Case Report

Journal of Forensic Chemistry and Toxicology
Volume 9 Number 1, January-June 2023
DOI: http://dx.doi.org/10.21088/jfct.2454.9363.9123.4

Reperfusion Induced Fatal Hemorrhagic Myocardial Infarction: A Case Report

Gokul G[1], Abdul Raoof MP[2], Abhishek Yadav[3], Amar Ranjan[4], Manivel. S[5]

How to cite this article:

Gokul G, Abdul Raoof MP, Abhishek Yadav, *et al.*/Reperfusion Induced Fatal Hemorrhagic Myocardial Infarction: A Case Report/J Forensic Chemistry Toxicol. 2023;9(1):53–57.

Abstract

Sudden death due to coronary artery disease is the leading cause of death globally. Occlusive coronary artery disease results in ischemia of myocardial tissue and subsequent infarction. Various treatment modalities like blood thinners, percutaneous coronary intervention (PCI) etc are being employed in the treatment of acute myocardial infarction (MI). However, these modalities have their own limitations. In this case, reperfusion therapy resulted in hemorrhagic myocardial infarction (HMI) with a fatal outcome. An adult male with history of sudden collapse was brought to emergency department, where he was declared as brought dead. He underwent reperfusion therapy and was on blood thinners, 4 days before the incident. On autopsy, we could find the features of hemorrhagic myocardial infarction grossly and the same was confirmed histopathologically. Though reperfusion injuries are commonly documented, deaths due to hemorrhagic myocardial Infarction, which is one of the rare complications of reperfusion therapy, are rarely reported. The important role of forensic pathologists in this case is to identify the rare causes, which led the patient to death during management of occlusive coronary artery disease.

Keywords: Occlusive coronary artery disease; Reperfusion therapy; Hemorrhagic Myocardial infarction; sudden death.

INTRODUCTION

Coronary artery disease is the leading cause of death worldwide.[1] Few reasons include urbanization, sedentary lifestyle, prevalence of alcohol and smoking in the developed societies.[2] After an acute myocardial ischemic episode, timely and efficient myocardial reperfusion with the use of primary percutaneous coronary intervention (PCI) or thrombolytic therapy is the most effective method for reducing the size of infarct and improving the outcome.

The restoration of blood flow to the ischemic myocardium may paradoxically reduce the beneficial effect and can lead to lethal reperfusion injury in some cases. It is defined as myocardial injury caused by the restoration of coronary blood flow after an ischemic episode. The injury culminates in the necrosis of cardiac myocytes that were viable immediately before reperfusion.[3]

Author Affiliation: [1,5]Junior Resident, [2]Senior Resident, [3]Additional Professor, [4]Additional Professor, Institute Rotary Cancer Hospital, Department of Forensic Medicine and Toxicology, All India Institute of Medical Sciences, New Delhi 110029, India.

Corresponding Author: Abhishek Yadav, Additional Professor, Department of Forensic Medicine and Toxicology, All India Institute of Medical Sciences, New Delhi 110029, India.

E-mail: drayad_in@yahoo.com

Received on: 11.10.2022 **Accepted on:** 13.11.2022

This form of myocardial injury, which induces death of cardiomyocyte and increases infarct size, may in part explain why, despite optimal myocardial reperfusion, the death after an acute myocardial infarction is not rare.[4]

The progression and presentation of ischemic heart disease is highly variable, ranging from silent MI to spontaneous cardiac rupture. Hemorrhagic Myocardial Infarction is one such potentially life-threatening complication of coronary revascularization following acute myocardial infarction. The authors report here a case of hemorrhagic myocardial infarction in an adult male diagnosed at autopsy and discuss its significance and implications in clinical outcome of such patients.

CASE HISTORY

A 40-year-old Japanese male was admitted with complaints of abdominal pain and vomiting to a super specialty hospital in New Delhi, India. He was managed initially under gastroenterology department, where symptomatic treatment was given. Due to persistent pain, multiple investigations including cardiac markers have been ordered. The serum CK-MB level was 183.8 ng/ml (Normal range: 0.6-6.3) and Trop-I was 22.08 ng/ml (Normal range:<0.02). In view of elevated cardiac markers, coronary angiography was ordered which revealed critical single vessel disease. Subsequently, the patient underwent PTCA (percutaneous transluminal coronary angioplasty) with stent (Xience XP Edition which was approved in Japan, introduced by Abbott) to Left anterior descending artery (LAD) under OCT (Optical coherence tomography) guidance on emergency basis with an uneventful course. The patient was discharged in stable condition after 3 days and was prescribed antiplatelet drugs (ecospirin, ticagrelor), statins (rosuvastatin), beta blocker (metoprolol), ACE-inhibitor (ramipril), anti-anginal drug (trimetazidine) and antibiotic (cefuroxime). Approximately 9 hours had already been passed before cardiac markers were taken since the arrival of patient to the hospital. By the time, stent was placed in the proximal segment of left anterior descending artery (LAD), it took further one hour.

In the following day, at the Police Control Room (PCR), a call was received regarding an adult male, found lying unresponsive in prone position at his residence. He was taken to a nearby hospital where he was declared as brought dead. His body was then sent for postmortem examination.

AUTOPSY FINDINGS

Rigor mortis was present over all parts of the body. Postmortem lividity was present on the right side of face, dependents parts of the body in prone position with contact pallor, which was not fixed. Conjunctivae were congested. No external injury is present over the body.

Pericardial sac was intact. Pericardial cavity contained about 40 ml of straw colored fluid. The anterior free wall of the left ventricle had patchy areas of dark reddish discoloration. The infarct zone was transmural and was extending till the endocardium (Fig. 1a, 1b).

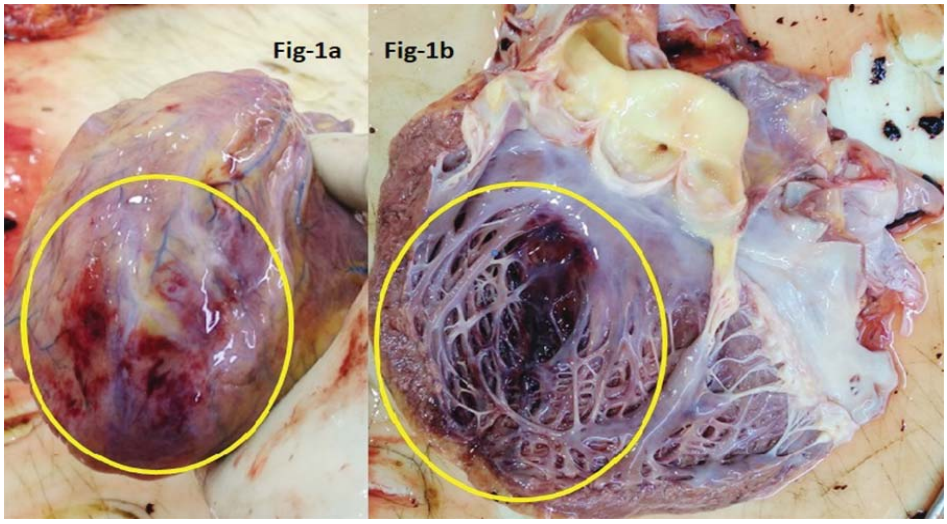

Fig. 1a: Reddish infarct on the anterior surface, **Fig. 1b:** Dark reddish infarct extending into the endocardium of LV

Left anterior descending artery had a metallic stent of length 4.8 cm along the proximal and middle one third of its course (Fig. 2). Left circumflex and right coronary artery were patent. The thickness of the left ventricle was within normal limits. Lungs were congested and edematous weighing 720 gm and 690 gm. Brain and liver were congested. All other internal organs were grossly unremarkable.

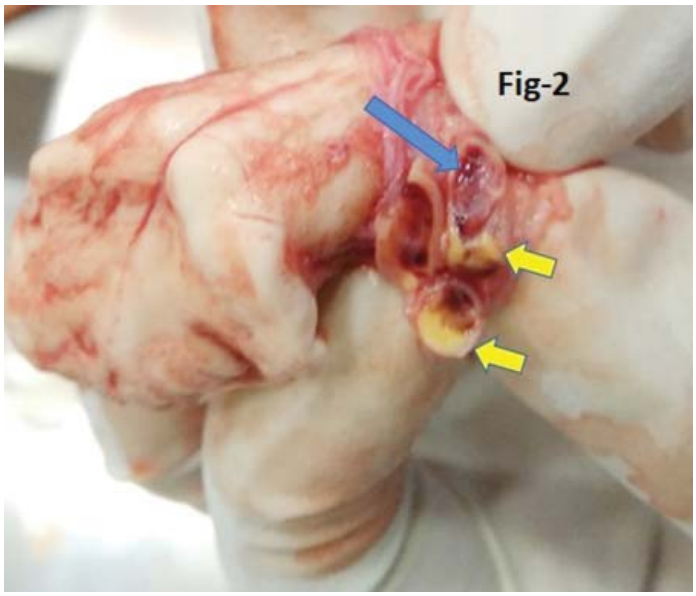

Fig. 2: Atherosclerosis in LAD (yellow arrows) with stent in-situ (Blue arrow)

HISTOPATHOLOGICAL EXAMINATION

Histopathological examination of the heart was performed. Patchy areas of necrotic muscle fibers are present in the anterior wall of left ventricle (Fig. 3a, 3b, 3c). In addition, extensive intramuscular hemorrhages are present in the anterior free wall of left ventricle. The lumen of the left anterior descending artery showed critical narrowing resulting in about 50-60 & occlusion of lumen due to atherosclerotic plaques, which are adherent to the vessel wall.

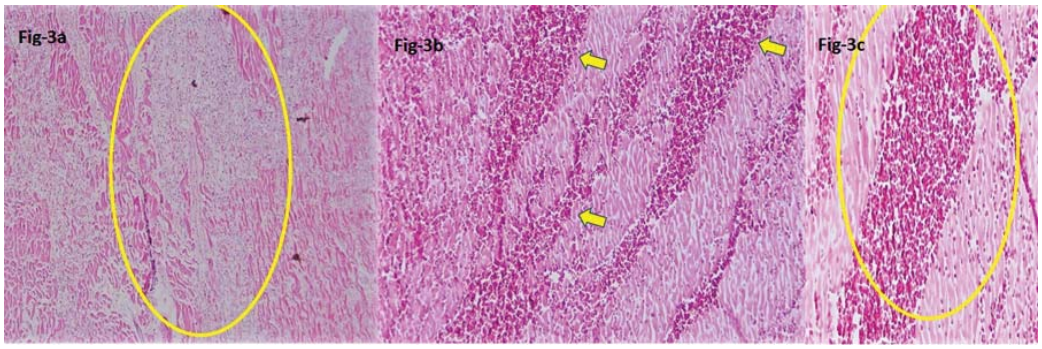

Fig. 3a: Pale areas of myocyte necrosis (Light microscopy-4X)
Fig. 3b: Intramyocardial hemorrhages (Light microscopy-10X)
Fig. 3c: Intramyocardial hemorrhages (Light microscopy-40X)

DISCUSSION

The aim of reporting this case is to discuss importance of acute hemorrhagic myocardial infarction (HMI) after re-perfusion therapy and morphological and histological findings of hemorrhagic myocardial infarction. Solving cases of sudden deaths are a daily challenge for the forensic pathologist. Acute coronary syndromes form a bigger part of the spectrum of sudden deaths and its incidence is more common in men than in women.[5] Myocardial infarction (MI) is becoming more frequent in the younger ages in the recent times.[2]

Infarction can be hemorrhagic or anemic (ischemic).[6] Myocardial infarction commonly

involves ischemic injury of the myocardium, which occurs when there is a negative balance in the perfusion and myocardial demand. The ischemic area undergoes metamorphosis subsequently depending on the amount of perfusion, type of myocardial resuscitation, the time taken for intervention and the preexisting hypertrophy of myocardium (most sensitive factor for necrosis).[7] The adverse effects of reperfusion are more evident when duration of ischemia crosses the golden period of 3 to 4 hours.[7,8,9] (As they say, Time is Myocardium). The infarct size is a directly related to severity of arrhythmia and mortality.[10]

In accordance with WHO, India ranks fifth among such deaths in the younger population.[11] Advancing research provides the healthcare personnel with various tools to be used in the management of Acute MI. This could be pharmacological thrombolysis or percutaneous coronary intervention. Reperfusion is a panacea in cases of acute myocardial infarction. Nevertheless, contradicting evidences are being stated by researchers for each technique, these modalities are virtually applied in almost all cases. Though the thrombolytic methods enable the clinician to establish reperfusion, the extent of reperfusion injuries and its adverse effects are not uncommon. Many theories of reperfusion like oxygen based free radicle theory, calcium theory, the PH theory, inflammatory response are proposed which in virtue of their own mechanism, cause extensive myocardial damage.[1] However, whether reperfusion by itself causes injury or it hastens the process of necrosis in irreversibly damaged myocardium is widely debated.

Mechanism of (Hemorrhagic Myocardial Infarction) HMI: When acute compromise to coronary blood flow occurs, the vascular endothelium in addition to the myocardium also undergoes ischemic damage. When perfusion is reestablished, the areas of endothelial damage become a potential site of hemorrhage into the surrounding myocardium. This is amplified by the therapeutic anticoagulation provided for reperfusion, increasing the probability of intramyocardial hemorrhage. The resulting hemorrhage into the myocardium increases the interstitial pressure, which has been already caused by tissue edema. This result in compromise of coronary blood flow in the area of at-risk-myocardium. These series of events cause a progressive wavefront like mechanism of myocardial injury in a patient with acute reperfusion.[9]

On gross appearance, the ischemic myocardial tissue shows soft, friable and tigroid appearance, as they evolve where as the hemorrhagic myocardial tissue is hard and dark red. Based on gross appearance, HMI can be classified as massive (gross + microscopic visibility) or focal (only microscopic visibility).[12] It can be graded as mild, moderate or severe based on the area of involvement.[13]

Histopathological examination of the area of interest shows accumulation of erythrocytes between the myocytes associated with areas of myocardial necrosis. Myocyte necrosis is not always mandatory since a remote infarct can cause hemorrhage in the adjacent myocardium.[14] Microscopically, it will appear as hemorrhage amidst between normal myocardial fibres.[13] This, in turn can potentially cause microinfarcts in the vicinity. In addition, the necrotic myocardial tissue, usually clearly by phagocytosis in ischemic infarcts are relatively dormant in hemorrhagic infarcts.[14] In cases of sudden death due to ischemic MI, due to lack of survival time and perfusion, gross pathological findings could not be appreciated at autopsy. However, in cases of hemorrhagic myocardial infarction cases, the survival time with reperfusion facilitates the necrosis of myocytes and the findings are appreciated grossly during autopsy.

HMI is a serious complication of reperfusion of acute MI and the diagnosis of which could be made by T2 weighted cardiac MRI.[15,16] The hemorrhagic conversion of ischemic area occurs approximately in one third of patients with STEMI and PCI.[17] In our case, almost 10 hours have been passed before the onset of reperfusion. Appropriate and timely management of patient with blood thinners and PCI will provide better prognosis.

CONCLUSION

The process of myocardial reperfusion itself, may induce injury to the myocardium, thereby reducing the beneficial effects of myocardial reperfusion even after the patient is discharged. HMI is underreported in underdeveloped and developing countries, due to limited facilities especially MRI. The forensic pathologists should not only restrict their expertise to unnatural deaths, but also explore the various causes and presentation of natural deaths with detailed histopathological examination in all cases of death due to acute coronary syndromes with reperfusion therapy. The role of forensic pathologist serves a significant part in the evolutionary development of evidence based medicine and new cardioprotective strategies

for the benefit of patients with acute myocardial infarction and toavoid myocardial reperfusion injury.

REFERENCES

1. Ambrosio G, Tritto I. Myocardial reperfusion injury. Eur Hear Journal, Suppl. 2002;4(B):1121–35.
2. Khan MA, Hashim MJ, Mustafa H, Baniyas MY, Al Suwaidi SKBM, AlKatheeri R, Alblooshi FMK, Almatrooshi MEAH, Alzaabi MEH, Al Darmaki RS, Lootah SNAH. Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study. Cureus. 2020 Jul 23;12(7):e9349.
3. Piper HM, García-Dorado D, Ovize M. A fresh look at reperfusion injury. Cardiovasc Res. 1998 May;38(2):291-300.
4. Yellon DM, Hausenloy DJ. Myocardial reperfusion injury. N Engl J Med. 2007 Sep 13;357(11):1121-35.
5. Jayaraj JC , Davatyan K , Subramanian, S, Priya, J. Epidemiology of Myocardial Infarction. In: Pamukçu, B, editor. Myocardial Infarction [Internet]. London: IntechOpen; 2018 [cited 2022 Jul 01]. Available from: https://www.intechopen.com/chapt.
6. Robbins & Cotran Pathologic Basis of Disease, 10e: South Asia Edition, 2 Vol SET - 10th Edition [Internet]. [cited 2022 Jul 12]. Available from: https://www.elsevier.com/books/robbins-&-cotran-pathologic-basis-of-disease-10e-south-asia-edition-2-vol-set/978-81-312-6211-5.
7. Bresnahan GF, Roberts R, Shell WE, Ross J, Sobel BE. Deleterious effects due to hemorrhage after myocardial reperfusion. Am J Cardiol. 1974;33(1):82–6.
8. Lang TW, Corday E, Gold H, Meerbaum S, Rubins S, Costantini C, et al. Consequences of reperfusion after coronary occlusion. Effects on hemodynamic and regional myocardial metabolic function. Am J Cardiol. 1974;33(1):69–81.
9. Reimer KA, Lowe JE, Rasmussen MM, Jennings RB. The wavefront phenomenon of ischemic cell death. 1. Myocardial infarct size vs duration of coronary occlusion in dogs. Circulation. 1977;56(5):786–94.
10. Ovize M, Baxter GF, Di Lisa F, Ferdinandy P, Garcia-Dorado D, Hausenloy DJ, et al. Postconditioning and protection from reperfusion injury: Where do we stand: Position Paper from the Working Group of Cellular Biology of the Heart of the European Society of Cardiology. Cardiovasc Res. 2010;87(3):406–23.
11. Sreeniwas Kumar A, Sinha N. Cardiovascular disease in India: A 360 degree overview. Vol. 76, Medical Journal Armed Forces India. 2020. p. 1–3.
12. Helmuth RA, Wills ER, Aust C, Orr C. Status of the myocardium and infarct-related coronary artery in 19 necropsy patients with acute recanalization using pharmacologic (streptokinase, r-tissue plasminogen activator), mechanical (percutaneous transluminal coronary angioplasty) or combined typ. J Am Coll Cardiol. 1987;9(4):785–801.
13. Fujiwara H, Onodera T, Tanaka M, Wu DJ, Kawai C, Hamashima Y. A clinicopathologic study of patients with hemorrhagic myocardial infarction treated with selective coronary thrombolysis with urokinase. Circulation. 1986;73(4):749–57.
14. Lie JT, Lawrie GM, Morris GC, Winters WL. Hemorrhagic myocardial infarction associated with aortocoronary bypass revascularization. Am Heart J. 1978 Sep 1;96(3):295–302.
15. Oka S, Nakamura J, Kai T, Hoshino K, Watanabe K, Abe M, et al. An autopsy case report of extensive intramyocardial hemorrhage complicated with acute myocardial infarction. J Cardiol Cases [Internet]. 2020;22(3):121–4. Available from: https://doi.org/10.1016/j.jccase.2020.05.021.
16. Ochiai K, Shimada T, Murakami Y, Ishibashi Y, Sano K, Kitamura J, et al. Hemorrhagic Myocardial Infarction after Coronary Reperfusion Detected in Vivo by Magnetic Resonance Imaging in Humans: Prevalence and Clinical Implications. J Cardiovasc Magn Reson. 1999;1(3):247–56.
17. Hawranek M, Wróbel M, Nożyński J, Pres D, Gierlotka M, Trzeciak P, et al. Hemorrhagic Myocardial Infarction: Mortality Compared With STEMI Patients Treated With Percutaneous Coronary Intervention. J Am Coll Cardiol. 2016;68(4):426–7.