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# An autopsy case of cardiac tamponade caused by a ruptured ventricular aneurysm associated with acute myocarditis

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**Abstract**

We report an autopsy case of hemopericardium caused by rupture of a ventricular aneurysm associated with acute myocarditis in an infant boy aged 2 years and 10 months. Three days before his death, the patient developed fever. On the day of death, he described an urge to defecate and attempted to do so in an upright position. While straining to defecate without success for a prolonged period, he stopped breathing and collapsed. On autopsy, his heart weighed 91.7 g and cardiac tamponade was evident, the pericardial cavity being filled with 140 mL of blood that had come from a 1.5-cm-long rupture in a 2.7 × 1.5 cm ventricular aneurysm in the posterior left ventricular wall. Patchy grayish-white discoloration was noted in the myocardium. Histologically, CD3-positive T lymphocytic infiltration accompanied by pronounced macrophage infiltration was observed in the myocardium. Hemorrhagic necrosis was detected in the area of the ventricular aneurysm. Staining for matrix metalloproteinase (MMP) expression revealed abundant MMP-2, MMP-7, and MMP-9. Polymerase chain reaction to detect viruses failed to identify any specific causative viruses in the myocardium. In this case of lymphocytic (viral) and histiocytic myocarditis with pronounced macrophage infiltration and upregulation of MMP expression, myocardial remodeling and associated wall weakening had resulted in formation and rupture of an aneurysm.

**Keywords:** myocarditis, ventricular aneurysm, immunohistochemistry

## 1. Introduction

Myocarditis is defined as “a process characterized by an inflammatory infiltrate of the myocardium with necrosis and/or degeneration of adjacent myocytes not typical of ischemic damage associated with coronary artery disease” [1]. It has a wide range of highly variable clinical presentations; thus, the diagnosis is frequently made at autopsy. Autopsy studies report a frequency of myocarditis ranging from 0.11 to 5.55% in the general population [2].

Spontaneous cardiac rupture leading to cardiac tamponade is one of the fatal outcomes of fulminant myocarditis. Spontaneous cardiac rupture is rare, most reported cases being caused by myocardial infarction. Other even rarer causes include myocarditis, mediastinitis, myocardial abscess, angiosarcoma of the heart, Chagas disease, and post-mitral valve replacement surgery. Cardiac tamponade following rupture of the heart occurs very rapidly, resulting in a fatal fall in cardiac output and consequent circulatory collapse. The interval between rupture and collapse is variable, but is usually short [1].

Rupture of the myocardium is classified into the following three types: (i) acute rupture, in which the patient characteristically dies within minutes, precluding hospitalization; (ii) small rupture, for which corrective surgery may be possible provided appropriate interventions occur within a few hours and adequate hemodynamic support is provided; and (iii) chronic rupture, which is associated with formation of a false aneurysm [3, 4].

Cardiac tamponade, also termed hemopericardium, is a clinical syndrome caused by accumulation of fluid in the pericardial space, resulting in reduced ventricular filling and subsequent hemodynamic compromise. Rapid accumulation of as little as 200 to 300 mL of blood can result in a marked increase in pericardial pressure and severely impede cardiac output; rapid accumulation of more than 400 mL can very quickly cause sudden death [5].

An aneurysm, a localized abnormal dilatation of a blood vessel or the heart, can be congenital or acquired [6]. Ventricular aneurysm formation and rupture is an infrequent complication of acute myocarditis; several case reports of subjects with acute myocarditis and associated left ventricular free wall rupture have been published [1, 5, 7–10]. However, ventricular aneurysmal changes have not been clearly described in these case reports.

In the present report, we describe a case of cardiac tamponade caused by a ruptured ventricular aneurysm associated with acute myocarditis.

## 2. Case report

The case subject was an infant boy aged 2 years and 10 months. Three days before his death, the patient developed fever and was brought to the hospital for assessment, after which he was sent home. The next morning he expressed an urge to defecate and attempted unsuccessfully, despite considerable straining, to do so in an upright position. His breathing became irregular and eventually ceased. He collapsed and an ambulance was called. On arrival at the emergency

department, the boy was in a state of cardiopulmonary arrest and could not be resuscitated despite immediate medical intervention. An administrative autopsy was performed on the same day.

### 2.1 Autopsy findings

The subject was 96 cm in height and weighed approximately 15 kg. No findings suggestive of trauma were detected. The heart weighed 91.7 g and the pericardial cavity was filled with 140 mL of blood mixed with soft blood clots, resulting in an autopsy diagnosis of cardiac tamponade. The blood had come from a 1.5-cm-long rupture in a 2.7 × 1.5 ventricular aneurysm that had formed in the posterior left ventricular wall (Fig. 1). Patchy grayish-white discoloration was noted in the myocardium from the interventricular septum to the posterior wall. The coronary arteries were smooth.

A small amount of viscous yellow fluid was observed within the trachea and bronchi and the mucosa of the airways was congested. The left lung weighed 94.2 g and the right lung 65.5 g. Although grossly the left lung appeared severely congested, there were no marked histological changes. The brain weighed 1181 g and had no marked gross or histological abnormalities. No abnormal findings were noted in any other organ. No ethanol was detected in the blood or urine.

### 2.2 Histological findings

Histologically, lymphocyte infiltration was observed in the myocardium,

indicating a diagnosis of lymphocytic myocarditis (Fig. 2A). Pronounced macrophage infiltration was also evident. Hemorrhagic necrosis was detected at the site of rupture of the ventricular aneurysm (Fig. 2B). No significant histologic changes were observed in the coronary arteries.

**2.3. Myocardial immunohistochemistry**

Infiltration of CD3-positive T lymphocytes and a small number of CD20-positive B lymphocytes was detected (Fig. 3A, B). CD4- and CD8-positive cells were also present, the latter being more numerous. Immunohistochemistry for granzyme B, which is secreted by cytotoxic CD8-positive T cells, was negative. Severe CD68-positive macrophage infiltration was also observed (Fig. 3C). Staining for expression of matrix metalloproteinase (MMP) revealed abundant MMP-2 (Fig. 3D), MMP-7, and MMP-9. Immunohistostaining with tenascin C was weakly positive in the surrounding myocardium, but negative in the necrotic area (Fig. 4).

The cause of death was determined as cardiac tamponade caused by rupture of a ventricular aneurysm associated with acute myocarditis.

**2.4 Virological examination**

Polymerase chain reaction (PCR) was performed on frozen myocardial tissues to determine whether any of the following viruses were present: adenovirus, enterovirus (including Coxsackie virus, echovirus, polio virus),

rhinovirus, respiratory syncitial virus, human metapneumovirus, parainfluenza virus, influenza virus, varicella-zoster virus, Epstein–Barr virus, cytomegalovirus, human herpes virus 6 and 7, BK virus, JC virus, parvovirus B19, rubella virus, measles virus, norovirus, rotavirus, sapovirus, parechovirus, mumps virus. None of these viruses were identified.

## 3. Discussion

Our case had lymphocytic and histiocytic myocarditis suspected to be caused by a virus; however, no causative virus was identified despite extensive PCR viral studies. In a previously reported case of rupture associated with myocarditis, massive inflammatory infiltrates and myocyte necrosis and degeneration at the rupture site were described [8]. However, in that case, immunohistochemical stains of the myocardium were not performed.

The differential diagnoses included myocardial infarction caused by coronary artery lesions associated with Kawasaki disease; however, this possibility was excluded based on the subject's medical history and coronary artery histology.

Generally, macrophage infiltration is observed 3–7 days after the initial inflammatory event [6]; thus, this finding was compatible with the history of onset of fever 3 days previously.

The pathology of the myocardium was characterized by pronounced macrophage infiltration with upregulation of MMP expression. MMPs, a family of

zinc-dependent proteases, are involved in the turnover of the extracellular matrix. They mediate a wide variety of biological processes, including normal embryonic development, wound healing, and pathological processes [11]. Activated MMPs degrade the collagen network, causing loss of structural support, distortion of tissue architecture, and wall thinning, all of which contribute to myocardial remodeling [12]. Thus, in our case, the increased expression MMP of MMP-2, MMP-7, and MMP-9 would have resulted in the observed myocardial remodeling, wall weakening, aneurysm formation, and rupture.

Tenascin C, an extracellular matrix protein, is one of the acute-phase proteins expressed in diseased sites undergoing tissue reconstruction [13]. It is expressed in the invasive portions of malignant tumors and has been established as a marker for myocardial injury and myocardial remodeling [13]. In our case, immunohistostaining with tenascin C was weakly positive in the surrounding myocardium, but negative in the necrotic area. Tenascin C can be considered a sensitive marker of active inflammation [14, 15]. The positive staining for tenascin C in our case may indicate the acute phase of myocardial remodeling process.

Taken together, the immunohistochemical findings in this case suggest that the myocardium was under ongoing remodeling, contributing to aneurysm formation and weakness of the free wall. The findings suggest that active inflammation had ceased in the ventricular aneurysm, whereas myocardial remodeling by macrophages was ongoing. Immunohistochemistry can assist in determining when an aneurysm has formed. This case highlights the need for forensic pathologists to perform a complete

autopsy to determine the cause of sudden unexplained death, including detailed histopathological, immunohistochemical, and virological examination of any myocardial lesions.

## 4. Conflict of interest

The authors declare that they have no conflicts of interest.

## 5. Acknowledgments

We thank Ms. Miki Ogi of the Infectious Diseases Research Division, Public Health Science Research Center, Hyogo Prefectural Institute of Public Health and Consumer Sciences, who performed the virological studies (PCR) in this case, and Ms. Chinami Nakagawa for helping to create the graphical abstract. We are also grateful to Edanz Group, Japan for editing the manuscript.

## References

[1] Gouda HS, Kumar L, Malur PR, Patil SY. Cardiac tamponade secondary to fulminant myocarditis: a case of custodial death. J Forensic Leg Med 2011;18:30–3.

[2] Carniel E, Sinagra G, Bussani R, Di Lenarda A, Pinamonti B, Lardieri G, et al. Fatal myocarditis: morphologic and clinical features. Ital Heart J 2004;5:702–6.

[3] Lin CH, Lu MJ, Chieng SHH, Hung CR. Spontaneous cardiac rupture. Ann Thorac Surg 2003;76,921–3.

[4] Bashour T, Kabbani SS, Ellertson DG, Crew J, Hanna ES. Surgical salvage of heart rupture: report of two cases and review of the literature. Ann Thorac Surg 1983;36:209–

13.

[5] Murty OP. Giant cell myocarditis with cardiac tamponade: a rare combination. Am J Forensic Med Pathol 2008;29:245–8.

[6] Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Cotran Pathologic Basis of Disease. 8th ed. Philadelphia: Saunders; 2010.

[7] Stock E, Lubbe T. Rupture of the right ventricle in acute myocarditis. Br Heart J 1968;30:135–7.

[8] Ito M, Tanabe Y, Suzuki K, Kumakura M, Kimura K, Masani F, et al. Left ventricular free wall rupture in acute fulminant myocarditis during long-term cardiopulmonary support. Jpn Circ J 1999;63:397–9.

[9] LeLeiko RM, Bower DJ, Larsen CP. MRSA-associated bacterial myocarditis causing ruptured ventricle and tamponade. Cardiology 2008;111:188–90

[10] Nwizu C, Onwuanyi AE. Acute myocarditis presenting as cardiac tamponade. J Natl Med Assoc 2004;96:1503–6.

[11] Vanhoutte D, Schellings M, Pinto Y, Heymans S. Relevance of matrix metalloproteinases and their inhibitors after myocardial infarction: a temporal and spatial window. Cardiovasc Res 2006;69:604–13.

[12] Yang Y, Ma Y, Han W, Li J, Xiang Y, Liu F, et al. Age-related differences in postinfarct left ventricular rupture and remodeling. Am J Physiol Heart Circ Physiol 2008;294:H1815–22.

[13] Imanaka-Yoshida K. Tenascin-C in cardiovascular tissue remodeling: from development to inflammation and repair. Circ J 2012;76:2513–20.

[14] Kataoka A, Takano H, Imaeda T, Lee K, Ueda M, Funabashi N, et al. A case of fulminant myocarditis ultimately diagnosed by tenascin C staining. Int J Cardiol 2012;157:e33–4.

[15] Morimoto S, Imanaka-Yoshida K, Hiramitsu S, Kato S, Ohtsuki M, Uemura A, et al. Diagnostic utility of tenascin-C for evaluation of the activity of human acute myocarditis. J Pathol 2005;205:460–7.

**Figure legends**

**Fig. 1** Macroscopic findings

AB: A 2.7 × 1.5 cm ventricular aneurysm (red arrows) has formed in the posterior left ventricular wall, accompanied by a 1.5-cm-long rupture (black arrows).

C: Patchy grayish-white discoloration and hemorrhagic necrosis is evident in the myocardium from the interventricular septum to the posterior wall.

**Fig. 2** Histological assessment of the myocardium

A: Lymphocyte infiltration is evident in the myocardium, indicating lymphocytic myocarditis. Pronounced macrophage infiltration is also evident. Inset: Lesion in which lymphocytic infiltration is predominant.

B: Hemorrhagic necrosis is present at the rupture site in the ventricular aneurysm. Hematoxylin and eosin stain. (A) 100×, (B) 40×.

**Fig. 3** Myocardial immunohistochemistry (inflammatory cells)

Infiltration of CD3-positive T lymphocytes (A) and a small number of CD20-positive B lymphocytes (B) is apparent. Severe CD68-positive macrophage infiltration is also present (C). Strong expression of matrix metalloproteinase (MMP)-2 is evident (D). (A) 200×, (B) 200×, (C) 200×, and (D) 200×.

**Fig. 4** Myocardial immunohistochemistry for tenascin C

Immunohistostaining with tenascin C is weakly positive in the non-necrotic myocardium, but negative in the necrotic area.

Original magnification 200×.

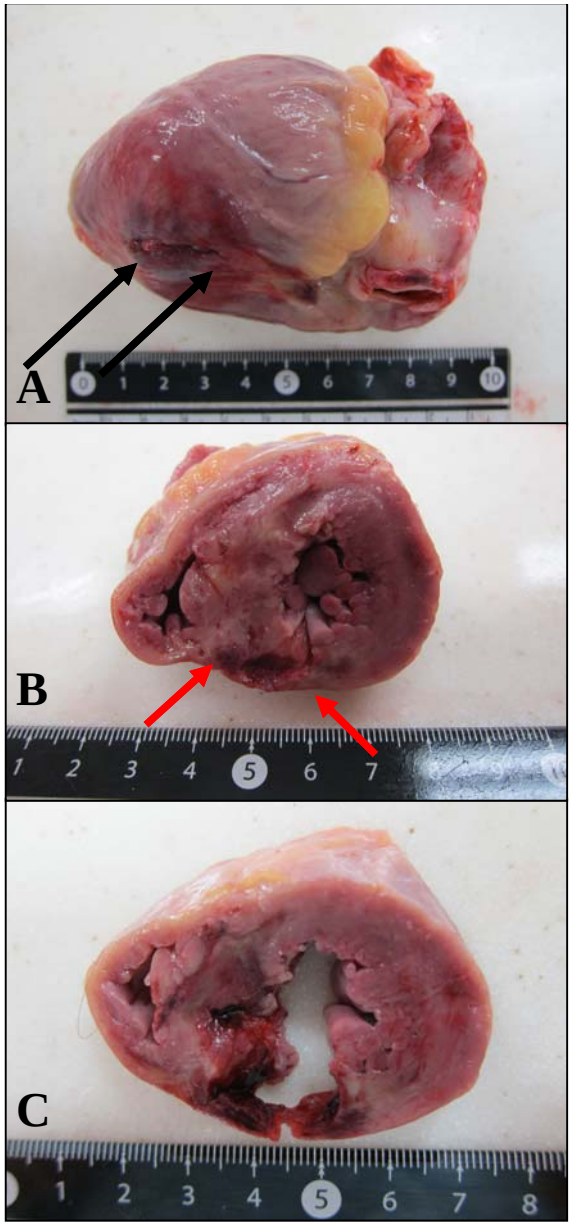



Fig. 1

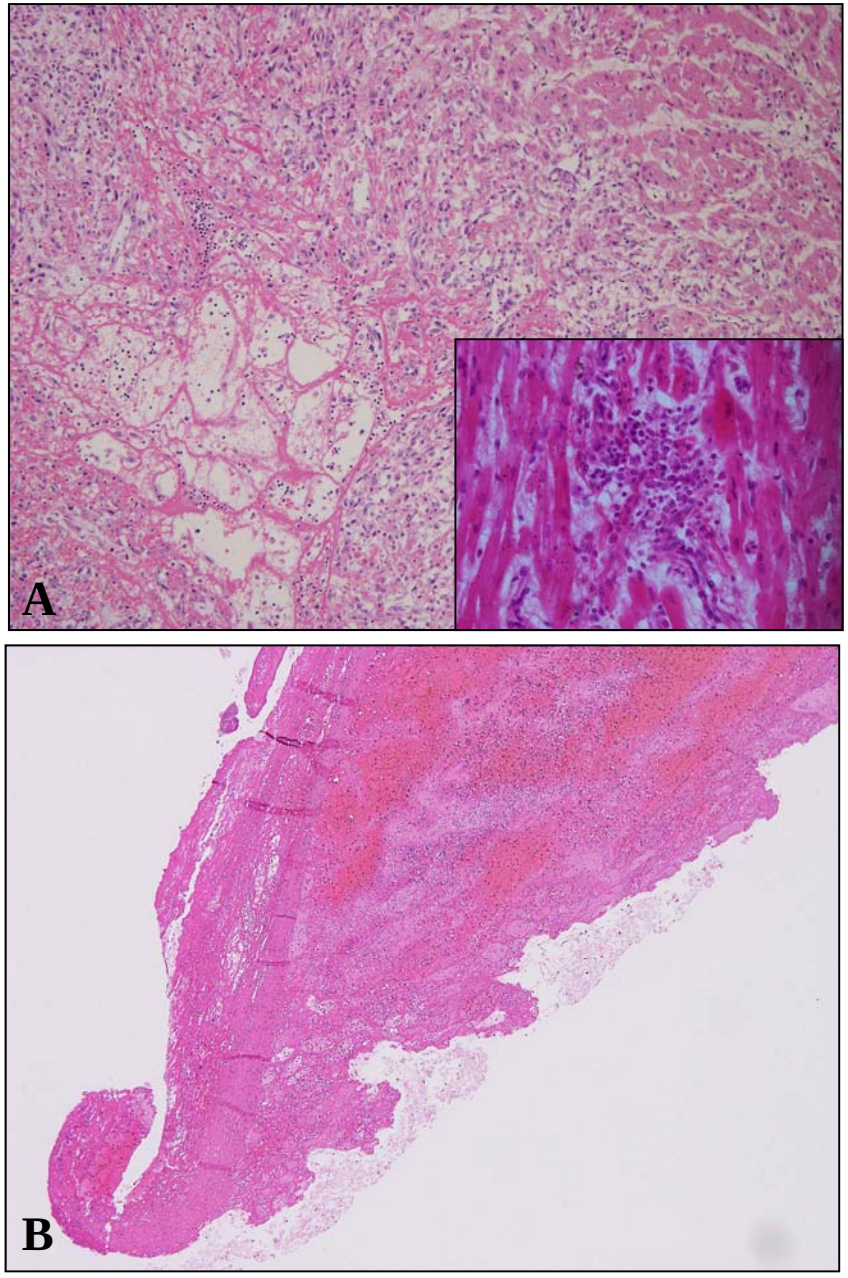



Fig. 2

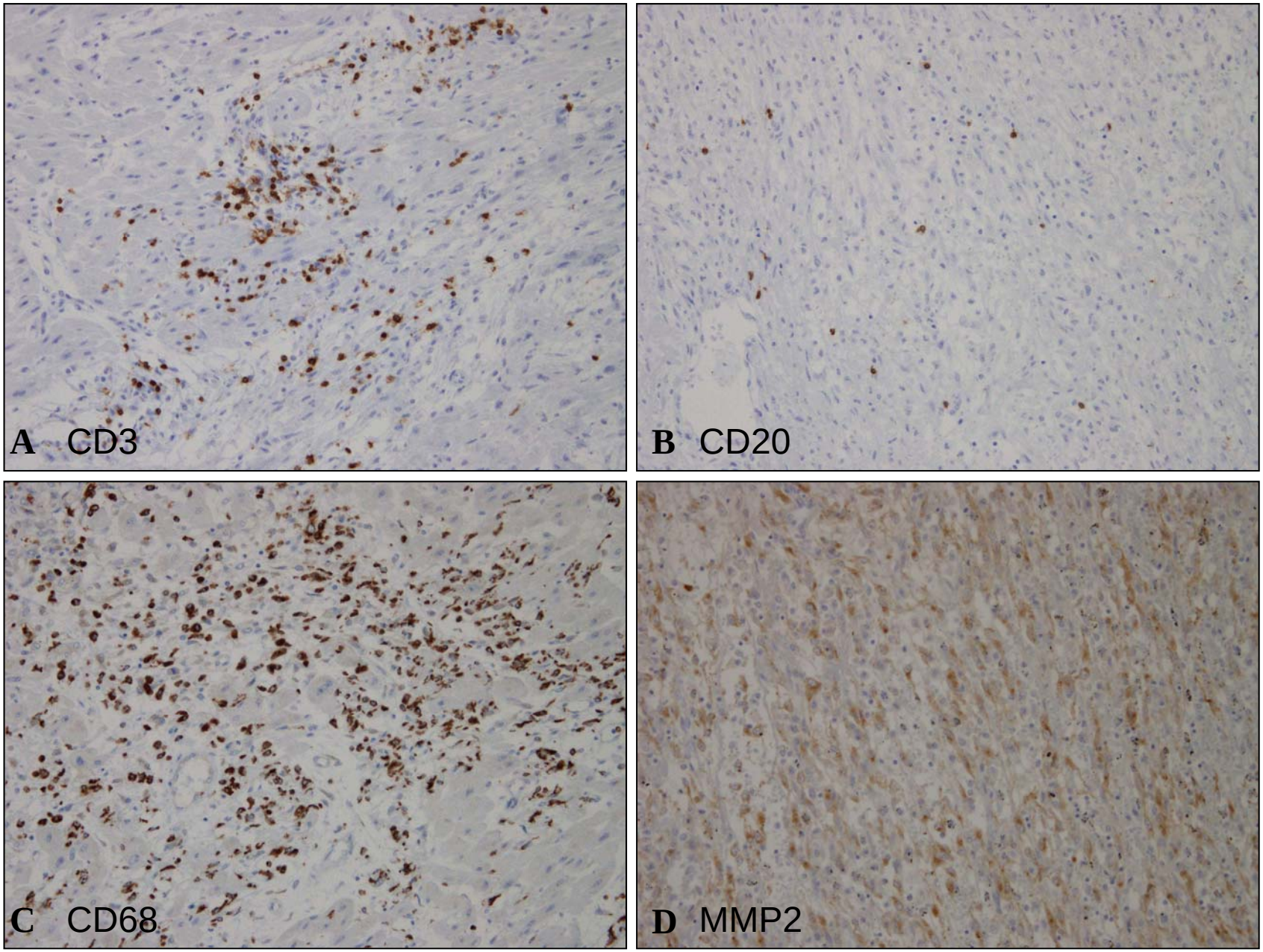



Fig. 3

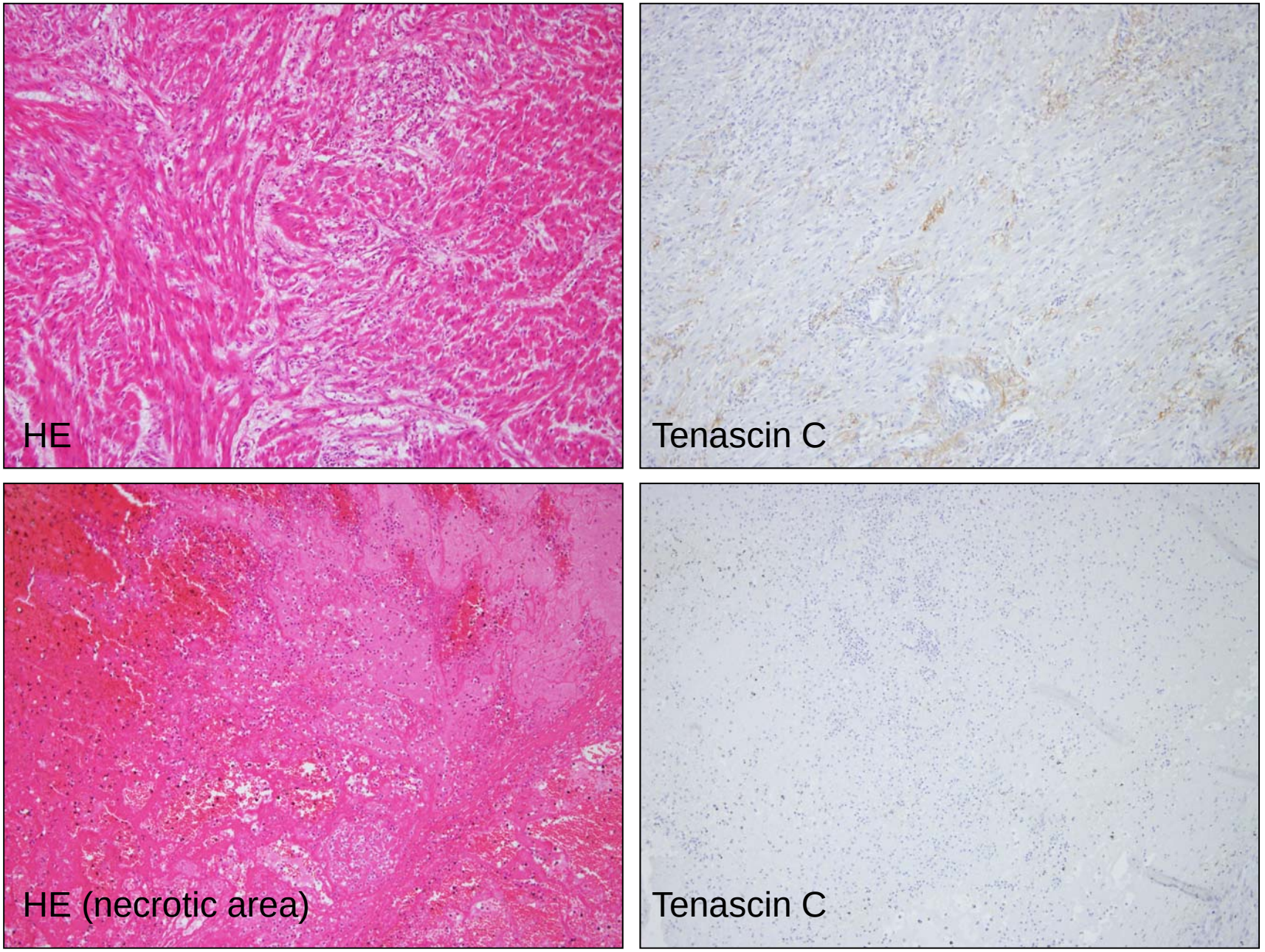
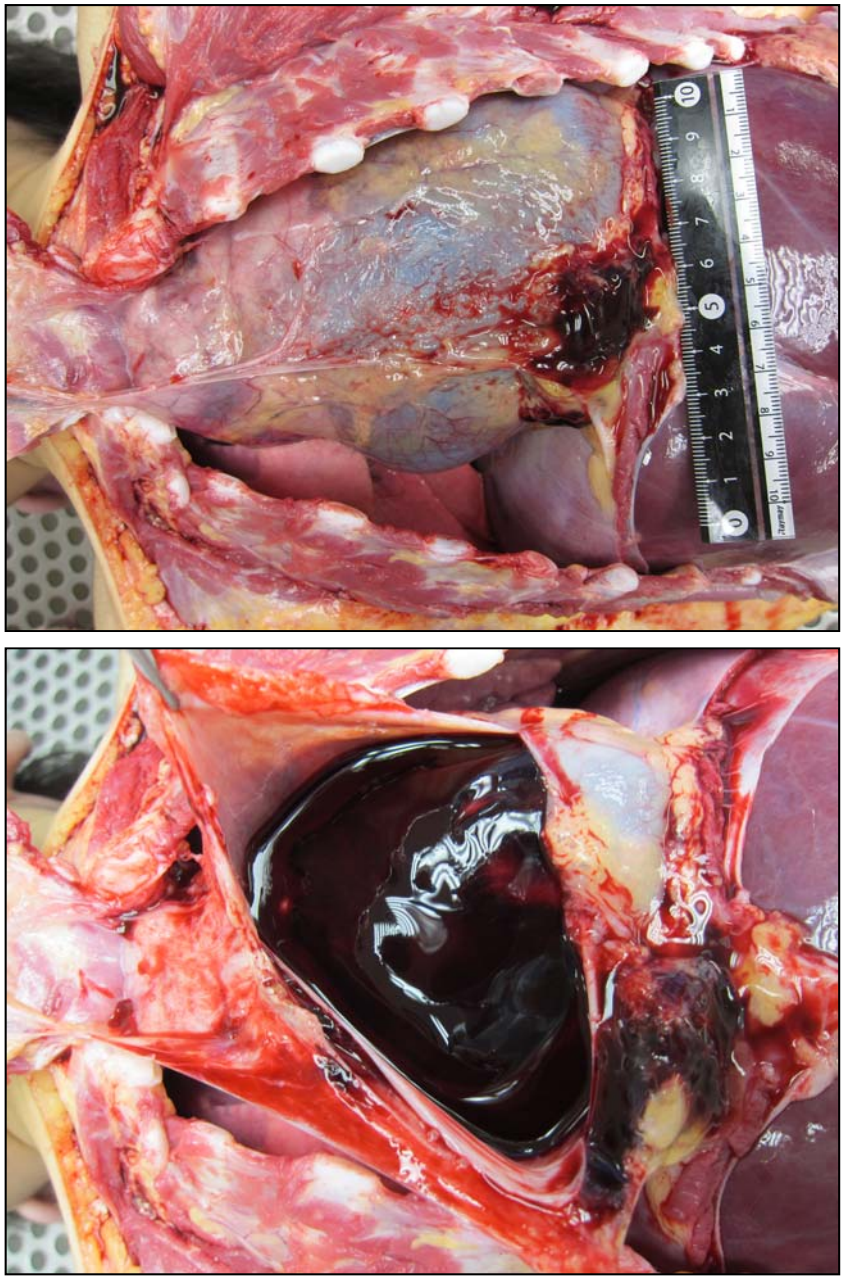
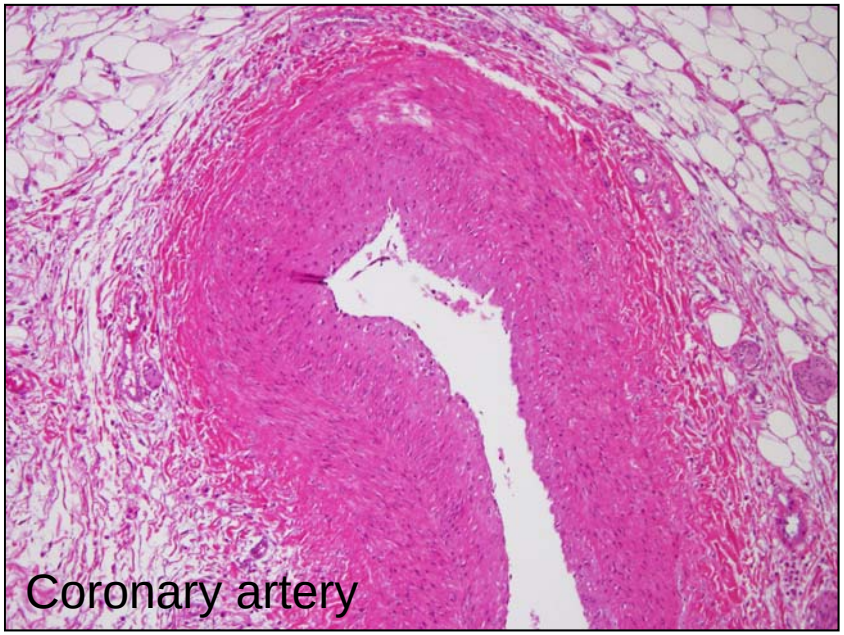



Fig. 4



Supplemental Figure 1: The heart weighed 91.7 g and the pericardial cavity was filled with 140 mL of blood mixed with soft blood clots.




Supplemental Figure 2: The coronary arteries were smooth and histologically normal.