H13 Natural Death Caused by Catecholamine Toxicity Due to Pheochromocytoma in a Young Adult

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After attending this presentation, attendees will understand the gross and microscopic characteristics of pheochromocytoma as well as laboratory findings associated with catecholamine toxicity.

This presentation will impact the forensic science community by enumerating the findings of pheochromocytoma and catecholamine toxicity and validating the necessity of complete autopsy examinations with histological analysis and ancillary laboratory testing.

A 22-year-old female with a questionable history of drug abuse complained of general malaise as well as a headache. She went to sleep in an attempt to alleviate her symptoms. She was found unresponsive on the floor next to the bed and was not able to be resuscitated. Her medical history is significant for a recently detected adrenal mass, recurrent hypertensive episodes, and elevated plasma and urinary catecholamines and their metabolites. Her family medical history is significant for von Recklinghausen disease (neurofibromatosis type 1).

At autopsy, multiple small cutaneous neurofibromas and café-au-lait spots were observed, supportive of a history of von Recklinghausen disease. The heart exhibited cardiomegaly and concentric left ventricular hypertrophy. Gross inspection of the right adrenal gland demonstrated a 5.5x5.0x3.5cm soft, brown, well-circumscribed mass arising from the medulla. Cut section of the lesion revealed soft, pink-brown tissue with multiple areas of hemorrhage. Microscopic examination of the mass showed large cells (some markedly pleomorphic) with basophilic cytoplasm, round nuclei, and prominent nucleoli in a nested arrangement with a rich intervening vascular network. A special laboratory chemistry request was made from a reference laboratory for measurement of free serum catecholamines. Chemistry of the plasma showed markedly elevated fractionated and free catecholamines (four orders of magnitude higher than the upper limit of normal). The cause of death was determined to be the result of catecholamine toxicity due to a pheochromocytoma of the right adrenal gland.

Pheochromocytoma is a rare neuroendocrine tumor that is seen in about 0.1% to 0.6% of people with hypertension. Estimates show an annual incidence of pheochromocytoma of approximately 1/100,000 people. Of those tumors, only 10% are found to be secretory. Pheochromocytomas generally follow the "10% rule" where approximately 10% of tumors are bilateral, extra-adrenal, show metastasis, and are seen in the pediatric population, respectively. Hereditary pheochromocytomas are seen in syndromes such as multiple endocrine neoplasia, Sturge-Weber, von Hippel Lindau, and von Recklinghausen disease. Familial tumors are more likely to be bilateral, multicentric, and are seen at a younger age.

Grossly, pheochromocytomas range from small to large with the mean of 7cm and 200g. They can be yellow, brown, or red and cut section may show a lobulated appearance, hemorrhage, or necrosis. Microscopically, pheochromocytomas are large cells with abundant basophilic or amphophilic granular cytoplasm with intracytoplasmic hyaline globules. The nuclei are round or oval with prominent nucleoli. There are rare-to-no mitotic figures. The cells can be arranged in a Zellballen, trabecular, or solid form and have a rich vascular network. Metastases are the best criteria for determining malignancy. Other criteria include mitotic figures, abnormal mitotic figures, spindling of tumor cells, necrosis, large nests of cells, high cellularity, and periadrenal adipose tissue invasion. Capsular and vascular invasion can be seen with benign or malignant lesions. Synaptophysin and chromogranin, immunohistochemistry stains are positive in tumor cells. S-100 can be used to stain the sustentacular cells. Hyaline globules within the cell stain positive with periodic acid-Schiff and resist degradation with diastase.

This case illustrates the broad range of diagnoses forensic pathologists must consider in their practice. Vigilance is required to ensure that proper collection techniques are performed for ancillary testing. For this case, a purple top tube of blood was required for the measurement of serum catecholamines, which is not a part of the autopsy standard operating procedure.

Pheochromocytoma, Catecholamine Toxicity, Adrenal Gland