H18 Genetic and Histopathological Factors in Thrombo-Embolic Disease: Results of a Preliminary Experimental Study

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After attending this presentation, attendees will understand how a comprehensive approach to fatal thrombo-embolism that includes the analysis of the clinical history of the patients, the research for genetic factors, and the histological age determination of thromboemboli may result in a better definition of the disease.

This presentation will impact the forensic science community by demonstrating the importance of the prophylactic measures in Venous Thrombo-Embolism (VTE).

VTE is the third most common cardiovascular disease after myocardial infarction and stroke. The mortality rate is high and there are many deficiencies in the diagnosis, prophylaxis, and therapy. In this study, a retrospective analysis of the reports of 500 autopsies performed at the Institute of Forensic Medicine of Catanzaro between 2005 and 2014 was performed. Twenty-two cases in which pulmonary embolism was recorded as the cause of death were identified, consisting of 13 males (59%) and nine females (41%) with a median age of 56 years (range 14-93 years). All subjects were Caucasian except one Negroid subject. The clinical histories of the patients who died were analyzed, with the identification of the risk factors for VTE. In the case of hospitalized patients, the measures of prophylaxis and therapy were evaluated. The role of genetic risk factors in the disease, particularly Factor V Leiden (G1691A) mutation, which is the most common genetic factor of thrombophilia, was studied. The presence of the mutation was researched in DNA extracted from blood samples. Additionally, in order to obtain a histological age of the process, the histopathological features of thrombo-emboli were studied using histological sections stained by Hematoxylin-Eosin (H&E) and trichromic stains (Masson).

The results of the clinical and epidemiological data showed that 18 subjects (81.8%) had at least one risk factor for VTE, while in four patients (18.2%) no clinical data that could be related to an increased thromboembolic risk was identified. Seven subjects (31.8%) were more than 65 years old at the time of the event, seven (31.8%) had major trauma, and seven (31.8%) were surgical patients. An immobility period was recorded in five subjects (22.7%), four subjects (18.1%) were obese, and two (9%) were receiving antipsychotic drugs. Central catheterization was present in two subjects (9%) and pregnancy and postpartum status were present in an additional two patients (9%). Finally, one subject (4.5%) was suffering from chronic respiratory failure and one subject (4.5%) had limb paresis.

The retrospective analysis also revealed that 13 deaths (59%) occurred in a hospital setting while nine subjects (41%) died before having the opportunity to receive medical care. Among hospitalized patients, ten subjects (77%) were hospitalized for other diseases and suffered an episode of fatal thrombo-embolism during the hospital stay. Three patients (23%) arrived at the hospital presenting with symptoms of VTE and none received a correct diagnosis. Among hospitalized patients, eight subjects received prophylaxis with low molecular weight heparin, while two subjects, despite the risk, received no prophylactic treatment for VTE. In 12 out of 22 subjects (54.6%), it was not possible to find the thrombotic site. In the other cases, five (50%) were femoral thromboses, two (20%) inferior-caval, two (20%) iliac, and one (10%) saphenous. The genetic results showed that none of the patients carried a Factor V Leiden (G1691A) gene variant, not even the younger subjects or those who did not show any clinical data that could expose them to an increased risk. The histopathological analysis revealed the age of the thrombi. The study of the morphological features of the thrombo-embolic samples reported that eight samples (36.3%) were between one and three days of age, eight samples (36.3%) were between three and five days of age, and six samples (27.3%) were between four and 20 days of age.

The results of this study highlight the importance of early identification of risk factors and the setting of primary prophylaxis measures in order to prevent the onset of the thrombotic process, especially as the clinical diagnosis of VTE is notoriously inaccurate. Moreover, it is known that even the non-fatal cases of VTE can result in serious chronic complications such as post-thrombotic syndrome and chronic pulmonary hypertension. It is clear that an accurate prophylactic treatment would be useful not only to prevent death but also morbidity. The results of this study indicate that even if the prophylaxis is correctly performed according to the guidelines, death cannot be completely avoided. This observation poses a question concerning the validity of current treatment approaches, despite the ongoing research in the field of thrombo-prophylaxis.

The genetic factors were determined to be non-significant in determining the risk compared to the environmental risk factors. The results of histopathological investigations showed that it can be a very large temporal range in which death can be avoided; therefore, early identification is important in order to prevent the progression of the disease to the fatal episode. In the histological age determination of thromboembolism, immunohistochemical investigations were not essential in establishing the cellularity of thrombo-embolic formation and are very expensive compared to basic histological investigations. The difficulty in finding the embolic source may be an important limitation in the age determination of the thrombotic process as it prevents evaluation of the residual thrombus. In this context, a decisive role could be played by postmortem computed tomography angiography. This imaging diagnostic method may be very helpful in the visualization of thrombus and may facilitate its subsequent detection during the autopsy.

In conclusion, there is a great need to implement diagnostic and prophylactic measures in VTE. It is necessary to pay more attention to the pathology and the risk factors, similar to what occurs with other cardiovascular diseases such as myocardial infarction. An accurate analysis of the clinical history of the subjects can be very useful to clarify the etiology of the disease while genetic investigation is not necessary. The histological age determination is essential to answer a number of questions about the nature and the evolution of the VTE, making it possible to establish the casual relationship between the exposure to certain risk factors and the occurrence of thrombosis.

Fatal Thrombo-Embolism, Histopathological Factors, Genetic Investigations