## H64 A Rare Case of Sudden Death From Hereditary Hemorrhagic Telangiectasia (HHT)

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**Learning Overview:** The goal of this presentation is to report on a rare case of sudden death from HHT.

**Impact on the Forensic Science Community:** This presentation will impact the forensic science community by emphasizing features of HHT, since many cases are undiagnosed and may present as sudden death. In previously undiagnosed cases, clinical and/or genetic testing of at-risk family members could be lifesaving.

Reported here is a rare case of sudden death due to HHT in a 66-year-old female with a history of high output heart failure and pulmonary hypertension. At autopsy, multiple Arteriovenous Malformations (AVMs) were throughout the lungs and liver. Additional AVMs were identified on the epicardial surface of the right atrium. Secondary effects of the disease identified at autopsy included cirrhosis of the liver and marked biventricular dilatation of the heart.

HHT is an autosomal dominant disorder with variable penetrance in which agenesis of capillaries results in a direct connection between veins and arteries, known as telangiectasias in mucocutaneous sites and AVMs in visceral organs.[1-4] HHT is associated with multiple gene mutations; the two most common are ENG (endoglin) and ACVRL1/ALK1 (activin receptor like kinase 1), with fewer than 5% of cases having mutations in SMAD4 or GDF2. All of these genes are part of the Transforming Growth Factor Beta (TFG-B) superfamily of regulatory proteins that play various fundamental roles in cellular function, including cell survival, proliferation, and differentiation. Mutations in any of these genes leads to malfunction of this signaling pathway and results in abnormal angiogenesis.[5]

The visceral organs most frequently involved include the lungs, brain, gastrointestinal tract, urinary tract, and liver. Approximately half of all affected individuals have lung involvement, resulting in an anatomical right-to-left shunt, the major consequence of which is impairment of gas exchange leading to local and systemic hypoxemia.[2] Another serious potential consequence of pulmonary AVMs is paradoxical emboli, which can lead to strokes and brain abscesses.[5-6] Although the majority of HHT cases have hepatic involvement, fewer than 10% of these are symptomatic.[3,7] Symptomatic cases often lead to high output heart failure and have a higher risk of portal hypertension, cirrhosis, and encephalopathy.[7]

Those affected by HHT can have a near-normal life expectancy with early initiation of treatment and monitoring.[1] When a case is diagnosed at autopsy, it can lead to identification of at-risk family members who can benefit from appropriate screening and treatment through clinical evaluation and possibly genetic testing.

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**HHT, Arteriovenous Malformations, Endoglin**