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MINI-FOCUS ISSUE: HEART FAILURE

INTERMEDIATE

CASE REPORT: CLINICAL CASE

A Boulder in the Chest

Case of Massive Pulmonary Artery Sarcoma

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ABSTRACT

A 79-year-old woman presented with dyspnea and cough. Workup revealed a pulmonary artery mass. After undergoing surgery, she was treated with adjuvant immunotherapy for an undifferentiated pulmonary artery sarcoma. Fifteen months after surgery, there was no evidence of recurrence. The case is discussed, imaging presented, and the published reports reviewed. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:1532–5) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 79-year-old retired nurse presented with 5 days of progressive dyspnea and dry cough. Outside hospital computed tomography angiography (Video 1) demonstrated a lobulated low-attenuation intraluminal mass in the right ventricular (RV) outflow tract (RVOT), extending into the right pulmonary artery (PA), and small filling defects in the distal segmental PA branches. She was started on heparin and transferred to our hospital. On presentation, she was afebrile with a heart rate of 81 beats/min, blood pressure 113/73 mm Hg, respiratory rate of 20 breaths/min, and oxygen saturation of 96% on room air. On exam, she appeared well and in no acute distress, and had clear bilateral breath sounds with no increased work of breathing. On cardiac exam, she had a regular rate and rhythm, normal S1 and S2, and an III/VI crescendo systolic murmur at the left upper sternal border. The abdomen was soft and nontender, and extremities were warm and well perfused, without edema.

LEARNING OBJECTIVES

- To recognize pulmonary artery sarcomas on imaging and understand their presentation, epidemiology, workup, treatment, and prognosis.

PAST MEDICAL HISTORY

Past medical history was significant for hypertension, hyperlipidemia, glaucoma, and stage III chronic kidney disease. She had a surgical history of cholecystectomy and hysterectomy.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis at this point included pulmonary artery thromboembolism and pulmonary artery tumor.

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INVESTIGATIONS

Transthoracic echocardiogram (Video 2) showed an ejection fraction of 55% to 60%, moderately enlarged RV, and moderately reduced RV function with flattening of the interventricular septum throughout the cardiac cycle consistent with RV pressure and volume overload. There was moderate tricuspid regurgitation. A large heterogenous mass was seen attached to the RV measuring approximately 5.3 by 3.2 cm and prolapsing across the pulmonic valve, partially obstructing the RVOT. The peak gradient across the pulmonic valve was 74 mm Hg with peak velocity 4.3 m/s. Only trace pulmonic insufficiency was noted. Estimated RV systolic pressure was 89 mm Hg. Cardiac magnetic resonance imaging (MRI) (Video 3) revealed an enhancing RVOT mass consistent with PA sarcoma causing RVOT and pulmonic valve obstruction with increased pressure and size of the right-sided chambers, as well as filling defects in the segmental PAs. Fluorodeoxyglucose (FDG)-positron emission tomography scan showed this mass to be hypermetabolic, along with several hypermetabolic lung nodules, increasing the concern for malignancy. Pre-operative coronary angiography revealed no significant coronary disease.

MANAGEMENT

The patient was taken to the operating room for surgical excision of the mass. In the operating room, we observed a very large, broad-based mass filling a large part of the RVOT near the atrioventricular groove, extending from the tricuspid annulus to pulmonic valve annulus and protruding through the pulmonic valve (Videos 4 and 5, **Figure 1**). Upon opening the right PA, another large mass was seen occupying most of the lumen with extension into the lobar branches of the right PA. Frozen sections were sent that identified thrombus. There was no obvious infiltration of the tumors into the epicardial surface; however, given the intraluminal extension and involvement of intracardiac structures, it was judged that complete resection would result in an irreparable RV defect and possible injury to the left and right coronary arteries. As a result, we performed a palliative debulking procedure, pulmonic valve replacement, and pulmonary thromboendarterectomy.

Pathology identified an undifferentiated pleomorphic sarcoma with distribution typical for an intimal sarcoma. It was noted to be arising from the subendocardium and intima of the PA. Programmed death-ligand 1 (PD-L1) testing with partial membranous staining demonstrated nearly 90% of tumor infiltrating immune cells strongly positive for PD-L1. Mouse double minute 2 homolog (mdm2) staining was negative.

Post-operatively, the patient initially required support for mixed cardiogenic and vasoplegic shock with inotropes, vasopressors, and inhaled pulmonary vasodilators. She had a mild acute chronic kidney injury, from which she ultimately recovered. After about a month in the hospital, she was discharged to acute in-patient rehab, where she was started on immunotherapy with pembrolizumab for this strongly PD-L1 tumor.

ABBREVIATIONS AND ACRONYMS

FDG = fluorodeoxyglucose

MRI = magnetic resonance imaging

PA = pulmonary artery

PD-L1 = programmed death-ligand 1

PE = pulmonary embolism

PPAS = primary pulmonary artery sarcoma

RV = right ventricle

RVOT = right ventricular outflow tract

DISCUSSION

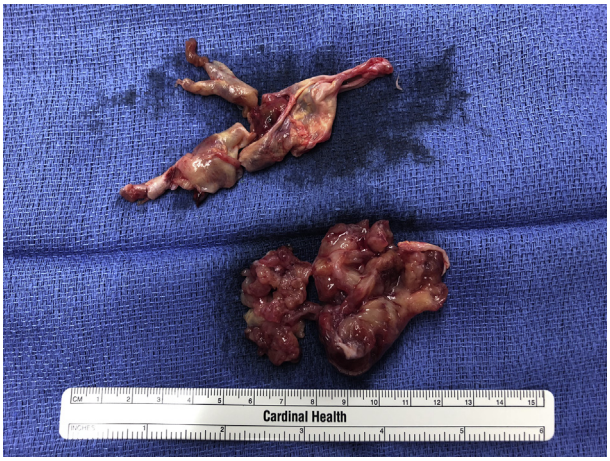
Primary PA sarcoma (PPAS) is rare, with only several hundred cases reported in the published reports. A retrospective report covering 20 years from the Cleveland Clinic identified just 10 cases (1). One reason for its rarity may be that PPAS is frequently misdiagnosed as pulmonary embolism (PE), with one study showing nearly one-half of patients initially treated for PE and early studies reporting around 60% of PPAS first recognized at autopsy (1,2). Patients typically present between 45 and 55 years of age, with a female-to-male predominance of 2:1 (3).

PPAS usually arise from the dorsal surface of the main pulmonary trunk (85%) with frequent involvement of the right PA (71%) and left PA (65%) (4). In about one-third of patients the pulmonic valve is involved (4). Commonly, there is a significant amount of intraluminal extension before growth outside the vessel is seen (5).

Histopathologically, 13 types of PPAS have been recognized, with leiomyosarcoma (20%) being most common, followed by spindle cell sarcoma (15%), fibrous histiocytoma (12%), and undifferentiated sarcoma (12%) (1). Bandyopadhya et al. (1) report that the median age of presentation is lowest for myofibralastic sarcoma (43 years) and undifferentiated sarcoma (48 years), and highest for rhabdomyosarcoma (66 years) and liposarcoma (67 years). Huo et al. (6) report longer survival associated with leiomyosarcoma and worse prognosis with rhabdomyosarcoma. Routine immunohistochemical staining includes desmin, cytokeratin, vimentin, and actin (5,7). These tumors frequently overexpress mdm2 (5,7).

On clinical presentation, PPAS often resembles PE, with the commonest symptoms being dyspnea (74%), chest pain (31%), cough (23%), and hemoptysis (15%)

FIGURE 1 Pulmonary Artery Sarcoma Specimen



Pulmonary artery sarcoma specimen in pieces resulting from debulking procedure.

(1). Initial misdiagnosis and treatment of PE delays proper management of these tumors, which increases mortality (8).

Given the ease with which PPAS may be mistaken for PE, multimodality imaging is critical for accurate diagnosis. Transthoracic echocardiogram typically shows a mobile mass with globular rather than filamentous morphology with attachment to the PA wall or pulmonic valve (8). Invasion of the vessel wall may be seen on transesophageal echocardiography (8). Gadolinium-enhanced MRI can differentiate PE from tumor because PPAS tends to enhance more than thrombus (5). FDG-positron emission tomography may demonstrate increased uptake within the tumor, helping distinguish it from thrombus, and also may reveal metastases, aiding in post-operative medical management and prognosis (5).

Optimal management for PPAS includes complete surgical resection and neoadjuvant chemotherapy. Neoadjuvant chemotherapy is advised to shrink the tumor size and improve the likelihood of curative resection as well as identify chemoresponders who are likely to benefit from surgery (8). In practice, as a result of misdiagnosis or clinical circumstances, few patients receive pre-operative chemotherapy (8). Likewise, curative resection is not always feasible, and resectability is usually impossible to determine before surgical exploration (5). Treatment with either chemotherapy or surgery alone is associated with poorer outcomes. Blackmon et al. (5) report that median and 5-year survival was 24.7 ± 8.5 months and 33.4%, respectively, for patients undergoing multimodality treatment compared with 8 ± 1.7 months and 30.6%, respectively, for patients who had only 1 modality of therapy.

Palliative surgical options include debulking, pneumonectomy, endarterectomy, and PA stenting. Patients who are not candidates for curative resection may still benefit from palliative procedures, although prognosis is poorer (5). Comparing curative resection with palliative surgery, Blackmon et al. (5) found that median and 5-year survival was 36.5 ± 20.2 months and 49.2%, respectively, for patients undergoing complete resection compared with 11 ± 3 months and 0%, respectively, for patients undergoing tumor debulking, palliative pneumonectomy, exploration, or thromboendarterectomy. In patients undergoing palliative procedures, recurrence is generally expected.

There is no consensus on the benefit of adjuvant chemotherapy, and there are no standard guidelines available on which agents to use. Doxorubicin and ifosfamide are frequently used as first-line neoadjuvant therapy with platinum-vinorelbine regimens reserved for those who fail doxorubicin-based treatment (8).

FOLLOW-UP

The patient was most recently seen in outpatient clinic by her oncologist 15 months after surgery, at which time surveillance computed tomography scan of the chest showed an overall decrease in size of the lung nodules, and transthoracic echocardiogram was stable, with normal ejection fraction and no evidence of recurrent mass.

CONCLUSIONS

PPAS are rare tumors with a poor prognosis. Their clinical presentation is often confused for PE, which delays appropriate treatment and worsens outcomes. Thorough workup and imaging with correct early diagnosis, aggressive curative surgical resection, and multimodality therapy offer patients the best chance of survival. We report here a patient with a large, metastatic tumor who was unable to receive neoadjuvant chemotherapy and underwent incomplete surgical resection but nevertheless has had a good clinical outcome at 15 months with targeted adjuvant immunotherapy.

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REFERENCES

1. Bandyopadhya D, Panchabhai TS, Bajaj NS, Patil PD, Bunte MC. Primary pulmonary artery sarcoma: a close associate of pulmonary embolism—20-year observational analysis. J Thorac Dis 2016;8:2592–601.

2. Krüger I, Borowski A, Horst M, de Vivie ER, Theissen P, Gross-Fengels W. Symptoms, diagnosis, and therapy of primary sarcomas of the pulmonary artery. Thorac Cardiovasc Surg 1990; 38:91–5.

3. Gan HL, Zhang JQ, Huang XY, Yu W. The wall eclipsing sign on pulmonary artery computed tomography angiography is pathognomonic for pulmonary artery sarcoma. PLoS One 2013;8: e83200.

4. Restrepo CS, Betancourt SL, Martinez-Jimenez S, Gutierrez FR. Tumors of the pulmonary artery and veins. Semin Ultrasound CT MR 2012; 33:580–90.

5. Blackmon SH, Rice DC, Correa AM. Management of primary pulmonary artery sarcomas. Ann Thorac Surg 2009;87:977–84.

6. Huo L, Moran CA, Fuller GN, Gladish G, Suster S. Pulmonary artery sarcoma: a clinicopathologic and immunohistochemical study of 12 cases. Am J Clin Pathol 2006;125: 419–24.

7. Moguillansky N, Verma N, Shah P, Knapik J, Mohammed TL. Pulmonary artery sarcoma: Case report and review of the literature. Respir Med Case Rep 2019;27:100857.

8. Al-Mehisen R, Al-Halees Z, Alnemri K, Al-Hemayed W, Al-Mohaissen M. Primary pulmonary artery sarcoma: A rare and overlooked differential diagnosis of pulmonary embolism. Clues to diagnosis. Int J Surg Case Rep 2019;65:15–9.

KEY WORDS imaging, pulmonic valve, right ventricle

APPENDIX For supplemental videos, please see the online version of this paper.