G92 Ehlers-Danlos Syndrome Type IV Revealed by Sudden and Unexpected Death: A Novel Point Mutation in the COL3A1 Gene

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The goal of this presentation is to describe the case of a 25-year-old man who presented with sudden death, consecutive to acute and extensive arterial dissection. Postmortem genetic analysis revealed heterozygosity for a novel point mutation in the COL3A1 gene leading to a diagnosis of Elhers-Danlos syndrome type IV.

This presentation will impact the forensic science community by showing the importance of considering Ehlers-Danlos Syndrome (EDS) diagnosis when confronted with spontaneous arterial rupture and then of alerting the family members of this hereditary and potentially fatal condition. Many health professionals are not familiar with EDS type IV syndrome, which is sometimes mistaken for coagulation disorders, Silverman syndrome, or physical abuse in children. Vascular Ehlers-Danlos syndrome can also be confused with other types of EDS, Marfan syndrome or Loeys-Dietz syndrome in adulthood.

Ehlers-Danlos syndrome (EDS) is a heterogeneous group of connective tissue disorders characterized by tissue fragility, excessive skin extensibility and joint mobility. Its prevalence in the general population varies between 1/10,000 to 1/25,000, with no ethnic predisposition. Type IV, also known as the vascular type represents 5% to 10% of all EDS types. It is an autosomal dominant disorder resulting from mutations in the gene for type III procollagen (COL3A1). The clinical diagnosis is made on the basis of four clinical criteria: easy bruising, thin skin with visible veins, characteristic facial features (acrogeria), and rupture of arteries, uterus, or intestines.

A 25-year-old white male died at home after sudden collapse and dyspnea. He had neither medical history nor cardiovascular risk factors except for tobacco consumption. Family members reported an addiction to cannabis.

A complete postmortem examination was performed. This man was 180cm tall and thin, and presented with dysmorphic facies (elongated face and acrogeria), elongated upper limbs and prematurely aged skin of the extremities, without evidence of recent trauma. The autopsy showed a massive hemo-pericardium of 200ml and a hemothorax of 330ml complicating a complete thoracic aortic dissection involving both the ascending and the descending aorta (type I of De Bakey, type A of Stanford). The dissection originated from the ascending aorta and extended into the abdominal aorta. The distal end of the dissection was situated in the superior mesenteric artery. Furthermore, aneurysms of both renal arteries and the celiac trunk without dissection were noted, with recent thrombosis in the left renal artery and the celiac trunk. Histological examination showed a complete aortic dissection localized to the media, the false channel being filled out by blood without any sign of organization or inflammation. There was also fibro-muscular dysplasia of the renal arteries and celiac trunk with thickening of the media due to hyperplasia, along with irregular arrangement of the smooth-muscle fibre. The diagnosis of EDS syndrome type IV was suspected and genetically confirmed. Molecular analysis of blood samples revealed heterozygosity for a causative mutation in exon 40 of COL3A1 gene. In research, this mutation has not been reported before.

The Villefranche classification identifies six clinical types of EDS, among which EDS type IV accounts for about five to 10% of cases. Complications were rare in childhood. Twenty-five percent of the patients had a first complication by the age of 20 years, and more than 80% had at least one complication by the age of 40. The mean life expectancy is between 48 and 54 years, most deaths resulting from arterial dissection or rupture with uncontrolled bleeding. The types of complications are not associated with specific mutations. Because of the autosomal dominant nature of this condition, family members should be informed of this genetic condition and submitted to genetic testing if they wish to. Based on this information, a particular check-up can be done with respect to obstetric complications and safety in everyday activities. Novel therapeutic modalities are under development.

Sudden Death, Ehlers-Danlos Syndrome, Aortic Dissection

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