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Giant Cell Myocarditis Diagnosed at Autopsy: Case Series

Otopsilerde Rastlanan Dev Hücreli Miyokarditler: Olgu Serisi

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ABSTRACT

Objective: In our study, we aimed to determine the accompanying cardiac pathologies and accompanying findings in other organs in the cases of giant cell myocarditis.

Methods: The histopathology reports of the autopsied cases between 2011 and 2020 were reviewed. Cases diagnosed with myocarditis were evaluated retrospectively according to their histopathological pattern. According to the histopathological pattern, it was divided into subgroups as neutrophilic, lymphocytic, lymphohistiocytic, eosinophilic, myocarditis accompanied by granulomas, and giant cell myocarditis. Age and gender distribution, death patterns, autopsy findings, concomitant cardiac pathologies, and histopathological findings in other organs of the cases diagnosed with giant cell myocarditis were evaluated retrospectively.

Results: Between 2011 and 2020, 558 of 49,612 autopsies performed in Morgue Department of the Council of Forensic Medicine were diagnosed as myocarditis in the histopathological examination. 1.02% (n=6) were giant cell myocarditis. Three of the cases with giant cell myocarditis were male and three were female. Histopathological findings were similar in all cases diagnosed with giant cell myocarditis. The mean age was found to be 55.66 (31-80). Heart weight ranged from 433-740 gram. Mononuclear cells, polymorphonuclear leukocytes and, eosinophils accompanying giant cells were seen in the inflammatory infiltrate with necrosis. On macroscopic examination, variegated discoloration and scarring on the ventricular wall was the most common finding. Giant cell myocarditis resulted was the cause of death in four cases. Lobular pneumonia was observed in the lungs in two cases. One case had acalculous cholecystitis.

Conclusion: Autopsy and histopathological diagnosis in sudden and unexpected deaths gain importance to diagnose giant cell myocarditis.

Keywords: Giant cell myocarditis, sudden death, autopsy



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ÖZ

Amaç: Çalışmamızda dev hücreli miyokardit olgularında eşlik eden kardiyak patolojileri ve diğer organlarda eşlik eden bulguları belirlemeyi amaçladık.

Yöntem: 2011-2020 yılları arasında otopsi yapılan olguların histopatoloji raporları incelendi. Miyokardit tanısı alan olgular histopatolojik paternlerine göre retrospektif olarak değerlendirildi. Histopatolojik paterne göre nötrofilik, lenfositik, lenfohistiositik, eozinofilik, granülomların eşlik ettiği miyokardit ve dev hücreli miyokardit olarak alt gruplara ayrıldı. Dev hücreli miyokardit tanısı alan olguların yaş ve cinsiyet dağılımı, ölüm şekilleri, otopsi bulguları, eşlik eden kardiyak patolojiler ve diğer organlardaki histopatolojik bulgular retrospektif olarak değerlendirildi.

Bulgular: 2011-2020 yılları arasında Adli Tıp Kurumu Morg İhtisas Dairesi'nde yapılan 49.612 otopside 558'ine histopatolojik incelemede miyokardit tanısı konuldu. %1,02 (n=6) dev hücreli miyokardit idi. Dev hücreli miyokarditli olguların üçü erkek, üçü kadındı. Dev hücreli miyokardit tanısı alan tüm olgularda histopatolojik bulgular benzerdi. Yaş ortalaması 55.66 (31-80) olarak bulundu. Kalp ağırlıkları 433-740 gram arasında değişmekteydi. Nekrozlu enflamatuvar infiltratta mononükleer hücreler, polimorfonükleer lökositler ve dev hücrelere eşlik eden eozinofiller görüldü. Makroskopik incelemede ventrikül duvarında alacalı renk değişikliği ve skarlaşma en yaygın bulguydu. Dört olguda ölüm nedeni dev hücreli miyokardit olmuştur. İki olguda akciğerlerde lobüler pnömoni görüldü. Bir olguda taşsız kolesistit vardı.

Sonuç: Ani ve beklenmedik ölümlerde otopsi ve histopatolojik tanı, dev hücreli miyokardit tanısında önem kazanmaktadır.

Anahtar Kelimeler: Dev hücreli miyokardit, ani ölüm, otopsi

INTRODUCTION

Giant cell myocarditis is a disease that was first described in 1905 and is characterized by an inflammatory infiltrate containing multinuclear giant cells that typically affects the young and middle-aged group (1). It may occur with arrhythmia and heart failure (2). Giant cell myocarditis, which shares some clinical and histological features with cardiac sarcoidosis, has a more aggressive course than sarcoidosis (3,4). Giant cell myocarditis, a fatal type of myocarditis, is associated with ventricular arrhythmia, atrioventricular block, and progressive congestive heart failure (4,5). It may be asymptomatic. Sudden death is the first finding, and it can be diagnosed by a forensic pathologist at autopsy (6). The incidence of this very rare condition was reported as 0.007% in a study conducted in 2019 (5).

In our study, we aimed to determine the accompanying cardiac pathologies and accompanying findings in other organs by retrospectively examining the clinical features and histopathological findings of giant cell myocarditis cases diagnosed in autopsies performed in our institution.

MATERIALS and METHODS

The histopathology reports of the autopsied cases between 2011 and 2020 were reviewed. Cases diagnosed with myocarditis were evaluated retrospectively according to their histopathological pattern. According to the histopathological pattern, it was divided into subgroups as neutrophilic, lymphocytic, lymphohistiocytic, eosinophilic, myocarditis accompanied by granulomas, and giant cell myocarditis. Age and gender distribution, death patterns, autopsy findings, concomitant cardiac pathologies, and histopathological findings in other organs of the cases diagnosed with giant cell myocarditis were evaluated retrospectively.

RESULTS

Between 2011 and 2020, 558 of 49,612 autopsies performed in the Morgue Department of the Council of Forensic Medicine were diagnosed as myocarditis in the histopathological examination. 39.43% (n=220) of these myocarditis cases were neutrophilic, 37.28% (n=208) lymphocytic, 14.87% (n=83) lymphohistiocytic, 5.02% (n=28) myocarditis accompanied by granulomas, 2.33% (n=13) were eosinophilic, 1.02% (n=6) were giant cell myocarditis.

Three of the cases with giant cell myocarditis were male and three were female. The mean age was found to be 55.66 (31-80). Heart weight ranged from 433-740 gram. Heart weight could not be reached in one case. Coronary arteries were open in all cases. On macroscopic examination, variegated discoloration and scarring on the ventricular wall was the most common finding.

Histopathological findings were similar in all cases diagnosed with giant cell myocarditis. Mononuclear cells, PMN leukocytes and, eosinophils accompanying giant cells were seen in the inflammatory infiltrate with necrosis (Figure A, B, D). All of them had scar areas, perivascular and interstitial fibrosis (Figure C).

In five of the giant cell myocarditis cases, it started with sudden illness, chest pain, and dyspnea and caused sudden death. One case was found dead. In the case of giant cell myocarditis who found dead, pulmonary embolism was detected in autopsy and histopathological examination. Giant cell myocarditis resulted was the cause of death in four cases. Lobular pneumonia was observed in the lungs in two cases. One case had acalculous cholecystitis.

The age and gender of the cases diagnosed with giant cell myocarditis, death patterns, autopsy findings, accompanying cardiac pathologies, and histopathological findings in other organs are given in Table 1 in detail.

DISCUSSION

Myocarditis has been defined as inflammation of the heart muscle and is an important cause of sudden death in adults and children. Its incidence varies between 0.12% and 12% in studies (7). According to the Dallas criteria established in 1987 for histopathological diagnosis in endomyocardial biopsies,

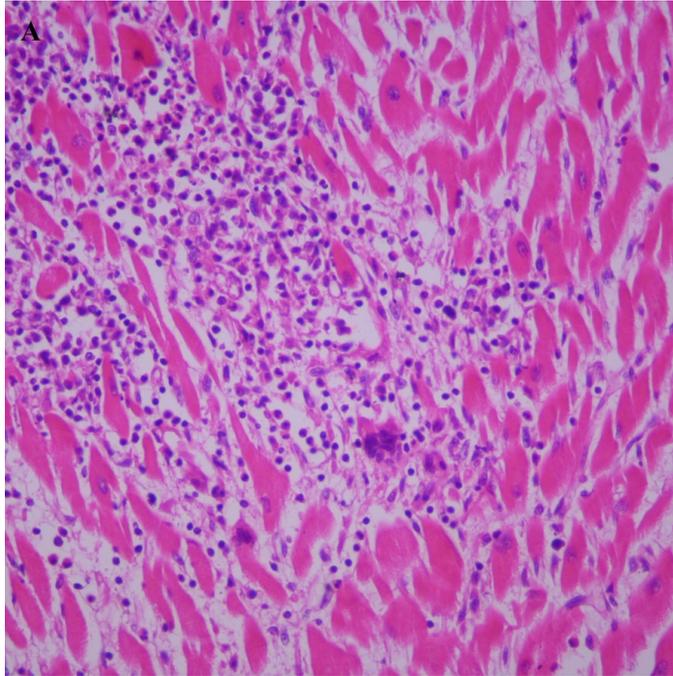


Figure A. Giant cell with mixed inflammatory infiltrate in the myocardium (H&E, x400)

H&E: Hematoxylin and eosin

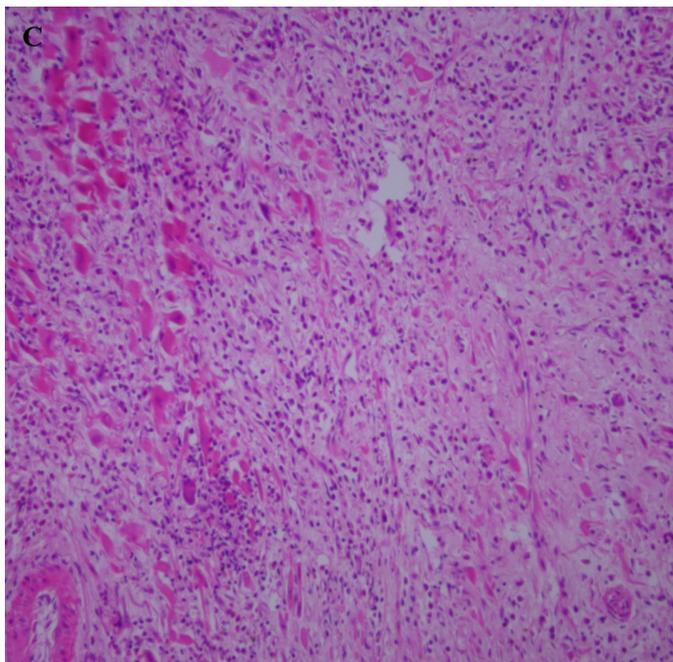


Figure C. Healing phase of giant cell myocarditis (H&E, x200)

H&E: Hematoxylin and eosin

myocarditis is the presence of inflammatory infiltration associated with myocyte necrosis or damage not associated with ischemia (8). There are infectious and non-infectious causes in the etiology. Viral infections are among the most common causes. Toxins, hypersensitivity reactions, autoimmune diseases, and systemic diseases are also among the causes

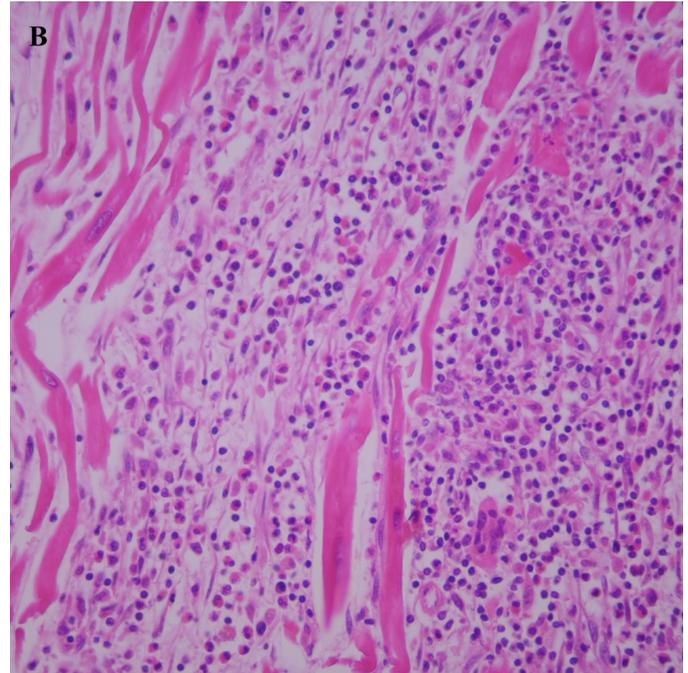


Figure B. Necrotic myocytes and eosinophils (H&E, x400)

H&E: Hematoxylin and eosin

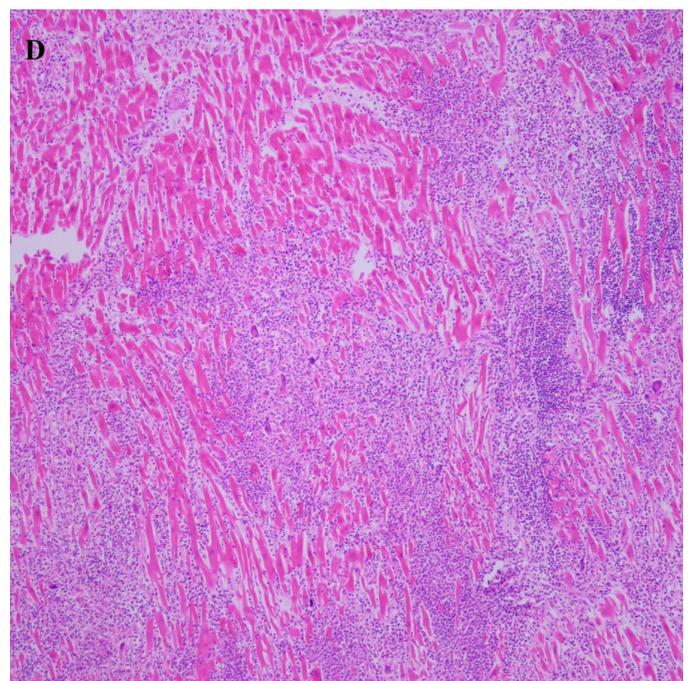


Figure D. Fulminant inflammation with giant cells and mixed inflammatory infiltration (H&E, x100)

H&E: Hematoxylin and eosin

Cases	Age	Gender	Symptoms	Heart weight (gr)	Coronary arteries	Macroscopic findings	Microscopic findings	Other organ findings	Cause of death
1	53	Female	Chest pain and dyspnea	Not known	Open	Widespread variegated appearance	Necrosis, lymphocytes, giant cell myocarditis with eosinophils, fibrosis	Acalculous cholecystitis, lobular pneumonia	Systemic disease of unknown cause
2	51	Male	Sudden illness, exitus in the hospital	520	Open	Haemorrhagic, white discoloration (scarring)	Giant cell myocarditis with lymphocytes, granulation tissue, scarring, fibrosis	Lobular pneumonia	Giant cell myocarditis
3	31	Male	Chest pain, sudden death	436	Open	Widespread variegated appearance, white discoloration (scarring)	Necrosis, giant cell myocarditis with lymphocytes, scarring, fibrosis	No features	Giant cell myocarditis
4	80	Female	Being found dead	433	Open	white discoloration (scarring)	Giant cell myocarditis with lymphocytes, scarring	Pulmonary embolism	Pulmonary embolism
5	68	Male	Sudden illness	740	Open	Haemorrhagic, white discoloration (scarring)	Giant cell myocarditis with lymphocytes, scarring	No features	Giant cell myocarditis
6	51	Female	Sudden illness	480	Open	Haemorrhagic, white discoloration (scarring)	Necrosis, giant cell myocarditis with polymorphonuclear leukocytes, scarring, fibrosis	No features	Giant cell myocarditis

of myocarditis (9). Histopathological examination plays an important role in the diagnosis of myocarditis in autopsy cases, but since the Dallas criteria are not designed for postmortem studies, it may not be appropriate to apply the Dallas criteria for postmortem histopathological evaluation (10).

Kitulwate et al. (10) emphasized in a study they conducted that grading myocardial inflammation is important for the diagnosis of myocarditis, especially seen in the mild form at autopsy. It has also been reported in studies that a few amounts of lymphocytes and macrophages between muscle fibers in sudden and unexpected infant deaths are at the same rate as infants who died by suffocation. For the forensic pathologist, it is difficult to diagnose myocarditis in the presence of uncertain histopathological findings. Because it is very important to distinguish whether this is incidental or the cause of death. In histopathological evaluation, it will be beneficial to determine the extent and degree of myocardial inflammation and to evaluate it carefully. In our study, we identified cases that were diagnosed with myocarditis histopathologically between 2011 and 2020, regardless of clinical history and cause of death. In our retrospective evaluation, we found 1.12% (n=558) cases diagnosed with myocarditis in 49,612 autopsies. This rate was also found to be consistent with the literature. When we looked at the histopathological patterns of these cases and the type

of inflammatory infiltration, neutrophilic and lymphocytic myocarditis were the most common types of myocarditis. Giant cell myocarditis was the least common group.

Giant cell myocarditis is an extremely rare fatal condition. In our study, it was seen in 1.02% (n=6) of myocarditis cases. The incidence in the 10-year autopsy series is 0.012%. Giant cell myocarditis, which is seen at an equal rate in men and women, was detected at an equal rate in our study (3).

It was initially defined as a mixed inflammatory cell infiltration accompanied by myocyte necrosis and giant cells, and then it was differentiated from sarcoidosis by non-granulomatous diffuse infiltration (4,11). Giant cells were previously thought to be regenerating myocytes similar to skeletal muscle cells, and later they were shown to be of monocytic-histiocytic origin. In a recent study, giant cells were found as CD68(+) macrophages at the border of active inflammation surrounding the area of necrosis. Accompanying lymphocytes were also found to be CD4 (+) T lymphocytes (3,12,13). In addition to lymphocytes, eosinophils are also involved in inflammatory infiltration. It is characterized by diffuse or multifocal inflammation and accompanying fibrosis (12). All of our cases diagnosed with giant cell myocarditis had widespread inflammation accompanied by fibrosis. Coronary arteries were open in all cases. All of our cases diagnosed with giant cell myocarditis had widespread

inflammation accompanied by fibrosis. Three histological stages of giant cell myocarditis have been described and these three stages can be seen simultaneously. These stages were defined as acute, healing, and healed. Among these stages, in the acute phase, which has similar features with sarcoidosis, mixed inflammatory cell infiltration containing histiocytes, T lymphocytes and plasma cells accompanying giant cells is observed. Myocyte necrosis and the presence of eosinophils are among the findings that distinguish it from sarcoidosis (14-17). In our cases, all three stages coexisted. Myocyte necrosis was also accompanying. We think that the fibrosis seen in our cases also showed a healed phase. The patency of the coronary arteries is important in terms of supporting the healing period of giant cell myocarditis, not the ischemic origin of the fibrosis we see.

In cases of giant cell myocarditis, cardiomegaly may develop secondary to cardiac failure with increased organ stress due to giant cell deposits that inhibit cardiac contractility. Cardiomegaly may also be manifested by an increase in heart weight. In giant cell myocarditis cases published in the literature, heart weight appears to be increased (6,18). In our cases, the heart weight increased similarly to the literature.

Giant cell myocarditis is often fatal and its etiology is unknown. Dyspnea, fatigue, chest pain, and palpitation are among the symptoms (6,18). Chest pain, dyspnea, and sudden illness, and sudden death were observed in our cases. One case was found dead. Although giant cell myocarditis usually affects young people, it can also be a cause of sudden death in children (3,6,19). Due to sudden death, the diagnosis can be made in postmortem histopathological examination.

Atherosclerotic diseases, which are among cardiovascular diseases, are responsible for most of the sudden and unexpected deaths. Less commonly, inflammatory diseases of the myocardium are among the causes of sudden death (6). Autopsy and histopathological diagnosis in sudden and unexpected deaths gain importance at this point.

CONCLUSION

The recognition and actual incidence of inflammatory diseases that will cause sudden death, which are difficult to recognize macroscopically, or which may be confused with ischemic diseases, can be revealed by histopathological examinations. Giant cell myocarditis can also be confused macroscopically with ischemic heart disease with the appearance of hemorrhagic and fibrotic areas. Macroscopically, we think that the absence of atheroma plaques in the coronary arteries should primarily suggest an inflammatory process. We think that the fact that this condition, which is so rare, comes to mind at the stage of macroscopy, is closely related to experience. Although giant cell myocarditis is rare, it is a cardiac pathological conditions

that come to mind in sudden death cases without a history of coronary artery disease.

Ethics

Ethics Committee Approval: For this study, permission was obtained from the Council of Forensic Medicine, Education and Scientific Research Commission with the date 04/10/2021 and number 21589509/2021/1027, and the Helsinki Declaration criteria were taken into consideration.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: A.B., T.D., Design: A.B., Data Collection or Processing: A.B., T.D., Analysis or Interpretation: A.B., Literature Search: A.B., T.D., Writing: A.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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