

# Coronary Artery Stenosis Caused by Primary Malignant Pericardial Mesothelioma in a 76-Year-Old Man

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*This report describes a 76-year-old man with diabetes mellitus who developed coronary artery stenosis from infiltration of a primary malignant pericardial mesothelioma. Three months before referral to the treating hospital, elevated liver function values and cardiac enzymes led to echocardiography, which revealed a motion abnormality in the anterior wall of the heart. The patient was diagnosed with congestive heart failure and admitted to the hospital, where chest computed tomography showed a tumor above the left atrial appendage that compressed the origin of the left anterior descending artery. He was referred to the treating hospital for surgery. Minimally invasive direct coronary artery bypass grafting was performed, but the mass was not resected because of its infiltrating nature and the potential for medical complications. Histologic examination of a biopsy specimen confirmed a primary malignant pericardial mesothelioma. The bypass procedure resolved the coronary artery stenosis caused by the tumor. Although the optimal treatment for primary malignant pericardial mesothelioma is controversial, minimally invasive methods, such as minimally invasive direct coronary artery bypass grafting, may be used successfully. (Tex Heart Inst J. 2022; 49(6):e207456)*

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**P**Primary malignant pericardial mesothelioma (PMPM) is an extremely rare tumor that has a poor prognosis because its asymptomatic nature delays detection.<sup>1,2</sup> There are no reports of minimally invasive direct coronary artery bypass grafting (MID-CAB) used to treat coronary artery stenosis caused by cardiac tumors, including PMPM. This report describes a successful application of MID-CAB for a patient with an infiltrating PMPM causing coronary artery stenosis. Herein, the team reports the first case, to their knowledge, in which MID-CAB was attempted for coronary artery stenosis caused by PMPM.

## Case Report

A 76-year-old man was noted to have elevated liver function values during a routine medical checkup. He was a nonsmoker with a history of insulin-dependent diabetes mellitus. His job as an electrician placed him at high risk for asbestos exposure, but there was no known specific exposure and no information about whether a *BAP1* mutation was present. He had no chest pain, dyspnea, or peripheral edema. Further laboratory testing revealed elevated cardiac enzymes, and echocardiography showed a dilated left ventricle (end-diastolic dimension, 58 mm), moderately reduced ejection fraction (36%), and a motion abnormality in the anterior wall of the heart (Fig. 1A).

The patient was diagnosed with congestive heart failure (HF) and admitted to the hospital, where chest computed tomography (CT) revealed a tumor measuring 35 mm × 78 mm extending from the left atrial appendage to the left pulmonary artery. A small pericardial effusion was present, and the mediastinal lymph nodes were enlarged (Fig. 1B). There was no pleural calcification or pleural effusion. Contrast-enhanced magnetic resonance imaging of the chest showed high intensity on T1-weighted images just above the left atrium, with thinning of the myocardium from the anterior wall to the anterior septum. Myocardial perfusion single-photon emission

CT demonstrated decreased blood flow in the region of the left anterior descending (LAD) coronary artery. Fluorodeoxyglucose (FDG) positron emission tomography showed abnormal uptake of FDG around the left atrium (diameter, 70 mm) and in a mediastinal lymph node (Fig. 1C). There was no evidence of metastasis or of a different primary tumor (Fig. 1D). Coronary CT showed compression causing 90% stenosis at the origin of the LAD, without calcification (Fig. 2).

The patient was discharged from the hospital after testing was completed; he remained asymptomatic. Three months later, outpatient contrast-enhanced CT showed that the tumor had grown by approximately 5 mm and was infiltrating the surrounding area of the heart; malignancy was suspected, with hemangiosarcoma and malignant lymphoma included in the differential diagnosis based on the imaging findings. Elevated blood levels of soluble interleukin-2 receptor (1,120 U/mL) supported the possibility of malignant lymphoma. At this point, the possibility of a primary pericardial malignancy was not considered.

The patient was referred to the treating hospital for surgical intervention. On arrival, his vital signs were stable, and physical examination showed no abnormalities. Laboratory testing revealed normal liver function but uncontrolled diabetes mellitus (hemoglobin A<sub>1c</sub>, 8.4%) and active inflammation (C-reactive protein, 8.35 mg/dL). Electrocardiography revealed abnormal Q waves on leads V<sub>1</sub> through V<sub>3</sub>, left anterior fascicular block, and complete right bundle branch block. No abnormalities were seen on chest radiography (cardiothoracic ratio, 54.5%). Transesophageal echocardiography demonstrated impaired left ventricular function (ejection fraction, 36.3%) and a dilated left ventricle (end-diastolic dimension, 67.8 mm) and left atrium (diameter, 41.5 mm). A tumor was observed extending from the ascending aorta and encircling the left pulmonary artery and the lateral wall of the left ventricle. No thrombus was noted in the left atrial appendage. The left main coronary artery was absent; the LAD and left circumflex artery had anomalous origins in the sinus of Valsalva.

Because percutaneous coronary intervention in a patient with anomalous coronary arteries is difficult, the surgeons initially planned to perform coronary artery bypass grafting and tumor resection through a median sternotomy. However, the possibility of infection with uncontrolled diabetes mellitus and the difficulty of resecting a tumor exhibiting myocardial infiltration prompted a revised approach. The surgeons decided to perform MID-CAB with a tumor biopsy, with postoperative chemotherapy and radiation pending the pathology results.

## Technique

The surgery was performed via a left fifth intercostal thoracotomy. The left internal thoracic artery (LITA)-to-LAD anastomosis was completed without any difficulty, but the field of view during MID-CAB was so narrow that the surgeons could not visualize the entire tumor and were unable to identify the enlarged lymph node because of dense adhesions. Thus, the lymph nodes could not be sampled and only the pericardium was biopsied. Frozen section examination during the operation of the pericardium biopsy revealed atypical epithelial cell proliferation and fatty tissue infiltration suggestive of malignancy. Histopathologic evaluation of a pericardial biopsy revealed proliferation of epithelioid cells with acidophilic cytoplasm and atypical nuclei (Fig. 3A). Immunohistochemical staining was strongly positive for calretinin (Fig. 3B), cytokeratin, D2-40, and WT1. The final diagnosis was malignant pericardial epithelioid mesothelioma.

## Follow-Up

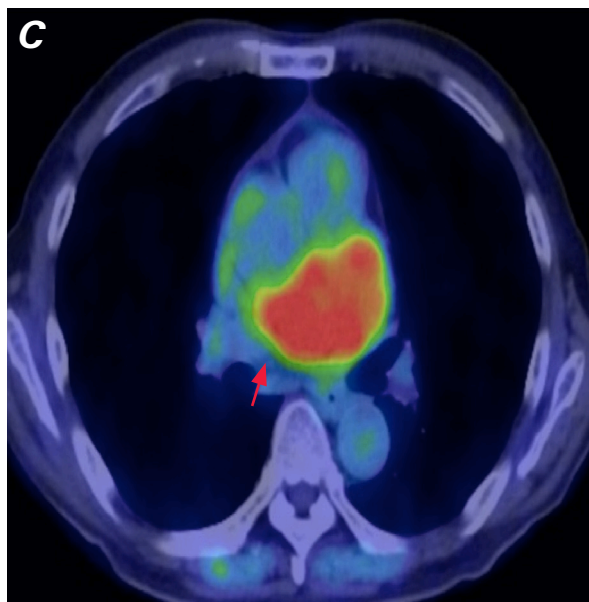
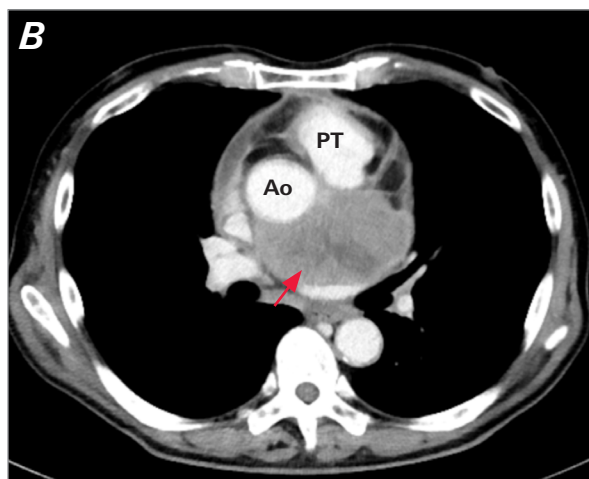
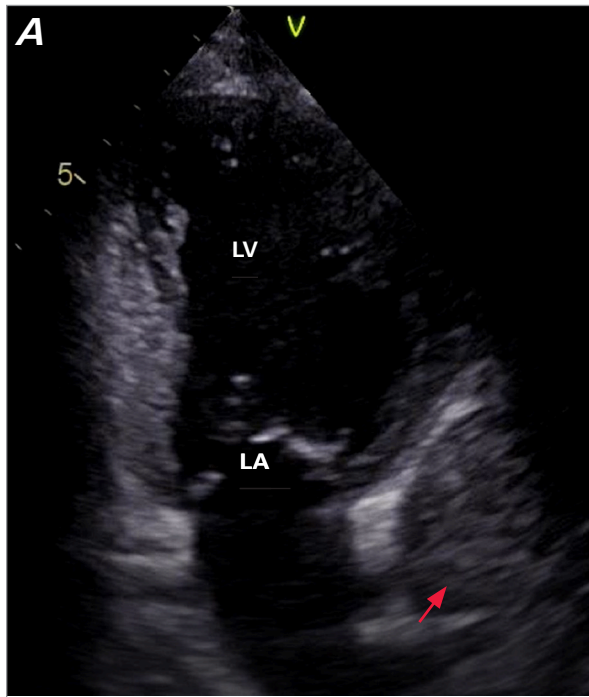
The patient was extubated on postoperative day (POD) 1 and recovered quickly. He was transferred from the intensive care unit to the ward on POD 4. Coronary CT on POD 7 confirmed the patency of the LITA-LAD anastomosis. On POD 14, he was discharged without any complications. The patient started chemotherapy with carboplatin and pemetrexed 1 month after hospital discharge.

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## Discussion

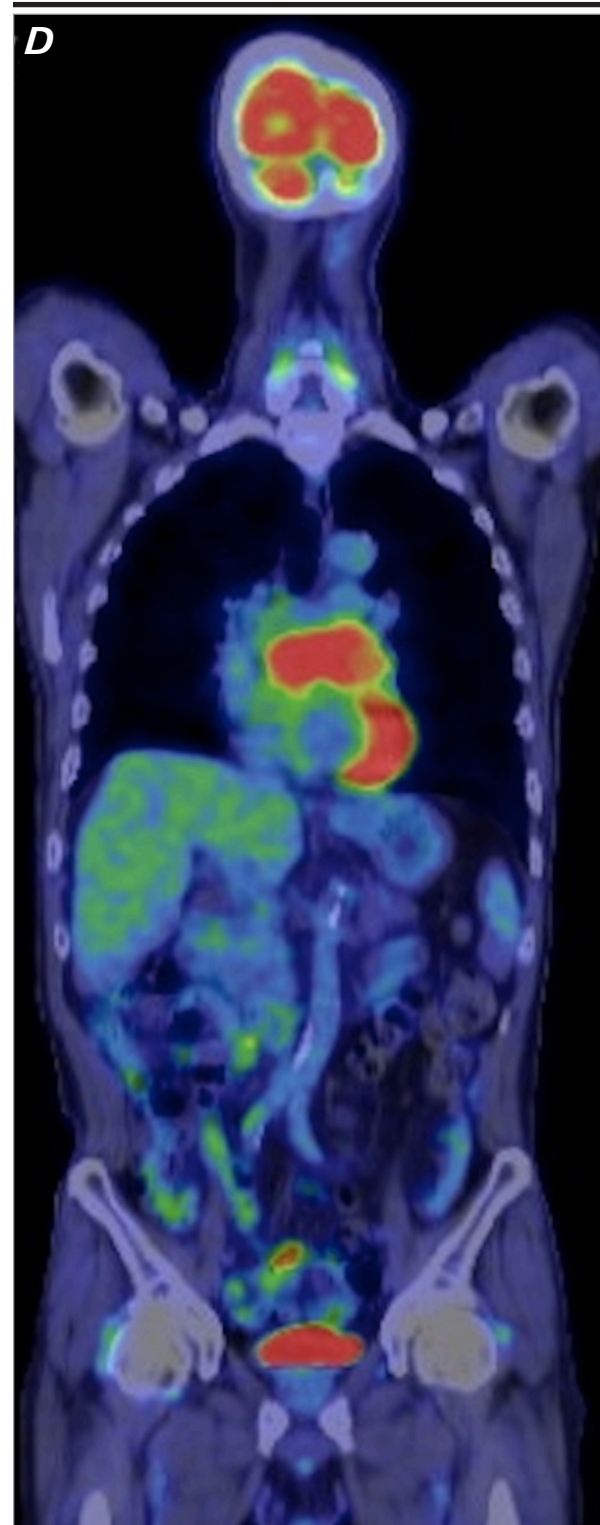
Although PMPM is extremely rare, with an incidence of less than 0.0022%, it accounts for up to 50% of primary malignant pericardial tumors<sup>1,2</sup> and is the third most common primary malignant cardiac tumor, after hemangiosarcoma and rhabdomyosarcoma.<sup>3,4</sup> Because it was not possible to determine the origin of this patient's tumor from the imaging studies, the differential diagnosis included primary cardiac malignant tumors and metastatic lesions from primary cancers including lymphoma, melanoma, or lung cancer. It was not possible to reach a definitive diagnosis without pathologic examination of tissue.

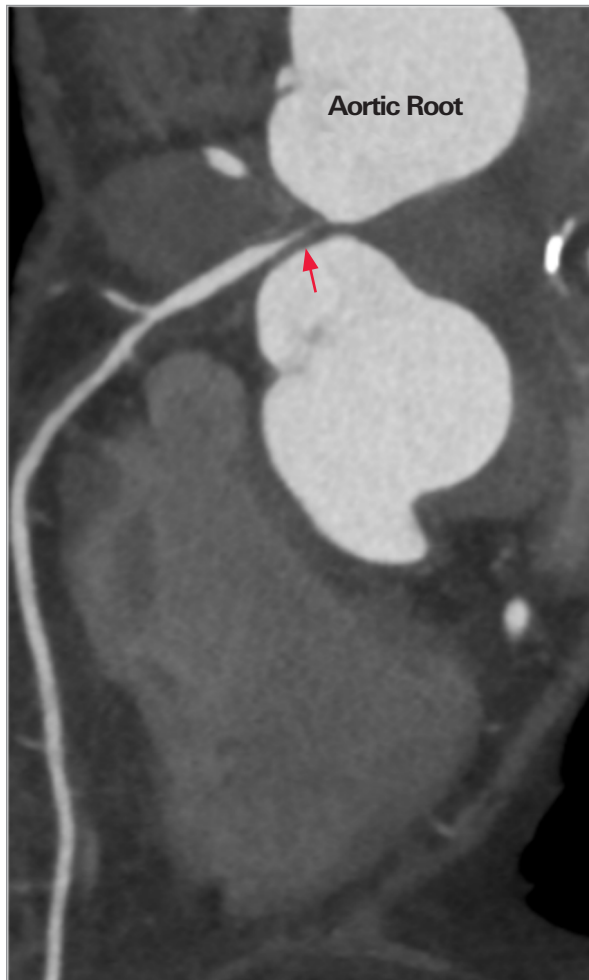
The clinical manifestations of pericardial mesothelioma are constrictive pericarditis, pulmonary embolism, cardiac tamponade, and HF caused by myocardial infiltration.<sup>3,5</sup> The most common causes of death are cardiac tamponade and HF.<sup>2</sup> However, nonspecific symptoms and long asymptomatic periods make early, accurate diagnosis difficult<sup>6</sup>; only 25% to 30% of patients are diagnosed before death.<sup>3,7,8</sup> In this asymptomatic patient, the tumor was found incidentally on CT scan, but the tumor invasion was advanced; this finding is consistent with those of previous studies showing a poor prognosis



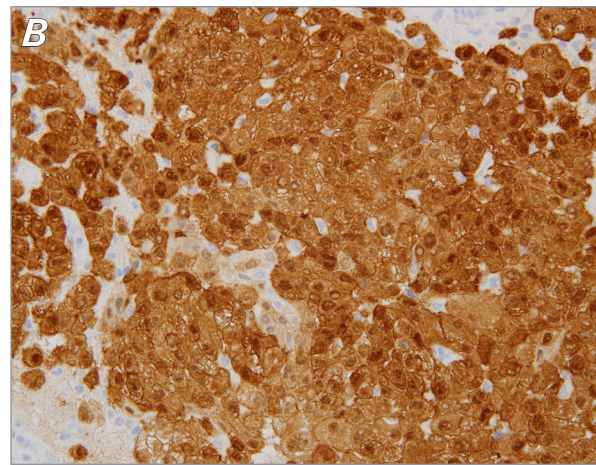
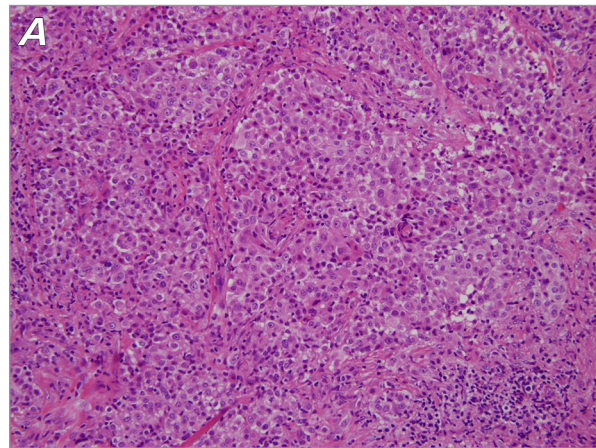
**Fig. 1** **A)** Preoperative transthoracic echocardiography shows a hypoechoic mass around the left atrial appendage (arrow); **B)** enhanced computed tomography shows a low-density area between the aorta and pulmonary trunk (arrow); **C)** FDG-positron emission tomography reveals abnormal uptake of FDG at the left atrium (arrow); **D)** the abnormal FDG uptake is confined to the pericardium.

Ao, aorta; FDG, fluorodeoxyglucose; LA, left atrium; LV, left ventricle; PT, pulmonary trunk.





**Fig. 2** Coronary computed tomography shows narrowing of the origin of the left anterior descending coronary artery caused by tumor invasion (arrow).



**Fig. 3** Photomicrographs of pericardial biopsy sections show **A)** proliferation of epithelioid cells with acidophilic cytoplasm and atypical nuclei (hematoxylin and eosin staining; magnification  $\times 20$ ); **B)** positive immunohistochemical staining for calretinin (magnification  $\times 40$ ).

once PMPM is discovered. The median survival time from symptom onset is reportedly 3 to 11 months.<sup>2,9</sup>

The diagnosis of PMPM is challenging. The lack of characteristic imaging findings, low prevalence, and nonspecific symptoms mean that pathologic diagnosis is typically required. Primary malignant pericardial mesothelioma can occur as a local solid tumor, a plaque-like thickening, or a diffuse infiltrate in the pericardium and adjacent structures, as in this patient. Pleural calcification is characteristically seen on imaging with pleural mesothelioma, but primary calcification in PMPM is not typical.<sup>10</sup>

Currently, no standard treatment for PMPM exists; however, surgery, chemotherapy, and radiation are commonly used as palliative therapy. Surgery plays a limited role in PMPM because of the high mortality associated with this tumor. Tumor resection is effective if the tumors are minimally adherent and localized; long-term survival is expected for patients in whom total resection is possible. However, this is a rare situation because few patients have resectable tumors at diagnosis. The most

frequently used techniques for patients with advanced PMPM are palliative surgery and pericardiectomy for palliation of symptoms. A pericardial window can be helpful for delivering chemotherapy.<sup>5,11</sup>

There are no previous reports of MID-CAB being used to treat coronary artery stenosis caused by PMPM or other cardiac tumors. Although asymptomatic, the patient in this report had mild congestive HF and a cardiac mass of unknown etiology. The decision to perform surgery was the correct one. Opinions vary on using bypass for coronary stenosis caused by PMPM, which has a poor prognosis. In this case, because of the fast growth of the tumor, myocardial ischemia could occur before chemotherapy and radiation therapy could be administered; therefore, bypass grafting was indicated. Although a tumor biopsy was considered, a medial sternotomy would put this patient at high risk for postoperative mediastinitis because of his uncontrolled diabetes. In addition, the results of the preoperative examinations indicated that the tumor was highly adherent and would be difficult to resect. In fact, the narrow

field of view during MID-CAB did not allow the full extent of the tumor to be visualized, and resection was impossible because of the dense adhesions. Adequate preparation for tumor resection will be required if the surgeons encounter similar patients in the future. However, given that total tumor resection is difficult for advanced-stage PMPM—and that most patients present with advanced PMPM—minimally invasive treatment, such as MID-CAB, may be reasonable and effective as palliative treatment.

## Conclusion

Although PMPM is an extremely rare and highly malignant tumor, the patient in this report was able to undergo effective and safe treatment of the resultant coronary artery constriction with MID-CAB. Optimal treatment for PMPM remains controversial, but minimally invasive approaches, such as MID-CAB, may be used as palliative therapy. More patients need to be studied to provide further validation of our findings.

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