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Case report

The use of lobectomy for management of clinically significant pulmonary vein stenosis and occlusion refractory to percutaneous intervention

Kevin J. O'Gorman[a,*], Tyson J. Sjulin[b], Donnell K. Bowen[c], Michael J. Morris[b,**]

[a] Department of Internal Medicine, Keesler Medical Center, Keesler AFB, MS, USA
[b] Department of Pulmonary/Critical Care, Brooke Army Medical Center, JBA Fort Sam Houston, TX, USA
[c] Department of Cardiothoracic Surgery, Brooke Army Medical Center, JBSA Fort Sam Houston, TX, USA

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ABSTRACT

Pulmonary vein stenosis (PVS) is a serious complication of radiofrequency ablation (RFA) for the treatment of atrial fibrillation. The prevalence of this complication was reported to be as high as 42% in 1999 when RFA was first implemented [1]. However, with improvements in operator technique including wide area circumferential ablation, antral isolation, and the use of intracardiac ultrasound, the incidence of symptomatic severe PVS following RFA ranges from 0% to 2.1% while the incidence of symptomatic pulmonary vein occlusion (PVO) following RFA was found to be 0.67% [2–8]. Despite a decrease in the incidence of clinically significant PVS following RFA, there have been increased reports of complications associated with PVS to include hemoptysis, scarring, lung infarction, and intraparenchymal hemorrhage [9]. Studies have shown that PVS is often misdiagnosed as pneumonia, pulmonary embolism, and lung cancer and as a result, patients are often subjected to unnecessary diagnostic procedures [2,10].

The current first line treatment for this condition is percutaneous balloon angioplasty with stenting; however, there are studies that have shown that there is a relatively high rate of restenosis despite optimal medical therapy [2–3,10,11]. Three case reports have described the use of lobectomy to treat patients with persistent respiratory symptoms in the setting of severe PVO with good outcomes [12–14]. We present a case of iatrogenic PVO and ipsilateral severe PVS following RFA who underwent attempted lobectomy for persistent exertional dyspnea and persistent hypoperfusion of the left upper lung lobe despite percutaneous intervention and six months of optimal medical therapy. The lobectomy was aborted due to the presence of a significant fibrothorax, and the patient continues to have significant exercise limitation despite participation in pulmonary rehabilitation.

1. Case presentation

A 51-year-old Caucasian male with a past medical history significant for Crohn's disease and atrial fibrillation status post RFA in September 2016 initially presented in January 2017 with a history of recurrent hemoptysis, cough, exertional dyspnea, and fever while on vedolizumab and clopidogrel. Computed tomography angiography (CTA) showed multifocal left upper lobe (LUL) opacities and an ipsilateral pleural effusion with no evidence of pulmonary embolism, (Fig. 1). Fiberoptic bronchoscopy revealed no endobronchial lesions, evidence of infection, or inflammatory lung disease. Diagnostic left thoracentesis revealed an exudative effusion with negative cytology and cultures. Ventilation/Quantitative perfusion scan (Figs. 2 and 3) showed hypoperfusion of the left lung (overall 95% perfusion in right lung, 5% perfusion in left lung) and reduced perfusion in the LUL (12% LUL vs. 88% left lower lobe). Transthoracic echocardiogram was unremarkable with an estimated left ventricular ejection fraction of 60% and mildly elevated pulmonary artery systolic pressure. Video assisted thoracoscopic biopsy of the LUL revealed venous infarcts associated with edema and fibrosis of interlobular septa, (Fig. 4). Following these findings, reassessment of the patient's initial CTA found thrombosis of the superior left pulmonary vein and a filling defect of the inferior left pulmonary vein. Dedicated CT coronary angiography revealed complete occlusion of the left superior pulmonary vein and stenosis of the left inferior pulmonary vein, (Fig. 5).

In April 2017, the patient underwent percutaneous intervention

Abbreviations: PVO, Pulmonary Vein Occlusion; PVS, Pulmonary Vein Stenosis; RFA, Radiofrequency Ablation

* Corresponding author. Department of Internal Medicine, Keesler Medical Center, 301 Fisher Street, Keesler Air Force Base, MS 39534, USA.
** Corresponding author. Pulmonary/Critical Care Service (MCHE-ZDM-P), San Antonio Military Medical Center, 3551 Roger Brooke Drive, Fort Sam Houston, TX 78234, USA.
E-mail addresses: kevinogormanmd@gmail.com (K.J. O'Gorman), michael.j.morris34.civ@mail.mil (M.J. Morris).

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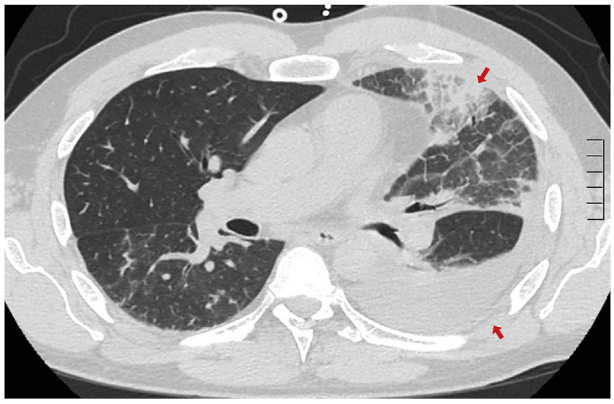

Fig. 1. CTA at initial presentation (January 2017).

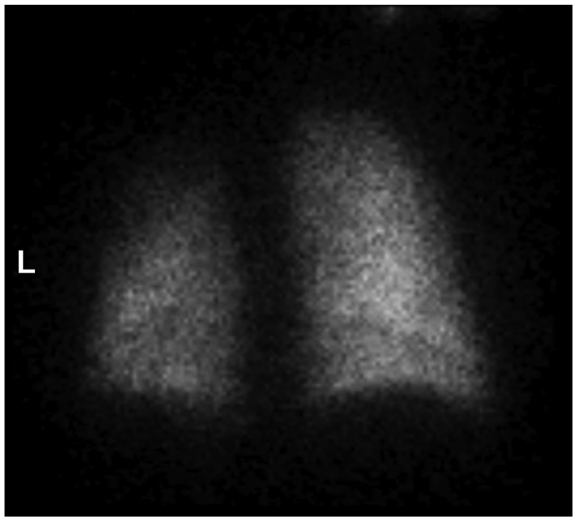

Fig. 2. V/Q scan ventilation.

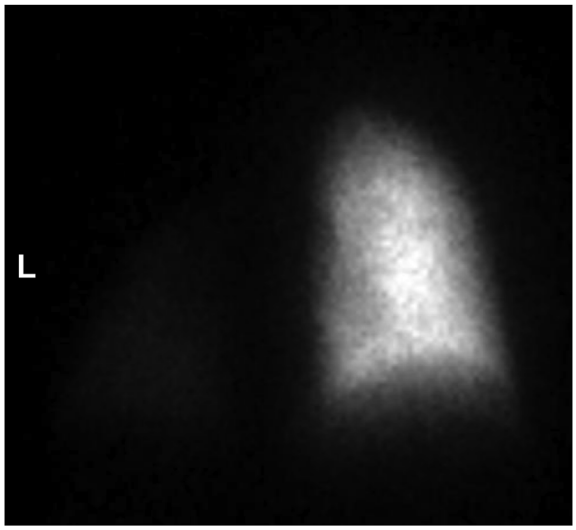

Fig. 3. V/Q scan perfusion.

(PCI) of the left inferior pulmonary vein by interventional cardiology; however, no intervention was attempted on the left superior pulmonary vein because the vein was completely occluded. Repeat CTA after the procedure noted almost complete resolution of the multifocal left upper lobe opacifications and resolution of the ipsilateral left sided pleural effusion, (Fig. 6). The patient was started on dual anti-platelet therapy

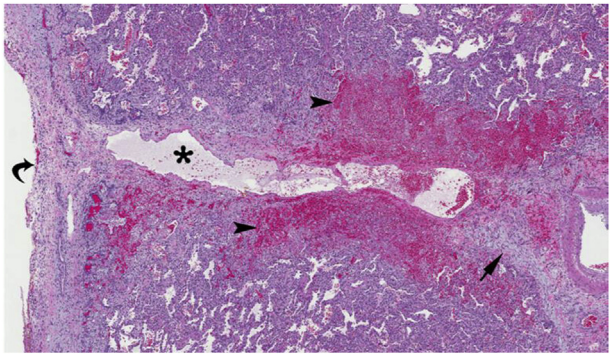

Fig. 4. Left upper lobe lung biopsy.

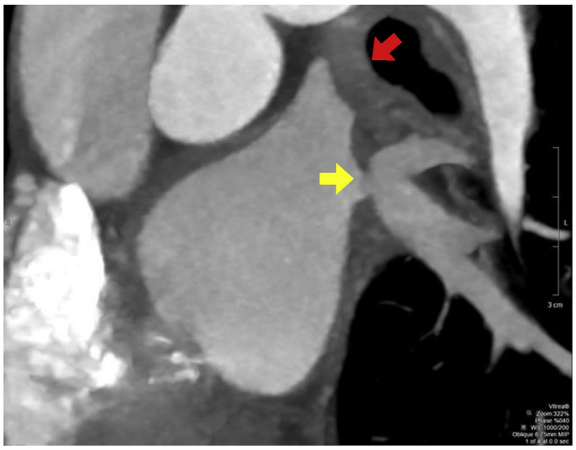

Fig. 5. CT Coronary Angiography (February 2017). Red Arrow: Complete occlusion of left superior pulmonary vein. Yellow Arrow: Moderate stenosis of left inferior pulmonary vein.

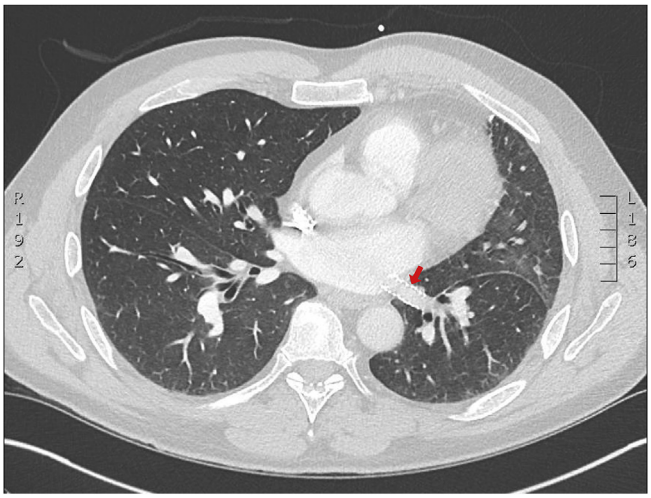

Fig. 6. CTA status post PCI of left inferior pulmonary vein.

with aspirin and clopidegrel in addition to rivaroxaban which had been previously initiated. At follow up, the patient reported significant improvement in his symptoms. He stated that his exertional dyspnea and cough had improved and was able to perform moderate intensity exercise for at least 20 minutes.

From October 2017 to January 2018, the patient presented to clinic on multiple occasions for recurrence of severe dyspnea on exertion. CT coronary angiography revealed complete occlusion of the left superior pulmonary vein and a patent stent in the left inferior pulmonary vein.

The patient was able to walk 450 m during a 6-min walk test with a lowest recorded pulse oximetry reading of 95%. Repeat pulmonary function testing showed no obstruction, normal lung volumes and normal diffusing capacity. Cardiopulmonary exercise testing was abnormal due to a ventilatory limitation as evidenced by a reduced ventilatory equivalent for carbon dioxide (VE/VCO_2). The patient otherwise had good exercise tolerance with VO_2 max of 92%, no evidence of cardiac ischemia with exertion, and no oxygen desaturations. The patient was referred to cardiothoracic surgery for a left upper lobectomy because he continued to have persistent symptoms of exertional dyspnea and significantly reduced perfusion in the LUL despite stenting of the left inferior pulmonary vein. Surgical findings included evidence of a left fibrothorax with complete visceral-parietal pleural fusion and dense adhesions to the diaphragmatic surface, pericardium, and posterior chest wall to include the descending aorta. The anterior hilum, fissure, and apex were frozen and unable to be freed despite an attempt at pneumolysis. The attempt at lobectomy was ultimately aborted. Despite participating in pulmonary rehabilitation, the patient continues to have significant exercise limitation.

2. Discussion

The reported rates of the incidence and prevalence of PVS after RFA for the treatment of atrial fibrillation in the literature have varied since the procedure was introduced [1]. The incidence of this complication appears to be decreasing as technical improvements have been discovered, and clinically significant PVS appears to occur from 0 to 2.1% of cases based on recent data, [2–7]. In 2006, DiBiase et al. reported that the incidence of PVO was 0.9% and the incidence of symptomatic PVO was 0.67% in 1780 patients studied who underwent RFA [8]. In a survey that collected information from 181 centers throughout the world between 1995 and 2002, significant PVS occurred in 1.3% of patients [4]. In 2003, Saad et al. reported that 3.4% of patients (21/608) developed a stenosis greater than 70% of the pulmonary vein lumen diameter; however, only 2.1% of patients (13/608) in the study developed symptoms from the PVS [2]. Packer et al. surmised that the incidence of iatrogenic PVS has decreased due to increased operator experience and technical improvements [3]. In this study, 11 of the first 100 patients that underwent RFA at their institution developed a stenotic lesion, but only one patient developed a stenotic lesion that required intervention in the last 100 cases prior to publication, [3]. Bertalgia et al. reported that only 0.4% (4 of 1011) of patients were found to have developed a PVS greater than 50%, and only 1 of those patients reported symptoms [5]. Finally, more recent studies published in 2018 reported a low rate of PVS. There were no cases of symptomatic PVS in 2750 RFA procedures at a single high-volume center, and in a larger cohort of 9633 patients, the rate of PVS from RFA was 0.79% [6,7].

2.1. Pathogenesis

The condition has been categorized into three subsets based on the percent narrowing of the pulmonary vein lumen diameter. Mild, moderate and severe PVS are defined as a stenosis with less than 50%, between 50% and 69%, and greater than or equal to 70% narrowing of the lumen diameter respectively [2,9]. The degree of PVS and the involvement of more than one pulmonary vein correlates with the presence and severity of symptoms, [2,8,15]. Patients with mild or moderate PVS (stenosis $< 70\%$) were asymptomatic, and 62% of patients with severe PVS (stenosis $\geq 70\%$) reported symptoms. This study reported that 86% of patients with severe PVS involving more than one pulmonary vein were symptomatic while only 28% of patients with severe PVS involving just one pulmonary vein reported symptoms [2]. In a different study, Saad et al. found that patients have a 12.5 times higher relative risk of developing symptoms if there is severe PVS present in more than one pulmonary vein [16]. Data from DiBiase et al. also supports this correlation as their study found that every patient with a cumulative stenosis greater than or equal to 75% of the cross sectional area of the pulmonary veins draining one lung had moderate to severe symptoms [8]. Although there is a strong correlation between the degree of PVS and symptoms, other studies have shown that patients with high grade PVS can be asymptomatic as illustrated by Fender et al. where 18% of patients with a stenosis greater than 75% were asymptomatic [10].

Pulmonary vein stenosis causes increased resistance to pulmonary venous drainage from the capillaries of the affected lung segment. If the stenosis is significant, this can result in decreased arterial blood flow to the affected segment, [3,8]. Stenosis greater than or equal to 70% typically results in a perfusion defect in the affected segment on nuclear medicine ventilation/perfusion imaging. Diminished perfusion and venous congestion leads to ischemia of the alveoli within the affected segment resulting in atelectasis, infarction, and increased susceptibility to developing pneumonia [8]. This mechanism explains why roughly 50% of patients with severe PVS will present with a lung consolidation on CT scan.

Additionally, with a small sample size of eleven patients, Arentz et al. found that none of the patients with severe PVS (at least one stenosis $> 70\%$) had pulmonary hypertension at rest but 7 of the 11 patients developed pulmonary hypertension during exercise with no decrease in pulmonary vascular resistance [17]. This finding would explain why exertional dyspnea is the most common symptom of patients with severe PVS. Yang et al. proposed that chronic pulmonary vein stenosis may result in irreversible venous and arterial morphologic changes throughout the lung based off of findings on histologic examination of their patient [18]. This finding may explain why pulmonary vein percutaneous angioplasty and stenting of the stenosis may not improve a patient's symptoms if irreversible remodeling of the pulmonary vasculature has already occurred.

2.2. Clinical presentation

Patients with severe PVS who are symptomatic present with symptoms of dyspnea, dyspnea on exertion, cough, and fatigue; occasionally, patients may also present with chest pain, pleuritic chest pain, hemoptysis, and flu-like illness [2,3,10,16]. The most commonly reported symptom was dyspnea on exertion which was endorsed by 69% and 83% of symptomatic patients in two different studies [3,10]. Forty-four percent of PVO patients endorsed severe dyspnea and roughly 17% presented with hemoptysis and pleuritic chest pain, [8]. The onset of symptoms typically ranges from one to seven months with a mean of 4 months following pulmonary vein RFA; but some patients endorsed symptoms immediately following the procedure [3,10,15].

The diagnosis of PVS is challenging because patients with the condition present with non-specific symptoms and in roughly 50% of cases, patients with severe PVS can present with abnormal radiographic findings which include lung consolidation and/or pleural effusion, [16]. One study reported that 55% of patients with PVS greater than 75% had a consolidation on CT scan, and another study discussed a case where a patient was found to have chronic LLL infiltrates on CT scanning, [10,19]. The constellation of non-specific symptoms and radiographic findings has led to incorrect diagnoses in patients with PVS. One study illustrated this problem and reported that PVS was not considered as a differential diagnosis in any of the patients with the condition. This same study reported that 78% of patients with a radiographic abnormality were misdiagnosed with pneumonia, lung cancer, or pulmonary embolism, [16].

2.3. Diagnostic imaging

Cardiac CT has been advocated to be the best test to evaluate the location and extent of the stenosis [3,15]. Barrett et al. reported that CT scan was able to detect the presence of PVS greater than 50% the lumen

diameter in 100% of cases [20]. Transesophageal echocardiography was found to have a sensitivity of 86% and a specificity of 95% in detecting the presence of PVS; however, Packer et al. reported that echocardiography was less useful for the evaluation of PVS than CT scan because it was unable to provide consistent views of the inferior pulmonary veins [3,20]. MRI is an effective alternative to CT for the evaluation of PVS as it has been shown to provide accurate evaluation of pulmonary vein anatomy [20]. Evidence has shown that the nuclear medicine ventilation/perfusion scan (V/Q) can distinguish mild and moderate PVS from clinically significant severe PVS. In one study, the finding of mismatch during V/Q scanning had a sensitivity of 100% to determine the presence of severe PVS (stenosis ≥70%) [2]. Significant perfusion defects corresponding to the lung region with PVS were present in 115 of 116 cases of patients with a pulmonary vein stenosis greater than or equal to 75% [3].

2.4. Treatment

The current first line treatment for PVS in symptomatic patients is percutaneous balloon angioplasty with stenting [9–11]. The Heart Rhythm Society suggests tretment with antiplatelet and anticoagulation therapy for 1–2 years following PCI until there is radiographic evidence of stable pulmonary vein stents [9]. Pulmonary vein occlusion (PVO) presents a challenging problem because not all patients are amenable to percutaneous BA or stenting, and patients with PVO are at a higher risk for developing severe pulmonary manifestations such as pulmonary venous congestion with subsequent infarction of the involved lung segment. The current treatment options for patients with PVO who are not candidates for angioplasty and stenting include: conservative management, angioplasty and stenting of the ipsilateral pulmonary vein if stenosis is present, and lobectomy. There is limited data concerning the efficacy of these options for this patient population; however, there are several case reports that have reported success. One case report described a patient with symptomatic PVO six months following RFA and was treated conservatively with supplemental oxygen, analgesia, antibiotics, mobilization, and no anticoagulation due to hemoptysis. This patient improved within one week and was able to return to exercise without symptoms [21]. Three case reports have described the use of lobectomy for the treatment of patients with persistent respiratory symptoms in the setting of iatrogenic severe pulmonary vein stenosis. In each case, the patient's symptoms resolved following lobectomy, and they experienced no significant complications [12–14]. However, Fender recently reported that two patients who underwent lobectomy following in-stent pulmonary vein thrombosis died in the immediate postoperative period due bleeding complications [3]. Surgical repair of PVS under cardiopulmonary bypass has been described in one case report and in one small retrospective study [7,22]. The study reported five patients who underwent surgical repair of a total of 13 pulmonary veins and found that all patients reported improvement of their symptoms at follow-up; however, the rate of restenosis (defined as narrowing > 70%) after an average of 60 months following the surgery was 38% [7].

3. Conclusion

Pulmonary vein stenosis following RFA is an uncommon condition that is often misdiagnosed for other pulmonary diseases. Patients who present with new pulmonary symptoms up to six months following RFA should have a dedicated coronary CT or MRI of the pulmonary veins to exclude PVS or PVO. Earlier recognition and treatment of this condition would have obviated lung biopsy in this patient. The use of lobectomy should be cautiously considered for symptomatic patients with PVO not amenable to PCI, or patients with PVO who have persistent symptoms and diminished lung perfusion following PCI despite use of optimal medical therapy and participation in pulmonary rehabilitation.

Conflicts of interest

None.

Disclaimer

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