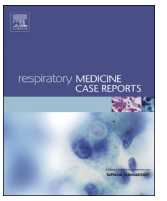
Respiratory Medicine Case Reports 48 (2024) 101998

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr



Case Report

Fibrosing mediastinitis resulting in unilateral pulmonary artery hypertension

Zackary Anderson [a, *], Alex Ashkin [a], Noelle Messina [b], Carl Ruthman [c], David Lindner [c]

[a] Internal Medicine Resident Physician, Naples Community Hospital, 311 9th St North Suite 201 Naples, FL 34102, USA
[b] Medicine Resident Physician, Naples Community Hospital, 311 9th St North Suite 201 Naples, FL 34102, USA
[c] Pulmonary and Critical Care Attending Physician Naples Community Hospital, 311 9th St North Suite 201 Naples, FL 34102, USA

ARTICLE INFO

Handling Editor: DR AC Amit Chopra

Keywords:
Fibrosing mediastinitis
Pulmonary hypertension
FM
PH-FM

ABSTRACT

Fibrosing mediastinitis (FM), a rare disorder that is further classified as excessive fibrous tissue that occurs within the mediastinum. Classically, presenting with manifestations dependent on where the fibrous tissue is located. In rare instances, compression of pulmonary vasculature can lead to Pulmonary Hypertension. Pulmonary Hypertension- Fibrosing Mediastinitis (PH-FM) represents a rare complication with minimal available data on incidence. In regards to all-cause mortality, no specific data regarding the prognosis of PH-FM exist. With the scarcity of data, this case aids in the advancement of literature due to unique unilateral obstruction and the need for further analysis on our current treatment.

1. Intro

Fibrosing mediastinitis (FM) is a rare disorder that is classified as excessive fibrous tissue that occurs within the mediastinum. FM most commonly occurs in females with an average age of presentation of 42 [1].This disease has a predominance in the Midwestern United States, with particular prevalence in the Ohio and Mississippi river watersheds. In North America, 78% of FM cases occur as a secondary complication from prior Histoplasmosis infection, occurring in a reported 3:100,000 of those infected with H. capsulatum [5]. Other forms of infections associated with granulomatous inflammation including aspergillus, blastomycosis, tuberculosis and Cryptococcus have been reported precipitants for the disease [2,3].

The precise pathophysiology of FM is not fully understood although generally stems around an inappropriate host immune response [1].This exaggerated host response causes an inflammatory cascade that generates excessive collagenous, and fibrous tissue. Infection remains the most common precipitant although autoimmune diseases, including Bechets, and IgG-4 related diseases have also been linked to cases [2,1].

Classically, this disease presents with cough, dyspnea, shortness of breath and/or hemoptysis. These general manifestations vary and are typically dependent on where the fibrous tissue is located.

With this fibrous tissue present, complications can frequently occur. In this disease process, complications such as obstruction of the airway and Superior Vena Cava syndrome have been reported [2,1,4]. With compression of such vital structures, it is always important to further investigate based on the area of concern. In even rarer instances, compression of pulmonary vasculature can lead to Pulmonary Hypertension. There are very few cases in the literature which demonstrate this complication and even less that demon-

* Corresponding author.
E-mail addresses: Zackary.anderson@nchmd.org (Z. Anderson), Alex.ashkin@nchmd.org (A. Ashkin), noelle.messina@nchmd.org (N. Messina), Carl.ruthman@nchmd.org (C. Ruthman), david.lindner@nchmd.org (D. Lindner).

https://doi.org/10.1016/j.rmcr.2024.101998
Received 11 November 2023; Received in revised form 21 February 2024; Accepted 22 February 2024
Available online 29 February 2024

strate a unilateral process [2,5]. Here we present a rare instance of FM causing unilateral pulmonary artery stenosis resulting in Pulmonary Hypertension.

2. Case presentation

This is an 80-year-old male who is a lifelong non-smoker who presented with a chief complaint of worsening shortness of breath. He first noted respiratory issues as a teenager after significant occupational exposure to sanding materials without the use of a mask. He described the symptoms as including significant wheezing with cough. In his twenties he went on to work in a bakery where he reported a prolonged period of inhalation of dust from the baking products such as sugars and flour which further exacerbated his respiratory symptoms. After graduating from college, he became a dentist where he again verbalized significant occupational exposure to inhaled irritants from performing tasks such as dental drilling without a mask on a regular basis. In his late thirties he developed significant shortness of breath and was found to have a pleural effusion. He underwent thoracotomy and mediastinoscopy which revealed granulomas. At this time, he was told that he likely had a prior tuberculosis exposure. However, there is no record confirming whether the granulomas were caseating or non caseating, and no confirmatory testing for tuberculosis. Approximately 10 years later he developed legionnaires disease which unfortunately continued to worsen his underlying respiratory complaints. In his early seventies he developed worsening respiratory symptoms and was seen by a pulmonologist who recommended a CT of the chest. The CT revealed diffusely calcified infiltrating soft tissue changes around the right hilum which were encasing the airways and obstructing the right bronchus intermedius. The infiltrating tissue was also found to obstruct the right pulmonary artery but not the main pulmonary trunk or left pulmonary artery tree (Fig. 1). Imaging also noted multiple calcified granulomas in the right lung consistent with the findings from prior thoracotomy. These findings were indicative of fibrosing mediastinitis and he was started on a regimen of inhaled tiotropium bromide along with arformoterol. Due to concern for pulmonary hypertension secondary to the fibrosing mediastinitis, he was referred to the pulmonary hypertension clinic for further evaluation.

Initial echocardiogram estimated right ventricular pressures of 40–45 mmHg. Pulmonary function testing showed moderate obstruction with FEV1 of 45% predicted, FEV1/FVC ratio 0.56, total lung capacity reduced at 74% predicted and diffusion capacity reduced at 59% predicted. Subsequent right heart catheterization showed right ventricular pressure of 41 mmHg/6 mmHg, mean pulmonary artery pressure of 32 mmHg on the right, PVR of 8 mmHg, mean pulmonary artery pressure of 28 mmHg on the left, and on the left the pulmonary capillary wedge pressure was 13 mmHg. The pulmonary capillary wedge pressure of the right was unable to be obtained secondary to pulmonary artery stenosis (Fig. 2). Based on these findings he was diagnosed with group 5 hypertension and

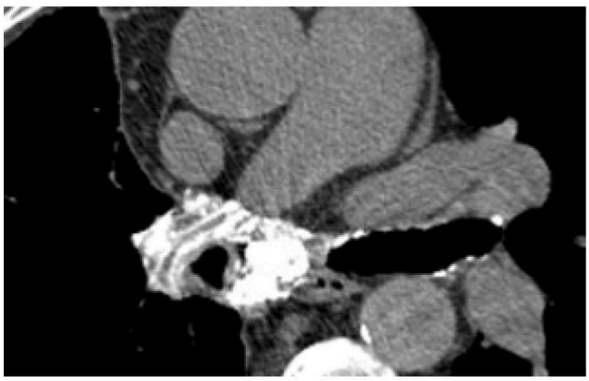


Fig. 1. CT Chest with contrast showing changes in the right mediastinum, compressing the Right PA to a small vessel as seen.

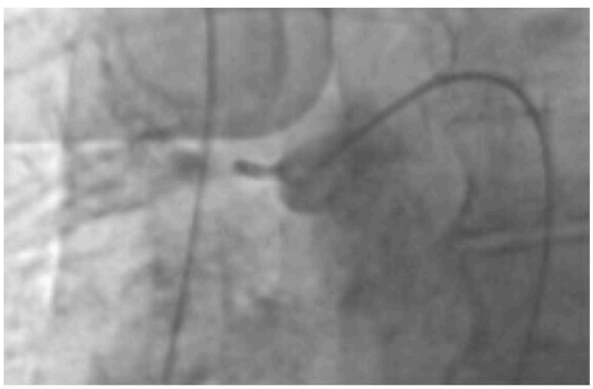


Fig. 2. Abnormal RHC consistent with a group 4.2 pulmonary arterial hypertension secondary to fibrosing mediastinitis other pulmonary artery obstructions.

subsequently initiated on pulmonary artery vasodilator therapy with macitentan, and tadalafil, with subsequent addition of selexipag as he had not reached goals of care and is being followed closely in the Pulmonary Hypertension Clinic.

3. Discussion

This case represents a rare instance of fibrosing mediastinitis complicated by pulmonary hypertension secondary to unilateral pulmonary artery compression. Due to the rarity of the disease, FM is often overlooked and not included in the differential diagnosis. Suspicion is often incidentally raised when a patient presents with cough, dyspnea, shortness of breath or hemoptysis.

When a patient presents with respiratory complaints the initial workup should at minimum include a Chest X-ray, complete blood count and basic metabolic panel. In cases such as these, they often yield nonspecific findings that fail to definitively yield a diagnosis of FM.

Due to nonspecific findings on roentgenography, contrast enhanced computed tomography (CT) chest is considered the imaging modality of choice, as the findings can be characteristic of the diagnosis [6]. The typical findings of infiltrative soft-tissue attenuation which obliterates the normal mediastinal planes and often encases or invades adjacent mediastinal structures can vary but can assist the clinician to further subclassify a focal vs. diffuse FM subtype [7,8].

A focal subtype of FM appears as a localized mass near the paratracheal or subcarinal regions of the mediastinum or in the pulmonary hila [8]. In contrast, The diffuse subtype affects multiple mediastinal compartments. Although not specific to FM, other imaging modalities can be used for further evaluation including MRI, esophagram and pulmonary angiography.

In this case of our patient, he had characteristics that further aligned with the classic features of imaging. Although there may be overlap in CT findings characteristics, he did not have evidence of lymphadenopathy that is more consistent with chronic beryllium disease. Additionally a presentation of occupational exposures, those patients presentation is often centered around additional symptoms such as fevers and weight loss. Our patient did not experience those factors making it less likely as the primary culprit.

Outside of the initial imaging, bronchoscopy can be helpful in the diagnosis of fibrosing mediastinitis but is limited and is typically used to assist in exclusion of other pathological concerns [9]. Biopsy remains the gold standard and a critical approach to rule out malignancy and establish a diagnosis. The pathology report typically shows varying degrees of nodular and hyperplastic fibrous tissues surrounding the mediastinal structures [3].

After establishing a diagnosis of FM, it is important to associate whether this is secondary or idiopathic as this can further dictate treatment. Evaluation for secondary etiologies of FM should include serological testing for H. capsulatum. Secondary H. Capsulatum can be diagnosed via high levels of antibody titers or rocott methenamine silver stains revealing *H. capsulatum* [3]. Additional infectious work-up should include TB PCR, and serologies for Aspergillus and Blastomycosis, which are necessary particularly if risk factors for these diseases are present. If suspicion warrants, investigation including autoimmune testing may be considered [3,10]. This testing should include total IgG and subtype levels, ANCA testing and consideration of other laboratory testing if clinical history warrant [10].

After a complete workup, the clinician's focus should be shifted to the evaluation of the location of fibrosis. Even with good general medical treatment, complications including airway compression, postobstructive, pneumonia, or atelectasis may commonly occur with FM. In our case, the presence of fibrotic changes led to compression of the right pulmonary artery and warranted a further investigation for Pulmonary Hypertension.

Initial evaluation of pulmonary hypertension typically includes EKG, transthoracic echocardiogram and PFT's. If initial work-up is suspicious for PH, PA catheterization remains the necessary gold standard diagnostic tool for diagnosis, and in this case provided for angiographic evaluation of the degree of pulmonary artery stenosis. Right Heart Catheterization provides the diagnosis by assessing PAP and pulmonary capillary wedge pressures. In this case, PFTs were consistent with PM-FH demonstrating a restrictive pattern with a reduced DLCO. The Right Heart Catheterization demonstrated elevated PA pressures confirming our suspicion of PH-FM.

In the case of our patient, PFTs were consistent with a mixed picture of obstructive and restrictive disease. This being one that can be further explained the patient's asthma history.

Pulmonary Hypertension- Fibrosing Mediastinitis (PH-FM) represents a rare complication with minimal available data on incidence or prevalence [2].WHO classifies PH-FM within its Group 5 classification. In literature review, the majority of cases demonstrate bilateral distribution of stenosis with a scarcity of case reports on unilateral stenosis.

Regarding PH-FM, further subclassification can be made based on the involvement of the pulmonary vessels [11]. Type I typically refers to stenosis confined within the pulmonary artery and bronchus without pulmonary vein involvement. Type II refers to stenosis within the pulmonary veins and bronchus without arterial involvement and Type III is more severe in which both the PAs, PVs, and bronchi are involved. In this case, subclassification as Type I PH-FM is most appropriate, as the stenosis was seen in the pulmonary arteries and adjacent bronchi, without pulmonary vein involvement [11].

The treatment of PH-FM is based on the subtype, and its clinical manifestations, and can include surgery, endovascular intervention, and/or medical therapy. The goal of surgery is to provide relief of the compression of the mediastinal structures. Commonly these procedures include airway reconstruction, pulmonary revascularization, mediastinal tissue resection and segmentectomy. These types of procedures are associated with a high mortality rate up to 20% due to the complexity of the operation. Even with these procedures, 42% of patients have been shown to relapse and require additional surgeries or alternative therapy [12,13]. Other therapeutic options include endovascular interventions which have a goal to relieving pulmonary artery obstruction. In a study where endovascular intervention was performed, 59 stents were placed in 47 separate pulmonary vessels (26 PAs and 21 PVs) [14]. The study showed reduction in pulmonary symptoms and only one case developed a restenosis of the pulmonary artery. Although this procedure is deemed highly effective, the risk of complications is high due to the brittle pulmonary vessel wall. These endovascular procedures

have high rates of complications compared to other endovascular procedures including lung or vessel injury and intrastent stenosis [14].

Our patient was not deemed a surgical candidate due to the protracted time period from diagnosis and instead was treated via medical therapy. Generally, treatment is aimed around hallmarks such as oxygen therapy, diuretics and digoxin. We treated our patient with pulmonary vasodilator therapy to reduce the symptomology of the elevated PAP pressures. Clinically, this was effective. The goal of medical treatment is łowering PA pressures. By achieving lower PA pressures, our goal was to reduce complications such as right heart failure.

Regarding mortality, inadequate data is available to accurately prognosticate for pulmonary hypertension secondary to FM. A retrospective study of 80 patients from Mayo Clinic spanning 1998 to 2007, showed that 2.5% patients had died from FM during a median 68 month follow up period [15]. The current scarcity of data means that this case aids in the advancement of literature due to unique unilateral obstruction and the need for further analysis on our current treatment protocols.

4. Conclusion

Fibrosing Mediastinitis is a rare disease that is often overlooked as a cause of respiratory symptoms. It can come with complications such as pulmonary hypertension that warrant further treatment and investigation. Due to the rarity of this disease and these complications, this case demonstrates an advancement in the literature for further investigation to improve patient outcomes.

Funding

The following authors have no financial disclosure to disclose.

CRediT authorship contribution statement

Zackary Anderson: Investigation, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **Alex Ashkin:** Conceptualization, Writing – original draft, Writing – review & editing. **Noelle Messina:** Writing – original draft. **Carl Ruthman:** Writing – original draft, Writing – review & editing, Supervision, Validation. **David Lindner:** Visualization, Writing – original draft, Writing – review & editing, Supervision, Validation.

Declaration of competing interest

The following authors have no interest to disclose.

References

[1] A.O. Kuranga, A.M. Eubank, M.R. Bowling, Fibrosing mediastinitis: a review of epidemiology, diagnosis and management, Int J Respir Pulm Med 5 (2018) 79, https://doi.org/10.23937/2378-3516/1410079.
[2] A. Wang, H. Su, Y. Duan, et al., Pulmonary hypertension caused by fibrosing mediastinitis, JACC (J. Am. Coll. Cardiol.): Asia 2 (2022 Jun) 218–234 (3_Part_1).
[3] Mathisen D.J., Grillo H.C. "Clinical Manifestation of Mediastinal Fibrosis and Histoplasmosis.
[4] C.F. Lagerstrom, H.G. Mitchell, B.S. Graham, J.W. Hammon, Chronic fibrosing mediastinitis and superior vena caval obstruction from blastomycosis, Ann. Thorac. Surg. 54 (1992) 764–765.
[5] A. Seferian, A. Steriade, X. Jaïs, O. Planché, L. Savale, F. Parent, D. Amar, R. Jovan, E. Fadel, O. Sitbon, G. Simonneau, M. Humbert, D. Montani, Pulmonary hypertension complicating fibrosing mediastinitis, Medicine (Baltim.) (2015 Nov) 94.
[6] J.B. Weinstein, D.J. Aronberg, S.S. Sagel, CT of fibrosing mediastinitis: findings and their utility, AJR Am. J. Roentgenol. 141 (1983) 247–251.
[7] S.H. Garrana, J.R. Buckley, M.L. Rosado-de-Christenson, S. Martinez-Jimenez, P. Munoz, J.J. Borsa, Multimodality imaging of focal and diffuse fibrosing mediastinitis, Radiographics 39 (2019) 651–667.
[8] Santiago E. Rossi, H. Page McAdams, L. Melissa, Rosado-de-Christenson, Teri J. Franks, Jeffrey R. Galvin, Radiographics 21 (3) (2001) 737–757.
[9] E.D. Manali, C.P. Saad, G. Krizmanich, A.C. Mehta, Endobronchial findings of fibrosing mediastinitis, Respir. Care 48 (2003) 1038–1042.
[10] S.B. Strock, S. Gaudieri, S. Mallal, et al., Fibrosing mediastinitis complicating prior histoplasmosis is associated with human leukocyte antigen DQB1*04:02 – a case control study, BMC Infect. Dis. 15 (2015) 206, https://doi.org/10.1186/s12879-015-0943-7.
[11] Y.S. Cao, Y.C. Duan, H.L. Su, Advances in diagnosis and therapy of pulmonary vascular stenosis induced by fibrosing mediastinitis, Zhonghua Xinxueguanbing Zazhi 48 (2020) 823-83i.
[12] S.P. Ponamgi, C.V. DeSimone, C.J. Lenz, et al., Catheter-based intervention for pulmonary vein stenosis due to fibrosing mediastinitis: the Mayo Clinic experience, Int J Cardiol Heart Vasc 8 (2015) 103–107.
[13] M.L. Brown, A.R. Cedeno, E.S. Edell, D.J. Hagler, H.V. Schaff, Operative strategies for pulmonary artery occlusion secondary to mediastinal fibrosis, Ann. Thorac. Surg. 88 (2009) 233–237.
[14] C.J. Smolock, S. Blackmon, Z. Garami, H.T. Hassoun, Endovascular management of carotid artery stenosis secondary to sclerosing mediastinitis, J. Vasc. Surg. 56 (2012) 492–495.
[15] J.E. Loyd, B.F. Tillman, J.B. Atkinson, R.M. Des Prez, Mediastinal fibrosis complicating histoplasmosis, Medicine (Baltim.) 67 (1988) 295–310.