Revista Portuguesa de Cardiologia 41 (2022) 431–432

Portuguese Society of CARDIOLOGY

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

EDITORIAL COMMENT

Vascular Ehlers-Danlos syndrome

Síndrome de Ehlers-Danlos

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Vascular Ehlers-Danlos Syndrome Type IV is generally considered the most severe form of Ehlers Danlos Syndrome; an inherited connective tissue disorder usually caused by a defect/mutation in the *COL3A1* gene and rarely by a mutation in the *COL1A1* gene.

The most comprehensive descriptions of clinical features and natural history derive from two types of studies: a cross-sectional and retrospective view obtained at the time of diagnostic testing[1] and a nearly 15-year-long cohort study from one group in France.[2] A retrospective review of the health history of more than 1200 individuals with Vascular Ehlers-Danlos Syndrome outlined the natural history of the disorder. The majority of individuals were diagnosed on the basis of a major complication (70%), at an average age of 30 years. Median survival in the population was 50 years, with a younger median survival in males (by 5 years) than in females, partially due to a higher rate of lethal vascular events in males than females before the age of 20. A similar rate of complications was reported in the French cohort of 215 individuals with Vascular Ehlers-Danlos Syndrome, however there was no difference in mean survival based on sex.[2] Clinical diagnostic criteria established in 2017[3] are useful to guide the approach to genetic testing.

The importance of establishing an early diagnosis is related to all complications being serious, usually requiring surgical intervention; they represent a high risk of morbidity and mortally. In children, the majority (60%) of individuals with Vascular Ehlers-Danlos Syndrome who are diagnosed before age 18 years are identified due to a positive family history; death that occurred in the first two decades of life almost always resulted from spontaneous artery rupture or dissection. In adults vascular rupture or dissection and gastrointestinal perforation or organ rupture are presenting signs in 70% of adults with a *COL3A1* pathogenic variant.[4] These complications are dramatic and often unexpected, presenting as sudden death, stroke and its neurologic sequelae, acute abdomen, retroperitoneal bleeding, uterine rupture at delivery, and/or shock.

Cardiovascular complications include rupture, aneurysm, and/or dissection of major or minor arteries, arterial ruptures may be preceded by aneurysm, arteriovenous fistulae, or dissection, or may occur spontaneously; ruptures of the chordae tendienae or ventricle of the heart are rare, venous varicosities can also occur. There may also be pulmonary, gastrointestinal, ocular or dental complications.

In general, surgical procedures should be performed by experienced surgeons.[5] The hospitalization of these patients in experienced and differentiated intensive care units can play a fundamental role in the recovery.

Despite the variability of this disease, its presentation and the way it manifests itself can be extremely aggressive and devastating both from surgical and medical point of view, involving as in some described clinical cases a first serious event,[6] varied complications and need for urgent hospitalization,. The published case in this issue of the Portuguese Journal of Cardiology illustrates in a complete, assertive and detailed way the natural history of a patient with a *COL3A1* gene mutation.

Currently, the major challenges after diagnosis are management, serial evaluations, treatment of manifestations,

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https://doi.org/10.1016/j.repc.2022.04.004

changes in lifestyle, genetic counseling and alternative therapies – angiotensin receptor blocker and celiprolol that somehow have a positive impact on survival; decreasing arterial complications and extending life expectancy is currently underway.

Conflicts of interest

The author has no conflicts of interest to declare.

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