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Giant cell myocarditis as a rare cause of sudden cardiac death in forensic medical practice – case report

Summary

Sudden non-traumatic deaths, especially of young and middle-aged individuals, usually raise doubts among investigators as to the circumstances and nature of the death. They also pose a diagnostic challenge for medical examiners and pathologists. One of the oligosymptomatic cardiac pathologies that can result in sudden cardiac death is myocarditis.

Key words: myocarditis, histopathology, forensic medical expertise, sudden death

Introduction

Sudden non-traumatic deaths, especially of young and middle-aged individuals, who have so far appeared 'healthy', usually raise doubts among investigators as to the circumstances and nature of the death (natural or sudden). They often also pose a diagnostic challenge for medical examiners and pathologists. who carry out post-mortem examinations and interpret their results (Baroldi, Fineschi, 2006).

One of the oligosymptomatic cardiac pathologies that can result in sudden cardiac death is myocarditis (Bury et al., 2010). A rare form of this condition is the so-called giant cell myocarditis (Shanmugam et al., 2015), an example of which, observed in the course of the authors' consultative practice, is presented below.

Case study

The corpse of a 44-year-old woman was revealed in the bathroom of a single-family house. Due to an unknown cause of death, the prosecutor ordered an autopsy. The examination and autopsy carried out in the forensic medicine department revealed left ventricular dilatation, numerous cysts of both ovaries and a state after laparoscopic resection of the gallbladder. The symptoms of sudden death and sudden and acute left ventricular circulatory failure manifested by cerebral and pulmonary oedema and fluidity, as well as blood stasis in the internal organs were also revealed. The macroscopic dimensions of the heart were 120 mm × 100 mm × 70 mm. The wall thickness of the left ventricle was 9 mm and of the right ventricle – 3 mm. The papillary muscles and muscular ridges of the left ventricle were clearly flattened. The cardiac muscle (myocardium) on the cross-sections was dark cherry in colour, with normal macroscopic appearance. No traumatic lesions have been revealed by the post-mortem examination. The gas chromatography method revealed no traces of ethanol in a woman's blood or intraocular fluid. Due to the location of the corpse (bathroom), blood tests for the presence of oxycarbonated haemoglobin as well as extended toxicological tests were performed, the former yielding a negative result, whereas the latter revealing only the presence of very small (trace) amounts of non-steroidal anti-inflammatory drug with analgesic and antipyretic effects – metamizole, as well as small amounts of its biologically active metabolites, i.e. 4-aminoantipyrin, 4-formylaminoantipyrin, 4-acetylamoantipyrin. Further evaluation of the cause of death was made dependent on the results of the commissioned histopathological examinations of internal organ sections.

The result of histopathological examination confirmed and expanded autopsy diagnosis, especially as regards the type of myocardial pathology. In the standard staining with haematoxylin and eosin (H&E), apart from the focal points of intensive hyperaemia observed, one of the cardiac sections showed medium intensity interstitial and perivascular lymphocytic infiltrations, necrotic lesions and numerous multinucleated giant cells in the above mentioned areas were observed (fig. 1). In two preparations, fatty degeneration was observed, occupying about 30% of the slice area. The filaments in these preparations were corrugated and focally fragmented. In all the preparations, the features of myocardial hypertrophy were present. In turn, Nielsen-Selye's staining method revealed extensive fuchsin-absorbing areas arguing in favour of fresh myocardial ischaemia. The additional tests were also supplemented with Masson's staining (fig. 2). In summary, the microscopic examination revealed a morphological image in favour of idiopathic giant cell myocarditis with ischaemic lesions. In the remaining organs, the microscopic examination revealed, among others, the characteristics of significant hyperaemia, oedema and emphysema (in the form of focal tearing of the vesicular septa) in the lungs with the presence of macrophages loaded with brown dye in the light of pulmonary alveoli (the so-called "heart failure cells"), large and small droplet steatosis of about 5% of hepatocytes, bile stasis, focal lymphocytic inflammatory infiltrations of low intensity within the portal triads, pancreatic fibrosis and follicular and simple ovarian cysts. No pathological changes were found within mediastinal lymph nodes.

Discussion and conclusions

Sudden cardiac death (SCD) is an unexpected, non-violent, natural death, i.e. caused by heart disease, heralded by abrupt loss of consciousness within one hour of the onset of acute symptoms. The existing heart condition may or may not be known. The time between the onset of symptoms and the death was in the past determined to be 24 hours, later on – 6 hours, and more recently, according to the definition introduced by the European Society of Cardiology – 1 hour (Chowaniec et al., 2007).

The diagnosis of sudden cardiac death is very important for a forensic pathologist, as an uncritical diagnosis may lead to overlooking cases of sudden

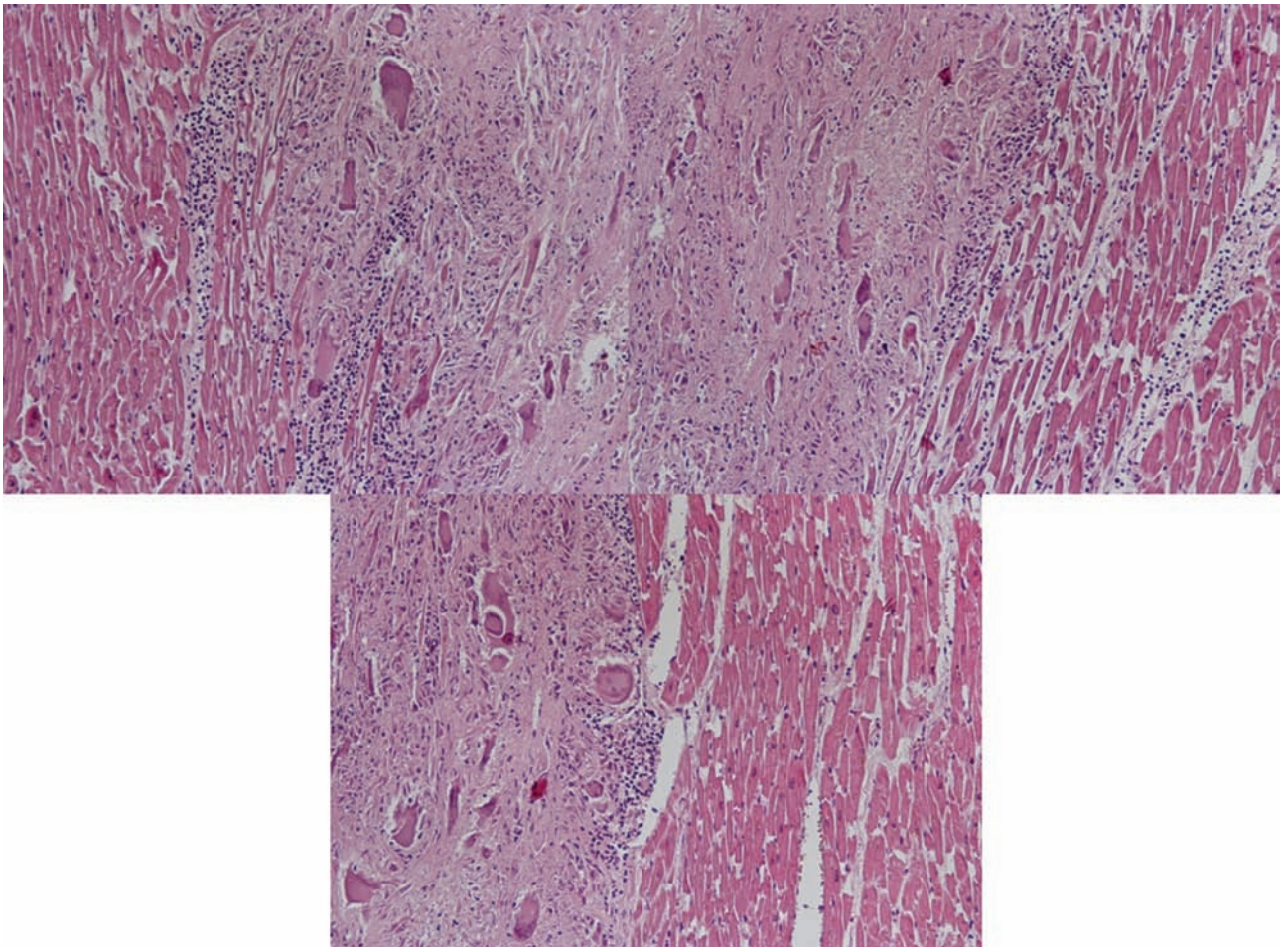

Fig. 1. Microscopic image of the myocardium with visible lymphocytic infiltrations, necrotic lesions and numerous multinucleated giant cells. 100x magnification.

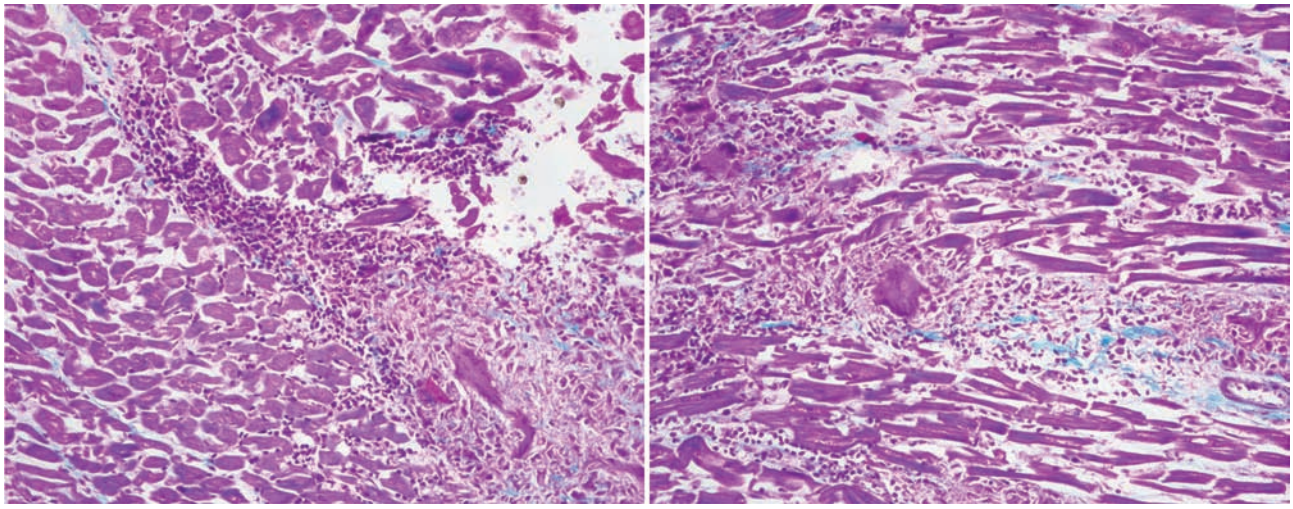

Fig. 2. Microscopic image of the myocardium stained with Masson's trichrome. 100x magnification.

death, where no characteristic macro- and microscopic morphological changes are observed. The most common causes of sudden cardiac death include acute myocardial ischaemia (coronary artery atherosclerosis with or without thrombosis), non-atherosclerotic coronary artery diseases, aortic stenosis, and diseases involving infiltrations and/or fibrosis of the cardiac muscle (myocarditis, sarcoidosis, fibrosis/scars, cardiomyopathy) (Winters, McManus, 2001).

Idiopathic giant cell myocarditis (IGCM), sometimes referred to as Fiedler's myocarditis, is a rare autoimmune disease affecting relatively young individuals (mean age: 42 years) who have not previously shown any signs of disease. The frequency of this diagnosis for endomyocardial biopsy samples from living individuals amounts to approximately 0.08% (Winters, Costanzo-Nordin, 1991). Despite its rare occurrence, it is one of the better characterized clinical and morphological forms of myocarditis. Apart from multinucleated giant cells, lymphocytes, plasmocytes, eosinophils and macrophages are also observed in mixed cell infiltrates, sometimes in the form of granulomas (Baroldi, Fineschi, 2006). The origin of the giant cells is still unclear (histiocytic or muscle), as is the nature of their correlation with systemic diseases such as rheumatic fever, thymoma, systemic lupus erythematosus, inflammatory bowel disease, autoimmune hepatitis, visceral disease or dermatomyositis (Winters, McManus, 2001). Histological differential diagnosis includes sarcoidosis, therefore it is important to pay attention to the presence of myocyte damage (myocytolysis) and examination of the mediastinal lymph nodes (Litovsky et al., 1996). It is also possible to differentiate between these diseases on the basis of the analysis of the expression profile of selected genes in the heart muscle (Lassner et al., 2014).

According to Krynicka et al. (2009), the diagnosis of IGCM, due to its sudden course and poor prognosis, should always be considered in patients with newly diagnosed left-sided heart failure resistant to standard treatment or with newly developed atrioventricular block. Median survival (from the onset of symptoms to the death) is 5.5 months (Cooper et al., 1997), but, occasionally, the first symptom to be noticed may be sudden cardiac death in the course of fatal ventricular arrhythmias, as it was most likely in the case reported herein. Therapeutic options, aside from immunosuppressive treatment trials, are essentially limited to heart transplantation. Occasionally, the diagnosis of this disease is first made on the basis of the results of microscopic examination of the explanted organ (Krynicka et al., 2009). Interestingly, after transplantation there is a risk of recurrence of the disease in up to 25% of recipients, which disappears after immunosuppressive treatment. Therefore some authors interpret this form of inflammation as a specific reaction of rejection in autoimmune patients (Wolfsohn et al., 1994).

On the basis the post-mortem results described above, it was assumed that the direct cause of sudden death of a woman was exacerbation of chronic circulatory insufficiency, which initially occurred on the basis of idiopathic giant cell myocarditis. Due to the lack of reliable morphological markers of acute ischaemia/heart muscle necrosis for the H&E staining method, as well as the questionable diagnostic value of the Nielsen-Selye staining method in diagnosing irreversible ischaemia-caused damage to cardiomyocytes (Rzepecka-Woźniak, 2008), the deceased woman was not diagnosed with myocardial infarction.

As the presented case shows, medical examiners should not limit themselves to taking individual sections from the myocardium (which unfortunately happens), because the key lesions may be multifocal or located within a small area of the heart (in individual sections). Therefore, the recommendations on securing organs for histopathological examination in forensic medicine made by Jankowski and Pieśniak (2007) remain fully

valid. At the time of taking cardiac tissue samples for histopathological examination, the necessary minimum is to cover the entire thickness of the interventricular septum, the right and left ventricular walls. Examination of multiple cardiac wall sections and other anatomical structures (atria, papillary muscles, excitatory and electrical conduction system, coronary arteries) increases the likelihood of diagnosing the cause of sudden cardiac death. Detailed guidelines for dealing with sudden cardiac death, developed by the Association for European Cardiovascular Pathology, were published in 2017 (Basso et al.). It is worth noting that in the case of sudden deaths, histopathological examination is an obligatory supplement of the autopsy and should be carried out as a matter of priority, along with the basic toxicological examination for the presence of ethanol. Sometimes, the interpretation of changes observed in the histopathological examination also requires the exclusion of the possibility of poisoning, by means of comprehensive toxicological examination.

In the article presenting two cases of interstitial myocarditis, Bury et al. (2010) also noted that supplementing the autopsy with a histopathological examination, even where the cause of death appears obvious and clear (e.g. trauma), is extremely important and can provide relevant information, including on the circumstances of death. Myocarditis, as well as ischaemic changes in the heart, may be the initial cause of a ground or air traffic accident, and may eventually lead to sudden death (Śliwka, Pikiel, 1971).

Sources of figures: Rafał Skowronek

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