Successful management of fibrosing mediastinitis with severe vascular compromise: Report of two cases and literature review

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ABSTRACT

Fibrosing mediastinitis is a rare disorder characterized by the invasive proliferation of fibrous tissue within the mediastinum. This fibrosis can result in compression of intrathoracic structures including the pulmonary vasculature leading to clinical symptoms and complications like pulmonary hypertension. Here, we present two cases of young patients with fibrosing mediastinitis complicated by pulmonary artery stenosis requiring medical and endovascular management with excellent results.

1. Introduction

Fibrosing mediastinitis (FM) is a rare disorder characterized by the invasive proliferation of fibrous tissue within the mediastinum. FM can result in compression of vital mediastinal structures which has been associated with substantial morbidity and mortality [1,2]. Its pathogenesis remains unknown, but it is believed that it represents an immune-mediated hypersensitivity response [3], and has been mainly associated to Histoplasma capsulatum, mycobacteria and other fungal microorganisms [1,4]. Even after extensive evaluation, many cases remain to have an unclear cause and are categorized as idiopathic. The majority of patients present with nonspecific respiratory symptoms due to the compression of mediastinal bronchovascular structures leading to complications including cough, shortness of breath, dysphagia, and pulmonary hypertension [1,3,5]. We present two cases of young patients with fibrosing mediastinitis complicated with pulmonary artery stenosis requiring aggressive management.

2. Case # 1

A 19-year-old female with ulcerative colitis, treated with vedolizumab, developed progressively cough, shortness of breath, and left pleuritic chest pain. A computed tomography (CT) scan of her chest was obtained and demonstrated a large left hilar soft tissue mass. She was referred to a tertiary care center and repeat imaging revealed progression of her disease with near occlusion of the left pulmonary artery, absent flow to the left upper lobe, and partial obstruction of the left lower lobe pulmonary artery with an associated pulmonary infarct in that area. Endobronchial biopsies were unrevealing and an endobronchial ultrasound sampling revealed rare positivity of IgG4+ cells and polyclonal lymphocytes with 20% of the B cells lacking either kappa or lambda light chain on flow cytometry. She had an extensive infectious and hematologic workup that was negative, including serologies for Histoplasma capsulatum, Cryptococcus neoformans and Bartonella spp. Additionally, serum IgG4, antinuclear and antineutrophil cytoplasmic antibody levels were normal.

The patient underwent mediastinoscopy and video-assisted thoracoscopic surgery because of the concern for lymphoma. The procedure was complicated because of dense fibrosis in the mediastinum and only lymph node sampling was obtained. All lymph nodes were negative for malignancy or granulomas. A positive emission tomography (PET)-CT scan revealed active disease in the mediastinal lymph nodes and in the fibrous tissue surrounding the left pulmonary artery (Fig. 1). She was started on high-dose corticosteroids and a course of rituximab based on recent medical reports [6,7]. Her symptoms improved dramatically, her chest CT demonstrated significant regression of her lesions, and a
follow-up PET scan showed resolution of all areas of avidity.

3. Case # 2

A 24-year-old man with diagnosed with pulmonary coccidioidomycosis, complicated by mediastinal fibrosis with significant scarring of the left upper lung, and involvement of the pericardium. The patient required a pericardial window and was referred to our institution. The fibrotic process had progressed over the subsequent 2 years resulting in complete occlusion of left pulmonary artery (PA), stenosis of the right PA, and compression of the superior vena cava (Fig. 2). These intrathoracic vascular occlusions resulted in severe pulmonary hypertension with right ventricular hypertrophy. At that time, his symptoms consisted of severe dyspnea on exertion (NYHA functional class III) and bilateral lower extremity edema.

The patient underwent a right heart catheterization that showed total occlusion of the left PA and severe stenosis of the right PA with a gradient of 50 mmHg across the stenosed vessel. One month later, right PA stenting was attempted; however, the procedure was aborted when the patient became acutely hypoxemic and developed signs of acute cor pulmonale requiring to be placed on extracorporeal membrane oxygenation (ECMO). Ultimately, the patient underwent right PA stenting where two overlapping, self-expanding vascular stents were placed with ECMO support (Fig. 2).

The patient was discharged and placed on clopidogrel indefinitely. Five years later, a computed tomography angiography showed no filling defect in segmental or sub-segmental areas of the right PA and the transthoracic echocardiogram demonstrated improvement in the right ventricular hypertrophy. The patient continues to do well with no dyspnea on exertion or lower extremity edema and has been able to return to work.

4. Discussion

FM is a rare disorder characterized by proliferation of locally invasive fibrous tissue within the mediastinum. In the United States, FM is most commonly associated with H. capsulatum; however, this is a rare complication of pulmonary histoplasmosis occurring in less than 1% of cases [1]. Although the etiology of this syndrome remains unclear it is usually associated with history of granulomatous disease such as sarcoidosis, tuberculosis or fungal infections. Rarely, it has been reported with Wuchereria bancrofti, prior radiation to the mediastinum and certain drugs (e.g. methysergide, cabergoline and bromocriptine) [3,8,9]. In the absence of a specific identifiable cause, FM is therefore categorized as idiopathic. FM is thought to represent an immune-mediated hypersensitivity reaction to fungus or other antigens. Up to one third of the patients with FM demonstrate histologic features of IgG4-related disease [10]. Unfortunately, measuring IgG-4 in serum has not been clinically relevant as it has not shown correlation with the presence of disease or its severity [2,10].

The clinical presentation of FM varies depending on which of the intrathoracic structures are compromised. Pulmonary, bronchial vasculature, superior vena cava (SVC), and esophageal compression can occur in up to 47%, 26%, 19% and 2% of cases, respectively [1,11]. Symptoms may be gradual in onset; often presenting with progressive shortness of breath and cough. Pulmonary artery occlusion may result in pulmonary hypertension leading to right-sided heart failure and patients can present with dyspnea on exertion, palpitations, syncope, or hemoptysis. When the SVC is involved, patients frequently complain of facial swelling, headache, and distension of the veins in the neck and/or chest wall.

In our first case, the etiology of FM was considered to be idiopathic; however, it was temporally related to the time that the patient was started on vedolizumab. This drug was stopped and reported to the Food
and Drug Administration as a possible adverse reaction. It is unclear if there is an association between her diagnosis of ulcerative colitis and the development of FM. We were unable to find other reports of FM in the setting of ulcerative colitis in the medical literature. Our second case was consistent with the literature as the patient developed FM secondary to coccidioidomycosis.

The association of inflammatory bowel disease (IBD) and mediastinal fibrosis has not been reported in the literature. In particular, “idiopathic” FM has been reported in patients with systemic vasculitis, such as Behcet, as well as in patients with idiopathic retroperitoneal fibrosis, sclerosing cholangitis, orbital pseudotumor and ANCA-associated vasculitis [12]. It is well described the presence of ANCA positivity in IBD [13], and in fact ulcerative colitis can be complicated with sclerosing cholangitis which has been described in patient with idiopathic FM. We hypothesized that the fibro-inflammatory component of IBD could potentially have played a role for the development of this patient’s mediastinal fibrosis.

Different imaging modalities are used to confirm the diagnosis of FM. Computer tomography (CT) scans of the chest show a focal lesion in 75–95% of the time, while approximately 25% of patients have bilateral lesions [1,5]. The presence and severity of stenosis can be assessed noninvasively by echocardiography, CT angiography or magnetic resonance imaging. Radionuclide perfusion imaging can be useful in the workup of malignancy. Tissue samples for histologic and immunohistochemistry staining for FM show predominantly CD-20 + B lymphocytes [1]. This was found in our first patient by endobronchial ultrasound sampling of the mediastinal lymph nodes which revealed polyclonal lymphocytes with 20% of the B cells lacking kappa or lambda light chain on flow cytometry (a feature suggestive of autoimmune disease or lymphoma).

Several treatment strategies for FM have been described including medical, surgical and non-surgical interventions. Based on case reports, there are different medical options that have provided significant symptoms relief in idiopathic FM which include steroids, methotrexate and rituximab to target B-cell proliferation in selected patients, especially if they have an underlying autoimmune disease [6,11]. The combination of corticosteroids and methotrexate has been reported to provide resolution of symptoms and improvement of hemodynamic parameters related to pulmonary hypertension [11]. Since fungal antigens are thought to play a role in the pathogenesis of the disease, antifungal therapy has been used as part of the medical treatment but has not shown efficacy and is not currently recommended [1]. In our first case, the patient was suspected to have an idiopathic form of mediastinal fibrosis, and we initiated aggressive management with a combination of high-dose steroids and rituximab, resulting in a dramatic improvement in the patient’s symptoms.

Our second patient showed more severe symptoms associated with pulmonary hypertension and right-side heart failure that limited his daily activities. He required endovascular right PA stenting under ECMO support, to achieve improvement in his hemodynamics resulting in improvement of his heart failure and reduction of his dyspnea. In patients with significant vascular occlusion with hemodynamic compromise, both stenting and surgical intervention (bypassing the occlusion) may be required to treat the vascular occlusion. Endovascular therapy is a safe and feasible treatment option with an acceptable safety profile with a high level of technical success [8]. Symptoms related to pulmonary hypertension can improve considerably, especially when proximal pulmonary arteries are involved [5]. A few case reports have documented that patients undergoing endovascular stenting of 80% stenosis of pulmonary artery have been symptom-free for up to 10 years [14,15]. Other associated approaches prior to endovascular stenting such as cutting balloon angioplasty have rarely been described in the literature [16].

Procedure-related complications associated with endovascular intervention for central vascular obstructions due to FM have been reported to occur in 24% of the cases according to a retrospective review of 40 interventions. The most common complications are hemoptysis, catheterization site bleeding and reperfusion lung injury; however, major complications and/or death following percutaneous intervention are rare [17–19]. The survival of patients with FM depends on the underlying etiology, the severity of its complications and possibly due to the therapeutic approach. Patients receiving only medical management with steroids have reported survival rates of 88%, 73% and 56% at 1, 3, 5 years, respectively [7]. To date, no clinical trials have been conducted.
to show whether endovascular interventions alone or in combination with medical therapy improves survival and further investigation is warranted.

Less frequently, operative strategies have also been associated with good outcomes in pulmonary arteries occlusion secondary to FM, including both, creation of a double-outlet right ventricle and complete reconstruction of the pulmonary artery confluence. Hybrid techniques of both conduit placement and stenting may also be considered for patients with occluded pulmonary arteries [15].

To our knowledge, this is the first case describing ECMO support for endovascular stenting of pulmonary artery occlusion related to FM. The durability of stents may be suboptimal because stents are susceptible to early and late restenosis and often require intervention within 1–2 years [1,4,8]. Our second patient has not required re-stenting of his right PA after 5-year follow-up. These cases document the benefit of aggressive therapy in select patients with fibrosing mediastinitis with pulmonary vascular compromise.

Declaration of competing interest
The authors declare no competing interests.

Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2019.100987.

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