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Survival After Acute Necrotizing Eosinophilic Myocarditis Complicating a Massive Left Ventricular Mural Thrombus: A Case Report

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Abstract

An 81-year-old man was referred to our hospital with exertional dyspnea following cold-like symptoms. Electrocardiography revealed ST elevation and positive T wave in leads Ⅰ, Ⅱ, aV_L, aV_F, and V_2–V_6. The diagnosis was acute myocarditis complicating heart failure. He was conservatively managed. On hospital day 8, brain infarction developed and echocardiography disclosed massive mural thrombus in the left ventricle. Left ventriculotomy was performed on hospital day 21 and histological examination showed inflammatory cell infiltration mainly composed of eosinophils and monocytes, degeneration of myocytes with replacement fibrosis, and fresh fibrin thrombus overlaying the endocardium. These findings were compatible with a diagnosis of acute necrotizing eosinophilic myocarditis (ANEM). He recovered uneventfully without specific therapy. This case suggests that a subtype of ANEM might be self-limiting.

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Key Words

■ **Myocarditis (acute necrotizing eosinophilic)**
■ **Thrombosis (left ventricular mural thrombus)**
■ **Cardiac surgery (left ventriculotomy)**

INTRODUCTION

The association between eosinophilia and heart disease is well known.[1–4] Eosinophil-related cardiac injuries involve various parts of the heart such as the endocardium, myocardium of both atria and ventricles or heart valves, and can be classified under the comprehensive term "eosinophilic heart disease".[5] In this continuum, acute necrotizing eosinophilic myocarditis (ANEM) is characterized by an acute and fulminant clinical course.[6–11] We describe a rare patient who survived ANEM complicating a massive mural thrombus in the left ventricle (LV).

CASE REPORT

An 81-year-old Japanese man with hypertension and hyperlipidemia developed fever, general malaise, polyarthralgia and exertional dyspnea in April 15, 2005. Four days later he consulted a gen-

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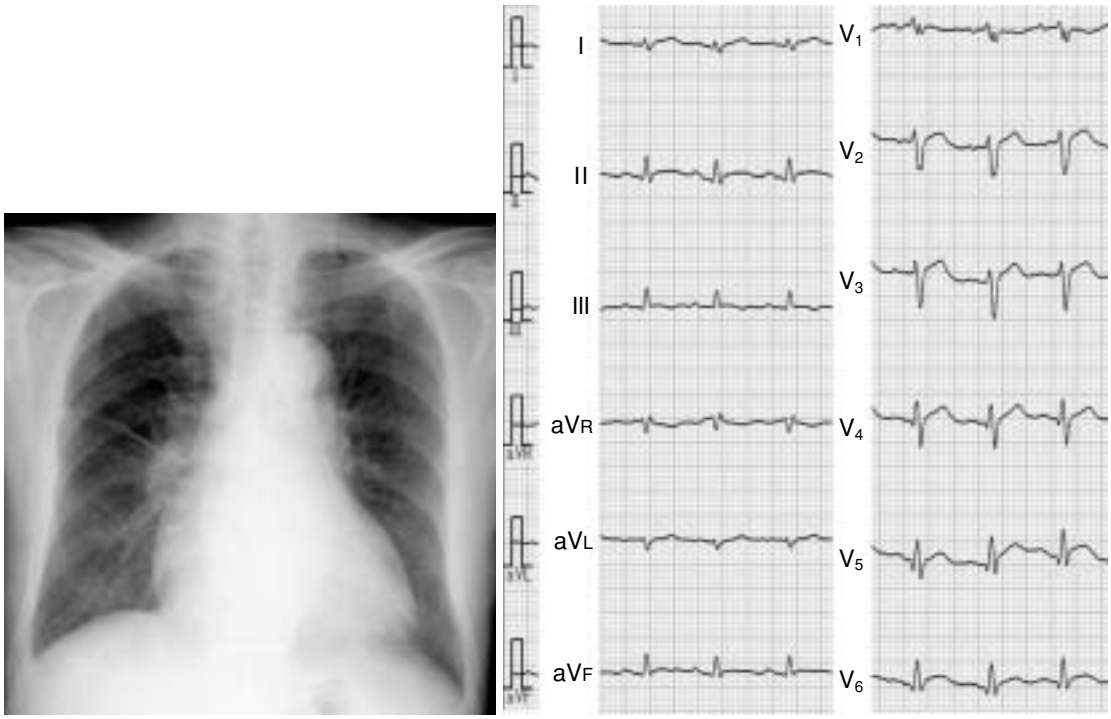

Fig. 1 Chest radiograph (*left*) and electrocardiogram (*right*) findings on admission
Chest radiography shows cardiomegaly, bilateral lung congestion and pleural effusion. Electrocardiogram shows sinus rhythm with ST elevation and positive T wave in Ⅰ, Ⅱ aVL, aVF, and V_2-V_6.

eral practitioner. Laboratory tests disclosed elevated aminotransferase levels and he was referred to our hospital. He had never developed allergic diasthesis, and had not received additional medication or a different prescription before the symptoms appeared.

On admission, he was afebrile with blood pressure of 170/44 mmHg and a pulse of 78 beats/min. Skin rash and edema were absent. Gallop rhythm, heart murmur, crackles or rubs were inaudible. The hepatojugular reflux was positive. Chest radiography showed cardiomegaly, bilateral lung congestion and pleural effusion (**Fig. 1−left**). Electrocardiography revealed sinus rhythm with ST elevation and positive T wave in leads Ⅰ, Ⅱ, aVL, aVF, and V_2-V_6 (**Fig. 1−right**).

Laboratory data demonstrated elevated white blood cell count without eosinophilia. Serum levels of lactate dehydrogenase and creatine kinase were elevated and the rapid assay for serum troponin T was positive. Arterial blood gas analysis showed metabolic acidosis accompanied by respiratory compensation. Blood coagulation markers such as fibrin degradation products and D-dimer were elevated (**Table 1**). Autoantibodies such as antinuclear

Table 1 Laboratory data on admission

WBC	11,200/μl	BUN	61.2mg/d*l*
Neutro	81.0%	Cr	1.3 mg/d*l*
Lymph	12.5%	Na	133 mEq/*l*
Eosino	0.0%	K	4.5 mEq/*l*
Baso	0.0%	Cl	95 mEq/*l*
Mono	6.5%	Troponin T	(+)
RBC	475×10⁴/μl	Myosin light chain 1	17.6 pg/m*l*
Hb	14.4 g/d*l*	CRP	24.9 mg/d*l*
Ht	42.9%	BNP	682.0 pg/m*l*
Plt	16.6×10⁴/μl	PT	19.9 sec (PT-INR 1.74)
		APTT	42.1 sec (control 32.9 sec)
ESR	70/101 mm (1 hr/2 hr)	Fbg	535 mg/d*l*
Urine		FDP	392.2 μg/m*l*
Blood	(2+)	D-dimer	58.5 μg/m*l*
Protein	(2−)	ATⅢ	60%
Ketone	(−)		
AST	3,426 IU/*l*	Arterial blood gas (room air)	
ALT	2,499 IU/*l*	pH	7.458
LDH	404 IU/*l*	Po_2	91.2 Torr
ALP	3,238 IU/*l*	Pco_2	25.0 Torr
γ-GTP	76 IU/*l*	BE	−4.7 mmol/*l*
CK	340 IU/*l*	SO_2	97.4%
CK-MB	31 IU/*l*		

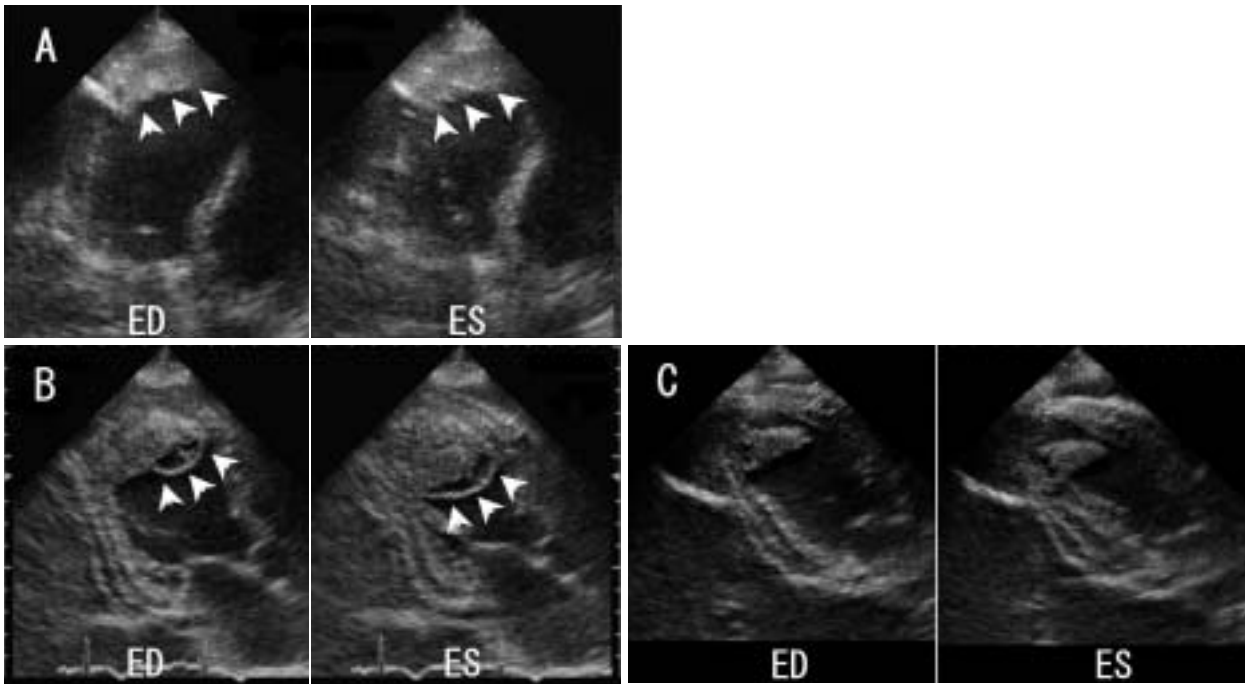

Fig. 2 Serial changes in echocardiograms
A: Mural thrombus in left ventricle was present on admission (*arrowheads*).
B: Massive mural thrombus was found in the apex of the left ventricle, partly floating in the left ventricular chamber (*arrowheads*) when cerebral infarction appeared on following day.
C: Left ventricular thrombus with reduced attachment to the lateral aspect of left ventricular endocardium near the apex with thin stalks and mobility in the left ventricular chamber on day 20 (24 hr before surgery).
ED = enddiastole; ES = endsystole.

antibody, anti-DNA and antineutrophilic antibodies as well as levels of serum antibodies to viruses were not elevated. Echocardiography demonstrated diffuse hypokinesis of the LV, especially severe in the anteroseptal to apical walls (**Fig. 2−A**). The LV wall was diffusely thickened and low echoic, suggestive of LV wall edema often seen in the acute phase of myocarditis.

An oral angiotensin converting enzyme inhibitor and spironolactone were administered based on a diagnosis of acute myocarditis, probably caused by viral infection with congestive heart failure, but peripheral edema became evident. Intravenous carperitide and dopamine were added, which ameliorated the lung congestion and peripheral edema.

Dysphagia, dysarthria and mild left hemiparesis appeared on hospital day 8. Brain magnetic resonance imaging demonstrated fresh cerebral infarction in the right cerebral cortex (**Fig. 3**). Echocardiography revealed a massive mural thrombus in the LV apex (**Fig. 2−B**), part of which was floating in the LV chamber (**Fig. 2−B,** *arrowheads*). Retrospectively, the thrombus was already visible on the echocardiogram on admission (**Fig. 2−A**). As the thrombus was thought to be the source of the cerebral embolism, unfractionated heparin was started and then switched to warfarin.

By hospital day 20, the size of the LV thrombus was reduced but it remained attached to the lateral aspect of the LV endocardium with thin stalks that were mobile in the LV chamber as a whole (**Fig. 2−C**). Global LV contractility was improved and the LV wall echogenicity was increased. Doppler studies of mitral inflow velocity showed an abnormal relaxation pattern with E/A ratio of 0.67 and diastolic descent rate (DDR) of 221 msec. Retrospectively, the echocardiogram on admission had revealed restrictive pattern of LV diastolic dysfunction, so-called 'pseudonormalization' (E/A ratio = 1.24, DDR = 165 msec).

He was transferred to the cardiovascular surgery department where left ventriculotomy was performed on the following day. Histological examination of the excised surgical specimen disclosed

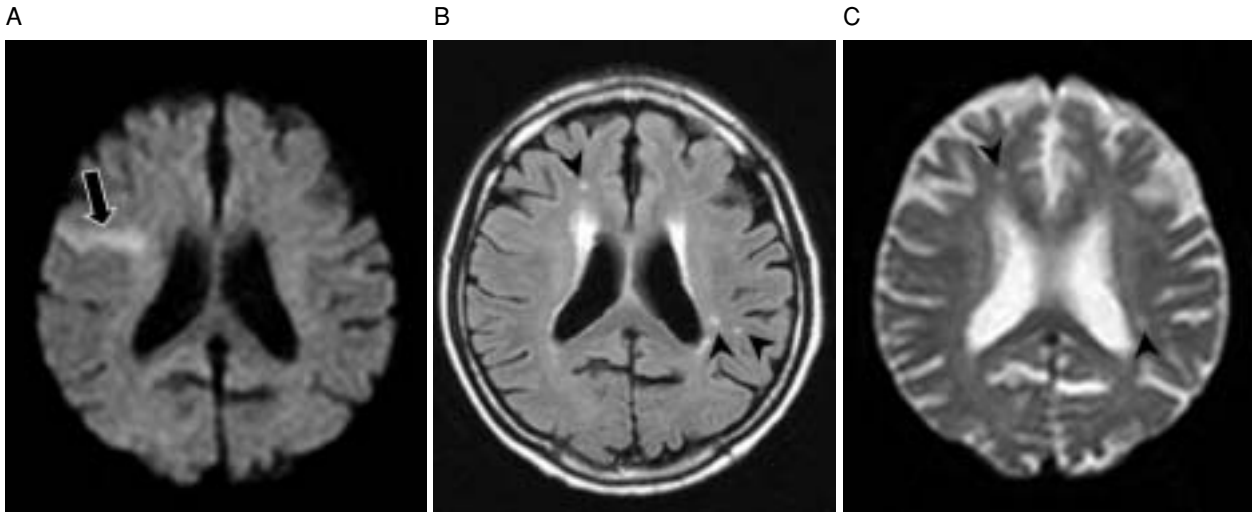

Fig. 3 Magnetic resonance images on hospital day 8
A: Diffusion-weighted image showed a high intensity area in the area of the middle cerebral artery of the right cerebral cortex (*arrow*), which suggested fresh cerebral infarction.
B, *C*: T1-weighted image (*B*) and T2-weighted image (*C*) disclosed old cerebral infarctions (*arrowheads*).

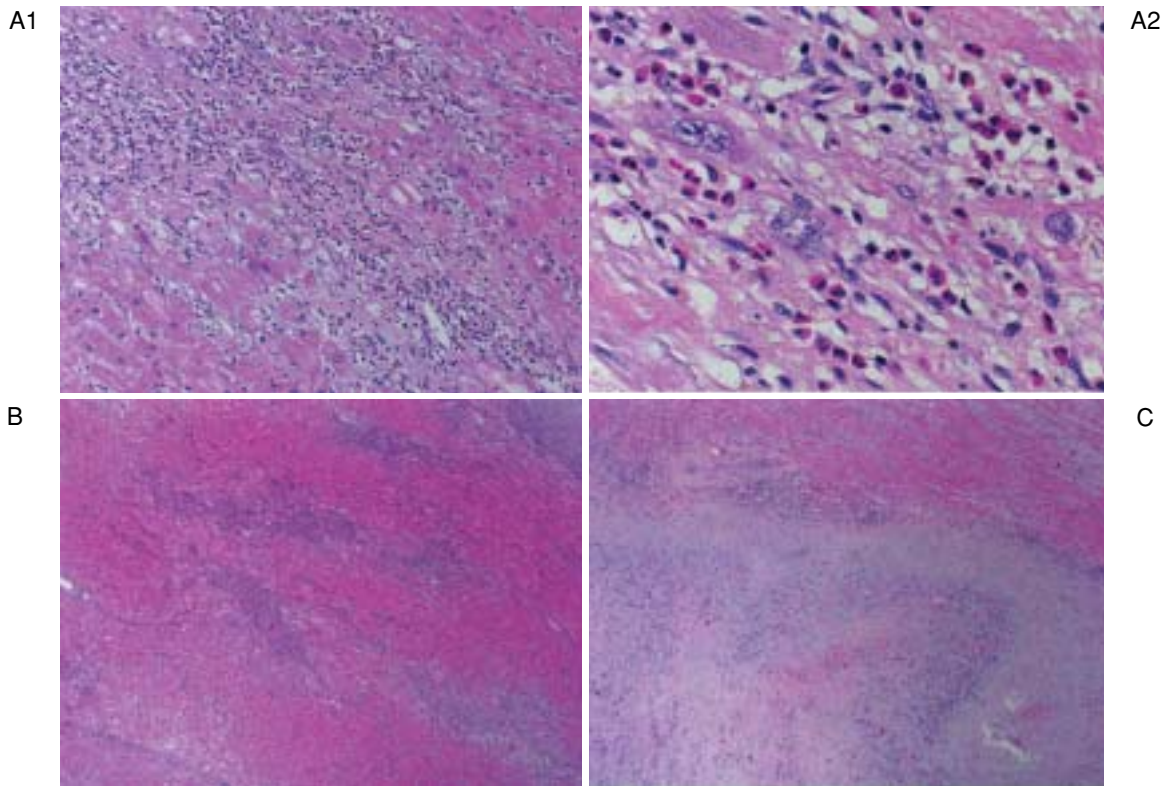

Fig. 4 Photomicrographs of excised left ventricular myocardium (hematoxylin-eosin staining)
A1, *A2*: Inflammatory cell infiltration mainly consisted of eosinophils and monocytes. Granulomas or multinucleated cells are absent (*A1*: × 100, *A2*: × 400).
B: Degeneration and necrosis of myocytes (× 20).
C: Granulation and fibrosis replacing degenerated myocytes (× 40).

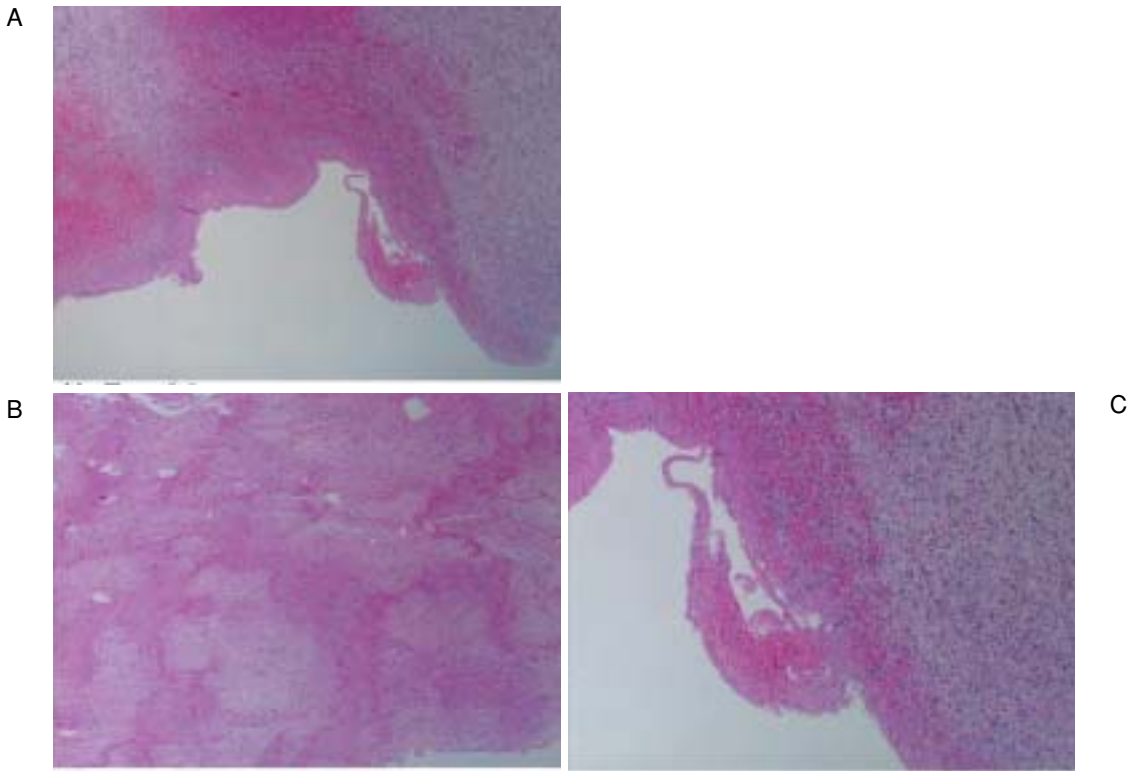

Fig. 5 Photomicrographs of excised left ventricular thrombus (hematoxylin-eosin staining)
A: Layer of fresh fibrin thrombus with sparse monocyte infiltration diffusely overlays endocardium (× 20).
B, *C*: Identical composition of mural thrombus and thin stalks anchoring thrombus, fibrin thrombus with sparse cellular infiltration (*B*, *C*: × 40).
Abbreviation as in Fig. 4.

inflammatory cell infiltration mainly composed of eosinophils and monocytes (**Figs. 4−A1, A2**). Degeneration and necrosis of myocytes (**Fig. 4−B**) was replaced by granulation and fibrosis (**Fig. 4−C**). Granulomas and multinucleated cells were absent. These findings were compatible with the features of ANEM. A layer of fresh fibrin thrombus with sparse monocyte infiltration diffusely overlaid the endocardium (**Fig. 5−A**), which is also a frequent feature of eosinophilic heart disease.[12, 13] The composition of the floating mass and stalks was the same (**Figs. 5−B, C**).

The blood eosinophil count peaked at 740/mm^3 on hospital day 27. The patient made an uneventful recovery and has remained well without immunosuppressive agents.

DISCUSSION

Within the spectrum of eosinophilic heart diseases, ANEM is the most lethal, and has such a fulminant clinical course that the diagnosis is often only established at autopsy or necropsy.[6,7,9] However, high dose corticosteroid after histological diagnosis with endomyocardial biopsy has had some success.[8,10] Only four cases of survival from ANEM have been reported.[8,10,11,14] In addition, the present patient had some intriguing features compared with other reports.

Firstly, he survived without specific therapy such as corticosteroid administration. A patient with ANEM rapidly recovered after pericardial drainage without corticosteroid therapy.[11] Elevated interleukin (IL)-5 concentration was found in the pericardial effusion during the acute phase of ANEM, suggesting that the reduction of IL-5 and of other cytokines such as IL-13 [15] in the heart induced by pericardial drainage might have reduced tissue eosinophil activities resulting in a benign clinical course. The pericardium of our patient was also opened and irrigated during surgery. However, in contrast to the previous patient, pericardiotomy was performed during the convalescent phase.

Therefore, the benign clinical course of our patient was not a likely consequence of the pericardiotomy and implies that a self-limiting subtype of ANEM may occur in patients with histologically undiagnosed acute myocarditis.

Secondly, blood eosinophilia did not appear during the entire clinical course. Other reports of patients who have survived ANEM often described absent or mild blood eosinophilia.[8,10] This suggests that a low blood eosinophil count indicates a good prognosis for patients with ANEM. On the other hand, the absence of blood eosinophilia makes it difficult to differentiate ANEM from lymphocytic myocarditis based only on the clinical presentation and noninvasive laboratory data. Therefore, early suspicion of ANEM and performance of endomyocardial biopsy, and early institution of corticosteroid therapy according to the histological diagnosis might be crucial for patient survival.

Thirdly, a massive LV mural thrombus led to cerebral thromboembolism in our patient, which is apparently unique in a living patient with ANEM. Eosinophilic heart disease is associated with endomyocardial inflammation and subsequent mural thrombi.[1,3–5,12,13] The histology of patients with Loeffler's endocarditis indicates that a stage of myocardial necrosis arises during the acute phase of the disease and leads to a thrombotic stage in which eosinophils cause endocardial damage and resultant ventricular mural thrombi.[12] Histological study has showed that eosinophils adhere to the endocardium with various degrees of endocardial thickening accompanied by diffuse myocyte necrosis,[11] which seems comparable with this acute necrotic stage.[12] Therefore, the pathophysiological likelihood of mural thrombi arising in ANEM is high. Conversely, the probability of eosinophilic heart disease should be determined by endomyocardial biopsy if intracardiac thrombi appear during the active phase of acute myocarditis.

The present patient had ANEM with unusual symptoms, suggesting that a benign self-limiting subtype of ANEM could be associated with absent or mild blood eosinophilia. We recommend that early histological diagnosis with prompt endomyocardial biopsy should be considered for patients with acute myocarditis irrespective of the degree of eosinophilia, especially if hemodynamic deterioration is rapid and/or mural thrombus is a complicating factor. This procedure would differentiate ANEM from other types of myocarditis and impact decisions about the application of corticosteroid therapy.

要　約

左室壁在血栓を合併した急性壊死性好酸球性心筋炎の1生存例

紺谷　真　　高島伸一郎　　大倉　清孝　　竹森　一司

前野　孝治　　田中　延善　　大橋　博和　　法木　左近

症例は81歳，男性．2005年8月，発熱・多関節筋肉痛に引き続き労作時息切れが出現した．4日後，近医にてアミノトランスフェラーゼ上昇を指摘され，翌日当院に紹介入院した．心電図上Ⅰ，Ⅱ，aV_L，aV_FおよびV_2−V_6誘導にST上昇と陽性T波を認めた．両心不全を合併した急性心筋炎と診断，保存的治療を開始した．第8病日に脳梗塞を発症，心エコー図検査により左室に壁在血栓を認めた．抗凝固療法を行うも血栓塞栓再発の可能性が高いと判断し第21病日に左室切除術を施行した．病理組織検査により主に好酸球と単核球からなる炎症細胞浸潤，置換性繊維化を伴う心筋細胞変性，心内膜全体を覆うフィブリン血栓を認めた．以上の所見から組織学的に急性壊死性好酸球性心筋炎と診断した．以後，特殊治療なしに自然軽快した．急性壊死性好酸球性心筋炎は急激な血行動態悪化を示し予後不良とされるが，予後良好な亜型が存在する可能性がある．

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