

## E49 How Many Times Does Forensic Pathology Have the Chance to Save Lives? A Case Report

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**Learning Overview:** The goal of this presentation is to show how autopsy and a complete genetic study play substantial roles not only in identifying the cause of death and serving justice, but also as a means of secondary prevention.

**Impact on the Forensic Science Community:** This presentation will impact the forensic science community by illustrating the importance of a familiar genetic investigation in cases of apparently unexplained Venous Thromboembolism (VTE) leading to sudden death. Genetic investigations can identify thrombophilic genetic mutations in patients with no other risk factors. This allows physicians to make a tailored plan of secondary prevention for relatives.

Secondary prevention aims to reduce the impact of a disease that has already occurred by detecting and treating pathology as soon as possible to halt or slow its progress and to prevent recurrence or long-term complications. Forensic pathology can rarely boast of playing a direct role in this context and, as far as sudden death is concerned, this is even more true.

VTE, consisting of Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE), plays an important role in sudden death, being the cause in approximately 15% of cases, exceeding the mortality rate for acute myocardial infarction, with a big socio-economic impact affecting millions of individuals worldwide. Half of the cases are idiopathic and occur without previous trauma, surgery, immobilization, or cancer. Several gene polymorphisms associate independently with an increased risk of VTE, among which the most common is Factor V Leiden (G1691A). Diagnosis of VTE can be a great challenge as its signs and symptoms are non-specific, constituting a large part of the misdiagnosis at autopsy.

The presented case concerns a 31-year-old Chilean man adopted with his two brothers by Italian parents. He was admitted to the local emergency department complaining of cough and dyspnea. His anamnesis was mute and his own family history was not achievable. The main vital parameters were: oxygen saturation 97%; heart rate 108/min, and blood pressure 110/80mmHg. Physical examination revealed reduced breath sounds, diffuse rhonchi, and wheezing. Echocardiogram, Electrocardiogram (ECG), and an arterial blood gas test were within normal limits. A thickening of right lung interstitial was observed at X-ray. Clinical chemistry reported an increase in D-Dimer (4,252ng/ml) and lactate dehydrogenase (569UI/L). A chest CT was advised but not performed because it was refused by the patient, who asked to be discharged. Two days later, he was found dead in his apartment.

The external examination only revealed a contusion in the parietal region of the head. During the autopsy, an embolus was identified in the pulmonary trunk, extending in its two branches, associated to pulmonary edema and infarct. At the examination of the lower limb vessels, a right popliteal vein thrombus was found. The toxicological analysis on blood and urine were negative. Because of the young age of the patient, his low VTE risk according to Wells criteria, and D-dimer increase, a genetic investigation was conducted on a spleen specimen collected during the autopsy. A Factor II gene mutation (IVS13 ds + 88 A > G) in heterozygosis was discovered. In the literature, this allele results in rising plasma prothrombin levels, constituting a pathological substrate on which a trigger event determines a higher risk of VTE.

In order to provide an early diagnosis of the family members, his two brothers and two sons underwent a specific genetic investigation. Among these, one single brother was proven to possess the same mutation as the dead man. This genetic finding allowed him to be informed about his thrombophilic haplotype, about interaction between life style and genetic factors, and about all risks of VTE, giving him the possibility of making informed choices about the most effective means to prevent disease and its complication, thus *Pursuing Justice* for his relatives *Through Truth in Evidence*.

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### Venous Thromboembolism, Sudden and Unexpected Death, Secondary Prevention