse varicosities on arms, chest, and hands

Multisystem Involvement

Cardiac:
- Small to moderate PDA s/p surgical closure age 7
- Aortic valve, ascending and proximal arch replacement for 8 cm aortic root and 5 cm aortic arch at age 21
- Redo ascending aorta replacement and arch replacement and endovascular repair of descending aortic aneurysm at age 45
- Progressive PA dilation to 7 cm
- Pulmonary hypertension with PVR of 7.7 WU responsive to vasodilators currently on dual PH therapy

Respiratory:
- Emphysema with chronic oxygen requirement
- Combined restrictive and obstructive lung disease
- Left bronchus compression from dilated PA and stented aorta

Musculoskeletal:
- Generalized hypermobility, early onset osteoarthritis and chronic pain
- Recurrent patellar dislocations
- Metatarsus adductus food deformity

Neurologic:
- Normal CT and MRA head

Hematologic:
- Chronic thrombocytopenia with severe post-op bleeding complications
- Non-traumatic hemarthrosis while on warfarin

Discussion

- Loss of function mutations in FLNA can be associated with congenital cardiac defects as well as physical and radiographic features of vascular Ehlers-Danlos syndrome
- Our patient had a novel frameshift mutation in *FLNA* associated with significant cardiac disease including aortic disease and PA dilation which has only been reported in one other affected female with an *FLNA* mutation.

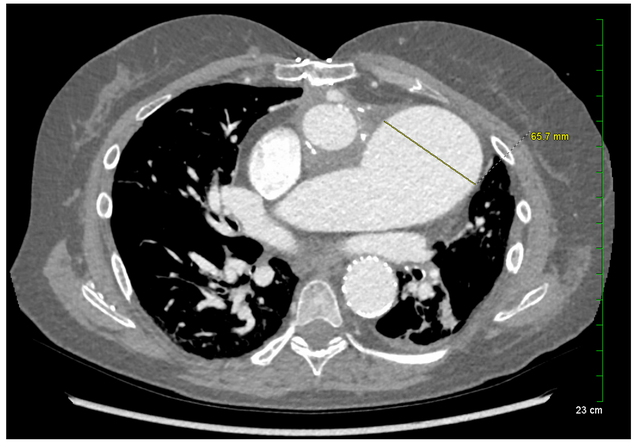

Figure 2: Chest CT scan showing PA dilation of 7cm.

Conclusion

- Case demonstrates a novel, pathogenic mutation of *FLNA* associated with severe PA dilation
- Our patient also has other clinical features suggestive of *FLNA* mutations including aortic disease, pulmonary hypertension, pectus excavatum and musculoskeletal symptoms
- *FLNA* mutations should be considered in any patient with bicuspid aortic valve and aortic dilation
- Patients with *FLNA* mutations should be monitored with serial imaging for progressive PA dilation