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# A Case of Giant Cell Myocarditis

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## ABSTRACT

**A case of granulomatous giant cell myocarditis diagnosed post-mortem is presented. Clinically, the 84-year-old patient showed progressive cardiac failure, atrial fibrillation and ECG changes suggestive of infarction. At autopsy granulomatous changes with mononuclear cells and giant cells were found exclusively in the left atrial myocardium. A review of recent literature on the subject is presented.**

## INTRODUCTION

The rare inflammatory condition of the myocardium named giant cell myocarditis has been occasionally discussed in the literature. The aetiology is unknown. The histo-pathological picture is dominated by mononuclear inflammatory cells with a contribution of multinucleated giant cells and histiocytes. Degenerated muscle cells are seen and fibrosis may be present (3). The infiltrations are mostly diffusely spread throughout the myocardium. Clinically, the disease is manifested by either rapidly progressive cardiac failure, cardiac arrhythmias, ECG changes suggestive of cardiac infarction or sudden unexpected death (9, 13). The disease is usually seen in young adults, although it has been observed in a 6-week old child (6) and a 76-year-old man (10).

This report deals with an 84-year-old woman who was admitted to hospital after 2 weeks of rapidly progressive cardiac failure. ECG suggested atrial fibrillation and infarction. Within 20 hours she died and at autopsy a giant cell myocarditis confined to the left atrium was found. The case is worthy of note in view of the patient's high age and the exclusive localization of the process.

## CLINICAL DATA

A woman (M. P., 840806), 84 years old, was admitted to hospital suffering from dyspnoea. As a child she had had scarlet fever. Ten years before admission she had been treated temporarily for hypertension. During the last 8 years she had been taking pilocarpine for chronic glaucoma in her right eye. During the last few years she had complained of dizziness. In the last 2 weeks before admission she had been suffering from dyspnoea, which had worsened progressively. She had also had a distressing cough with transient hemoptysis.

*Clinical findings on admission:* Cyanosis of the lips, dyspnoea at rest and marked pretibial oedema. The jugular veins were dilated. Blood pressure 125/85 mmHg (recumbent position). Heart auscutation negative. Slight bilateral dullness of the chest on percussion. Crepitant rales over the right lung. The liver was palpable 3–4 cm below the costal arch. In the right eye there was myosis due to pilocarpine and a cataract. Examination of the left ocular fundus revealed minimal arteriolar narrowing (FH I according to Keith-Wagener).

*Laboratory data on admission:* Hb 12.5 g/100 ml, white blood cell count 6 700 (1 % band neutrophils, 83.5 % segmented neutrophils, 0.5 % basophils, 8 % lymphocytes, 4 % monocytes). Thrombocyte count 182 000. Sedimentation rate 30 mm/h. Serum electrolyte content normal. Serological test for syphilis was negative. SLDH 280 Wroblewski units. ECG indicated a slightly irregular supraventricular rhythm without discernible P waves, possibly atrial fibrillation; a localized Q wave together with ST elevation in V4 aroused suspicions of infarction; 15 hours later the ST–T changes were accentuated. Cytology of pleural effusion was negative.

*Treatment and course:* On the day of admission, treatment was initiated with digitalis injections, diuretics, and theophyllamine. Twenty hours after admission she developed a pulmonary oedema which could be alleviated only temporarily before she died.

## AUTOPSY FINDINGS

Autopsy was performed within 24 hours of death. Oedema was noted in the lower extremities. In the pericardium 100 ml of yellow transparent fluid was found. In the heart (weight 370 g) the left atrial wall was thickened (thickness 8 mm). The cut surface of the left atrium was pale and lustreless. The rest of the myocardium was of normal appearance. In the left auricle a thrombus the size of a walnut was found. The valves were fibrosed. In the coronary arteries and the aorta atheromatous changes were seen. Bilateral pleural effusion (right pleura 800 ml, left pleura 1 000 ml) was observed. In the lungs, atelectasis was seen in both lower lobes. Moderate amounts of oedema were noted in both lungs.

The thyroid was diffusely enlarged, each lobe being the size of a golfball. The cut surface was glass-like and exhibited some minor haemorrhages, calcifications and necroses. The

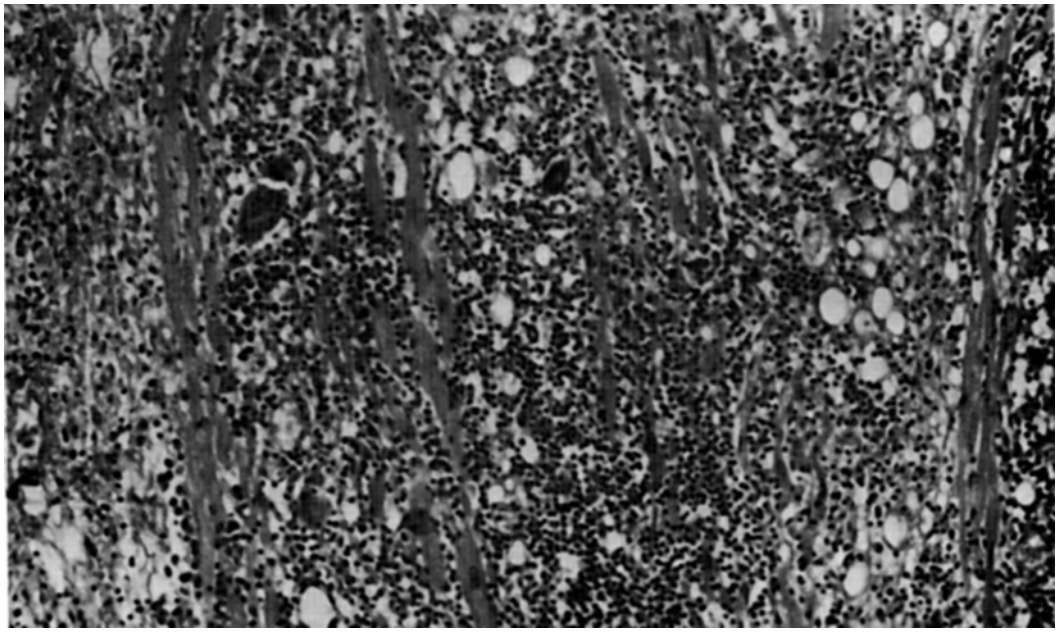

*Fig. 1.* Microphotograph of specimen from left atrial myocardium showing dense granulomatous infiltration with mononuclear inflammatory cells, a few giant cells of different appearance and degenerated muscle cells. Hematoxylin-eosin, × 150.

liver (weight 1 250 g) was congested. In the gall bladder a walnut-sized stone was found. The kidneys (weight 2 × 90 g) were nephrosclerotic. There was a calcified myoma in the uterus.

Microscopically, specimens from the myocardium showed granulomatous infiltrations with destruction of the muscle bundles exclusively in the left atrial wall. These dense infiltrations were observed in all parts of the left atrium and contained mostly lymphocytes and plasma cells (Fig. 1). Giant cells were also found intermingling with the other cells. These were mainly of the Langerhans' and foreign body types and contained no inclusion bodies. The giant cells were faintly more basophilic than surrounding cells (Fig. 2*a–b*). No fibrosis could be seen, but a few fibroblast-resembling cells and histiocytes were observed. No neutrophils or eosinophils could be seen with certainty. A few fairly large mononuclear cells resembling epithelioid cells were present, scattered or in clusters, but no distinct epithelioid cells were present. No tubercles, areas of caseation or rheumatoid lesions were observed. In some areas the muscle cells were highly degenerative with loss of cross striation and nuclei (Figs. 1–2). A few muscle fibres were hypertrophic with enlarged nuclei (Fig. 3).

In the wall of the left ventricle no infiltrations of the kind described above were observed. The subendocardial and subepicardial connective tissue was thickened, however, and infiltrations of mostly lymphocytes were seen. A few plasma cells were seen, but no giant cells. (Fig. 4). Stains for fungi (methenamine, PAS) were negative. Stain for acid-fast bacteria (Ziehl-Neelsen) was also negative.

## DISCUSSION

On the basis of the histo-pathological findings presented above the condition was considered to be a chronic process with granuloma-like lesions. The possibility that the changes in the atrial wall in the case presented were associated with the thrombus found in the left auricle was rejected on the basis of the same histo-pathological findings. On this basis the possibility of a cardiac myxoma in the atrial wall was also refuted. Neither of these interpretations was in accordance with the presence of giant cells and degenerated muscle fibres (4). The findings seemed consistent with those in giant cell myocarditis.

Approximately thirty cases of giant cell myocarditis have hitherto been reported. Dilling (3) presented a review of 13 cases published during 1900–1952 and added one case of her own. The age at death in these cases ranged from 20 to 57 years. Eight of the patients were male and six female. The duration of illness was at least several days, but in 11 of the cases the death was considered more or less sudden and unexpected. Farrish (12) mentioned in his report six cases published after 1956

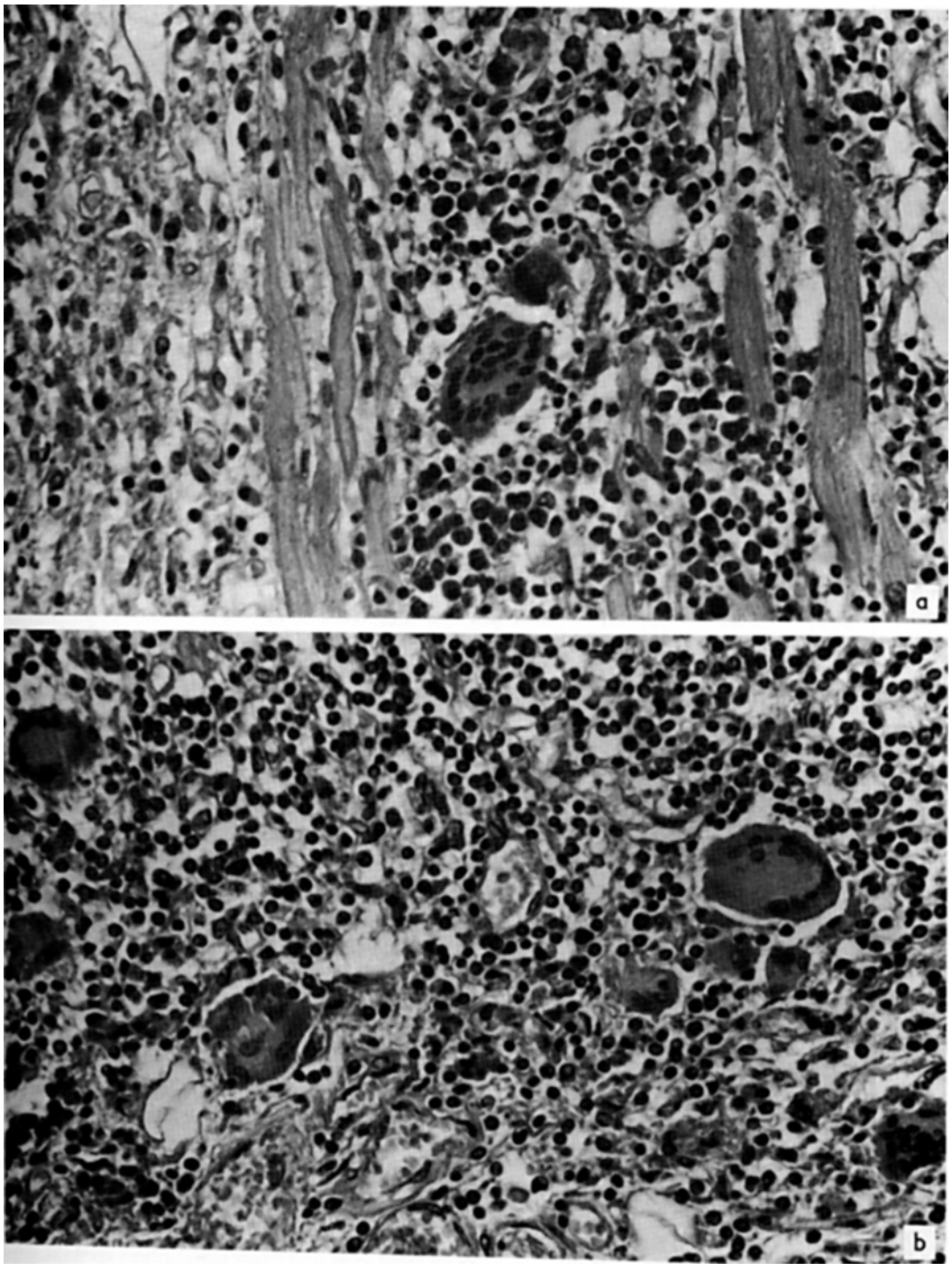


*Fig. 2.(a–b)* Microphotographs showing the cellular composition of the infiltrate—numerous lymphocytes and plasma cells, a few giant cells of Langhans and foreign body types and large mononuclear cells. H–E, × 360.

and added one case of his own. The ages at death ranged between 19 and 54 years. Three of the patients were male, four were female. It is concluded that the condition is extremely rare. Only two of the observed cases have been noted by the same investigators (10). The disease is seen in

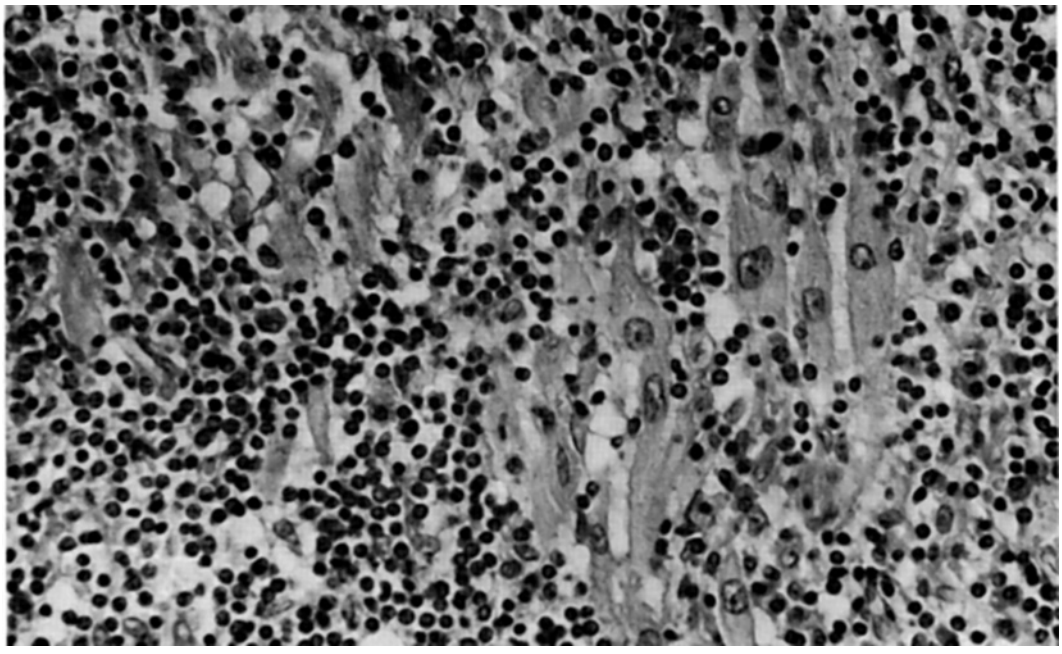

*Fig. 3.* Microphotograph showing a few hypertrophic muscle cells with large nuclei. H–E, × 360.

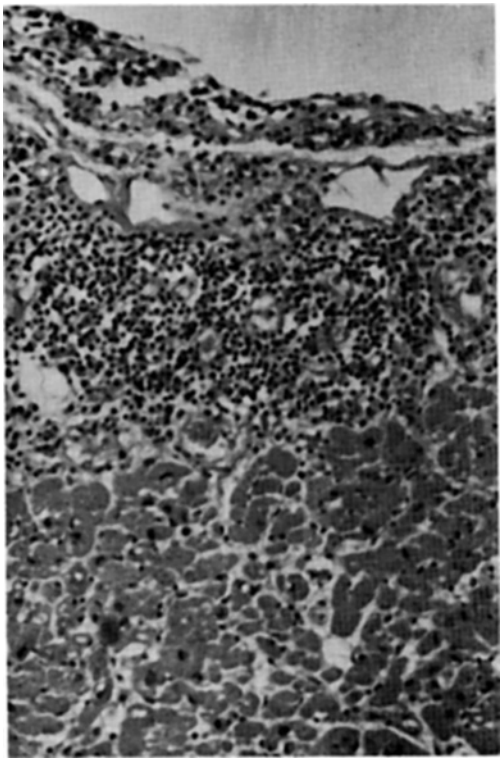

*Fig. 4.* Microphotograph of specimen from the left ventricular myocardium with endocardial mononuclear cell infiltrate. H–E, × 150.

relatively young people. O'Donnel & Mann (10) mentions a median age of 34 years. There seems to be no sex predisposition.

On the basis of histo-pathological findings giant cell myocarditis is considered to be a chronic process with granuloma-like lesions and sometimes extensive fibrosis (14). The pathological changes are usually consistent with those generally seen with protracted inflammation (10). The chronic inflammation is probably systemic in character, since in 10 of 23 cases extracardiac lesions were found (10) On this basis the designation "isolated myocarditis" is rejected by some authors.

Two problems have been subjected to considerable discussion in preceding reports: (i) the pathogenesis of the giant cells; (ii) the aetiology of the lesion.

There seems to be general agreement that the myocardial giant cells arise from muscle cells. Giant cells are seen in continuity with muscle fibres (9). Both giant cells and myocardial fibres contain intracytoplasmic PTAH positive fibrillar structures and lipochrome pigments (9). Electron microscopic studies have confirmed these observations (13). The giant cells are considered either to represent attempts at regeneration by muscle cells or to be derivatives of degenerated muscle cells (9, 13).

The aetiology of the cardiac lesion has been much debated. Attempts at demonstrating bacteria, vira, fungi, spirochetes, helminths or other specific agents have failed. Recent discussions on the aetiology have concentrated on three possible alternative factors: (i) viral infection, (ii) sarcoidosis, and (iii) auto-immune or hypersensitivity reaction.

Tesluk (16) concluded on the basis of the histopathological appearance of the lesion that viral infection is possible. He cited Rivers (15) and stated that the action of viruses at first frequently resulted in a hyperplastic response. He failed, however, to demonstrate the viral factor in cytopathogenicity studies on tissue cultures. Recently Pyun et al. (13) reported that they had observed no virus particles in the giant cells in electron microscope examinations.

The possible role of sarcoidosis in the aetiology was discussed by Rab et al. (14). They concluded, however, that a lack of multiple organ invasion and absence of a clinical history of the disease made the diagnosis difficult. But the possibility that giant cell myocarditis might represent a case of solitary myocardial sarcoidosis remained. They cited Forbes & Usher (5), who found 25 cases of myocardial sarcoidosis, two of them without multiple organ invasion. Johansen (7) concluded that as long as the real nature of sarcoidosis has not been elucidated the possibility that it bears relation to some of the lesions in giant cell myocarditis cannot be quite rejected. Pyun et al. (13) found, however, that the histological features of giant cell myocarditis differed from a typical sarcoid lesion in many details.

Though Dilling (3) believed allergy to be an unlikely cause of giant cell myocarditis many authors have found this interpretation fairly probable. Parrish (12) considered that the picture was not imcompatible with an autosensitization reaction to heart muscle proteins. In the case of giant cell myocarditis presented by Palmer & Michael (11), concomitant giant cell arteritis was found. They suggested that a hypersensitivity reaction could be the basis of both lesions. O'Donnell & Mann (10) put forward the same interpretation in a case of concomitant giant cell myocarditis and acute interstitial nephritis. Miller et al. (9) considered that the character of the inflammatory infiltrate was suggestive of an experimental delayed hypersensitivity reaction. Further, myocardial giant cells have been found in cases of thymoma (2) and Wegener's granulomatosis (8), both conditions with immunpathological significance.

The possibility that interstitial myocarditis of unknown aetiology has an immunological basis has experimental support. Bing et al. (1) found granulomatous myocardial lesions in certain homografted canine hearts. Miller et al. (9), however, was unable to demonstrate bound gammaglobulin in the myocardial lesions by the immunofluorescent technique in their case of giant cell myocarditis.

Besides the fact that no aetiological agent has been found in the case presented above it has nothing to contribute to the discussion on the aetiology of this disease. The giant cells were seen in association with degenerated muscle cells and could have arisen from muscle tissue though no special procedure was undertaken to demonstrate this.

The localization of the lesion is of special interest in this case. Several authors have reported previously that the inflammatory lesion is always found in the left ventricular wall; frequently it extends to the interventricular septum and right ventricle (3). In one of the reviewed cases the auricles were involved. In the case published by Parrish (12) it was estimated that 80% of the myocardium was destroyed. Miller et al. (9) found pathological changes only in the left ventricle and interventricular septum. Pyun et al. (13) found changes in all parts of the myocardium. Though McCrea & Childers (8) were able to diagnose a case of giant cell myocarditis during life from examination of the left atrial appendage removed at mitral valvotomy, nothing is known about the distribution of the lesion in other parts of the myocardium. In the present case lesions were only found in the left atrium. This has not been reported earlier.

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