H84 Idiopathic Arterial Calcification of Infancy: A Case Report With Postmortem Computed Tomography (PMCT) and Histologic Findings

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After attending this presentation, attendees will understand the rare genetic disorder of Idiopathic Arterial Calcification of Infancy (IACI) and advanced radiographic, gross, and histologic findings.

This presentation will impact the forensic science community by describing the different pathological and clinical diagnostic modalities and by increasing awareness of this rare genetic disorder.

This presentation reports the Postmortem Computed Tomography (PMCT) and histologic findings of IACI, a rare genetic disorder with approximately 180 cases reported in the literature. IACI is characterized by extensive generalized arterial calcification and intimal proliferation of large- and medium-sized arteries. In 75% of cases, the affected infants are either homozygous or compound heterozygous for an Ectonucleotidepyrophosphatase/Phosphodiesterase 1 (ENPP1) gene mutation. ENPP1 is a cell surface enzyme that generates extracellular pyrophosphate, which regulates vascular smooth muscle differentiation and inhibits soft tissue calcification. The critical vascular stenosis and reduced vessel compliance in IACI causes severe heart failure with hydrops fetalis, hypertension, postnatal cardiomegaly, respiratory failure, and myocardial infarction. Most affected infants are diagnosed at autopsy. *In utero* diagnosis of IACI is based on the presence of dystrophic calcifications by fetal echocardiography. Although several cases of prolonged survival with persistent cardiovascular sequelae have been reported, the majority of affected infants will not survive beyond six months of age, especially when coronary arteries are involved. Although a curative treatment for IACI and medical management of cardiovascular effects has generally been unsuccessful, the use of prostaglandin E1 and bisphosphonate such as etidronate, a chelating agent, have been used to treat hypertension and to prevent and reduce further arterial calcification, respectively. In addition, spontaneous remission of the disorder has been reported.

An infant was the first born to an 18-year-old Caucasian female at 37 weeks and 4 days gestation. The prenatal care, which started at 11 weeks gestation, was reportedly unremarkable. Family history was remarkable for three miscarriages involving her paternal half-brother, a neonatal death to a paternal aunt, and a maternal aunt with two miscarriages. The baby was born vaginally with some difficulty in extraction with left shoulder dystocia and asymmetric Moro reflex. The arm movement rapidly improved, but she still had asymmetric Moro reflex at the time of discharge two days after delivery. The post-discharge course was unremarkable with normal feeding and weight gain. Two days before her death, she was noticed to be more restless and fussy and appeared to be straining and stretching her legs, but her feeding was still normal. She was found unresponsive on the 20th day of her life.

As per routine protocol, a full-body PMCT was performed at the Office of the Chief Medical Examiner in Baltimore, which showed extensive bilateral calcification of the following arteries: carotid and its facial branches, subclavian, axillary, brachial, ulnar, radial, aorta, all coronaries, main pulmonary and distal branches, intercostal branches, mesenteric, splenic, renal, common iliac, internal and external iliac, femoral, and tibial. Additionally, significant cardiomegaly with dilated chambers was noted.

The gross examination showed a normally developed female infant, weighing 2,500 grams and approximately 52cm long. The review of organ systems was remarkable for hepatosplenomegaly, palpable calcifications throughout the vascular system, cardiomegaly (42 grams, normal predicted weight 24 grams), four chamber dilatation, and bilateral remote cerebellar infarcts.

Histologic sections of the cardiovascular system showed biventricular circumferential subendocardial acute infarction with wavy and hypereosinophilic fibers and acute inflammatory infiltrates, diffuse calcification of internal elastic laminae and significant luminal narrowing with intimal proliferation in all three coronary arteries, calcified intimal plaques, and calcification of internal elastic lamina with marked intimal proliferation. Microscopic sections of the lungs showed diffuse calcification of internal elastic laminae of large- and medium-sized pulmonary arteries and intimal proliferation. The review of other organ systems was unremarkable, except for calcifications of periadrenal and perilaryngeal small vessels. The cause of death was certified as cardiac arrhythmia due to IACI.

Early screening and genetic counseling are recommended in future pregnancies of all affected families.

IACI, Postmortem CT, ENPP1