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Apoptosis concept: 30 years later

KEYWORDS: Apoptosis; Caspases; Cell death

Apoptosis concept introduced three decades ago was based primarily on morphological characteristics of dying cells suggestive of an active process of cellular deconstruction and fundamentally different from necrosis. A broader biological significance was attributed to this process on the basis of its presence in numerous physiological and pathological conditions that soon brought to equalizing apoptosis with programmed cell death. During last decades, numerous molecular mechanisms involved in triggering and execution of the apoptotic "program" were discovered, including identification of a family of cystein proteases (caspases), as well as, numerous molecules involved in fine regulation of apoptosis, such as bcl-2 protein family and inhibitory apoptosis proteins. Specific subcellular distribution and mode of activation of these molecules enabled understanding of the role of individual organelles, in particular mitochondria, in the mechanisms of death signal detection and transduction. In parallel with these discoveries, a development of various techniques for identification of apoptosis occurred, that enabled detection of specific forms of cell death which could not be classified as either necrosis or apoptosis, such as lathiptosis, paraptosis, apoptosis-like cell death, and others. These findings brought to a significant change in appreciation of apoptotic concept, and instead of dichotomic classification of cell death into apoptosis and necrosis, attempts for new classification appeared in order to include observed intermediary forms of cell death. Furthermore, the opinion that apoptosis and necrosis represent only extreme morphological forms of cell death of the otherwise common process, which, depending on specific circumstances, express itself in various forms.

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Forensic medicine and public

KEYWORDS: Forensic medicine; Public

For forensic medical doctors, the public means every person with whom he or she may come into a contact, starting from relatives of a damaged person or a victim, through investigators and police inspectors to the media persons, not excluding friends, acquaintances and family members. A forensic medical doctor generally does not worry about what he or she has said or done but it happens that his or her work is wrongly interpreted or understood. Therefore a forensic medical expert must develop a system of protecting integrity of his own personality because this issue has never been practically anywhere legally regulated, or at least not sufficiently enough and not in every detail. A personal protection is mostly based on rather personal than on other persons' negative experiences what is not good. It is necessary to establish the rules, either within the legislation or within the profession, about the relationship between a forensic expert and public audience. These rules should relate to the following: with whom a forensic medical expert can communicate, in what way, a scope and a quality level of information on the findings, time of communication and similar.

Meeting abstract
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Diagnostic applications of Cytokeratins 20 and 7

KEYWORDS: Cytokeratins; Metastasis; Immunohistrochemistry

Cytokeratin immunophenotyping has become a routine additional diagnostic method in tumor pathology. The relatively limited expression of cytokeratins 20 and 7 in adenocarcinomas has been intensively studied. Detection of cytokeratin 20 in urine, blood, tumor tissue or some reactively changed tissue assists the pathologists in making their diagnostic decisions. However, good technical quality, personal experience, and use of database are strongly recommended in interpretation of cytokeratin phenotypes. We also advocate a probabilistic approach, which means an information about the statistical probability of a diagnostic statement based on a certain immunophenotype. Our presentation is going to be focused on the use of cytokeratins 20 and 7 in tracing primary tumor location from metastases. We reviewed 29 related studies from the literature, including five own studies, containing more than 3500 reported cancer cases. The results of the review are going to be presented in connection to demonstration of typical cases. The cytokeratin 20 positive / cytokeratin 7 negative phenotype is highly characteristic for colorectal adenocarcinomas. Detecting this phenotype in a metastasis carries an 80 - 85% probability to find the primary tumor in the colorectum. The cytokeratin 20 negative / cytokeratin 7 negative phenotype in a metastasis indicates the location of the primary tumor in the prostate with about 60% probability, the second probable localization being the colorectum (17%). The cytokeratin 20 positive / cytokeratin 7 positive phenotype is mostly expressed by ovarian mucinous carcinomas, urothelial carcinomas, carcinomas of the pancreas and the stomach, but a considerable percentage of other primary adenocarcinomas may also express this phenotype. The cytokeratin 20 negative / cytokeratin 7 positive phenotype is characteristic for lung, breast and non-mucinous ovarian adenocarcinomas. Cytokeratins 20 and 7 have a well - established diagnostic role in assisting the clinical investigations in cases of metastatic adenocarcinomas of unknown primary site.

Extended abstract
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Classification of blunt injuries to the thoracic aorta

KEYWORDS: Thoracic aorta; Blunt injuries; Classification

INTRODUCTION

Traumatic injuries to the thoracic aorta consist of sharp (penetrant, direct) and blunt (non-penetrant, indirect) injuries. Blunt injuries occur in traffic, aircraft and workplace accidents, and falls from height. Due to the direction of the force, the aortic wall is injured from intima to adventitia. There are several forms of blunt injuries to the thoracic aorta, from limited lacerations of the intima to complete transection of the aorta. Various authors use different terms to describe various kinds and forms of the blunt injury to the aorta. Since no unified terminology and nomenclature is in place to describe all kinds and forms of blunt aortic injury, both the idea and the need arose for the introduction of a systematic classification of the pathomorphological changes that result from a blunt injury to the aorta that would enable a better overview, higher quality of discussion and comparability of studies of this problem.

Classification of morphological changes of blunt injuries to the thoracic aorta. According to pathomorphological changes in blood vessel walls, aortic ruptures were classified into three basic groups or types, and corresponding subtypes: Type I: Incomplete (intramural) ruptures: Type IA: rupture of the intima, Type IB: rupture of the intima and the innermost (subendothelial) layer of the media, Type IC: rupture of the intima and media up to the adventitia, Type ID: post-traumatic pseudoaneurysm; Type II: Complete (transmural) ruptures, Type IIA: partial rupture, Type IIB, total rupture or transection, Type IIC: rupture of post-traumatic pseudoaneurysm; Type III: Several (multiple, graduated) ruptures, Type IIIA: several ruptures of type I, Type IIIB: several ruptures of types I and II, Type IIIC: several ruptures of type II.

MATERIALS AND METHODS

In the course of retrospective research conducted from 2000 to 2002, we analyzed the autopsy records of the IFM where blunt injury to the aorta were present. We defined forms, kinds, extent and number of injuries to the aorta, and classified them accordingly into types and subtypes of the proposed classification. We determined the occurrence and frequency of the individual morphological changes that occur due to blunt injury to the thoracic aorta.

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RESULTS

In 69 cases of fatal injury, 130 injuries to the walls of the thoracic aorta were present. In 43 cases (62%) the aorta was damaged in one place; in the other 26 cases (38%) the aorta was damaged in several places simultaneously. We established 61 (47%) incomplete or intramural and 69 (53%) complete or transmural ruptures of the aorta. Morphological changes with blunt injuries to the thoracic aorta were classified into corresponding types and subtypes of the proposed classification. Injuries of type I were established in eight subjects (12%): type IA was established in one case, type IB in three cases, type IC in one case, and type ID in three cases. Morphological changes to the aorta of type II occurred in 35 subjects (50%): type IIA in 24 cases, type IIB in ten cases and type IIC in one case. Multiple ruptures of type III were discovered in 26 cases (38%): type IIIA in five subjects, type IIIB in 13 subjects and type IIIC in eight subjects.

DISCUSSION

Rupture is a synonym for blunt injury to the aortic walls, which means damage to the straight edges that run perpendicular to the axis of the blood vessel. There are two kinds of rupture: incomplete or intramural ruptures that do not go through the whole aortic wall, and complete or transmural ruptures, where the whole wall is ruptured. They are also classified according to the area of circumference they affect, the two categories being partial and total aortic ruptures. Clinical symptoms depend on the site, number and type of blood vessel trauma. At the site of intima injuries (type IA), thrombosis can occur, with possible peripheral embolic complications. An incomplete rupture of the media (type IB) can lead to intramural hematoma, dissection of the aortic walls and the occurrence of late post-traumatic aneurysm. Traumatic pseudoaneurysm (type ID) can occur due to invasion of the blood through the complete rupture of the muscular layer beneath the adventitia that peels and arches the blood vessel wall. A hematoma beneath the adventitia can prevent the outpouring of blood for a short time (type IC). At the sites of intramural injuries, a complete rupture of aortic walls can occur that causes belated clinical symptoms (type IIC). The most common blunt injury to the thoracic aorta in cases of fatal accidents is a partial transmural aortal rupture (type IIA), which causes bleeding into the pericardium, mediastinum and chest. Complete transmural ruptures or transections of the aorta (type IIB) are incompatible with life due to rapid bleeding. Rupture of the aorta usually occurs at one site, while in 30-40% of cases several intra- and/or transmural (multiple, graduated) ruptures of the aorta occur simultaneously (type III A-C), which usually run parallel to each with a distance of 5-25 mm.

CONCLUSIONS

Blunt injuries to the aorta can be classified into three basic types: type I (intramural), type II (transmural) and type III (multiple), and corresponding subtypes. The proposed classification enables a systematic overview of all kinds and forms of blunt injuries to the aortic wall, a more uniform and better discussion, and the comparability of the studies on this medical issue.

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Significance of biochemical parameters obtained by serum analysis post-mortem in determination of cause of death

KEYWORDS: Biochemistry; Post-mortem analysis; Death

The significance of the biochemical parameters determination such us: degradation products - Urea, Creatinine; enzymes - AST, ALT, γGT, CK, LDH, ALP; electrolytes - Na, K and Ca, as well as Glucose, for the need of the clinical investigation a.i in determination of clinical diagnosis, is well known and it is very well established in the medical science. The motive of this research comes from the need to comprehend the significance of those same parameters in a post mortem serum analysis during expertise investigation, with the purpose to be used as one more argument in precising the cause of death and histopathological mechanisms that brought to it, in a correlation with other investigations: pathoanatomical findings, histological analyses and other specific investigations, depending on the specifics of each analyzed case. A total of 22 cases have been analyzed, whose autopsies had been performed at the Institute for Forensic Medicine in Skopje. In 11 of 22 cases a pathoanatomical finding has been determined, that we could objectively expect changes of the investigated biochemical parameters, conditions as pyelonefritis, sepsa, hepatorenal syndrome, infarctus myocardi acuta, as well as one case of chronicle starvation (inanitio marazam); in 9 controlled cases the death occurred momentary or quickly either by traumas, and in 2 of the cases, taken as special controls, death occurred by intoxication. The analyses were performed by specific methods and reagents for separate biochemical parameters on COBAS Integra photometer, biochemical analyzer. The results of this pilot-study that represents the beginning of a larger research, point to selective significance of the separate biochemical parameters which added to pathoanatomical findings (microscopical as well as histological) could be used as a significant evidence in the determination of the cause of death.