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Internal Medicine

ACUTE COR PULMONALE AS THE PRESENTING FEATURE OF LIMITED SYSTEMIC SCLEROSIS: A CASE REPORT

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ABSTRACT Systemic sclerosis (SSc) is a complex, multisystem disease characterized by fibrosis and excessive collagen deposition within the skin and internal organs, chronic inflammation, autoimmune dysregulation, and microvascular endothelial dysfunction. There are two forms of SSc that are characterized by the extent of skin involvement – Limited SSc and Diffuse SSc. Pulmonary vascular disease, primarily PAH, occurs in 10 to 40 percent of patients with SSc, more common in patients with longstanding limited cutaneous disease without associated ILD. It can also happen secondary to ILD, particularly in those with diffuse SSc. Dyspnea with exertion and diminished exercise tolerance are the most common initial symptoms but are commonly absent until the disease is fairly advanced. PAH is fairly progressive, and if severe, can lead to cor pulmonale and right sided heart failure. A 65 year old female patient presented with breathlessness and bilateral lower limb swelling since 6 months which progressed in the last 10 days to dyspnea at rest and bilateral pedal edema upto knees. She is a known case of Hypothyroidism on treatment. On examination bilateral infrascapular fine crepitations were present with loud P2 and early diastolic murmur at pulmonary area along with visible jugular venous pulsations and bilateral pedal edema. No significant cutaneous features could be identified. On further investigations she was diagnosed with Pulmonary Arterial Hypertension (RVSP -70 mm Hg) and Cor Pulmonale (RA and RV dilated; IVC dilated non collapsible). ANA By IF came strongly positive with centromere pattern (+3) leading to the diagnosis of Limited Systemic Sclerosis which was confirmed by **CENP B antibody** being strongly positive on the ANA profile. Treatment was initiated with Sildenafil and diuretic therapy with patient being discharged on LTOT. The patient showed dramatic clinical improvement in follow up.

KEYWORDS :

INTRODUCTION:

Systemic sclerosis (SSC) is an orphan disease of unknown etiology, complex pathogenesis, and variable clinical presentations. Patients with SSC can be broadly segregated into two major subsets defined by the pattern of skin involvement and associated with characteristic clinical, serologic features and natural history- Limited Cutaneous SSc and Diffuse Cutaneous SSc. Pulmonary manifestations of SSC include but are not limited to, pulmonary vascular diseases such as pulmonary arterial hypertension (PAH) and pulmonary veno-occlusive disease (PVOD), interstitial lung disease (ILD), and increased susceptibility to lung neoplasms. Pulmonary arterial hypertension affects up to 8-12% of patients with SSc with a 50% mortality rate within 3 years of PAH diagnosis.[1] It usually occurs as a late isolated complication in patients with longstanding limited cutaneous disease without associated ILD and presents with signs and symptoms of right-sided heart failure as evident in the following case.

CASE PRESENTATION:

A 65- year- old female patient presented with breathlessness on exertion since 6 months which progressed to dyspnea at rest over the last 10 days. This was associated with bilateral lower limb swelling since 6 months; insidious in onset and gradually progressive. She is a known case of Hypothyroidism since 1 year on treatment. On arrival at the hospital, the patient was tachypneic with respiratory rate of 32 breaths/minute and maintaining oxygen saturation at 96% on room air. The blood pressure was 118/80 mm Hg with a pulse rate of 106/min. On general examination, it was noted that her neck veins were engorged with visible jugular venous pulsations along with bilateral lower limb pitting, non-tender edema upto knee joint. There were no visible signs of anemia, jaundice, clubbing, or cyanosis. **No significant cutaneous features; skin thickening or any sequelae of Raynaud's phenomenon were present**. On cardiovascular and respiratory system evaluation, bilateral infrascapular fine crepitations were present with loud P2 at pulmonary area and holosystolic murmur heard at the tricuspid area.

Noteworthy investigations included a **BNP level of 404 pg/ml**; **CRP of 11.31 mg/L** and an elevated d-Dimer value of 2105 ng/ml. 2D echo showed dilated Right Atrium, Right Ventricle and Pulmonary Artery with a normal Left Ventricle; LVEF- 50% and RVSP- 70 mm Hg. The echo findings were suggestive of severe PAH (Pulmonary Artery Hypertension) and Severe TR. To identify the cause of this severe PAH; HRCT Thorax was done which was suggestive of significant fibrotic changes with inter and intralobular septal thickening involving the left lower lobe. CT pulmonary angiography showed cardiomegaly with pericardial effusion. A normal Lower Limb Venous Doppler was noted. Finally ANA by IF was sent and it was positive with **3+ Centromere pattern** suggestive of progressive systemic sclerosis-limited form. This was further confirmed with ANA profile showing **Antibody against CENP-B** positive thus leading to the diagnosis of Limited SSc.

The patient was treated with Sildenafil (Phosphodiesterase-5 inhibitor) and supportive management in the form of diuretics and oxygen supplementation. She was discharged with LTOT and had a marked improvement in symptoms and signs on follow up.

Figure 1.

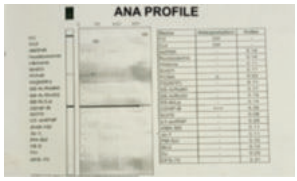

Figure 2.

DISCUSSION:

Scleroderma is a complex disease that involves the interaction between various factors, including environmental factors, host factors, and pathogenic factors. One of the key events in the pathogenesis of scleroderma is endothelial injury, which is not fully understood. This event is also coupled with the depletion of bone marrow-derived endothelial vascular progenitor cells, which impairs the ability to repair vascular damage. This is particularly relevant in the pathogenesis of SSc-PH, a disease characterized by intimal proliferation, medial hyperplasia, and adventitial fibrosis in the small pulmonary arterioles.[2]

Systemic sclerosis (SSc) frequently gives rise to the occurrence of pulmonary arterial hypertension (PAH), a complication that manifests with notable frequency. [3] Pulmonary arterial hypertension (PAH) is characterized by a mean pressure exceeding 20 mmHg in the pulmonary artery while maintaining a pulmonary capillary wedge pressure below 15 mmHg and exhibiting a pulmonary vascular resistance surpassing 3 Wood units. The disease often begins as a functional problem of vasoconstriction due to an imbalance between up-regulated endothelium-derived vasoconstrictors and down-regulated endothelium-derived vasodilators. Over time, the effects of endothelial-derived vasoconstrictors, along with profibrotic cytokines such as transforming growth factor 1, lead to structural changes in the pulmonary vasculature, resulting in an obliterative arteriopathy and eventual pulmonary vascular rarefaction. Additionally, coexistent parenchymal fibrosis (interstitial lung disease) contributes to the pathogenesis of pulmonary hypertension by entrapment and obliteration of small arterioles within the fibrotic tissue. The micro vasculopathy in SSc-PH alters the hemodynamics in the pulmonary circulation, resulting in elevated pulmonary vascular resistance and sustained right ventricular pressure overload. Although compensatory right ventricular hypertrophy occurs initially, eventually the right heart fails, and cardiac output and cardiac index decline. Understanding the complex interplay between the different factors involved in the pathogenesis of scleroderma and SSc-PH is essential for developing screening methods and effective treatments for these diseases. [4]

The majority of patients with systemic sclerosis (SSc) exhibit the presence of antibodies targeting the angiotensin II type-1 receptor, endothelin-1 receptor type A, anti-endothelial cell antibodies, and anti-fibroblast antibodies. These antibodies are known to have substantial involvement in the process of vascular remodeling. Anticardiolipin antibodies are associated with pulmonary hypertension in SSc, suggesting that endothelial injury and small vessel thrombosis may play important roles in the pathogenesis of SSc-PAH.[3]

Risk factors associated with the development of pulmonary arterial hypertension (PAH) in patients with systemic sclerosis typically encompass late-onset disease, as well as additional factors such as a solitary decrease in the diffusing capacity of the lungs for carbon monoxide (DLCO) and a forced vital capacity (FVC)/DLCO ratio exceeding 1.6. A combined decrease in the ratio of Diffusing lung capacity to carbon monoxide (DLCO)/alveolar volume with an elevation of serum N-terminal pro-brain natriuretic peptide (N-TproBNP) levels is also an associated risk factor. Some statistics also show that the post-menopausal onset of disease in female patients can act as a risk factor.[5]

Patients with isolated PAH suffer from limited SSc disease developing PAH after 10-15 years. [6]Usually these patients present with cutaneous features and are diagnosed at any earlier stage by the cutaneous features and signs and symptoms other than those due to PAH.In contrast, it has been observed that individuals diagnosed with diffuse systemic sclerosis (SSc) face a higher likelihood of developing interstitial lung disease (ILD) within the initial five years following the diagnosis of SSc. This period is characterized by the most significant rate of decline in forced vital capacity (FVC).[7]

However, patients with Systemic Sclerosis, with limited or diffuse disease, may present at any stage in the course of their disease with pulmonary hypertension, whether associated or not with Interstitial Lung Disease(ILD).[8]

Pulmonary arterial hypertension (PAH) is the primary factor contributing to the mortality rates observed in patients diagnosed with systemic sclerosis (Ssc), thereby exacerbating overall survival outcomes.[5,9]

In our case, the patient presented with signs and symptoms of right-sided heart failure due to pulmonary hypertension as evident by the 2D Echo findings. After ruling out other possible causes of pulmonary hypertension, ANA by IF was sent which was strongly positive with a +3 centromere pattern; diagnosis of limited systemic sclerosis was put forth which was confirmed by CENP B antibody being strongly positive on the ANA profile. **This case is unique in a way that the patient presented with cor pulmonale without any cutaneous or other systemic features of Limited Systemic Sclerosis.**

Serum levels of NT-proBNP correlate with the presence and severity of PAH, as well as survival. While it can be used for screening purposes it is not specific for PAH and may occur in other forms of left and right sided heart failure.

Radiological evaluation is crucial in diagnosing and quantifying the extent of pulmonary damage in SSc patients. High-resolution computed tomography (HRCT) is a sensitive and specific tool for detecting pulmonary pathology due to rheumatic disease, and different scores such as visual score, Goh's score, Wells' score, and Warrick's score are used to evaluate radiological alterations in lung tissue. Additionally, signs such as the diameter of the pulmonary artery, the pulmonary artery to aortic diameter ratio, and the segmental pulmonary arteries' diameter to relative bronchial tube diameter are used to diagnose the presence of pulmonary hypertension (PH) with CT. These methods of diagnosis and evaluation are essential in managing the complex disease of SSc and providing proper treatment to patients. [10]

Hemodynamic studies, such as transthoracic echocardiogram and right heart catheterization, are also performed to assess the function of the heart and the blood vessels. Ideally, cardiac catheterization is required to confirm the diagnosis of suspected PAH; assess its severity, including the degree of right heart dysfunction: rule out veno-occlusive disease and other cardiac (postcapillary) causes of pulmonary hypertension, and provide prognostic parameters. However, it is not routinely performed in our hospital settings.

Presently, no guidelines are available to identify patients with limited SS complicated by PAH for screening. [11]

Although systemic sclerosis-associated pulmonary arterial hypertension (SSc-PAH) exhibits more favorable hemodynamics, its prognosis is comparatively worse and treatment response is inferior when compared to idiopathic pulmonary arterial hypertension (IPAH) which makes early diagnosis and initiating treatment more imperative.

Treatment in our case was started with sildenafil (Phosphodiesterase-5 inhibitor) and supportive management in the form of diuretic therapy and oxygen supplementation. The patient was discharged with LTOT. On follow-up, marked improvement in signs and symptoms was noted.

Phosphodiesterase-5 inhibitors (PDE5i) such as sildenafil, tadalafil, and vardenafil are commonly used for the treatment of pulmonary arterial hypertension (PAH). These drugs help dilate blood vessels, improve exercise capacity, and enhance the quality of life for PAH patients. It is advisable to be cautious when using PDE5 inhibitors (PDE5i), such as sildenafil, tadalafil, and vardenafil, in patients who are taking nitrates or nitric oxide donors. Combination therapy with other PAH drugs like prostacyclin analogues, endothelin receptor antagonists, and soluble guanylate cyclase stimulators has been shown to provide greater benefits for patients. Close monitoring of patients with regular assessments is necessary to determine the best treatment plan, which may include oxygen therapy, diuretics, and anticoagulation, among other interventions. PDE5i should not be used as monotherapy but as part of a comprehensive treatment plan.[12]

Lung transplantation continues to be a viable alternative for a specific subset of patients diagnosed with systemic sclerosis (SSc) and pulmonary arterial hypertension (PAH) who do not respond to conventional medical treatments. The two-year survival rates for these patients, which stand at 64%, are similar to those observed in individuals with idiopathic interstitial lung disease (ILD) or PAH.[3]

Thus, to conclude cases have been reported with acute cor pulmonale as the presenting feature of systemic sclerosis. Due to the elevated incidence of PAH in SSC, the differential diagnosis of systemic sclerosis should be borne in mind in any patient presenting with cor pulmonale. Acute cor pulmonale in the setting of Systemic Sclerosis

portends a poor prognosis with associated 50% mortality. More studies are therefore needed to identify strategies for early identification that will improve outcomes in this population.[9]

REFERENCES:

1. Chaisson NF, Hassoun PM. Systemic sclerosis-associated pulmonary arterial hypertension. Chest. 2013 Oct;144(4):1346-1356. doi: 10.1378/chest.12-2396. PMID: 24081346; PMCID: PMC3787920.
2. Kuwana, M., Okazaki, Y., Yasuoka, H., Kawakami, Y., & Ikeda, Y. (2004). Defective vasculogenesis in systemic sclerosis. The Lancet, 364(9434), 603–610. doi:10.1016/s0140-6736(04)16853-0 10.1016/s0140-6736(04)16853-0
3. Aithala R, Alex AG, Danda D. Pulmonary hypertension in connective tissue diseases: an update. Int J Rheum Dis. 2017;20(1):5–24.
4. Chatterjee S. Pulmonary hypertension in systemic sclerosis. Semin Arthritis Rheum. 2011 Aug;41(1):19-37. doi: 10.1016/j.semarthrit.2010.08.004. Epub 2010 Nov 2. PMID: 21047671.
5. Hassoun PM. Lung involvement in systemic sclerosis. Presse Med. 2011 Jan;40(1 Pt 2):e3-e17. doi: 10.1016/j.lpm.2010.08.006. Epub 2010 Dec 30. PMID: 21195581; PMCID: PMC3066150.
6. Steen V, Medsger TA Jr. Predictors of isolated pulmonary hypertension in patients with systemic sclerosis and limited cutaneous involvement. Arthritis Rheum. 2003 Feb;48(2):516-22. doi: 10.1002/art.10775. PMID: 12571862.
7. Steen V. Predictors of end stage lung disease in systemic sclerosis. Ann Rheum Dis. 2003 Feb;62(2):97-9. doi: 10.1136/ard.62.2.97. PMID: 12525376; PMCID: PMC1754422.
8. Chang B, Wigley FM, White B, Wise RA. Scleroderma patients with combined pulmonary hypertension and interstitial lung disease. J Rheumatol. 2003 Nov;30(11):2398-405. PMID: 14677184.
9. NAVNEET KAUR, ADNAN KHALIF, ACUTE COR PULMONALE AS THE INITIAL PRESENTATION OF LIMITED SYSTEMIC SCLEROSIS, Chest, Volume 154, Issue 4, Supplement, 2018, Page 1048A, ISSN 0012-3692, https://doi.org/10.1016/j.chest.2018.08.946.
10. Zompatori M, Leone MB, Giannotta M, et al. Pulmonary hypertension and systemic sclerosis: the role of high-resolution computed tomography. La Radiologia Medica. 2013 Dec;118(8):1360-1372. DOI: 10.1007/s11547-013-0934-1. PMID: 23716290.
11. Jentzer JC, Mathier MA. Pulmonary Hypertension in the Intensive Care Unit. J Intensive Care Med. 2016 Jul;31(6):369-85. doi: 10.1177/0885066615583652. Epub 2015 May 5. PMID: 25944777.
12. Galiè N, Corris P, Frost A, et al. Updated Treatment Algorithm of Pulmonary Arterial Hypertension. J Am Coll Cardiol. 2013 Dec, 62 (25_Supplement) D60–D72. https://doi.org/10.1016/j.jacc.2013.10.031