

Visceral Pleural Lung Graft for Myocardial Injury: Case Report

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The literature is sparse regarding the treatment of myocardial substance loss.¹ Immediate thoracotomy and cardiorrhaphy have been used in the past primarily for the purpose of hemostasis.² However, such a technique renders the area of damaged myocardium unvascularized and thus nonfunctional. Research efforts are needed to explore various ways to provide blood supply to as well as tissue replacement of ischemic myocardium. We present a case of myocardial muscle loss caused by a missile and its repair with a visceral pleural lung (VPL) graft that may prove to be helpful in such a situation.

CASE REPORT

An 18-year-old African-American male patient was admitted to the Harlem Hospital emergency room after having sustained three gunshot wounds. The first of these was to the fourth intercostal space to the left of the sternum. The second was to the left chest at the level of the eighth intercostal space. The third bullet was to the left flank. The patient had a palpable blood pressure only, which was recorded as 88 mm Hg. In the emergency room, a closed left thoracotomy tube drainage was instituted that drained 1800 mL of blood. Chest and abdominal radiographs were consistent with a diagnosis of a left hemothorax and a chip fracture of the left iliac crest. In addition, a bullet was detected in the epigastrium. Fluid resuscitation with lactated Ringer's was started, and the patient was taken to the operating room within 20 minutes.

Abdominal exploration revealed a through and through gunshot wound of the stomach and splenic flexure. These injuries were repaired first. Because of continuous bleeding from the left thoracostomy tube (an additional 1000 mL of blood at this time), an exploratory left anterolateral thoracotomy was then performed. Exposure revealed a left thoracic cavity filled with blood. Active bleeding from the lower lobe and lingula of the left lung was controlled by partial lung resections with TA-90 and TA-50 staples. Further exploration revealed bleeding from the heart, requiring a pericardiectomy and revealing injury to the left ventricular wall with gross loss of myocardium. The large caliber bullet, exiting through the

anterior chest, had tangentially taken away part of the left ventricular wall, leaving a crater of $3 \times 2 \times 1.5$ cm, pulsating at its center with intact endocardium. The patient had intraoperative electrocardiographic evidence of an anterolateral infarction. Attempts were made to close the open heart muscle defect using pericardial plaquets, but the damaged muscle would not hold the sutures. An improvised new technique was then applied. A flat piece of the resected lingula, with intact visceral pleura, measuring 0.5 cm in thickness was used to patch the myocardial defect. The graft was sutured from the visceral pleural side toward the epicardium, a free VPL graft, with interrupted 3-0 silk sutures; hemostasis was achieved in a matter of minutes (see Fig. 1).

At final exploration, no active bleeding was noted. An additional left thoracostomy tube was inserted and the chest was closed. In total, the patient received 14 units of packed red blood cells, 2000 mL of cell saver, 6 units of fresh frozen plasma, and 12 units of platelets. Anesthesia was tolerated without complications. The patient was transferred the following day to Columbia Presbyterian Medical Center (CPMC) for observation in the cardiac intensive care unit for expectant management of the left ventricular injury where an open-heart procedure might be required.

On postoperative day 1, the temperature rose to 38.7°C. All other vital signs were stable. The cardiac examination revealed a regular rate and rhythm without any rub, murmur, or gallop. Decreased breath sounds were heard at bilateral lung bases, indicative of some atelectasis.

The CPMC admission chest radiograph revealed an enlarged mediastinum and a left pleural effusion with left lower lobe haziness. The electrocardiogram (EKG) showed sinus tachycardia of 112 with ST elevations in leads I and V3-V6. The hematocrit at admission was 32, and the blood urea nitrogen/creatinine ratio was 11/1.1.

On hospital day 2, the patient was afebrile. The abdominal distension decreased and the nasogastric tube was discontinued. He was transferred out of the cardiac intensive care unit and advanced to a clear diet, which he tolerated well. By hospital day 3, he was having normal bowel movements and was tolerating a regular diet. The patient underwent cardiopulmonary rehabilitation. With respect to his cardiac condition, the patient remained in normal sinus rhythm, and telemetry was discontinued on day 3. He was treated with 3.1 g i.v. of Timentin (SmithKline Beecham, Philadelphia, Pa) until day 3 (which was postoperative day 5), when it was discon-

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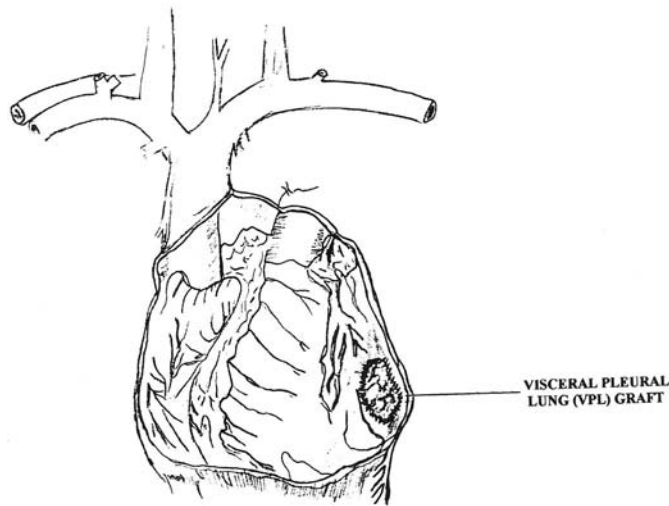


FIG 1. Illustration of VPL graft.

tinued. Serial chest radiographs continued to show persistent bibasilar atelectasis, and serial EKGs consistently revealed ST elevations in the anterolateral chest leads. The patient remained afebrile with a normal white blood cell count. On the 6th postoperative day, the chest tube was removed. The patient was discharged home in stable condition on the 7th postoperative day.

The patient was lost to follow-up until June 1998, when a repeat EKG was obtained. It revealed evidence of anterolateral ischemia and when compared with the patient's previous EKG, the most probable diagnosis was a subendocardial infarct.

DISCUSSION

Patches of adjacent pericardium as well as omentum have been used in the past for the replacement of myocardial loss. In addition, intercostal muscle, serving as a vascularized pedicle, as well as a patch of diaphragm have also been previously reported to repair myocardial defects. We now propose an additional alternative for such a situation, i.e., a VPL graft. The possibility exists that the free VPL graft may have acted as a myocardial cover for heart muscle substance loss, providing both a hemostatic as well as structural basis for healing without rupture of the ventricle. For research purposes, we also propose the model of a free or pedicle VPL graft possessing the potential to act as a matrix for the growth of heart muscle under the influence of insulin-like growth factor-I (IGF-I) or growth hormone.

Animal studies have shown that enhanced cellularity of the small intestine occurs with the administration of growth hormone. Byrne et al.³ hypothesize that the administration of growth factors (e.g., growth hormone) could enhance further compensation of the remnant intestine (in patients having undergone intestinal resection) and thereby improve absorption. They demonstrated a 39% improvement in absorption in such patients on a regimen of diet plus glutamine plus growth hormone.³ Davis et al.⁴ have treated mouse embryonic fibroblasts with 5-azacytidine and successfully converted them to myoblasts at a frequency suggesting alteration of one or only a few closely linked regulatory loci. Myogenesis was re-

ported to have occurred in some of these cell lines.⁴ Furthermore, Florini et al.⁵ reported that "the IGF's play a central role in the control of growth and differentiation of skeletal muscle." Such a role is emphasized by the results of gene knockout experiments in which it has been found that muscle formation is severely reduced or eliminated when an IGF gene is inactivated.⁵

The above studies describe the beneficial effects of growth factors regarding cellularity and function (of intestinal cells) as well as supporting evidence for the potential conversion of one primitive cell type (fibroblasts) into another (myoblasts). Inspired by the work of the aforementioned researchers, our goal was to create a matrix by which fibroblasts can be converted to myoblasts, ultimately culminating in new muscle growth. A VPL graft is proposed as the matrix for such a conversion to take place: embryonic fibroblasts could be injected into the graft (after harvest but before transplantation) and subsequently treated with 5-azacytidine. Lung tissue, composed primarily of alveolar and connective tissue cells (as opposed to muscle cells) could potentially provide a better environment for embryonic fibroblast survival. In addition, after the transplantation of the VPL graft, the influence of the well-defined trophic effects of administered growth factors (e.g., IGF-I or growth hormone) could potentiate myoblast growth and differentiation.

Another potential avenue of research in the attempt to repair infarcted myocardium would be the transplantation of myoblasts or fetal cardiomyocytes directly into the VPL graft (after suturing the lung tissue to the myocardium). Engrafted fetal cells are a potential source of growth factors and can be used for cardiomyocyte-based gene therapy. Leor et al.⁶ induced myocardial infarctions in rats and then injected fragments of cultured human fetal ventricles into the myocardial scar. Their results showed that the engrafted fetal tissues stained positive for alpha-actin, commonly expressed in human cardiomyocytes, but highly unusual for adult rat myocardium. They concluded that "fetal myocyte tissue can be implanted and survive in the infarcted myocardium".⁶ Furthermore, Scorsin et al.⁷ demonstrated the "feasibility of transplanting allogeneic cardiomyocytes into the border zone of myocardial infarction areas." Transplantation of cardiomyocytes along the VPL graft-myocardial interface (a myocardial infarction border zone) certainly makes theoretical sense on the basis of such data. It is important to remember that the VPL graft would serve two purposes in such a model: it would function as a matrix for myocyte growth and also behave as a myocardial cover for heart muscle substance loss. Finally, Van Meter et al.⁸ subjected adult swine to transplantation of neonatal porcine myocytes (allogeneic), murine atrial tumor cells (xenogeneic), and human fetal cardiomyocytes (xenogeneic) into the left ventricular wall. The transplanted cells formed close associations with host myocytes, contained myofibrils and other cell architecture resembling the transplanted cell lines, and appeared to produce an angiogenic influence resulting in the proliferation of surrounding microvasculature. They believed that "these findings indicate successful xenogeneic and allogeneic myoblast cell transplantation in a large animal model."⁸ Such research

opens up several potential research projects with not only VPL graft allogeneic transplantation, but with xenogeneic transplantation as well.

It is important to note that the length of follow-up in the described case is approximately 20 months. Further follow-up is certainly mandated, because such an individual is at increased risk for a ventricular aneurysm. The patient, therefore, will require additional medical examinations for the next several years. He is currently, however, without any cardiac or respiratory symptoms.

In summary, we propose several avenues of research as potential mechanisms of repair of injured myocardium. The use of transplanted growth factors, embryonic fibroblasts, and/or fetal myocytes in conjunction with the use of a VPL graft (for the purpose of serving as a matrix as well as providing both hemostatic and structural support) is described in detail. These proposals hope to set the stage for future studies to assess the feasibility of a VPL graft as well as the ability of these transplanted cells to survive, contract, and potentially repair infarcted myocardium. Such models may have future implications in the treatment of myocardial muscle loss, regardless of the cause.

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