W7 A Multidisciplinary Approach for Cardiovascular Deaths: Breakthrough Technologies and Their Applications

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Learning Overview: After attending this presentation, attendees will better understand the use of modern technologies by immunohistochemistry, metabolomics, genetics, and imaging introduced recently in postmortem evaluation of cardiovascular pathologies, not only for natural cases but also for traumatic and post-cardiac surgery cases involving medical liability. Participants will understand the advantages and limitations as well the possible pitfalls of these methods.

Impact on the Forensic Science Community: This workshop will impact the forensic science community by presenting new technologies (immunochemistry, genetics, and imaging) and their current role and prospective. By including discussion with participants, the usefulness of these methods will be clearer to the forensic science community.

Any sudden, unexpected or unexplained death, mainly in the young, is a reason for a medicolegal investigation. The underlying cause of sudden death is most frequently cardiovascular with coronary atherosclerotic disease as the leading cause of death in elderly victims, while genetically determined cardiomyopathies as hypertrophic or arrhythmogenic cardiomyopathy and canalopathies prevail in the young. Modern immunohisto-chemical markers and untargeted metabolomics allow the progress in the detection of early myocardial ischemia. Autopsy-negative Sudden Cardiac Deaths (SCDs) are most often thought to be the consequence of sudden arrhythmic death syndrome, and so-called molecular autopsy is recommended. Radiological examination has been used in forensic and clinical pathology in specific situations of natural and violent deaths for many years, as an additional diagnostic tool, for documentation and for research, and is very useful for cardiovascular pathologies.

Many immunohistochemical markers have been proposed to diagnose early myocardial infarction, which include proteins from the complement cascade (C5b9), fibrinogen and fibronectin, and some of them seem promising in terms of early expression and specificity. Untargeted Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry (MALDI IMS) imaging was also evaluated. These methods need to be tested and validated for application in routine postmortem diagnosis. The interpretation of immunohistochemical staining should consider cardiopulmonary resuscitations and other agonal events that may affect marker expression. Current insight is that immune stains cannot reliably detect myocardial ischemia at an earlier time point than conventional staining. However, they can be valuable for the confirmation of diagnosis and demonstration of the extent of myocardial necrosis in the heart.

The potential genetic origin of cardiac pathologies involves the forensic pathologist in the multidisciplinary management of surviving family members. The role of the forensic pathologist is to perform and store the postmortem samples according to legal and ethical guidelines and orients the relatives of SCD's victims to the genetic counselling. Most of the laboratories today use Next Generation Sequencing (NGS), and it is possible to screen several genes at the same time, but the interpretation of the results requires a close collaboration with clinicians.

In forensic investigations, a significant progress has been made with the introduction of modern radiological methods, such as Multiple Detector Computed Tomography (MDCT), MDCT-angiography, and cardiac Magnetic Resonance Imaging (MRI). These methods are also practiced for cardiovascular pathologies, mostly ischemic heart disease. The advantages and disadvantages of various radiological methods for whole-body imaging are related to logistic and financial questions, as well as those concerning the image quality. The training necessary to interpret postmortem radiological images is a subject of discussion. The question concerning the value of minimally invasive autopsy techniques has appeared.

In sudden cardiac death cases, Postmortem Computed Tomography (PMCT) is helpful to estimate the heart size and to visualize hemopericardium, calcified plaques and valves, as well as to identify and locate cardiovascular devices. Angiographic methods are useful to provide a detailed view of the coronary arteries and to analyze them, especially regarding the extent and location of stenosis and obstruction. In post-surgical cases, it allows verifying and document patency of stents and bypassing grafts before opening of the body. Postmortem Magnetic Resonance Imaging (PMMRI) is available in only a few academic centers and is practiced to investigate the soft tissues, such as the myocardium; Postmortem Magnetic Resonance-angiography (PMMR-angiography) is today in development; detection of myocardial ischemic injury in PMMRI has been reported, but images are susceptible to being affected by postmortem changes, and further work is ongoing in order to increase understanding of radiological aspects of the ischemic myocardium. In violent and post-surgery cases, the value of postmortem imaging of the heart is reported essentially for diagnostic and documentation purposes. It is recognized that postmortem radiological examination is most often not sufficient to establish the exact cause of cardiac death and, at present, autopsy remains the gold standard.

Postmortem Radiology, Sudden Cardiac Death, Postmortem Genetic Testing