

Histopathological Examination in Medicolegal Autopsies: Unmasking Early Myocardial Infarction in Two Cases of Sudden Death

Singh PK, Ojha P, Neupane S, Oli P, Rajak S, Simkhada S, Shrestha N

Department of Forensic Medicine and Toxicology,
Kathmandu University Hospital, Dhulikhel Hospital,
Kathmandu University School of Medical Sciences,
Dhulikhel, Kavre, Nepal.

Corresponding Author

Pankaj Kumar Singh
Department of Forensic Medicine and Toxicology,
Kathmandu University Hospital, Dhulikhel Hospital,
Kathmandu University School of Medical Sciences,
Dhulikhel, Kavre, Nepal.
E-mail: drpankaj_s@yahoo.co.in

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ABSTRACT

Sudden unexpected cardiac death remains one of the most challenging diagnoses in forensic pathology, particularly when gross autopsy findings are uncertain. Myocardial infarction in the first few hours after symptom onset may produce faint or absent gross morphological changes, making microscopic evaluation necessary. In Nepal, histopathological examination is not routine in medicolegal autopsies.

We present two cases of sudden unexpected natural death involving middle-aged men who presented with nonspecific symptoms shortly before and were declared brought dead upon arrival at health care facilities. Medicolegal autopsies revealed minimal gross cardiac findings. First case, a localized whitish patch was identified over the right ventricular surface without significant coronary artery obstruction. Histopathological examination demonstrated early myocardial infarction involving the left ventricular wall and interventricular septum, accompanied by focal lymphocytic myocarditis and early coronary atherosclerosis. Second case, gross examination revealed severe calcific narrowing of the left anterior descending coronary artery. Microscopic examination confirmed early myocardial ischemic injury of the right ventricular myocardium with advanced atherosclerotic plaque characterized by cholesterol clefts and foamy macrophages.

Routine histopathological examination should be strongly considered in medicolegal autopsies involving sudden unexplained deaths. Integrating microscopic evaluation into standard forensic practice improves diagnostic precision, reduces uncertainty in determining the cause of death, and enhances the scientific credibility of medicolegal investigations in resource-limited settings.

KEY WORDS

Coronary artery diseases, Early myocardial infarction, Forensic pathology, Histopathology, Medicolegal autopsy, Nepal, Sudden cardiac death, Sudden unexpected death

INTRODUCTION

Medicolegal autopsy remains the gold standard for investigating sudden, suspicious, unexplained, and unnatural deaths.^{1,2} Besides determining the medical cause of death, forensic autopsy plays an important role in establishing the manner of death, reconstructing the circumstances surrounding the fatal event, documenting injuries, recovering forensic evidence, and assisting judicial investigations.^{2,3} Accurate autopsy findings are basic to criminal justice, mortality statistics, epidemiological surveillance, and public health planning.² Modern forensic pathology promote a multidisciplinary approach

that combines gross examination with histopathology, toxicology, microbiology, molecular investigations, postmortem imaging, and other supporting techniques to improve diagnostic accuracy and strengthen medicolegal conclusions.⁴⁻⁶

Cardiovascular disease remains the leading cause of mortality worldwide, accounting for approximately 20 million deaths annually, with ischemic heart disease representing the largest contributor.⁷ Sudden cardiac death (SCD), defined as an unexpected natural death due to

cardiac causes occurring within one hour of symptom onset or within 24 hours of the individual last being seen alive, constitutes a significant proportion of these deaths.^{6,8,9} Although many cases result from advanced coronary artery disease, sudden death may also occur during the earliest phase of acute myocardial ischemia, when gross morphological changes are absent or inadequate to be detected during routine autopsy.^{6,10,11}

Early myocardial infarction is a well-recognized diagnostic challenge in forensic pathology.¹ During the first few hours after coronary artery occlusion, the myocardium may appear grossly unremarkable despite irreversible cellular injury.^{12,13} Histopathological examination can reveal characteristic early changes, including myocyte waviness, hypereosinophilia, loss of cross-striations, nuclear pyknosis or disappearance, contraction band necrosis, and interstitial edema, followed later by inflammatory cell infiltration.^{8,12,13} Identification of these microscopic features requires systematic tissue sampling and expert interpretation, making histopathology essential in the investigation of sudden cardiac deaths.^{1,3,6}

Recognizing its diagnostic value, the Association for European Cardiovascular Pathology recommends comprehensive histological examination of the myocardium and coronary arteries in all cases of sudden unexpected cardiac death.^{14,15} Likewise, the Royal College of Pathologists and other international forensic organizations advocate routine cardiac histopathology whenever the cause of death remains uncertain or cardiovascular disease is suspected.⁸ These recommendations address that microscopic examination frequently detects pathological changes not evident on gross examination alone.^{9,16}

Several studies have shown that histopathological examination significantly increases the diagnostic yield of medicolegal autopsies by establishing, confirming, or modifying the cause of death in cases initially considered uncertain after routine autopsy.^{4,5} Histology is particularly valuable for identifying early myocardial infarction, myocarditis, cardiomyopathies, infiltrative myocardial diseases, vasculitis, and occult infections.^{5,6,9} Correlation of microscopic findings with clinical history, gross pathology, and toxicological investigations enhances the scientific reliability of forensic opinions and improves the accuracy of death certification.^{1,17}

Despite these advantages, routine histopathological examination is not universally practiced in many low- and middle-income countries because of limited laboratory infrastructure, financial constraints, shortages of trained personnel.^{4,5} In Nepal, medicolegal autopsies in sudden, suspicious, and unnatural deaths are performed by authorized government medical officers or forensic specialists under the prevailing legal framework.¹⁸ However, tissue sampling for histopathology is generally reserved for selected cases with uncertain gross findings or suspected specific pathology.¹⁹ As a result, faint myocardial lesions

and early ischemic changes may remain undiagnosed when microscopic examination is omitted.^{10,16}

This case series describes two middle-aged men who died suddenly following nonspecific symptoms, in whom conventional medicolegal autopsy failed to fully explain the fatal event. Histopathological examination of the myocardium demonstrated characteristic features of early acute myocardial infarction, enabling definitive determination of the cause of death. These cases highlight the important role of routine cardiac histopathology in improving diagnostic accuracy, strengthening medicolegal conclusions, and supporting the incorporation of systematic microscopic examination into medicolegal autopsy protocols, particularly in resource-limited settings such as Nepal.

CASE REPORT

Case 1

Clinical History

A 40-year-old Nepalese male with no documented history of chronic medical illness suddenly developed severe epigastric discomfort while spending the evening with friends in his rented room. According to the police inquest report, the discomfort was acute in onset and progressively worsened over a short period. Recognizing the severity of his symptoms, his companions immediately transported him to the nearest healthcare facility. Despite immediate transportation, he was declared brought dead on arrival. There was no reported history of preceding trauma, seizures, intoxication, or fever. Due to the sudden and unexplained nature of death, a medicolegal autopsy was ordered by the investigating authority to determine the cause and manner of death.

External Examination

The autopsy was performed at the Department of Forensic Medicine, Kathmandu University School of Medical Sciences, Dhulikhel Hospital, Kathmandu University Hospital. The deceased was moderately built and had early postmortem changes, consistent with the reported postmortem interval. Multiple superficial abrasions were present over both lower limbs and the lower back. These injuries were recent, superficial, and non-fatal, and were considered compatible with minor contact during collapse or transportation. No significant external injuries or other findings indicating poisoning and mechanical asphyxia.

Internal Examination

Systematic internal examination demonstrated no evidence of significant traumatic injury involving the thoracic, abdominal, or cranial cavities.

The heart weighed approximately 300 g, which was within the expected range, a localized whitish patch was observed over the anterior aspect of the right ventricle. The

pericardium was intact without hemorrhage or effusion. The cardiac chambers were normally configured, and the myocardium maintained its usual consistency. Cardiac valves, papillary muscles, chordae tendinae, and great vessels appeared grossly unremarkable. The coronary arteries appeared patent on routine gross inspection without significant luminal narrowing or thrombosis.

Examination of the lungs, liver, spleen, kidneys, brain, and gastrointestinal tract revealed no significant pathological abnormalities that could account for death. Because the gross examination failed to establish a definitive cause of death, the entire heart was preserved and submitted for detailed histopathological evaluation.

Histopathological Findings

Gross Pathology

The intact heart measured 10x9x8 cm.

The ventricular wall thicknesses were as shown in table 1.

Table 1. Ventricular wall thickness.

Cardiac Structure	Thickness (cm)
Right ventricular wall	1.4
Left ventricular wall	2.4
Interventricular septum	1.8

External examination confirmed the presence of focal whitish discoloration over the right ventricular surface. Serial sectioning failed to demonstrate obvious hemorrhage, fibrosis, infarction, calcification, or myocardial scarring. The cardiac valves were structurally normal. The right coronary artery and left anterior descending (LAD) coronary artery appeared grossly patent.

Microscopic Examination

Representative sections were obtained from both ventricles, interventricular septum, atria, major coronary arteries, aortic root, and pulmonary trunk.

Histological sections from the left ventricular myocardium and interventricular septum demonstrated characteristic features of early myocardial ischemic injury, including:

- Wavy myocardial fibers. (Fig. 1A in 10X and Fig. 1B in 40X)
- Loss of cross-striations (Fig. 1C)
- Loss of nuclear staining (Fig. 1C)
- Patchy lymphocytic inflammatory infiltrates (Fig. 1C)

These microscopic alterations were consistent with the earliest stages of acute myocardial infarction. Section from the right ventricular myocardium were largely unremarkable.

Microscopic examination of the left coronary artery demonstrated focal intimal atheromatous plaque formation without critical luminal obstruction (Fig. 2A in 10X and Fig. 2B in 40X). The remaining coronary arteries, pulmonary

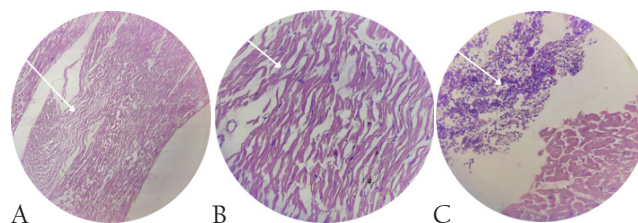


Figure 1. Sections from the left ventricular wall and interventricular septum show some muscle fibers with increased waviness (Fig. A in 10X and Fig. B in 40X), loss of nuclei and cross striations, and lymphocytic infiltrations (Fig. C).

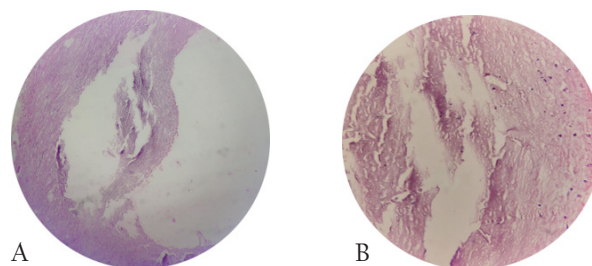


Figure 2. Sections from the left coronary artery show the vessel wall with focal atheromatous plaque (Fig. 2A in 10X and Fig. 2B in 40X).

artery, aortic wall, and cardiac valves showed no significant pathological abnormalities.

Final Pathological Diagnosis

The combined gross and microscopic findings established the diagnosis of

- Early acute myocardial infarction involving the left ventricular wall and interventricular septum.
- Mild coronary atherosclerosis involving the left coronary artery.
- Focal non-infective lymphocytic myocarditis.

The absence of significant extracardiac pathology, together with the histopathological evidence of acute ischemic myocardial injury, supported ischemic heart disease as the cause of sudden natural death

Case 2

Clinical History

A 52-year-old Nepalese male experienced severe abdominal pain while staying at a local guest house. According to the police inquest report, the pain developed suddenly during the early morning hours. He was transported urgently to a nearby hospital but was declared dead at 06:40 hours before resuscitative measures could be initiated. Available investigative records revealed no history of recent trauma, assault, poisoning, or prolonged illness. Given the sudden unexplained nature of death occurring outside a healthcare setting, a medicolegal autopsy was requested.

External Examination

The deceased was a moderately built and postmortem examination revealed multiple superficial abrasions over both lower limbs and the lower back, like those observed in

case 1. These injuries were insignificant. No other external injuries were present, leading to no obvious cause of death could be identified.

Internal Examination

The cranial, thoracic and abdominal cavities contained no abnormal fluid collections or traumatic injuries. The heart demonstrated a smooth glistening epicardial surface without pericardial hemorrhage.

Careful examination of the coronary arteries identified marked pathological change involving the left anterior descending coronary artery (LAD). Approximately 5 cm distal to its origin. A 1 cm segment exhibited marked calcification with complete luminal occlusion by a firm atherosclerotic plaque. No acute coronary thrombosis was identified grossly.

Cardiac valves, papillary muscles, and chordae tendinae appeared structurally intact. No ventricular rupture or gross myocardial infarction was identified on serial sectioning.

The remaining thoracic and abdominal organs were grossly unremarkable. Because gross myocardial infarction was absent despite severe coronary artery disease, the entire heart was submitted for histopathological examination.

Histopathological Findings

Gross Pathology

The heart measured 12 x 10 x 7.5 cm.

The myocardial wall thicknesses were as shown in table 2.

Table 2. Myocardial wall thickness

Cardiac Structure	Thickness (cm)
Right ventricular wall	1.3
Left ventricular wall	1.6
Interventricular septum	2.1

Serial sectioning demonstrated yellow-white atherosclerotic deposits producing marked narrowing of the LAD lumen, consistent with autopsy findings. The remaining coronary arteries showed no grossly significant disease. No gross myocardial fibrosis, infarction, hemorrhage, or scar formation was identified.

Microscopic Examination

Histological sections from the left atrium, left ventricle, right atrium, and interventricular septum demonstrated preserved myocardial architecture without significant pathological abnormalities.

In contrast, sections obtained from the right ventricular wall demonstrated early ischemic myocardial injury characterized by:

- Wavy myocardial fibers (Fig. 3)
- Loss of cross-striations (Fig. 3)
- Nuclear fading (Fig. 3)

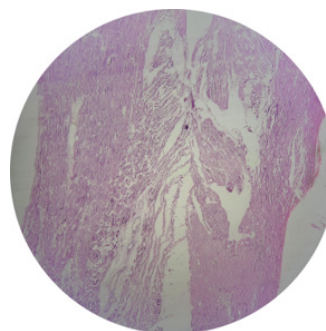


Figure 3. Sections from the right ventricular wall show some muscle fibers with increased waviness, loss of nuclei, and cross striations.

These findings were consistent with the earliest microscopic stage of acute myocardial infarction.

Microscopic examination of the LAD revealed advanced fibroatheromatous disease characterized by:

- Severe intimal thickening with flattened endothelium (Fig. 4)
- Cholesterol clefts (Fig. 4)
- Numerous foamy macrophages (Fig. 4)
- Fibrous cap formation (Fig. 4 and Fig. 5)
- Marked luminal compromise (Fig. 4 and Fig. 5)

The right coronary artery, left circumflex artery, ascending aorta, pulmonary artery, and cardiac valves showed no significant microscopic abnormalities.

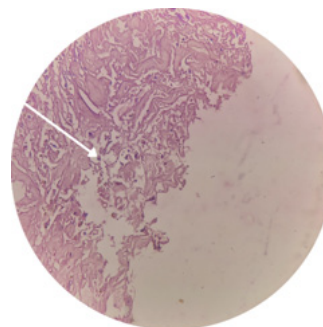


Figure 4. Sections from the left anterior descending artery show a vessel wall linked by flattened endothelium with a compromised lumen. The subendothelial region shows cholesterol clefts and foamy macrophages.

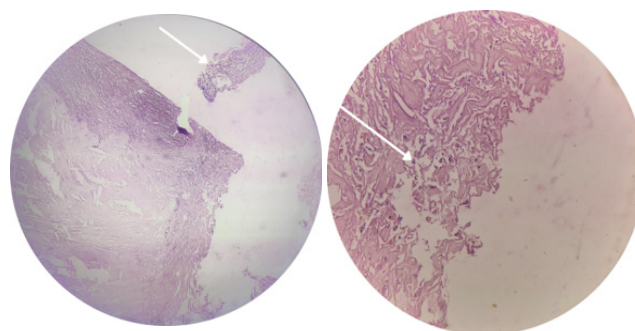


Figure 5. Sections showing atherosclerosis plaque in the left anterior descending artery (Fig. A in 10X and Fig. B in 40X)

Final Pathological Diagnosis

Histopathological examination established:

- Early acute myocardial infarction involving the right ventricular myocardium.
- Advanced calcific atherosclerosis of the left anterior descending coronary artery with critical luminal stenosis.
- Ischemic heart disease, secondary to severe coronary artery atherosclerosis.

The correlation of gross coronary pathology with microscopic evidence of acute myocardial ischemia established ischemic heart disease as the definitive cause of sudden natural death.

Comparative Summary of Both Cases

Despite differences in age and gross pathological findings, both decedents presented with sudden death following nonspecific symptoms and exhibited either absent or minimal gross evidence of acute myocardial infarction at autopsy. Histopathological examination proved decisive in both cases by revealing early ischemic myocardial injury that would likely have been overlooked on macroscopic examination alone. While the first case demonstrated slight coronary atherosclerosis associated with early myocardial infarction and focal lymphocytic myocarditis, the second case showed advanced calcific atherosclerosis of the left anterior descending coronary artery with corresponding early myocardial ischemic changes.

Together, these cases illustrate the indispensable role of routine cardiac histopathology in medicolegal investigations of sudden unexpected death, particularly when conventional autopsy findings are equivocal or insufficient to explain the fatal event. This clinicopathological correlation forms the basis for the expanded discussion that follows, emphasizing the diagnostic, forensic, and public health significance of histopathological examination in sudden death.

DISCUSSION

Medicolegal autopsy is the reference standard for investigating Sudden, unexpected, suspicious, and unnatural deaths.^{20,21} While gross examination establishes the cause and manner of death in most cases, it may be insufficient when fatal pathological changes are small or occur before recognizable macroscopic alterations develop.^{1,13} In such situations, supplementary investigations, particularly histopathological examination, provide critical diagnostic evidence that strengthens medicolegal opinions and improves the accuracy of death certification.^{4,5}

Cardiovascular disease remains the leading cause of mortality worldwide, with ischemic heart disease

accounting for most sudden cardiac deaths.^{7,9} Although advanced coronary artery disease is frequently identified at autopsy, fatal myocardial ischemia may occur during the early stages of infarction when gross examination reveals no significant abnormalities.^{13,22} Failure to recognize these early lesions may result in an incorrect or uncertain cause of death, potentially affecting judicial investigations, mortality data, and public health surveillance.^{1,20}

Histopathological examination plays a important role in resolving this diagnostic challenge.^{1,6} Early myocardial infarction is characterized by microscopic changes including myocyte waviness, hypereosinophilia, contraction band necrosis, nuclear pyknosis, and interstitial edema that precede gross pathological findings and may provide the only objective evidence of acute ischemic injury.^{13,23} Accordingly, histopathology frequently establishes or confirms the cause of death when conventional autopsy findings are uncertain, particularly in cases of sudden unexpected cardiac death.^{4,5,16}

Recognizing its diagnostic importance, the Association for European Cardiovascular Pathology and the Royal College of Pathologists recommend systematic histological examination of the myocardium and coronary arteries in unexplained sudden cardiac deaths or when cardiovascular disease is suspected.^{6,24} Multiple studies have demonstrated that microscopic examination improves the diagnostic yield of medicolegal autopsies by identifying occult myocardial infarction, myocarditis, cardiomyopathies, infiltrative myocardial disorders, and other cardiac pathologies that may not be apparent on gross examination.^{4,5,16}

Despite these recommendations, routine cardiac histopathology remains inconsistently practiced in many low- and middle- income countries because of limited laboratory infrastructure, financial constraints, and shortages of trained forensic pathologists.^{4,5,18} In Nepal, histopathological examination is generally performed selectively when gross autopsy findings fail to explain death or when a specific pathological process is suspected.¹⁹ Consequently, early myocardial infarction may remain undiagnosed, reducing diagnostic certainty and potentially compromising medicolegal conclusions.

The present case series describes two sudden unexpected deaths in which conventional medicolegal autopsy failed to identify the fatal pathology. Histopathological examination of the myocardium demonstrated characteristic features of early acute myocardial infarction, enabling definitive determination of the cause of death. These cases highlight the forensic significance of routine cardiac histopathology in resolving diagnostically challenging autopsies and support its wider incorporation into medicolegal autopsy protocols, particularly in resource-constrained settings.

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