

Case report of 2 sudden deaths after surgery for bone fracture

Usefulness of immunohistochemical analysis of coronary artery for identifying acute myocardial infarction

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Abstract

Rationale: Death following orthopedic surgery has become rare, but does occur. Acute myocardial infarction (AMI) can be a cause of such death, but diagnosis of AMI is often challenging, even by autopsy.

Patient concerns: We have recently experienced 2 cases of sudden death after bone fracture surgery, in which AMI and pulmonary thromboembolism were clinically suspected as causes of death. Case 1 was a 60-year-old male with a history of diabetes mellitus who died 7 days after surgery for Lisfranc dislocation fracture. Case 2 was a 75-year-old female who died several hours after surgery for proximal femur fracture.

Diagnoses: At autopsy, slight myocardial change suggestive of AMI, severe coronary stenosis, and pulmonary congestion were noted in case 1. No signs for AMI were observed, but diffuse fat emboli were identified in the pulmonary vasculature in Case 2. Thus, postmortem pathological diagnosis was AMI in case 1 and it was suggestive of fat emboli in case 2.

Interventions: Immunohistochemical analysis of smooth muscle markers in the coronary artery was performed in both cases.

Outcomes: The positivity ratio of h-caldesmon to α -smooth muscle actin indicative of maturity of neointimal smooth muscle cells was preserved in case 2 but diminished in case 1, where coronary occlusion may have been caused via plaque rupture.

Lessons: Immunostaining of smooth muscle markers in the coronary artery may serve as a supporting tool in establishing or disregarding AMI at autopsy.

Abbreviations: AMI = acute myocardial infarction, CPA = cardiopulmonary arrest, LAD = left anterior descending branch, LCX = left circumflex branch, PTE = pulmonary thromboembolism, SMA = smooth muscle actin.

Keywords: acute myocardial infarction, autopsy, orthopedic surgery, smooth muscle cells, sudden death

1. Introduction

Although incidence of death following orthopedic surgery has recently decreased because of advances in surgical techniques and management, fatal complications including death do occur.^[1] Major causes of these deaths include acute myocardial infarction (AMI), pulmonary thromboembolism (PTE), and fat embolism.^[1,2] Among these causes, the diagnosis of AMI is

occasionally challenging even by autopsy because histological evidence in myocardium only becomes apparent several hours after onset of the ischemic attack.^[3] Here, we introduce immunohistochemical analysis of smooth muscle markers in coronary artery as a supporting tool to verify AMI, by presenting 2 autopsy cases of sudden death after surgery for bone fracture.

2. Case presentation

Case 1 was a 60-year-old male with a history of diabetes mellitus from the age of 44 years. He presented with swelling and reddening of the left foot, which was however painless because of the presence of diabetic neuropathy. He was then diagnosed with Lisfranc dislocation fracture. One month later, surgery was performed under general anesthesia. Seven days post surgery, he was discovered to have undergone cardiopulmonary arrest (CPA) in the ward and died despite attempted cardiopulmonary resuscitation. AMI or PTE was suspected as a cause of death. Heart weight was 400 g at autopsy and AMI was not evident on gross observation of the myocardial cut surface, although old MI, 3 x 1.5 cm in size, was identified in the left anterior ventricular wall. Histologically, striation of the myocardium disappeared focally in the lateral ventricular wall, indicative of coagulative necrosis, along with contraction band necrosis and slight neutrophilic infiltration (Fig. 1), suggesting early AMI. These changes were

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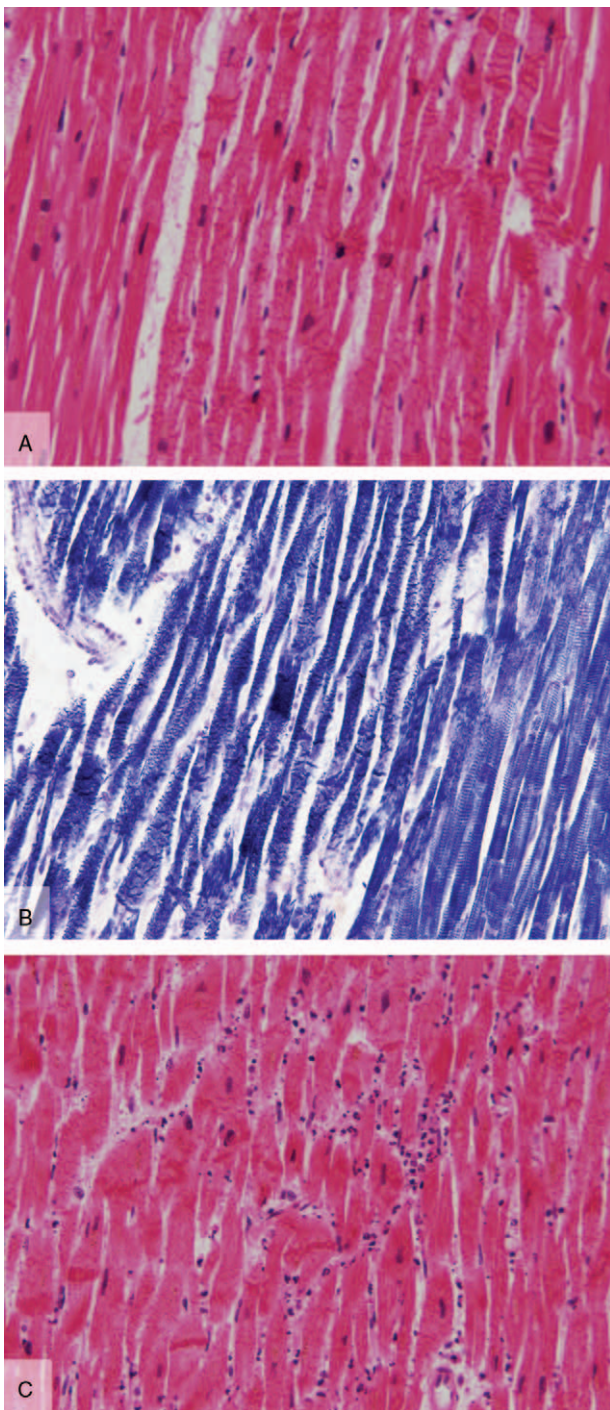


Figure 1. Histology of myocardial damage in case 1. (A) Contraction band necrosis (HE staining), (B) diminished myocardial striations (PTAH staining), and (C) neutrophilic infiltration (C: HE staining). HE=hematoxylin and eosin, PTAH=phosphotungstic acid hematoxylin.

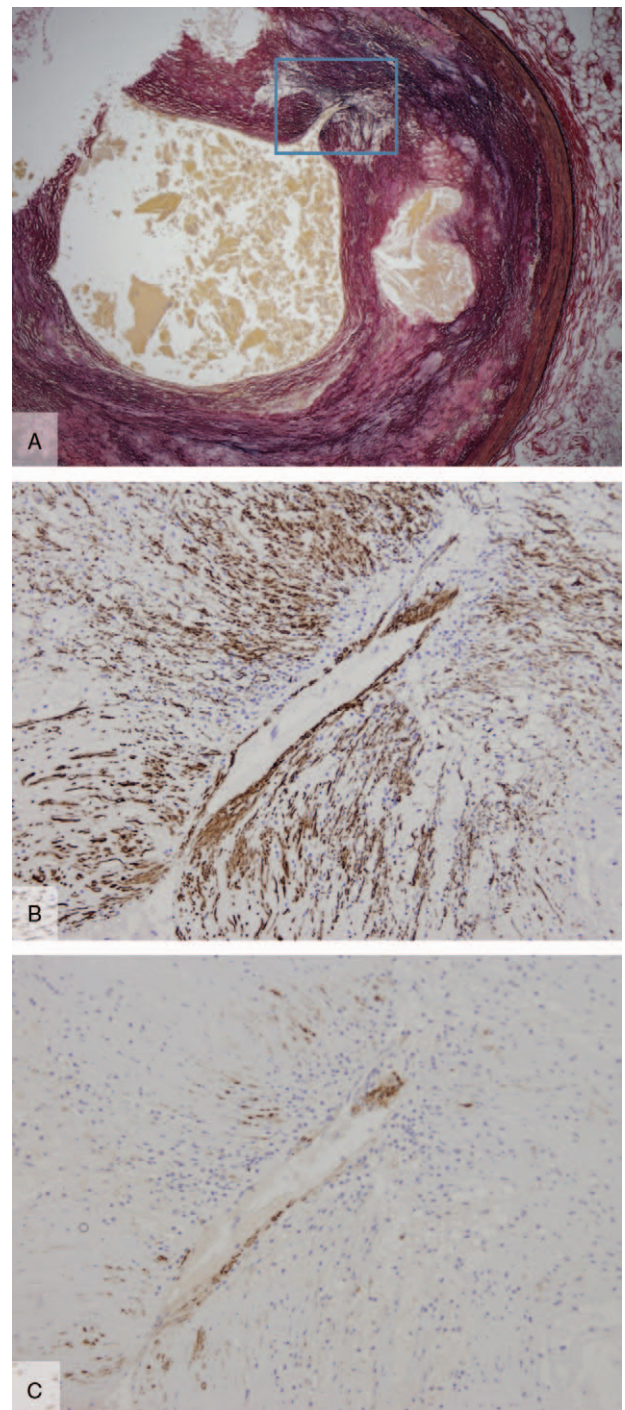


Figure 2. Marked stenosis of the coronary artery with immaturity of intimal smooth muscle cells in case 1. (A) Atherosclerotic stenosis with luminal thrombus (EVG staining), (B) neointimal smooth muscle cells (square field in A, α -smooth muscle actin immunostaining), and (C) decreased positivity ratio of h-caldesmon in smooth muscle cells (the same area as B, h-caldesmon immunostaining). EVG=Elastica van Gieson.

scattered throughout the left lateral ventricular wall, but the precise extent of AMI was undetermined, since most of these changes were subtle. Marked atherosclerotic stenosis up to 80% to 95% in 3 branches of the coronary artery was observed. These atheromatous lesions were predominantly fibrous cap atheroma or thin fibrous cap atheroma defined by Virmani et al,^[4] and luminal thrombus was focally observed in the left circumflex

branch (LCA) (Fig. 2A). Pulmonary congestion (lt. 620/rt. 600g) with occasional edema in the interlobular septa was noted, and PTE was not identified. Sudan III staining revealed fat globules in the pulmonary vasculature only sporadically. Other autopsy findings included diabetic nephropathy and moderate atherosclerosis of the aorta.

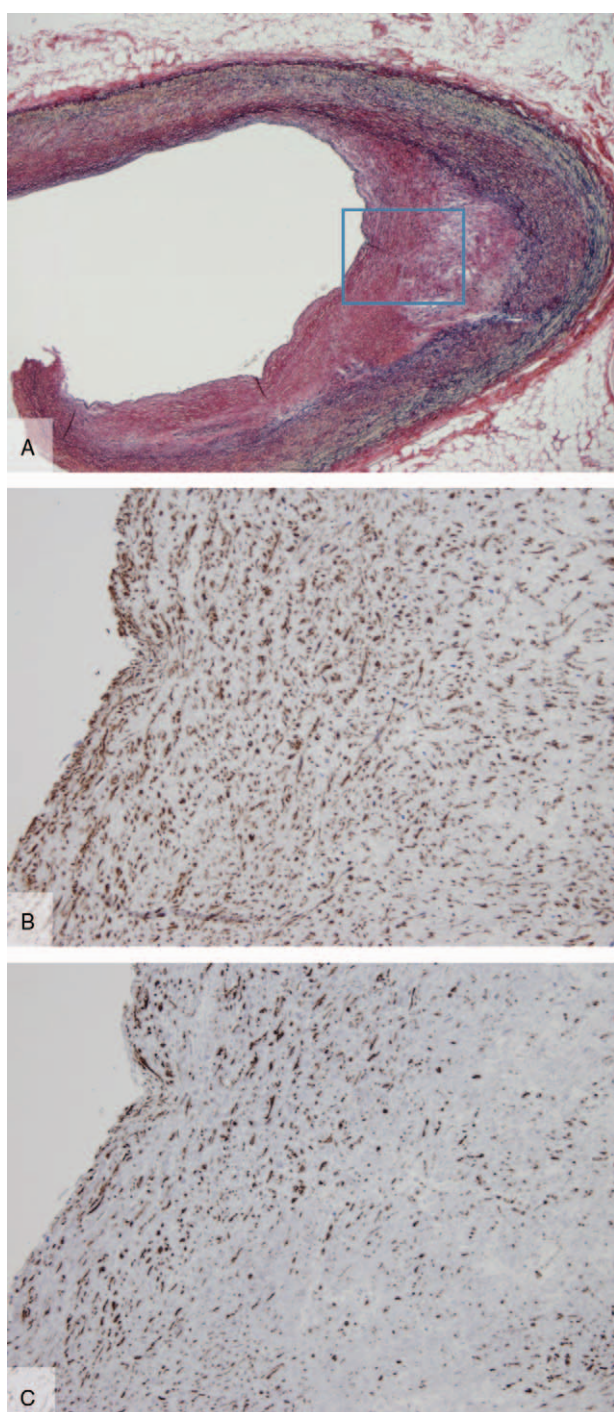


Figure 3. Mild stenosis of the coronary artery with mature intimal smooth muscle cells in case 2. (A) Stenosis with mild intimal thickening (EVG staining), (B) neointimal smooth muscle cells (square field in A, α -smooth muscle actin immunostaining), and (C) preserved positivity ratio of h-caldesmon in smooth muscle cells (the same area as B, h-caldesmon immunostaining). EVG = Elastica van Gieson.

Case 2 was a 75-year-old female with a chronic history of rheumatoid arthritis. She experienced a fall at home, which impacted on the left hip. Following removal to hospital by ambulance, she was diagnosed with left proximal femur fracture. As she was under oral administration of acetylsalicylic acid, surgery (open reduction and internal fixation of the proximal femur fracture) was performed 2 weeks later under general

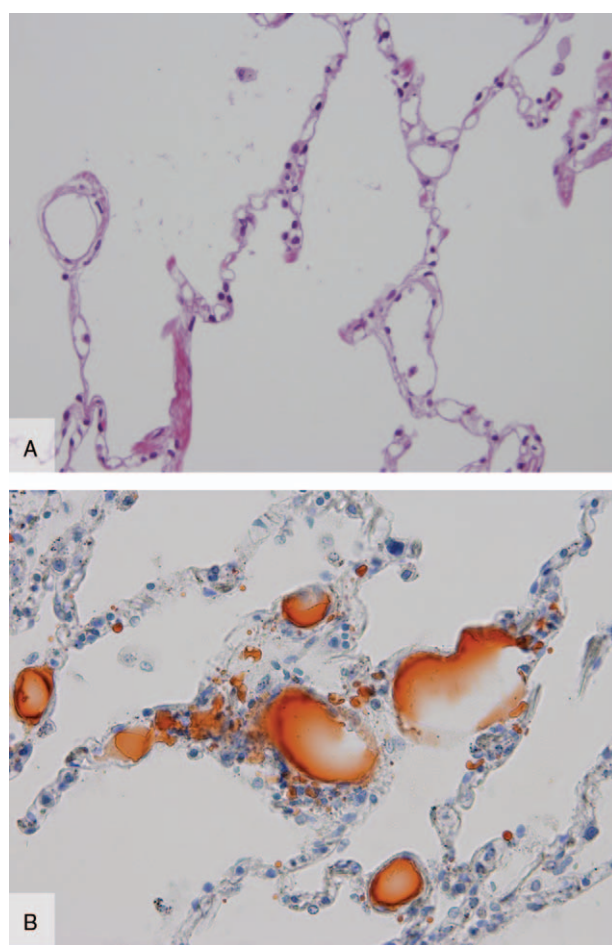


Figure 4. Histology of pulmonary fat emboli in case 2. (A) Occasional dilatation of pulmonary capillaries (HE staining), (B) wherein fat droplets of various sizes are identified (Sudan III staining). HE = hematoxylin and eosin.

anesthesia. Two hours after surgery, she pressed the call button and complained of pain. Soon afterwards, she went into CPA and died 5 hours after surgery despite attempted cardiopulmonary resuscitation. AMI or PTE was suspected as a cause of death. Heart weight was 340 g at autopsy and the myocardium appeared normal on gross and histological examination. Atherosclerotic stenosis was mild, at up to 40%, in 3 branches of the coronary artery (Fig. 3A). These atheromatous lesions were predominantly pathological intimal thickening with an admixture of fibrous cap atheroma defined by Virmani et al.^[4] Lungs (lt. 320g/rt. 260g) exhibited a normal gross appearance without PTE, but dilatation of capillaries was occasionally observed histologically (Fig. 4A). Sudan III staining revealed diffuse fat globules in the pulmonary vasculature (Fig. 4B). Atherosclerosis of the aorta was slight.

Immunohistochemical analysis of smooth muscle markers in 3 branches of the coronary artery was performed in both cases using the avidin-biotin-peroxidase complex according to standard methods. As this was postmortem analysis, ethical approval is not necessary, but department of safe management of our university approved the method. A monoclonal antibody to α -smooth muscle actin (SMA) (clone 1A4, working dilution 1:400, Dako) was used to identify all smooth muscle cells, whereas h-caldesmon (clone h-CD, working dilution 1:50, Dako) was used to identify smooth muscle cells beyond intermediate differentiation. The ratio of h-caldesmon⁺ cells to α -SMA⁺ cells was counted

at least 6 sites in the neointima where SMA⁺ cells were abundant using $\times 200$ fields in any branch. The average h-caldesmon/ α -SMA ratio (\pm standard deviation) in the coronary neointima in left anterior descending branch (LAD), LCX, and right coronary artery were $28.3\% \pm 22.9\%$, $17.5\% \pm 11.5\%$ (Fig. 2B and C), and $32.5\% \pm 28.1\%$, respectively, in case 1; and $55.0\% \pm 10.1\%$ (Fig. 3B and C), $64.2\% \pm 6.1\%$, and $60.1\% \pm 10.6\%$, respectively, in case 2. These ratios were not greatly varied among the different categories of the plaque defined by Virmani et al^[4] within the same branch of the coronary artery.

3. Discussion

These 2 autopsy cases are common in sudden death after surgery for bone fracture in elderly patients, wherein AMI or PTE is suspected as a cause of death. The postmortem pathological diagnosis was AMI in case 1 because of scattered myocardial damage in the lateral ventricular wall, severe coronary stenosis with focal luminal thrombus in LCX, and pulmonary congestion, whereas the diagnosis was suggested to be fat emboli in case 2 because of the absence of AMI and PTE in heart and lungs and findings of diffuse fat emboli in the pulmonary vasculature.

To establish or disregard the existence of AMI at autopsy in sudden death is often problematic. Neutrophilic infiltration is conclusive, but becomes apparent as early as 6 to 12 hours after the onset of the ischemic injury. The earliest histological findings such as wavy fibers, coagulative necrosis including cytoplasmic homogenization and hyper eosinophilia, and nuclear alterations may be subtle and nonobvious,^[3] as is shown in the present case 1. Here, we have recently reported that decreased h-caldesmon/ α -SMA ratio in the coronary neointima indicates immaturity of neointimal smooth muscle cells and is a good marker for vulnerable plaque, leading to AMI through plaque rupture and coronary occlusion, using autopsy materials.^[5] In the present cases, reduction of this marker to 17.5% in LCX in case 1 is indicative of vulnerable plaque, whereas preservation of this marker to $>50\%$ in any branch of coronary artery in case 2 is compatible with stable plaque. We deem that presence of diabetes mellitus in case 1 contributed not only to the risk for atherosclerosis, but also painless AMI because of diabetic neuropathy. Although categories of the atheromatous plaque varied including pathological intimal thickening and fibrous cap atheroma among different branches and even within the same branch of the coronary arteries, h-caldesmon/ α -SMA ratio was not greatly different within the same branch. Indeed, our previous study in the carotid artery also showed that this ratio was uniform among different neointimal regions in the same plaque.^[6]

The findings of myocardial change suggestive of AMI, severe coronary stenosis along with decrease in neointimal h-caldesmon/ α -SMA ratio, and pulmonary congestion found in case 1 were all lacking in case 2. Instead, diffuse fat emboli in the pulmonary

microcirculation, shown by Sudan III staining, were observed. These fat emboli are a major cause of intraoperative death in bone fracture, partly because of excessive intramedullary pressurization, for example, when using long stems during cementing.^[2] However, fat emboli in the lungs originating from sternal or rib fractures owing to chest compression may be seen after cardiopulmonary resuscitation.^[2] Indeed, fat emboli in the pulmonary vasculature were also observed, albeit sporadically, in case 1. However, it has been reported in a previous autopsy study that pulmonary embolized tissue areas associated with cardiopulmonary resuscitation are much fewer than those owing to bone traumatic fractures.^[7] Therefore, we consider that diffuse fat emboli in case 2 were attributable to bone surgery and brought about death, whereas patchy fat emboli in case 1 merely reflected cardiopulmonary resuscitation.

4. Conclusion

In conclusion, we have presented 2 currently rare cases of sudden death after bone surgery. Autopsy findings were indicative of AMI in left lateral ventricular wall in case 1 and were highly suggestive of fat emboli in case 2. Immunohistochemical analysis indicated that h-caldesmon/ α -SMA ratio in the neointima of the coronary artery was reduced especially in LCX in case 1 and was preserved in case 2. These findings were helpful in establishing the existence of AMI in case 1 and disregarding it in case 2. This immunohistochemical method may serve as a supporting tool in verifying postmortem diagnosis of AMI.

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