GIANT CELL MYOCARDITIS WITH ASTEROID BODIES DIAGNOSED AT AUTOPSY: A RARE CASE REPORT

Prasenjit Sarkar*,1, Debadrita Sen*, Sumona Ghosh* and Abhijit Datta*
*PG RESIDENTS HOSTEL, AGMC, AGARTALA.

ABSTRACT Giant cell myocarditis (GCM) is an extremely rare and rapidly fatal cardiovascular condition with high morbidity and mortality. It usually affects young, healthy individuals and may be associated with autoimmune disorders. In most cases, the course of the disease is in the form of fulminant myocarditis. The basis of its diagnosis is an endomyocardial biopsy (EMB). Even with optimal medical care, GCM has a bad prognosis. Herein we report a 54-year-old female who presented with difficulty in breathing and was clinically diagnosed with acute myocardial infarction in cardiogenic shock and died on the 3rd day of admission. After the autopsy, histopathologically, it was diagnosed as a case of giant cell myocarditis.

We intend to raise awareness of this rare disease process and its potential to cause sudden cardiac death without any previous symptomatic heart disease.

KEYWORDS Giant cell myocarditis, Asteroid bodies, Myocyte necrosis, Autopsy

Introduction

Giant cell myocarditis (GCM) is an extremely rare and rapidly progressive form of myocarditis that occur for unknown reasons (idiopathic). The incidence of GCM has been reported to be 0.007% in a large Japanese autopsy study and 0.051% in India.[1] Till now, less than 300 cases have been reported in the medical literature.[2] The first case was described in 1905 by Saltykow as a case of widespread myocardial inflammation with multinucleated giant cells and myocyte necrosis.[3] The development of diagnostic tools, such as endomyocardial biopsy (EMB), cardiac MRI, fluorodeoxyglucose (FDG)-positron emission tomography (PET), has allowed diagnosis and treatment in living patients only after the mid-1980s, prolonging transplant-free survival and life expectancy.[4] The definitive diagnosis is based on the histopathologic findings obtained by EMB. However, the procedure’s invasiveness is often not done early enough, and results are thus delayed. Most cases occur in young or middle-aged adults (median age 42 years), with equal gender distribution. The most common initial manifestations are symptoms of congestive heart failure, ventricular arrhythmia, atrioventricular block. However, rarely, it may also present as sudden cardiac death.

In the right clinical context, such as an acute presentation of unexplained new-onset heart failure and arrhythmia, it is very important to maintain high suspicion of such a rare disease.

Case report

A 54 years old female with no significant past medical history presented difficulty breathing for one day. She received the Covid-19 vaccination 21 days back. On admission, her oxygen saturation (Spo2) was 59% in room air. On initial investigations Electrocardiogram (ECG) showed ventricular premature contraction (VPC) with left bundle branch block (LBBB) (Fig-1). Serum CPK-MB was raised, and Serum cardiac Troponin I was positive. She was diagnosed with acute myocardial infarction in cardiogenic shock in a case of adverse event following immunization (AEFI). She was treated aggressively with Oxygen, intravenous inotropic and fibrinolytic agents. Echocardiography (ECHO) revealed a left ventricular ejection fraction (LVEF) of 30% without evidence of valvular dysfunction. Cardiac function deteriorated despite standard heart failure therapy. On the third day of her admission, she was declared dead after several unsuccessful
attempts at resuscitation with the diagnosis of acute myocardial infarction in cardiogenic shock in the case of AEFI.

An autopsy was performed as per protocol. The decedent’s external examination revealed no abnormality. The heart weighed 400 grams, ventricular wall thickness and coronary arteries were normal. Upon sectioning, the myocardium was grossly unremarkable (Fig-2).

**Microscopic examination:**

Histologically upon extensive sectioning of the heart, the myocardium revealed a diffuse inflammatory infiltrate consisting primarily of lymphocytes, plasma cells, eosinophils and histiocytes with numerous giant cells. The cytoplasm of a few giant cells showed star-shaped asteroid bodies. Marked myocyte-necrosis was noted (Fig-3 & 4). There was no well-formed granuloma in any section of the heart. No microorganisms were identified in and around the giant cells. Ziehl Neelsen stain did not show any acid-fast bacillus. No fungal element was identified on Periodic acid Schiff (PAS) staining. A large mural thrombus was seen in the left auricle. The endocardium and pericardium were normal. Pericardial vessels were normal. Finally, a diagnosis of giant cell myocarditis was made. Gross and histopathology of other organs like lungs, liver, kidney, brain showed no significant abnormality.

**Discussion**

Giant cell myocarditis is a rare and frequently fatal disorder with a mortality rate of approximately 90% if untreated. The majority of cases occur in healthy young adults; the median age reported is approximately 42 years (range 10days-88years) with equal gender distribution. From 1905 to 1980, all reported GCM cases were diagnosed at autopsy.[5] The exact aetiology and pathogenesis are unknown. It has been postulated to be autoimmune. Numerous autoimmune disorders have been associated with GCM in various case reports. (Box-1). The most influential evidence supporting autoimmune aetiology was an animal study in 1990. Researchers were able to induce GCM in rats using autoimmunization with myosin. It is mainly mediated by T-lymphocytes and tumour necrosis factor-alpha (TNF-α), the later stimulating the multinucleation of macrophage.[6]
Criteria for GCM
Presence of widespread inflammatory infiltrates with multinucleated giant cells associated with myocyte damage.
The absence of non-necrotizing granuloma in this background was sufficient to classify this case as GCM.

Criteria for CS
Presence of at least 1 non-necrotizing granuloma, with or without foci of lymphocytic myocarditis, necrosis or presence of isolated giant cells.

Table 1: Summary of criteria used for diagnosis of GCM & CS (article by Nordenswan et al.)

Box-1: Autoimmune and other diseases associated with giant cell myocarditis

1. Crohn’s disease
2. Ulcerative colitis
3. Thyroid disease
4. Cryofibrinogenaemia
5. Pernicious anaemia
6. Rheumatoid arthritis
7. Optic neuritis
8. Common variable immunodeficiency

Figure 4: High power view 40X H&E - shows multinucleated Giant cells with star shaped asteroid bodies admixed with dense exuberant inflammatory infiltrate consisting mainly of mononuclear cells.

Figure 5: A- Low power view10X – mural thrombus B- 40X- muscle necrosis: pale areas within muscle (black arrow).
CD4+ T-lymphocytes were the main cell type implicated in the initial phase of the disease in the rat model, whereas in human GCM, CD8+ T-cells predominate. [7] CD8+ cells may outnumber CD4+ in the acute stage of disease in human GCM. The ratio may vary at different stages of the disease. A multicenter GCM registry showed upto 75% of patients presented with heart failure, 14% with ventricular tachycardia (VT), 6% with myocardial infarction, 5% with atrioventricular block. The median survival from onset of symptoms to death was estimated at around 5.5 months without transplantation. [8]

The definitive diagnosis of GCM is made by histological examination of endomyocardial biopsy. The typical myocardial histological finding is widespread mixed inflammatory infiltrates including histiocytes, T-lymphocytes and multinucleated giant cells causing myocyte damage. [4]

Thus, maintaining a high index of suspicion in the appropriate clinical settings is critical in enabling early diagnosis.

In this case, the decedent was a post-covid-vaccination patient who was admitted with symptoms of myocardial infarction with cardiogenic shock, with no previous history of any underlying condition. On autopsy history, all organs, including lungs, were normal, except the heart, which showed features of giant cell myocarditis with extensive myocyte-necrosis (Fig-5). The cytoplasma of a few giant cells showed asteroid bodies. Asteroid bodies are small, intracytoplasmic, eosinophilic star-shaped structures usually seen in sarcoidosis but can also be present in tuberculoid leprosy, foreign body giant cell reactions or fungal infections. No such reason was present in the present case.

Giant cell myocarditis has to be distinguished from other forms of myocarditis like lymphocytic, eosinophilic, hypersensitivity, necrotizing eosinophilic and sarcoid myocarditis, as GCM is associated with a poor prognosis. Distinction from cardiac sarcoidosis solely depends on the histopathology of the myocardium. In 1956, Tesluk differentiated the diffuse non-granulomatous infiltrate of GCM from well organized granulomatous lesions of Cardiac sarcoidosis. Organized noncaseating interstitial granulomas without myocyte necrosis are the key to diagnosing sarcoidosis. The absence of sarcoid granulomata distinguishes it from cardiac sarcoidosis (CS). [8]

This case satisfied those criteria (Table 1). Clinically GCM and CS distinguish themselves quite clearly. Although congestive heart failure, ventricular arrhythmias, and heart block have been associated with both GCM and CS, patients with GCM are more likely to present with a fulminating course with a shorter period from onset to death than CS. 5 year disease-free survival is worse for GCM 27%, compared to 77% in CS. Sarcoidosis of other organs does not exclude the diagnosis of GCM. [10]

Incidence and prevalence
A review of 377,841 autopsies throughout 20-years found myocarditis in 0.11% but giant cell myocarditis in only 0.007% of the cases. Considering that patients passed away before reaching the hospital, this incidence rate might even be higher. [11]

The incidence of myocarditis and pericarditis following post-covid vaccination is rare and mainly seen in adolescents and young males, notably after the second dose. Most cases appear to be mild and respond well to supportive treatment and follow-up. [12]

However, in this case, we could not establish that giant cell myocarditis has occurred due to the covid-19 vaccination. More studies, further workup and standard investigations may give us more insight into this extremely rare and fatal disorder.

Conclusion
Giant cell myocarditis is rare and rapidly progressive myocarditis that affects young to middle-aged adults. GCM has more rapid progression than lymphocytic myocarditis (presumed viral). The disease usually manifests as ventricular arrhythmia, congestive heart failure, or sudden cardiac death. The exact aetiology of the disease is not known. However, an autoimmune mechanism is considered to play a vital role in developing the disease. So this condition should be considered in patients with autoimmune diseases presenting with cardiac complications.

This case presented features of acute myocardial infarction in cardiogenic shock without any past relevant medical history. The disease took a fatal course and led to the early demise of the decedent. The rapid and fulminating course of the disease needs prompt diagnosis and intensive cardiac care and opens new questions necessitating future research on this disease.

Acknowledgement
We wish to thank Dr Arunabha Dasgupta, Professor, Department of Medicine, Agartala Government Medical College, for his support and encouragement.

Funding
This work did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest
There are no conflicts of interest to declare by any of the authors of this study.

References
1. Izumi T, Kodama M, Sibata A. Experimental giant cell myocarditis induced by cardiac myosin immunization. Eur Heart J 1991;12(Suppl D):166-8. https://doi.org/10.1093/eurheartj/12.suppl-d.166.
2. Zeigler JP, Batalis NI, Fulcher JW, Ward ME. Giant cell myocarditis causing sudden death in a patient with sarcoidosis. Autops Case Rep[Internet], 2020;10(4):e2020238.
3. Saltykow S. Uber diffuse myocarditis. Virchows Arch Pathol Anat Physiol Klin Med. 1905;182(1):1-39.
4. Xu J, Brooks EG. Giant cell myocarditis: a brief review. Arch Pathol Lab Med 2016;140:1429-34. https://doi.org/10.1007/s0005900500231.5858/arpa.2016-0068-3S.
5. L.T.Cooper Jr, J.M. Hare, H.D.Tazelaar, Edwards DW, Starling CR, Deng CM et al.Usefulness of immunosuppression for giant cell myocarditis. Am J Cardiol, 102(2008), pp.1535-39
6. Sorimachi K, Akimoto K, Tsuru K, Niwa A. The involvement of tumor necrosis factor in the multinucleation of macrophages. Cell Biol Int 1995;19:547-
7. Litovsky SH, Burke AP, Virmani R. Giant cell myocarditis: an entity distinct from sarcoidosis characterized by multifac- tic myocyte destruction by cytotoxic T cells and histiocytic giant cells. MOD PATHOL 1996;9:1126-34.
8. Kandolin R, Lehtonen J, Salmenkivi K, Sokolowski AR, Lommi J, Kupari M. Diagnosis, treatment, and outcome of giant-cell myocarditis in the era of combined immunosuppression. Circ Heart Fail 2013;6:15-22. https://doi.org/10.1161/CIRCHEARTFAILURE.112.969261.

9. Nordenswan HK, Lehtonen J, Ekstrom K, Sokolowski AR, Vihinen T, Miettinen H et al. Manifestations and outcome of cardiac sarcoidosis and idiopathic giant cell myocarditis by 25-year nationwide cohorts. J Am Heart Assoc. 2021;10:e019415. DOI: 10.1161/JAHA.120.019415.

10. David H. Birnie, MB ChB, Nair Vidhya et al. J Am Heart Assoc. 2021;10:e020542. DOI: 10.1161/JAHA.121.020542

11. Of lazer P. Giant cell myositis and myocarditis revisited. ACTA MYOLOGICA 2020; XXXIX: p. 302-306. doi:10.36185/2532-1900-033. 12. Myocarditis and Pericarditis Following mRNA COVID-19 vaccination | CDC https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.htm