Type B Aortic dissection in a patient with MYLK variant.

TEVAR or Open?

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Disclosure of Interest

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• I do not have any potential conflict of interest
Case Report

- 63 YO male
- PMH: Hypertension
  Dyslipidemia
  Coarctation
- Admitted for interscapular pain
- Hemodynamically stable
Type B Aortic Dissection
Follow-up

Genome sequencies showed MYLK variant
Mutations in Myosin Light Chain Kinase Cause Familial Aortic Dissections

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Mutations in smooth muscle cell (SMC)-specific isoforms of α-actin and β-myosin heavy chain, two major components of the SMC contractile unit, cause familial thoracic aortic aneurysms leading to acute aortic dissections (FTAAD). To investigate whether mutations in the kinase that controls SMC contractile function (myosin light chain kinase [MYLK]) cause FTAAD, we sequenced MYLK by using DNA from 193 affected probands from unrelated FTAAD families. One nonsense and four missense variants were identified in MYLK and were not present in matched controls. Two variants, p.R1480X (c.4438C>T) and p.S1759P (c.5275T>C), segregated with aortic dissections in two families with a maximum LOD score of 2.1, providing evidence of linkage of these rare variants to the disease (p = 0.0009). Both families demonstrated a similar phenotype characterized by presentation with an acute aortic dissection with little to no enlargement of the aorta. The p.R1480X mutation leads to a truncated protein lacking the kinase and calmodulin binding domains, and p.S1759P alters amino acids in the α-helix of the calmodulin binding sequence, which disrupts kinase binding to calmodulin and reduces kinase activity in vitro. Furthermore, mice with SMC-specific knockdown of Mylk demonstrate altered gene expression and pathology consistent with medial degeneration of the aorta. Thus, genetic and functional studies support the conclusion that heterozygous loss-of-function mutations in MYLK are associated with aortic dissections.

The American Journal of Human Genetics 87, 701–707, November 12, 2010

A novel variant in MYLK causes thoracic aortic dissections: genotypic and phenotypic description

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Abstract

Background: Mutations in MYLK cause non-syndromic familial thoracic aortic aneurysms and dissections (FTAAD). Very little is known about the phenotype of affected families. We sought to characterize the aortic disease and the presence of other vascular abnormalities in FTAAD caused by a deletion in MYLK and to compare thoracic aortic diameter and stiffness in mutation carriers and non-carriers.

Methods: We studied FTAAD in a 5-generation family that included 19 living members. Exome sequencing was performed to identify the underlying gene defect. Aortic elastic properties were measured by TTE, MRI and pulse wave velocity were then compared between mutation carriers and non-carriers.

Results: Exome sequencing led to the identification of a 2-bp deletion in MYLK (c.3272_3273del, p.Ser1091*) that led to a premature stop codon and nonsense-mediated decay. Eleven people were mutation carriers and eight people were non-carriers. Five aortic ruptures or dissections occurred in this family, with two survivors. There were no differences in aortic diameter or stiffness between carriers and non-carriers of the mutation.

Conclusions: Individuals carrying this deletion in MYLK have a high risk of presenting with an acute aortic dissection or rupture. Aortic events occur over a wide range of ages and are not always preceded by obvious aortic dilatation. Aortic elastic properties do not differ between carriers and non-carriers of this mutation, rendering it uncertain whether and when carriers should undergo elective prophylactic surgery.

Keywords: Thoracic aorta, Aortic dissection, Gene mutation, MYLK

Abbreviations: AoA, Ascending aorta; BSA, Body surface area; FTAAD, Familial thoracic aortic aneurysms and dissections; MYLK, Myosin light chain kinase; PWV, Pulse wave velocity; SMCs, Smooth muscle cells; SNVs, Single-nucleotide variants; SoV, Sinuses of Valsalva
What is the best solution?

- Open Surgery?
- Tevar?
- No treatment......?