



When is myocarditis indeed the cause of death?

Alessandro Bonsignore^{a,*}, Cristian Palmiere^b, Francesca Buffelli^c, Eloisa Maselli^d,
Andrea Marzullo^e, Giulio Fraternali Orcioni^f, Francesco Ventura^a, Francesco De Stefano^a,
Alessandro Dell'Erba^d

^a Department of Health Sciences (DISSAL) – Section of Legal and Forensic Medicine, University of Genova, Italy

^b CURML, University Center of Legal Medicine, Lausanne University Hospital, Switzerland

^c Fetal and Perinatal Pathology Unit, Istituto Giannina Gaslini, Genova, Italy

^d Department of Interdisciplinary Medicine (DIM) – Section of Legal and Forensic Medicine, University of Bari, Italy

^e Department of Emergency and Organ Transplantation (DETO) – Section of Pathology, University of Bari, Italy

^f Department of Pathology – Anatomic Pathology Division, IRCCS-AOU San Martino-IST Teaching Hospital, Genova, Italy



ARTICLE INFO

Article history:

Received 19 October 2017

Received in revised form 7 January 2018

Accepted 30 January 2018

Available online 7 February 2018

Keywords:

Myocarditis
Cause of death
Incidence
Autopsy
Histopathology

ABSTRACT

Attribution of death to myocarditis continues to be a controversial issue in forensic pathology, despite the existence of established histopathological criteria as well as complementary investigations. The aim of the study was two-fold: (a) to retrospectively analyse the data obtained from a series of clinical and forensic autopsies in order to assess the number of cases with death attributed to myocarditis, and (b) to reevaluate these cases in order to assess how properly the histopathological diagnosis of myocarditis conformed to established criteria and therefore how accurately these were used on the basis of all postmortem investigation findings to conclude the cause of death. 2474 clinical and forensic autopsies were taken into consideration. Myocarditis was recorded as the official, underlying cause of death in 48 cases. Of those, 8 cases were considered to accurately conform to the histopathological Dallas criteria for the presence of myocarditis and could therefore be classified as cases of fatal myocarditis. In 19 out of 48 cases, description of focal myocarditis was considered to accurately fulfill the histopathological Dallas criteria for the presence of myocarditis. However, data provided by histological analysis and virology testing result reevaluation allowed alternative causes of death to be speculated. In another 21 out of 48 cases, description of focal myocardial inflammation was considered to inaccurately meet the histopathological Dallas criteria for the presence of myocarditis. The findings of our own study appear to be in agreement with previous observations in similar study groups and highlight that since myocarditis may occur in association with many diseases, a great deal of evidence is required before settling on categorical conclusions.

© 2018 Elsevier B.V. All rights reserved.

1. Introduction

Attribution of death to myocarditis continues to be a controversial issue in forensic pathology, despite the existence of established histopathological criteria as well as complementary investigations [1].

If, on the one hand, the clinical diagnosis of myocarditis remains challenging and often under-recognized due to sign and symptom heterogeneity that may overlap with other cardiac diseases, on the

other hand the postmortem diagnosis of myocarditis as the main cause of death may prove even more questionable and uncertain with the real incidence of fatal myocarditis in the forensic setting probably overestimated, for a myriad of reasons [1,2].

Focal myocarditis may potentially lead to sudden death in otherwise healthy young people in the absence of any prodromal symptom, since it may precipitate fatal arrhythmia despite normal ventricular function and basal electrocardiogram [1,3].

Nevertheless, though focal myocardial inflammatory infiltrates and myocyte necrosis may explain the death individually considered when alternative causes of death can be excluded through in-depth postmortem investigations, these same findings are relegated to the category of incidental and non-contributory elements when a more flagrant cause of death might be postulated based on other evidence. This means that, as highlighted in the

* Corresponding author at: Department of Health Sciences (DISSAL) – Section of Legal and Forensic Medicine, University of Genova, Via De Toni 12, 16132 Genova, Italy.

E-mail address: alessandro.bonsignore@unige.it (A. Bonsignore).

past, myocarditis may be falsely recorded as the cause of death if no other cause can be found or investigated [4].

The purpose of the study presented herein was two-fold: (a) to retrospectively analyse the data obtained from a series of clinical (hospital) and forensic (medicolegal) autopsies performed over a period of ten years in two university hospitals in order to assess the number of cases with death attributed to myocarditis, and (b) to reevaluate these cases in order to assess how properly the histopathological diagnosis of myocarditis conformed to established criteria and therefore how accurately these were used on the basis of all postmortem investigation findings to conclude the cause of death.

2. Materials and methods

2.1. Study design and study population

The present study was performed in 2016, designed as a retrospective, double-center study. 2474 clinical and forensic autopsies were taken into consideration as such: 600 hospital cases, including 434 males and 256 females, and 1874 medicolegal cases, including 1217 males and 657 females. Autopsy age ranged from 6 months to 89 years and included 1561 male cases and 913 female cases overall. The autopsies were performed over a ten-year period from January 1, 2006 to December 31, 2015 in two university hospitals.

Clinical autopsy cases originated from hospital practice and were performed by hospital pathologists upon family and/or clinical staff request (only with family consent) exclusively on inpatients who died in hospital.

Medicolegal cases originated from forensic practice and underwent medicolegal investigations (performed by forensic pathologists) as requested by local inquiring authorities (the public prosecutor).

Both clinical and forensic autopsies were jointly performed by two pathologists (forensic or clinical pathologists, at least one of whom board-certified) in accordance with both local standards and international guidelines.

To address the first aim of the study, death certificates listing morphological findings and causes of death were retrospectively obtained from the records of each center involved in the study.

To address the second aim of the study, the following data were retrospectively revised: complete autopsy protocols, analyzed histological samples (formalin-fixed and paraffin-embedded preparations as well as slides stained with hematoxylin and eosin and immunohistochemical slides when available), results from any other postmortem investigations (death scene investigation reports, toxicological and biochemical results, postmortem bacteriology and virology testing results) as well as any available medical and/or clinical data (including laboratory results, electrocardiograms, and imaging information), and comorbidities listed in death certificates.

Viral genome re-analysis was not performed in those cases that had myocarditis recorded as a cause of death. Microbiological analysis results were revised only in those cases that had myocarditis recorded as a cause of death (48 cases) and had available results (9 out of 48 cases).

As a control, one hundred randomly chosen autopsy protocols, histological samples, and results from other postmortem investigations were selected among non-myocarditis cases, in order to check whether (and how many) false negative cases of histologically identifiable myocarditis had gone unnoticed.

2.2. Histopathological diagnosis

To address the second aim of the study, three myocardial formalin-fixed paraffin-embedded preparations and slides stained

with hematoxylin and eosin per subject were provided on the average for all the cases with myocarditis recorded as the underlying cause of death (as well as for controls). Paraffin slides were cut at 4–5 μm . Full-thickness sections from both ventricles included endocardium and pericardium. In a number of cases in which histological findings were inconclusive, deeper cuts were prepared.

Histological re-evaluation was systematically performed in all the cases that had myocarditis recorded as a cause of death (48 cases).

Immunohistochemical re-evaluation was performed in all the cases that had myocarditis recorded as a cause of death (48 cases) and that had available immunohistochemical slides (21 out of 48 cases).

Performed immunohistochemical investigations included antibodies against leukocytes (CD45), T lymphocytes (CD3), and macrophages (CD68).

All preparations were evaluated independently and irrespective of postmortem investigation results and available medical/clinical data by two board-certified clinical pathologists according to the histopathological Dallas criteria for the presence of myocarditis. When opinions differed, assessment was double-checked and consensus was reached by discussion.

Myocarditis was sub-categorized according to the predominant type of inflammatory cell characterizing the infiltrates.

The extent of inflammatory cell infiltration of the myocardium was classified under microscopic examination into focal and diffuse (inflammatory cell infiltration of the myocardium distributed over the sections).

2.3. Statistics

The obtained results were statistically compared. A difference was considered significant with a p value <0.05 .

3. Results

Myocarditis was recorded as the official, underlying cause of death in 48 cases. Of those, 8 cases (all Caucasians, 5 males, 3 females, 17% of all initially recorded cases and 0.32% of all collected autopsies) were considered to accurately conform to the histopathological Dallas criteria for the presence of myocarditis and could therefore be classified as cases of fatal myocarditis (5 cases of lymphocytic myocarditis out of 8 myocarditis cases, mean 59 lymphocytes/ mm^2). No alternative causes of death were identified or postulated based on all postmortem investigation findings. Autopsy type (medical versus forensic) did not affect the proportion of Dallas criteria-positive myocarditis. No significant seasonality or annual changes over the years was identified.

Mean age at death was 32 years. 5 out of 8 cases occurred in the age group under 30 years and, of these, only 1 case occurred in the 0–1 year age group. No case was recorded in the population aged over 55 years.

5 out of 8 cases demonstrated heart weight within the normal range and with a normal appearance upon postmortem macroscopic examination. Pericardial effusion and evidence of chamber dilatation were observed in 2 out of 8 cases. Histologically, lymphocytic myocarditis (5 out of 8 cases) and focal infiltration (6 out of 8 cases) were the most common types. In 3 out of 8 cases, the left ventricular myocardium was the location of focal lymphocytic myocarditis. Myocyte necrosis and interstitial edema was systematically present and confirmed by histological/immunohistochemical reevaluation. Pericardium (2 out of 8 cases), endocardium (1 out of 8 cases), and conduction tissue (2 out of 8 cases) involvement were occasionally observed.

In 19 out of 48 cases (40% of all initially recorded cases, 15 out of 19 cases in individuals aged less than 40 years), description of focal myocarditis was considered to accurately fulfill the

Download English Version:

<https://daneshyari.com/en/article/6551201>

Download Persian Version:

<https://daneshyari.com/article/6551201>

[Daneshyari.com](https://daneshyari.com)