Myocardial infarction in normal coronary artery (MINCA): Death in healthy military personnel

Nadiawati Abdul Razak[1,2,4,] *, Faridah Mohd Nor[2], Nur Najmi Mohamad Anuar[3], Ahmad Zakuan Kamarudin[4]

[1]*Forensic Unit, Pathology Department, Faculty of Medicine and Defence Health, National Defence University of Malaysia, 57000 Kuala Lumpur, Malaysia.*
[2]*Forensic Unit, Pathology Department, Faculty of Medicine, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia, 56000 Kuala Lumpur, Malaysia.*
[3]*Programme of Biomedical Science, Center for Toxicology & Health Risk Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300, Kuala Lumpur, Malaysia.*
[4]*Pathology Department, Hospital Angkatan Tentera Tuanku Mizan, 53300, Kuala Lumpur, Malaysia.*

*Correspondence: nadiawati@upnm.edu.my

ABSTRACT

Sudden unexpected death among healthy military personnel leads to a false allegation from family members. However, majority of the deaths were related to an abnormal cardiac condition. Objective: The occurrence of patent coronary vessels in sudden deaths demands histological examination and/or molecular study to detect underlying diseases, which need to be highlighted especially in a centre with limitation of post-mortem computed tomography (PMCT) or virtopsy. In this article, a case of a young healthy male personnel, who died during routine training was reported. He collapsed after a 10-minute jog. An autopsy was performed to determine the cause of death. The autopsy showed a moderately built male. No fatal external injuries were found. Internal examination showed cardiomegaly and patent coronaries. The cardiac markers were markedly raised with normal toxicological analysis. Histology of the heart showed a recent myocardial infarct, hence the cause of death was determined as myocardial infarction in normal coronary artery (MINCA). Conclusion: Annual medical screening is highly recommended to detect any cardiac abnormalities among military personnel. Screening may be extended for a genetic study in suspicious and strong family history to exclude a conduction defect or channelopathy.

Keywords: Sudden cardiac death; cardiomegaly; myocardial infarction in normal coronary; military personnel and MINCA

INTRODUCTION

Sudden and unexpected death among healthy military personnel causes bereavement from family members that often leads to false allegations associated with abuse or mistreatment by a superior. Majority of the cause of death is related to cardiac diseases such as atherosclerotic of the coronary artery. A technical report (Ahmad, 2021) showed that deaths due to coronary artery disease (CAD) are increasing among army personnel in Malaysia from 18.1% in 2015 to 23.2% in 2016. The report also stated that coronary artery disease occurred as early as in the mid-30s. The typical age of death in those with myocardial infarction with 'normal' coronary arteries (MINCA) is under the 50s (Tun & Khan, 2000). MINCA was first documented more 75 years ago when autopsy reports detailed myocardial necrosis in the absence of significant coronary atherosclerosis (Agewall et al., 2016). There is no previous history of angina pectoris or myocardial infarction, and they are mostly without any risk factors (Khan & Ansari, 1998).

The European Society of Cardiology (Agewall et al., 2016) developed the first international position article on MINCA and proposed the following MINCA criteria: (1) Acute myocardial infarction (AMI) criteria as defined by the "Third Universal Definition of Myocardial Infarction" (Thygesen et al., 2012); (2) non-obstructive coronary arteries as per angiographic guidelines (Scanlon et al., 1999), with no lesions ≥50% in a major epicardial vessel; and (3) no other clinically overt specific cause that can serve as an alternative cause for the acute presentation. Fundamental to the definition of MINCA is the diagnosis of AMI with an elevated cardiac biomarker, typically a cardiac troponin >99th percentile of the upper reference level with a rise or fall in the level on serial assessment.

Histologically, the infarct sizes are smaller in MINCA, however the symptoms and electrocardiographic (ECG) changes are similar to that with AMI with coronary disease (Raymond et al., 1988.). The prognosis is better as its complications such as malignant arrhythmias, heart failure and hypotension are much reduced (Raymond et al., 1988; Sharifi et al., 1995). The mechanism of death is attributed to coronary vasospasm, coronary thrombosis, cocaine abuse and carbon monoxide poisoning (Sharifi et al., 1995).

Herein, we reported a case of a young, healthy military male personnel, who died during routine training. This paper aimed to highlight the concept of structurally patent coronary vessels in sudden death and the need for histology and/or molecular study to detect an underlying disease, that may cause death especially in a centre with a limitation of postmortem CT (PMCT) or virtopsy.

CASE REPORT

A 26-year-old healthy male, a heavy smoker was found collapsed after ten minutes of a morning jog. He complained of shortness of breath and chest pain while jogging. On further history, there was no previous major childhood infection, no history of medication allergy, and no family history of heart disease, cardiac rhythm abnormality or auto-immune disease. However, despite vigorous resuscitation performed, he succumbed to death. He was brought in dead by the police for an autopsy to determine the cause of death.

Since PMCT is not available in our centre, the body was proceeded for post-mortem examination. External examination of the body showed a moderately built male, fully clad in an army sports attire. Subcutaneous dissection was performed to investigate for any subcutaneous and muscle haemorrhage, which can be concealed by dark skin complexion. Subcutaneous dissection showed no evidence of fatal external injuries were found on the body, which disapproved allegations of abuse. Post-mortem internal examination showed unremarkable changes of other organs except for the heart.

The heart weighed 400 grams and was hypertrophied. The left ventricle wall was thickened with cavity dilatation. The myocardium was normal without any haemorrhage or fibrosis. The coronary arteries i.e. the left anterior descending artery (LAD), left circumflex artery and right coronary artery showed no atheroma. Post-mortem blood analysis demonstrated significantly raised troponin-I and creatine kinase-myocardial band (CKMB), which signify myocardial necrosis. Neither presentation or autopsy findings hint at an allergic reaction, blood markers for allergy testing (tryptase and Immunoglobulin E level) were not submitted. Microbiological analysis showed no evidence of bacterial or viral infection. Toxicology analysis of blood and urine showed no common drugs such as paracetamol, antihistamines, steroids and analgesic drugs or ethyl alcohol. Histology of the left ventricle and interventricular septum of the heart tissue revealed areas showing hypertrophied cardiomyocytes, associated with patchy areas of fibrosis, while other areas show infiltration by inflammatory cells, predominantly neutrophils in the interstitium with adjacent myocardial necrosis and contraction band necrosis (Figure 1). There was no evidence of myocarditis or auto-immune related cardiac changes seen in the histology sample of the heart. The cause of death was determined as myocardial infarction in a normal coronary artery (MINCA).

DISCUSSION

AMI with normal coronary arteries is typically diagnosed in young patients. MINCA accounts for 5 – 8 % of an acute coronary syndrome (Cheema et al., 2021). Most cases occur under 50 years of age. It is worth noting that women, particularly the young ones, have a higher prevalence of non-obstructive coronary arteries among AMI patients. (Tamis-Holland & Jneid, 2018). There is usually no history of angina, and traditional risk factors for CAD are almost absent (Ammann et al., 2000), except for cigarette smoking (Scanlon et al., 1999). A study had shown that there is a high risk for MINCA in all men with heavy smoking habits (range 47-68 years), women with no history of smoking (Kardasz & de Caterina, 2007) with bimodal distribution in sex and age in the younger age group (range 31-43 years).

Smoking habit is rampant among military personnel. Smoking causes hypercoagulability and thrombosis. Additionally, it causes endothelial dysfunction in the form of inflammation or vasospasm, which may result in coronary atherosclerosis. The decedent was a heavy smoker, and there are no other known risks of myocardial infarction. As a result, we conclude that cigarette smoking is his only risk factor. (Zuhdi et al., 2013)

reported that out of 1595 patients, 16% were categorized into the young coronary artery disease group (less than 45 years of for men and less than 55 years old for women), who were significantly associated with active smoking and obesity compared to the older group.
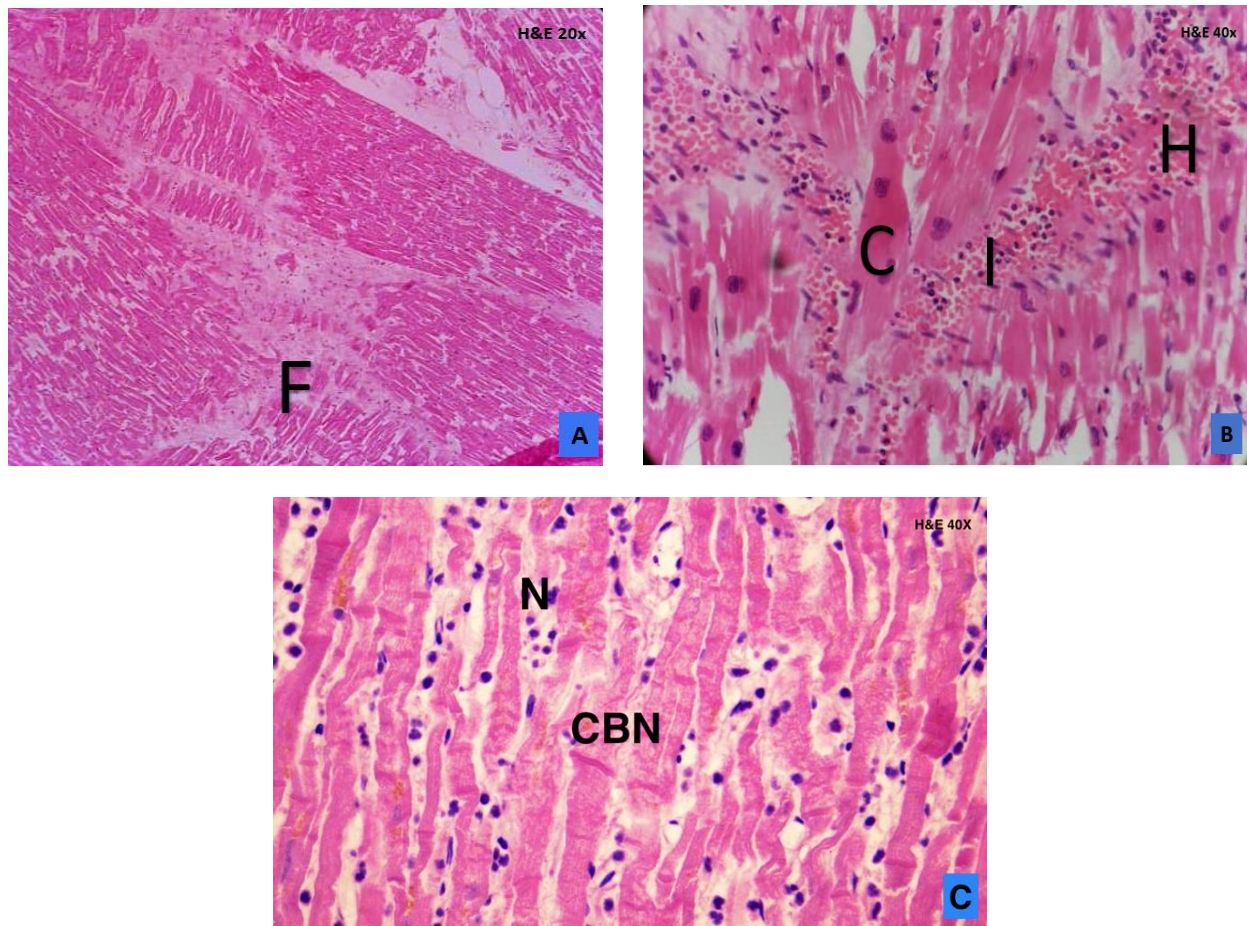

Figure 1: Heart tissue taken during autopsy and stained with haematoxylin and eosin (H&E) staining. (A) Replacement fibrosis (F) of the myocardium. (B) Inflammatory cells predominantly neutrophil (I) infiltration into the myocardial interstitium and adjacent haemorrharge (H) with a background of cardiomyocytes hypertrophy (C). (C) Neutrophils (N) infiltration into interstitium with a background of myocardial necrosis and contraction band necrosis (CBN).

This case report highlights the need for a thorough autopsy with complete histology death especially in a centre with a limitation of postmortem CT or virtopsy. A detailed autopsy not only disapproves concealed fatal injury but also helps to determine the exact cause of death. MI can occur in a young patient; the eventual diagnosis is difficult unless supported by other ancillary investigations and histology. Additional testing to determine the underlying aetiology is required to adopt etiology-targeted therapy. A comprehensive clinical history, including a complete examination of the presenting symptoms, as well as a family and social background, can help with diagnosis. Additional testing, such as cardiovascular magnetic resonance imaging (CMRI) tests with intravascular ultrasonography or optical coherence tomography, thrombophilia testing, provocative testing for coronary vasospasm, and cardiac magnetic resonance imaging should be considered when needed and if resources permit in a suspected patient.

Sudden death with a normal heart morphology is a prominent finding in necropsy that worth to be explored. Genes have been identified for several disorders responsible for arrhythmias and sudden death. These genes encode ion channels and are referred to as channelopathy genes, that regulate the electrical activity, but cannot be detected morphologically at the time of post-mortem examination (Raymond et al., 1988). Hence, a molecular study is needed to reveal the association between myocardial infarction and genetic factors. Inherited arrhythmia (IA) syndromes are a group of disorders marked by a higher risk of sudden cardiac death (SCD), aberrant cardiac electrical function, and, in most cases, a structurally normal heart. Examples are long QT syndrome (LQTS), Brugada syndrome (BrS), catecholaminergic polymorphic ventricular tachycardia (CPVT), short QT syndrome (SQTS), early repolarisation syndrome (ERS) and idiopathic ventricular fibrillation (IVF). They share a genetic aetiology in which disease-causing genetic variations can result in the absence or dysfunction of proteins essential in the formation and propagation of cardiac action potentials. Abnormal ECG in the absence of ischaemic and structural heart disease or unexplained ECG abnormalities in an asymptomatic patient or through family

screening for a specific diagnosis or following a sudden unexplained death raise clinical suspicion of IA (Melor et al., 2021).

The possible mechanisms leading to myocardial infarction in the presence of apparently normal coronary arteries are proposed in Figure 2. A qualitative assessment of 46 publications evaluating the underlying pathophysiology responsible for MINOCA revealed the presence of a typical myocardial infarct on cardiac magnetic resonance imaging in only 24% of patients, with myocarditis occurring in 33% and no significant abnormality in 26%. Coronary artery spasm was inducible in 27% of MINOCA patients, and thrombophilia disorders were detected in 14%. (Pasupathy et al., 2015).
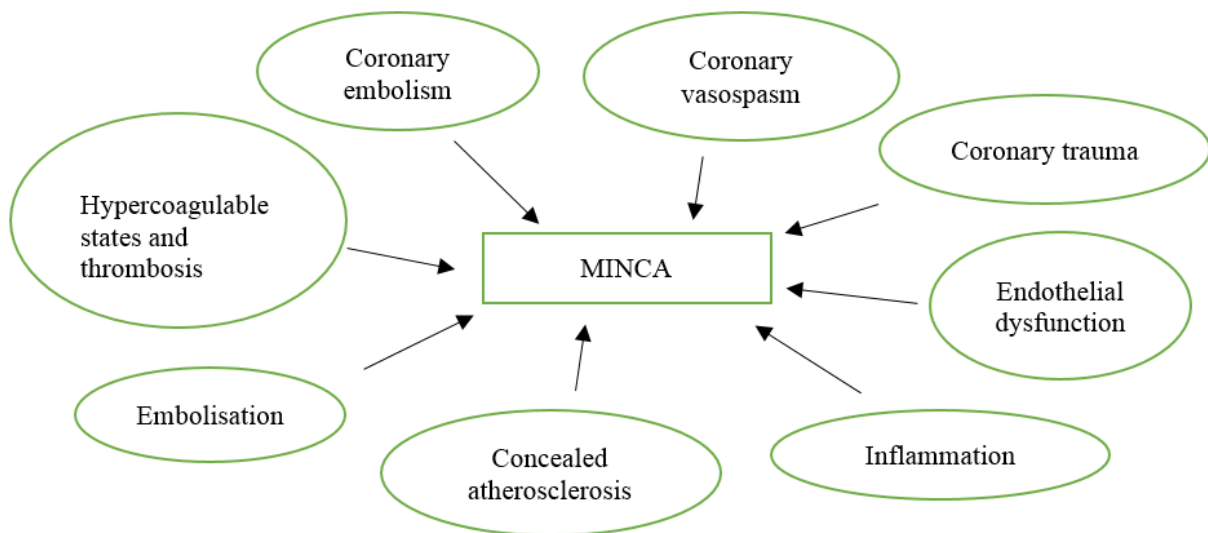

Figure 2: Probable pathogenic mechanisms of myocardial infarction with normal coronary arteries (MINCA).

CONCLUSIONS

Non-atheromatous cause of sudden cardiac death is considered a diagnostic challenge for pathologists. A normal heart is an important negative indicator in the investigations, as it warrants referral of living relatives to a cardiologist for genetic screening. The normal heart grossly may exhibit microscopic disease, hence histological analysis is mandatory to determine a specific diagnosis. In addition, post-mortem tissue and/or blood samples should be sent for genetic testing in questionable cases. Prior to autopsy, the use of PMCT serves as an ancillary investigation in determining the cause of death. The Malaysian Armed forces implement stringent and comprehensive medical screening based on the current medical guidelines (Mohd Zin Bidin & Mohd Ghazalli Mohd Taha, 2012; Muslan, 2021) for early detection of infectious and lifestyles diseases to ensure that each military personnel is physically and mentally fit so that they can perform their duties efficiently. The current health screening conducted in military medical institutions is sufficient in determining cardiovascular fitness among military personnel. We recommend that genetic screening and/or CMRI should be incorporated in a medical screening in a suspicious and strong family history of young death to exclude conduction defect or channelopathy. Obligation for medical screening, a healthy lifestyle and a no smoking policy should be strictly enforced. Most importantly, each military personnel should be responsible for their health and fitness.

LIMITATIONS

This case report has limitations. The most important limitation is genetic testing for heart conduction problems and/or channelopathy was not undertaken due to financial constraints imposed by the next-of-kin. Furthermore, because this was an autopsy case, CMRI is not applicable on a dead body, and PMCT is not available at our facility.

AUTHOR CONTRIBUTIONS

Nadiawati Abdul Razak was in charge of the case clinically and was a major contributor in writing the manuscript. Faridah Mohd Nor, Nur Najmi Mohamad Anuar and Ahmad Zakuan Kamarudin reviewed the literature, analysed and contributed to the article writing. All authors read and approved the final manuscript.

ETHICS APPROVAL

Ethics approval was not sought for the case report because the anonymity of the subject and confidentiality were well preserved. Verbal informed consent was obtained from the next-of-kin of the deceased for the publication of this case report and accompanying images. The next-of-kin was informed regarding the findings after the post-mortem and the usage of the tissues for this case report remains anonymous.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest in this work.

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