H9 Fibroplasia Ossificans Progressiva (FOP): Could Autopsy Define Syndromic Features?

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Learning Overview: After attending this presentation, attendees will better understand this rare genetic disorder, characterized by ossification of soft tissues, and be aware of the most frequently associated causes of death: thoracic insufficiency syndrome, recurrent respiratory infections, and accidental trauma.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by providing attendees with the understanding that postmortem investigations could discover additional features, unknown in the clinical setting, improving the knowledge about the pathophysiology of rare diseases. This could directly impact also on earlier diagnosis, prevention of complications, and rehabilitation of patients.

This study describes the autopsy findings in a 27-year-old woman affected by FOP who died after a fall from a stairway. Cardiopulmonary resuscitation was unsuccessfully performed by responders. While the death was suspected to be attributable to traumatic head injury and intracranial hemorrhage, an autopsy was requested due to the unclear circumstances of the fall.

FOP is a rare (1/2.000.000 inhabitants) autosomal dominant disorder resulting in progressive bone formation in soft tissues due to the mutation of the Activin Receptor 1 (ACVR1) gene, which encodes for Bone Morphogenetic Protein type-1 Receptor (BMPR1). The ossification of muscles, tendons, ligaments, and other mesenchymal tissues, in association with congenital skeletal malformations, leads to a severe reduction of joint mobility and therefore to severe disability.

At autopsy, rigor mortis was difficult to evaluate due to FOP-related firm rigidity as the upper and lower extremities were diffusely fixed in flexion. An ogival palate with tooth overcrowding was also seen. There was kyphoscoliosis of the spine and major deformity of the chest wall resembling pectus carinatum. Hallux valgus was also observed.

There was evident trauma of the head, including a laceration of the scalp in the vertex region and a diastatic median skull fracture originating from the vertex and involving the fused metopic suture, crossing the anterior cranial fossa and ending in the sella turcica. Associated diffuse subdural hemorrhage and subarachnoid hemorrhage, especially in the cerebellum and around the brainstem, was evident. There was also a right periorbital hematoma with bruising of the left forearm, the back side of the left hand, and the right leg. Microscopic sections of the brain demonstrated recent cerebral hemorrhage. The spine was intact, whereas ribs were fractured on both sides. Both lungs showed subpleural petechiae, edema, and congestion. Microscopic sections of the lungs showed acute emphysema and intra-alveolar hemorrhage, with areas of edema. The thyroid gland appeared grossly unremarkable, but histologically showed diffuse lymphocytic infiltration and some fields of fibrosis. In a histologic sample of muscular tissue (quadriceps femoris), small areas with necrosis of myocytes and hyperplasia of fibroblasts were seen, indicating an initial thin fibrosis. Also, the tendon of the left pectoralis major muscle was completely ossified.

The cause of death of this young woman was certified as being due to severe head and brain trauma. Joint stiffness could explain the walking disability and thus the fall. The investigation led to the manner of death being certified as accidental. The finding of thyroiditis—although clinically silent—appeared consistent with the other reports and probably correlated to the gene mutation. Even non-affected muscle areas already exhibited microscopic foci of inflammation and degeneration. Further study of these elements could better help define characteristics of FOP syndrome.

Fibroplasia Ossificans Progressiva, Thyroiditis, Fibrosis