



Forensic Pathological Identification Report of Early Death after Orthotopic Heart Transplantation: A Case Study

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Abstract: This report aims to determine the cause of death from a forensic pathological perspective in a case of early death after heart transplantation. Using methods such as external examination, autopsy, and histopathological examination, we analyze the multiple factors leading to death in this case, particularly focusing on the heart donor aspects. Heart donors must meet strict criteria regarding structural abnormalities, age, low body weight, cold ischemia time, donor infection, and poisoning, and heart function. However, this case suggests the need for further refinement of these standards. Preoperative pathological diagnosis of the donor heart is necessary to determine any primary diseases, establish pathological diagnostic standards, evaluate heart survival indices, and ensure the quality of life for recipients, thereby avoiding deaths caused by primary diseases of the donor heart.

Keywords: forensic pathology; autopsy examination; histopathological examination; early death after heart transplantation; heart donor selection

1. Basic Clinical Information of the Case

The patient was a 61-year-old male. On August 10, 2020, he was admitted due to chest discomfort and a history of dilated cardiomyopathy for eight years, with progressively worsening heart function. Clinical diagnosis: end-stage dilated cardiomyopathy. Hospitalization was recommended to await a donor for heart transplantation and to complete relevant preoperative examinations and symptomatic treatment. On the day of the heart transplantation, the patient was sent to the operating room under general anesthesia and cardiopulmonary bypass support after confirming the availability of a donor heart from a remote location. The donor heart had a warm ischemia time of 12 minutes and a cold ischemia time of 380 minutes. Upon arrival at the operating room, the heart transplantation was performed immediately, but difficulties in heart resuscitation were encountered during the operation. ECG showed significant acute anterior wall ischemia, and exploration revealed a significant stenosis in the proximal-middle segment of the left anterior descending artery. Therefore, an internal thoracic artery coronary artery bypass grafting was performed. Postoperatively, the heart resumed beating but required vasopressors and inotropes to maintain blood pressure and heart function. The patient developed heart failure that was difficult to improve and died on the sixth postoperative day (August 19, 2020). The hospital's clinical cause of death diagnosis was heart transplant status, multi-organ failure. However, the patient's family questioned the cause of death and the clinical management, leading to a medical dispute. To clarify the cause of death and properly resolve the dispute, a forensic pathological judicial identification was requested.

2. Findings from the Autopsy Examination

2.1 External Examination

The deceased was a middle-aged male, measuring 165 cm in height, with black and white hair of 6.0 cm in length and an obese body type. The head showed no abnormalities, and no significant fractures were palpable on the skull. The conjunctiva of both eyes and eyelids appeared pale without petechiae, and both corneas were cloudy, with the pupils bilaterally dilated and cloudy. The tongue was within the dental arch. The mucosa of the lips showed no abnormalities, and the left upper teeth numbered 1-3 were dentures, with the teeth arranged neatly. The nail beds of all ten fingers were mildly cyanotic, while the nail beds of both feet were normal. There was a sutured incision about 1 cm long on the right side of the neck. A longitudinal sutured incision approximately 26 cm long was present from the top of the sternum to the xiphoid process, with four additional sutured wounds of about 1 cm each below it. There were also sutured incisions of 1.0 cm on the right elbow crease and left wrist, a slanted 9.5 cm long sutured incision on the left groin, and a 1.0 cm sutured incision on the right groin. The left lower leg was wrapped with negative pressure suction dressing.

2.2 Internal Examination

A routine combined thoracoabdominal incision was made from the submandibular area to the pubic symphysis. The neck muscles showed no abnormalities, and there were no fractures of the thyroid cartilage or hyoid bone. The sternum was split in the middle, with four stabilizers in place. The chest wall had 1.0 cm thick fat, and no rib fractures were seen. There was 820 ml of dark brown fluid in the right pleural cavity and 700 ml in the left pleural cavity. No significant abnormalities were observed in the main bronchi, bilateral bronchi, or esophagus. The pericardial sac contained 155 ml of bloody fluid, and blood clots and absorbable hemostatic materials were attached to the base of the heart. The transplanted heart was examined in situ, with sutures in place at the superior and inferior vena cava, atria, and aorta, showing no abnormalities. The aortic arch appeared normal. The transplanted heart was significantly enlarged, with a substantial amount of fat tissue deposited on its surface. The left anterior descending artery's mid-upper segment showed changes due to the left internal mammary artery to coronary artery bypass grafting. The heart and lungs were removed together for further examination. Both lungs were edematous, with foamy liquid exuding from the cut surfaces upon compression; the left lung weighed 836 g, and the right lung weighed 901 g. Samples were taken and fixed for pathological examination. The transplanted heart, bypass graft, and aorta were removed as a whole and fixed for pathological examination.

The abdominal wall had 2.5 cm thick fat. The abdominal organs were in place, with no visible lesions or signs of injury. The stomach was empty, with a smooth mucosa. The intestines showed no ruptures, obstructions, ischemia, or necrosis, but there were scattered petechiae within a 9.0 cm x 8.0 cm area at the root of the mesentery. The liver weighed 1073 g, appeared gray-yellow, with a smooth capsule and yellow cut surface. The gallbladder was in the gallbladder bed, filled with bile, with a smooth mucosa. The spleen weighed 189 g, had a shrunken surface, and showed signs of ischemia. The kidneys weighed 217 g (left) and 208 g (right), with intact capsules and signs of ischemia, and a clear corticomedullary junction. The pancreas showed evident autolysis.

Routine scalp incisions revealed no significant abnormalities on the scalp surface. Both temporalis muscles showed no bleeding. The skull was sawed open, revealing no epidural or subdural hemorrhage, and no skull fractures were noted. The whole brain weighed 1263 g. No hemorrhages or contusions were observed in the cut surfaces of the cerebrum. The cerebellum and brainstem showed no significant surface or sectional hemorrhages or contusions.

2.3 Histopathological Examination

Samples from the aforementioned major tissues and organs were fixed in formalin solution, and the sections were prepared and observed under a microscope:

Brain, Cerebellum, and Brainstem: The pia mater and subarachnoid space showed no signs of hemorrhage or inflammation. The cortical neurons appeared normal in morphology and quantity, with no signs of contusion, hemorrhage, softening, or other ischemic changes.

Heart: Subepicardial tissue in both atria showed extensive fat infiltration. The myocardial fiber layer was thinned and disrupted by the infiltrating fat, presenting as island-like changes. Additionally, fat infiltration in the apex of the left ventricle was significant. Cardiac sections revealed myocardial fiber rupture, contraction band necrosis, and wavy changes. The endocardium was not significantly thickened, but subendocardial myocardial fibers were disorganized and presented a whorled pattern, with substantial fat infiltration in the subendocardial and interstitial regions. Some areas showed myocardial cell hypertrophy and swelling, while others exhibited atrophy and partial dissolution of myocardial fibers. The myocardial interstitium showed arteriosclerosis of small vessels, causing eccentric thickening of the vessel walls and approximately grade III stenosis. The subepicardial anterior descending branch of the coronary artery showed atherosclerotic changes with grade IV stenosis (Figure 1 and Figure 2).



Figure 1. Cardiac view showing significant deposition of adipose tissue in the atria, especially in the right atrium. Left ventricle and interventricular septum are obviously hypertrophic.

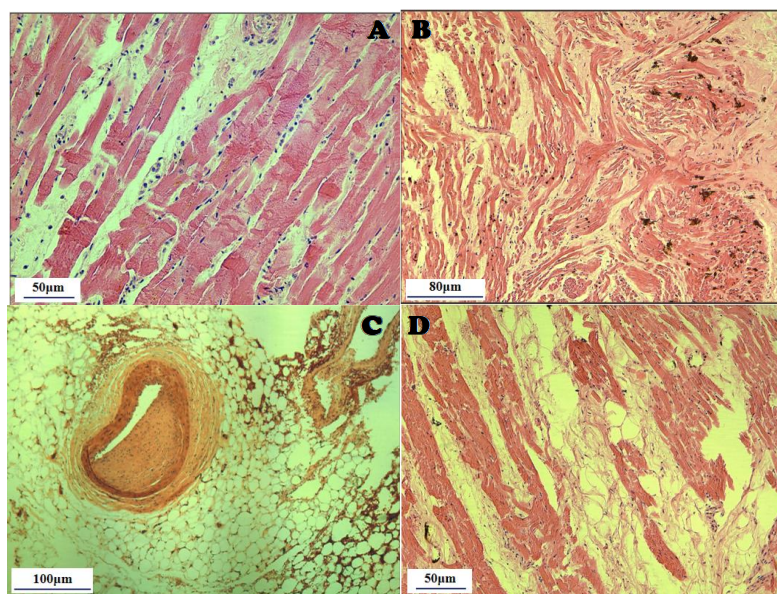


Figure 2. A shows extensive necrosis of contractile bands of myocardial fibers; B shows disorder of myocardial fibers and fibrous hyperplasia; C shows significant intimal hyperplasia and high stenosis of distal lumen in anterior descending coronary artery; D shows obvious fat tissue infiltration and myolysis among myocardial fibers.

Lung Tissue: The pleura was not significantly thickened, and no apparent inflammatory tissue was observed in the lumens of the small and terminal bronchi. Some areas showed alveolar collapse and carbon deposition. Other areas showed pulmonary edema, congestion of small blood vessels, and focal inflammation in localized regions. The pulmonary interstitium displayed arteriosclerosis of small blood vessels.

Liver Tissue: The hepatic lobular structure was normal. Hepatocytes showed signs of lysis and partial fatty degeneration, with no abnormalities in the portal tracts.

Spleen Tissue: The capsule was intact, with clear red and white pulp structures. The germinal centers of the lymphoid follicles appeared normal. The splenic arterioles displayed thickened, sclerotic walls, and the splenic cords were thickened.

Kidney Tissue: The glomerular capillary tufts in the cortical region were swollen, with cloudy proximal tubular cells and focal inflammatory cell infiltration in the interstitium. Some glomeruli exhibited fibrosis and hyalinization. The distal convoluted tubules and collecting ducts in the medullary region showed no significant abnormalities, but the interstitium was edematous. The renal arterioles had thickened walls, and the small blood vessels were congested.

3. Examination of the Fixed Transplanted Heart

The transverse short-axis slicing method was used to examine the transplanted heart.

The weight of the heart ventricles was 367 grams (excluding the atria and aorta). A large amount of fat tissue was deposited on the heart's surface, particularly on the left and right atria, right ventricle, and apex. The left atrial wall thickness was 1.8 cm (with a fat layer thickness of 1.5 cm), and the left ventricular wall thickness was 1.6 cm. The right atrial wall thickness was 2.3 cm (with a fat layer thickness of 2.0 cm), and the right ventricular wall thickness was 0.7 cm. The interventricular septum was 1.9 cm thick. The circumferences of the aortic, mitral, tricuspid, and pulmonary valves were 6.0 cm, 7.0 cm, 8.0 cm, and 8.5 cm, respectively. No abnormalities were observed in the heart valves. The left and right ventricular chambers were slightly reduced, the interventricular septum was slightly thickened, and the papillary muscles were coarse. No abnormalities were found at the openings of the left and right coronary arteries. The lumen of the left anterior descending branch of the coronary artery was narrowed. The lumen of the internal mammary artery used for the bypass was patent without narrowing, but the distal coronary artery lumen at the bypass site was narrowed.

4. Discussion

Heart transplantation involves the complete removal of a human heart from a donor who has been declared brain-dead and successfully matched, and its implantation into the chest cavity of the recipient. This allogeneic transplantation surgery primarily targets end-stage congestive heart failure and severe coronary artery disease. The origin of heart transplantation dates back to 1967 when Christian Barnard performed the world's first clinical heart transplant in South Africa, with the patient surviving for 18 days [1]. In China, the first heart transplant was performed in 1978 by Zhang Shize and others at

Shanghai Ruijin Hospital, which was also the first in-situ heart transplant in Asia, with the patient surviving for 109 days.

In this case, the identified person died 6 days after undergoing an in-situ heart transplantation. Through autopsy and pathological section examination under a microscope, it was found that the transplanted heart of the identified person had significant underlying pathological changes. These changes were primarily manifested as the deposition of a large amount of adipose tissue on the surface of the heart, especially on the left and right atria and ventricles, resulting in an increased heart size and weight. The circumferences of the mitral and tricuspid valves were reduced, and there was significant narrowing of the left coronary artery's anterior descending branch. Microscopically, there was notable adipose tissue infiltration in the left and right atria, myocardial fiber atrophy, fragmentation, subendocardial adipose tissue infiltration, and scattered disorganized whorled arrangement of myocardial fibers. There was also hypertrophy of myocardial cells, atrophy of myocardial cells in some areas, a reduction in the number of myocardial cells, and interstitial hyperplasia. The degree of coronary artery stenosis in the subepicardial anterior descending branch was Grade IV, and the stenosis of small arterioles in the myocardial interstitium was Grade III. Additionally, the transplanted heart showed pathological signs of acute myocardial ischemia, such as myocardial cell degeneration, contraction band necrosis, waviness, and fragmentation of myocardial fibers. These pathological findings indicate that the transplanted heart had characteristics of adipositas cordis, hypertensive heart disease, coronary atherosclerotic heart disease with severe narrowing of the left anterior descending branch, as well as ischemia-reperfusion injury characteristics post-transplantation.

The findings of this forensic examination indicate that the transplanted heart had significant characteristics of adipositas cordis, hypertensive heart disease, and coronary heart disease with severe stenosis of the left anterior descending branch. During the transplantation, an internal mammary artery-left coronary artery anterior descending branch bypass was performed. However, severe stenosis remained in the mid-distal segment of the anterior descending branch post-bypass, leading to ischemic impact of Grade IV. Combined with the severe adipositas cordis, the duration of extracorporeal time, and ischemia-reperfusion factors, the transplanted heart exhibited clinical manifestations of arrhythmia and heart failure, ultimately resulting in death due to circulatory failure and multiple organ failure.

Post-heart transplantation complications can occur at different stages, including right ventricular failure, ischemia-reperfusion injury, acute rejection, Quilty lesions, infection, and chronic rejection characterized by transplant coronary artery disease. Endomyocardial biopsy (EMB) is currently the most accurate diagnostic method for these complications [2], but ensuring the recipient's quality of life is paramount, making the selection of a healthy donor heart extremely important.

This case is a classic example of post-heart transplantation death. Forensic pathological examination revealed that the transplanted heart had significant characteristics of adipositas cordis, hypertensive heart disease, and coronary heart disease with severe stenosis of the left anterior descending branch as the main cause of death. With the rapid development of China's economy and the improvement of national literacy levels, both heart donors and heart transplant surgeries are increasing. To reduce postoperative mortality and extend survival time, strict standards must be adhered to regarding donor heart structural abnormalities, age, body mass, cold ischemia time, donor infection, and toxicity, and donor heart function. Only those meeting these standards should undergo surgery [3,4]. However, this case suggests that these standards need further refinement, and preoperative pathological diagnosis of the donor heart is necessary to determine if there are any primary diseases. Establishing pathological diagnostic criteria and assessing the heart's viability index aims to ensure the quality of life for the heart and the recipient, avoiding deaths due to primary diseases of the donor heart.

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