G66 Ehlers-Danlos Syndrome Type IV (Vascular): An Atypical Presentation and Unexpected Diagnosis in a Medical Examiner Setting

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After attending this presentation, attendees will have a basic knowledge of the pathophysiology of the Ehlers-Danlos Syndrome, particularly the most severe form, Ehlers-Danlos Syndrome Type IV. They will also learn some of the basics of the genetic testing performed and be made aware of resources available should this diagnosis be suspected.

Because Ehlers-Danlos Syndrome can result in premature death, which may be related to trauma or even mistakenly thought to be due to trauma, this presentation will impact the forensic science community by demonstrating how it is important for medical examiners and forensic investigators to be aware of this clinical entity and have a basic understanding of the pathophysiology.

Ehlers-Danlos Syndrome is a group of genetically inherited defects in collagen synthesis characterized by a wide array of clinical manifestations and with diverse clinical presentations. Because Ehlers-Danlos Syndrome can result in premature death, which may be related to trauma or even mistakenly thought to be due to trauma, it is important for medical examiners and forensic investigators to be aware of this clinical entity and have a basic understanding of the pathophysiology. This presentation will accomplish those goals using a recent case as an example.

There are six recognized major types of Ehlers-Danlos Syndrome, all of which vary somewhat in biosynthetic defect, mode of inheritance, and clinical presentation. The common feature among the subtypes is decreased tissue tensile strength, particularly tissues rich in collagen. Elhers-Danlos Syndrome type IV is the most severe form because the defect involves type III collagen and may result in the rupture of large blood vessels or organs. Complications include arterial and bowel rupture and, in pregnancy, rupture of the uterus at delivery.

A recent case at the Office of the Armed Forces Medical Examiner- Pacific Region demonstrated the importance of considering diseases like Ehlers-Danlos Syndrome in the differential diagnosis. An adolescent female developed right flank pain and was treated presumptively for a urinary tract infection. After a week of both outpatient and inpatient management her condition did not improve. The patient collapsed while getting out of a vehicle and sustained a large scalp laceration. She subsequently went into cardiac arrest in the Emergency Department and died in the operating room of the local medical treatment facility.

During the autopsy the medical examiner was struck by the friability of the patient's connective tissue, particularly the mesentery. Multiple vascular defects and complete avulsion of one kidney with partial avulsion of the vascular pedicle of the other kidney were noted. A connective tissue abnormality, such as Ehlers-Danlos Syndrome, was suspected based on the gross anatomic findings. A microscopic examination demonstrated organizing hemorrhage outside of the adventitia of the right renal artery, indicating that the rupture had evolved over a period of time.

The medical examiner consulted with a research laboratory that specializes in the Ehlers-Danlos Syndromes. Frozen tissue specimens were provided and spleen was used to extract DNA for analysis. The researchers identified a mutation in one allele of the COL3A1 gene that is located on chromosome two. The effect on the gene product was deletion of 18 amino acids from the protein, accounting for the clinical presentation and autopsy findings.

In retrospect the family related that their daughter had always bruised easily and sustained unusually severe lacerations for seemingly minor trauma as a child. She also had some of the characteristic facial and skin features of Ehlers-Danlos Syndrome as well as the classic finding of joint laxity. Routine laboratory studies performed years earlier to evaluate the problem of easy bruising were all within normal limits.

An accurate diagnosis was extremely important to provide closure for a family that was attempting to understand how their daughter could be diagnosed with a urinary tract infection and die one week later. Establishing a diagnosis was critical for the clinicians who took care of this patient, all of whom were initially left wondering if there was anything they could have done to change the outcome. It was also essential to recommend genetic counseling for the parents and siblings of the deceased, particularly since Ehlers-Danlos Syndrome Type IV is typically inherited in an autosomal dominant mode.

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