The EuroBiotech Journal
SHORT ARTICLE

Familial aneurysms of great vessels in young people

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Abstract

The major structural proteins of the vascular wall are collagen and elastin. Genetic connective tissue diseases lead to degeneration, aneurysms and spontaneous dissection or rupture of arteries. The best-known are Marfan syndrome, vascular Ehlers-Danlos syndrome (type IV), Loeys-Dietz syndrome and familial aortic aneurysms and dissections. Objective. This review addresses the current status of endovascular treatment options for major connective tissue diseases.

The treatment of choice for patients who are mostly affected at a young age is primarily conservative or open repair. There is only limited evidence in favour of endovascular aortic repair (EVAR) of abdominal aneurysms or thoracic endovascular aortic repair (TEVAR) because disease progression and dilation leads to secondary endoleaks and high reintervention rates with uncertain long-term results. There is therefore consensus that EVAR and TEVAR should be limited to exceptional cases and emergency situations in patients with genetic aortic diseases.

Keywords: aneurysm, young people, dissection, thoracic, abdominal

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Published online: 28 December 2017
doi:10.24190/ISSN2564-615X/2017/S2.02

Introduction

The classification of inherited, predominantly thoracic aortic aneurysms (TAAs) includes familial syndromic forms, familial non-syndromic forms and sporadic forms (1). This clinical classification allows the identification of a large number of genes responsible for syndrome forms and some non-syndromic genes (2-3).

Thoracic ventricular aneurysms

TAA syndromes are defined as aneurysms that occur in patients together with other abnormalities in different systems or organs, thus constituting a syndrome. The best-known are the syndromes of Loeys-Dietz, Marfan and Ehler-Danlos. In other cases, such as Turner's syndrome, aneurysms are only one possible manifestation.

Non-syndromic familial thoracic aneurysms

Familial TAAs defined as "non-syndromic" were identified in 1980. They occur as the sole pathological manifestation, without other diffuse phenotypic abnormalities, but nevertheless have familial, often autosomal dominant inheritance with reduced penetrance (especially in female family members) and variable expression. The TAA response rate in first-degree relatives of TAA patients is 11-19%.

Specifically, six different gene loci have been recognized in families with non-syndromic familial TAAs but only three genes have been identified: TGFBR2 in TAA type 2, ACTA2 in TAA type 4 and MYH11 in familial TAA with pervious arterial duct. Other loci are 5q13-14 (found in TAA type 1, in about 10-30% of not syndromic familial cases), locus 11q23.3-24 (found in TAA type 1 in less than 5% of non-syndromic familial cases) and locus 15q24-26 (found in TAA type 3 in about 10-20% of non-syndromic familial cases).

Sporadic thoracic aneurysms

Sporadic TAAs manifest as an isolated event not associated with other phenotypic anomalies and are not inherited. They include a wide range of etiological agents, but precise pathogenetic, cellular and molecular mechanisms remain unclear. They may be secondary to degenerative, inflammatory (Horton arteritis), autoimmune (rheumatoid arthritis, Takayasu, or Reiter syndrome), infectious (tuberculosis or syphilis) or traumatic mechanisms. Most are characterized by infiltration of the aortic wall by immune and inflammatory cells, causing degeneration and fragmentation of the elastin.

Pharmacological treatment

Pharmacological therapy for familial aneurisms and genetic aortic diseases is generally targeted at minimising the risk of major events such as rupture of an aortic aneurysm or development of acute aortic dissection. Since these events are directly proportional to aortic bulb size, beta-blocking drugs are used to reduce heart stress from aortic wall stress and its negative chronotropic effects through protection of the aortic root. The dose must be sufficient to achieve maximum effect, typically at a resting heart rate of 60 bpm.

Open Surgery

When aortic dilation reaches risk size, surgery may be needed. Surgical intervention is indicated: 1) for maximum aortic root dilation >55 mm; 2) for maximum aortic dilatation >50 mm in patients with a family history of dissection, or rapid increase in aortic dilation (>2 mm per year), or severe aortic and/or mitral regurgitation; 3) for maximum aortic root dilation >45-50 mm, if the surgeon thinks that the aortic valve can be spared; 4) for maximum aortic dilation >44 mm in a patient contemplating pregnancy; 5) for progressive dilation or diameter of other aortic segments >50 mm; 6) for severe mitral regurgitation or progressive dilation/dysfunction of the left ventricle (4-6).

Improved survival of patients after aortic root replacement is also due to an increase in the number of patients with distal aortic disease subject to monitoring. Surgical treatment is more aggressive than for pathogenic atherosclerotic aneurysms due to the greater risk of rupture.

Endovascular treatment

There are few reports of endovascular treatment of the thoracic aorta (TEVAR) in patients with genetic aorta disease. Data available in the literature indicates that TEVAR can be performed safely with few complications and low perioperative mortality. However, in young patients, the advantages compared with open surgery in specialized centers with high volumes are less evident. The major problem regards follow up, as shown by the high rate of re-intervention with open surgery, since these patients have longer survival. Thus it is still unclear from the literature whether TEVAR can be a long-term solution. It is clearly useful as bridging treatment in emergencies, where it may be truly life-saving (7-10).

Conclusions

In the past decade, molecular biology and its techniques have provided insights into the cell and molecular mechanisms that lead to the formation of aneurysms and aortic dissections, while continuing research and collaboration are clarifying the hereditary and sporadic forms of this disease. It is paramount for the prevention of premature deaths from thoracic aortic disorders to recognize carriers of these genetic mutations. In traditional surgery it is crucial to minimize the amount of residual aortic tissue and reduce mechanical stress at anastomoses, especially by separate revascularization of visceral vessels. The use of endovascular techniques in patients with connective tissue disease is feasible, but questionable due to their young age, as well as the frequency of endoleaks and re-interventions due to progression of the disease. Low morbidity and mortality can justify its use as a bridging measure in emergency situations. Careful follow-up is nevertheless mandatory.

Conflicts of interest statement

The authors have no competing interests or conflicts of interest to declare.

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