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Fatal Perioperative Myocardial Infarction in Four Patients with Cardiac Amyloidosis

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AMYLOIDOSIS is caused by the accumulation of amyloid fibrils in vital organs, leading to functional disturbances. Approximately 40% of patients with primary amyloidosis have had cardiac amyloidosis.[1–3] In cardiac amyloidosis, right heart failure is the predominant sign, whereas left heart function is preserved until late in the disease.[1–3] Because of the cardiac involvement, when patients with cardiac amyloidosis undergo surgery, anesthesia can present special risks.[4,5] In addition to the conduction disturbance and cardiac failure that are the main causes of death in cardiac amyloidosis, ischemic changes have been reported extensively.[6–9] However, there have been no reports concerning perioperative myocardial ischemia in patients with cardiac amyloidosis. Here we report on four patients with cardiac amyloidosis who developed fatal perioperative cardiac arrest resulting from myocardial infarction.

Case Reports

Preoperative electrocardiogram (ECG) data and postmortem findings for each patient are shown in table 1. Patient no. 1 received a Holter ECG examination 6 months before operation, and neither conduction disturbance nor ST-T changes were noted. Patients no. 2–4 did not receive other cardiac examinations because few clinical signs indicating myocardial ischemia were detected and because a preoperative diagnosis of cardiac amyloidosis was not made. On the day after resuscitation, patients no. 1–3 were diagnosed clinically as having myocardial infarction by marked elevation in myocardial enzymes (*e.g.*, heart fatty acid–binding proteins, myoglobin, MB isoenzyme of creatine kinase, myosin light chain) and ST-T changes. Myocardial infarction was confirmed by postmortem study. The epicardial coronary arteries were free of > 75% atherosclerotic narrowing in all patients.

Case 1

A 48-yr-old man weighing 65 kg gradually lost consciousness 3 h after a traffic accident. A diagnosis of acute subdural hematoma was made, and an emergency operation with general anesthesia was scheduled. The patient had a 1-yr history of nephrotic syndrome and an 8-yr history of amyloidosis secondary to pulmonary tuberculosis. Although cardiac amyloidosis had been detected by echocardiographic examination 6 months previously, his cardiac signs were minimal, and his preoperative heart rate and blood pressure were 80 beats/min and 135/80 mmHg, respectively. We administered mannitol and furosemide to decrease intracranial pressure and prevent postoperative aggravation of renal function. The intraoperative course was uneventful, but at the end of surgery, the patient's heart rate increased (120 beats/min) and blood pressure decreased (85/60 mmHg). Three hours postoperatively, marked ST-T elevation and complete atrioventricular block were noted on his ECG, followed by cardiac arrest a few minutes later. The patient was successfully resuscitated with 1.5 mg epinephrine within minutes. Although critical arrhythmia could be controlled by intravenous lidocaine, progressive congestive cardiac failure could not be arrested by digoxin, dopamine, furosemide, and even epinephrine. He died 6 days postoperatively.

Case 2

A 62-yr-old woman was diagnosed as having a bleeding duodenal ulcer, and emergency surgery was scheduled. She had been receiving medical treatment for rheumatoid arthritis for 5 yr, but a diagnosis of amyloidosis had not been made. She had no signs that suggested cardiac failure or ischemia. Preoperative blood chemistry tests showed moderate hepatic and renal dysfunction. Because of intraoperative bleeding (1,200 ml), her heart rate and blood pressure were stabilized by fluid replacement and blood transfusion. The patient had no intraoperative arrhythmia or conduction disturbance. Three hours postop-

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Table 1. Preoperative Cardiac Data and Postmortem Findings

No.	Preoperative ECG findings	Cause of Death	Amyloid Deposition in Heart	Other Abnormal Cardiac Findings	Other Amyloid Deposition
1	Low QRS voltage; ventricular extrasystole; right bundle branch block; psuedoinfarction pattern	Myocardial infarction (anterior and anterolateral); transmural necrosis of left ventricular wall	Atria, ventricular wall, and septum; mitral and tricuspid valves; intramural coronary arteries	Narrowing of ventricular cavities; thickening of ventricular wall and septum	Kidney; spleen; liver; intestine
2	Low QRS voltage; right bundle branch block; pseudoinfarction pattern	Myocardial infarction (antero-lateral and inferior); mitral valve prolapse	Ventricular wall and septum; all four valves; intramural coronary arteries	Narrowing of ventricular cavities; atrioventricular thrombi	Kidney; liver; lung
3	Low QRS voltage; flattened T wave (V1–V3); left anterior hemiblock	Myocardial infarction (anterior and anterolateral); transmural necrosis of left ventricular septum	Atria, ventricular wall, and septum; mitral and tricuspid valves; intramural coronary arteries	Narrowing of ventricular cavities with atrial dilation; thickening of ventricular wall and septum	Liver; kidney; lung
4	Low QRS voltage; pseudoinfarction pattern; atrial fibrillation; right bundle branch block	Myocardial infarction; rupture of left ventricular wall	Ventricular wall and septum; all except aortic valve; intramural coronary arteries	Narrowing of ventricular cavities; marked thickening of ventricular septum	Kidney; liver; skin; spleen

Amyloid deposition was confirmed by Congo red staining.
Low QRS voltage = QRS $\leq$ 15 mm in I + II + III.

eratively, complete arteriovenous block and marked ST elevation were detected on ECG, followed by ventricular fibrillation. The patient was rapidly resuscitated with 0.5 mg epinephrine and cardioversion. However, she did not respond to cardiotonics and antiarrhythmics such as dobutamine, epinephrine, and lidocaine and died of congestive cardiac failure 7 days postoperatively. Amyloidosis was confirmed postmortem.

Case 3

A 63-yr-old man underwent a transurethral resection of the prostate. The patient had no clinical signs that suggested cardiac failure or ischemia. The findings on a chest radiograph showed mild pleural effusion but a normal cardiac shadow, and no further examination was performed. A diagnosis of amyloidosis was not made preoperatively. His 2.5-h intraoperative course was uneventful. At the end of surgery, plasma sodium level decreased to 129 mM, compared with a preoperative level of 137 mM. A diagnosis of mild dilutional hyponatremia was made, and he was treated with furosemide and fluid restriction. No abnormal cardiac signs were noted at this time. However, 2 h postoperatively, he became dyspneic and cyanotic, and ventricular fibrillation ensued. Initial resuscitation with 0.5 mg epinephrine and cardioversion was successful within 10 min. The plasma sodium level 30 min after resuscitation was 129 mM. Despite treatment with dobutamine, digoxin, furosemide, and lidocaine, the patient died of congestive cardiac failure 5 days later. Postmortem study revealed that 200 ml of pleural effusion containing amyloid fibrils was present.

Case 4

A 71-yr-old woman underwent a low anterior resection of the rectum. Preoperative blood chemistry showed moderate hepatic and renal dysfunction, but a diagnosis of amyloidosis was not made. She had no signs that suggested cardiac failure or ischemia. Despite intraoperative hemorrhage (2,100 ml), her heart rate and blood pressure were within acceptable limits upon fluid replacement and blood transfusion. Just after completion of homeostasis and rectal anastomosis, marked ST-T elevation was detected on her ECG, followed by cardiac arrest within 5 min. Resuscitation was unsuccessful.

Discussion

Cardiac amyloidosis is very resistant to cardiosupportive treatment. Cardiotonic agents are considered to be useless because diastolic dysfunction is the predominant feature of cardiac amyloidosis. In addition, negative inotropic support such as treatment with calcium channel blockers worsens cardiac amyloidosis.[10] The administration of digitalis is of no benefit and may cause heart block.[1,2] Treatment for cardiac amyloidosis has consisted of careful restriction of fluid and sodium.

Among possible surgical and anesthetic factors, fluid imbalance might have been critical in our cases. Exten-

sive fluid replacement and blood transfusion in cases 2 and 4, and hypervolemia as suggested by dilutional hyponatremia in case 3, might lead to an increase in the myocardial preload. In case 1, intraoperative furosemide and mannitol might have caused dehydration and tachycardia, resulting in an increase in myocardial oxygen demand.

It is very important to understand that cardiac symptoms are observed only late in the course of cardiac amyloidosis.[1–3] In fact, although postmortem study in our patients revealed that cardiac function was seriously affected by the deposition of amyloid, few clinical signs indicating myocardial ischemia were detected. According to Barbour and Roberts,[8] none of their eight patients with cardiac amyloidosis who had transmural necrosis or fibrosis of the myocardium had clinical signs of myocardial ischemia.

Therefore, preoperative diagnosis and estimation of cardiac function are mandatory when patients with cardiac amyloidosis undergo anesthesia. However, clinical signs are rarely helpful, because they are too nonspecific to prompt consideration of such an uncommon disease. We encountered these cases among approximately 250,000 anesthesia cases over 12 yr, and three of the four patients were diagnosed postmortem.

We consider abnormal ECG findings very important clues for a preoperative diagnosis of cardiac amyloidosis.[6–8] Low voltage of the QRS complex and bundle branch block on the ECG were observed in all four of our patients (table 1). Low voltage of the QRS complex is particularly important, because this finding is observed when there is serious cardiac involvement, including cardiomyopathy, myocardial infarction, and pericarditis. Roberts and Waller[7] reported that 63% of patients with cardiac amyloidosis had low voltage of the QRS complex on ECG. Echocardiographic examination is useful for diagnosis and estimation of the severity of cardiac amyloidosis.[1–3,8]

We did not insert a pacemaker in patient 1 because Holter ECG monitoring did not show any serious conduction disturbance. A temporary pacemaker is advisable in patients with conduction disturbance, as suggested by Eriksson *et al.*[5] Intraoperative transesophageal echocardiography is beneficial because the examination is relatively noninvasive, and because immediate detection of changes in cardiac function is possible.

The anesthetic treatment of patients with cardiac amyloidosis depends on the severity of cardiac involvement. Anesthetic drugs or techniques that do not greatly decrease venous return, produce bradycardia, or depress the myocardium should be used. Our cases emphasize that a variety of common anesthetic and surgical factors, including blood loss and fluid replacement, hemodynamic changes caused by surgical stress, and surgical stimulation, may lead to severe myocardial ischemia and death in patients with cardiac amyloidosis.

In summary, patients with cardiac amyloidosis are at risk of fatal myocardial infarction at any time during and after surgery. Findings on routine preoperative examination as well as clinical signs are nonspecific. Abnormal ECG findings followed by examination by echocardiography can be used in the diagnosis of the disease or in the estimation of its severity. For a successful outcome, perioperative intensive cardiac care is mandatory.

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