A Rare Presentation of Pulmonary Arterial Hypertension as an Initial Manifestation of Systemic Lupus Erythematosus in a young girl

Abstract

There is a great dilemma in diagnosing sinus venosus ASD with eisenmengerisation and primary pulmonary hypertension (PPH) in younger patients. In the majority of children, PAH is associated with structural cardiac abnormality leading to Eisenmenger syndrome. Early presentation of pulmonary arterial hypertension (PAH) in patients ~~of~~ with systemic lupus erythematosus (SLE) is a rare presentation in patients worldwide. There are multifactorial causes of the occurrence of pulmonary hypertension. ~~Usual~~ The usual occurrence of PAH is seen in patients with full-~~-~~blown SLE or ~~after~~ months or years later in the disease course. We describe a case of a 10 ~~year's~~ year female who presented with PAH a presenting feature of SLE after ruling out all other causes of PAH. ~~Patient~~ The patient was started with vasodilators and immunosuppressants, with a partial response to treatment on serial follow-up.

Introduction

Till today there is a great diagnostic dilemma of pulmonary hypertension (PH) in younger patients. SLE Being a chronic illness, Pulmonary manifestations include pleural effusion, pleuritis, diffuse alveolar hemorrhage, shrinking lung syndrome, interstitial lung disease, pulmonary thromboembolism, and pulmonary hypertension (1). PH is defined as mean pulmonary artery pressure of more than or equal to 20 mmHg. Later there is a vascular remodelling setting in leading to right heart failure (2). In Patients of SLE occurrence of pulmonary complications doesn't correspond to the duration of the disease (1). Pulmonary arterial hypertension (PAH) is a rare and ~~a~~ life-threatening complication and its diagnosis is usually delayed to due rarity and more than 40 percent patients with early PAH remain~~s~~ asymptomatic (2). Out of various ~~antibody~~ antibodies used to diagnose SLE, anti-PCNA (proliferating cell nuclear antigen) antibodies is seen in approximately 2% patients of SLE. Occurrence of anti PCNA antibody is considered as a disease specific antibody in diagnosis of SLE (5). ~~Usual~~ The usual prevalence of PAH in patients of SLE is 2.8 to 23.3 % (6).

Here we describe a rare case of a young female who presented as a case of suspected sinus venosus atrial septal defect (ASD) with eisenmengerisation and on thorough investigations was found to be suffering from PH with SLE.

Case Presentation

A 10 ~~year's~~ year female was referred as a case of suspected sinus venosus ASD with eisenmengerisation to our hospital. Patient was having chronic exertional breathlessness which gradually progressed from New York Heart Association (NYHA) class II to III over the past 3 years. There was no evidence of icterus, clubbing, lymphadenopathy, edema. She was afebrile, her pulse was 96/min, her blood pressure of 90/60 mm Hg, respiratory rate was 24/minute. Examination of the cardiovascular system revealed grade III parasternal heave and a loud pulmonary component of the second heart sound. Examination of other systems was within normal limits. Her routine blood and urine investigations including thyroid function, renal function, hepatic function tests were within normal limits.
Her chest radiograph was suggestive of cardiomegaly, with bilateral hilar prominence~~'s~~.

Her electrocardiogram (ECG) showed sinus tachycardia, right ventricular hypertrophy, right axis deviation, p-pulmonale, tall R waves in V1, right ventricular strain. Patients trans-thoracic echo was

Commented [Er1]: Order of references needs correction.

Commented [Er2]: Plagiarized from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7920217/
Suggestion: Paraphrase and Rewrite

Commented [Er3]: Plagiarized from: https://www.brainscape.com/flashcards/aha-pals-8734436/packs/14915785
Suggestion: Paraphrase and Rewrite

suggestive of dilated right atrium and ventricle with severe pulmonary hypertension, inter atrial septum drop out of 2.5 mm was noted. Bubble contrast was suggestive of right to left shunt through PFO. Transesophageal echocardiography was not done as the patient was uncooperative. Patients' cardiac catheterization study was suggestive of MVO2 of 52.4 %, Qp/Qs of 0.6, and PVR of 34.26 WU was concluded for having either ~~of~~ ASD with eisenmengerisation or PAH with reversal of shunt through PFO. A Cardiac CT of patient was done to rule out sinus venosus ASD. It was suggestive of an oblique slit-like defect between the septum primum and septum secundum of 2 mm in mid portion of inter atrial septum without any obvious jet suggestive of patent foramen ovale and cardiomegaly with dilated right atrium (6.0 X 5.2 cm) and right ventricle (4.9 cm in mid ventricle level in diastole) with reflux of contrast in hepatic veins suggestive of right heart strain pattern. At this point, we ~~came to the conclusion~~concluded that the patient is having primary PAH with reversal of shunt through PFO. We started evaluating for the aetiology of primary PH. CT pulmonary angiography was done to rule out any pulmonary AV malformations and AV fistulas and any extracardiac shunts and it was suggestive of a dilated main pulmonary artery, left and right branch of pulmonary artery with P/A ratio of > 1 suggestive of PAH. Ultrasound of the abdomen and hepatoportal doppler was done to look for intra-hepatic shunts and it was within normal limits. CECT abdomen and pelvis was done to look for any porto-systemic shunt and it was suggestive of normal study. Later in course of hospitalization patient's Antinuclear antibody profile was done and was strongly positive for PCNA antibody (1:320 titre) which was suggestive of SLE. Retrospectively it was found that patient never had a history of photosensitivity to the skin, arthralgias of the small joints of the fingers of the hands and wrists, hair loss, or rash over the forehead and face. There were no joint swellings, alopecia, or rash on her general examination.

Discussion

Our patient presented with increasing intensity of dyspnea on exertion in a younger age and cause of which, from the clinical history and examination, appeared to be cardiac. Echocardiography findings were suggestive of severe PAH with dilated right atrium (RA), and right ventricle (RV). The differential diagnosis then considered ~~were~~ was sinus venosus ASD with eisenmengerisation or PPH with right to left shunt through PFO. Later after a stepwise workup of the patient, she was found to have pulmonary hypertension secondary to SLE.

SLE is an autoimmune disease characterized by spectrum of clinical and immunological abnormalities (1). Occurrence of PAH in SLE is not uncommon but the occurrence of PAH in patients of SLE in younger age groups is a rare entity (1, 3, 6). In majority of children, PAH is associated with structural cardiac abnormality leading to Eisenmenger syndrome. Clinically differentiating patients with PPH with Eisenmenger syndrome is difficult (3). It was there is no significant association between the duration of SLE and the occurrence of pulmonary complications (1). PH is defined as mean pulmonary arterial pressure (mPAP) ≥ 25 mm Hg (2, 6). There is remodelling leading to right heart failure. RVH is defined as precapillary PH with a mPAP ≥ 25 mm Hg, pulmonary artery wedge pressure (PAWP) < 15 mm Hg, and pulmonary venous resistance (PVR) > 3 Wood units (2, 6). According to French registry mean age of PAH is 52 ± 15 years, with 25% of patients with > 60 years (2, 6). There is chronic change in pulmonary vasculature resulting in remodelling of pulmonary vasculature, inflammation, and thrombosis within small arteries and arterioles. Histologically, there is intimal hyperplasia, medial hypertrophy, and proliferation of adventitia. Increase in levels of vasoconstrictor like thromboxane, endothelin, serotonin levels and decrease levels of vasodilators like prostacyclin, nitric oxide (NO), and vasoactive intestinal polypeptide. This in turn leads to increase in pulmonary vascular resistance (2). Echocardiography can determine pulmonary artery systolic pressure by estimation of tricuspid regurgitation (TR) jet velocity and using Bernoulli's equation. Also, RV assessment can be done by measuring the size and function of both the right atrium and ventricle (2, 3). Enlarged or hypertrophied

Commented [Er4]: Plagiarized from: https://www.sciencedirect.com/science/article/pii/S1930043323003321
Suggestion: Rewrite text

Commented [Er5]: Plagiarized from: https://www.ncbi.nlm.nih.gov/books/NBK535405/
Suggestion: Paraphrase and Rewrite

Commented [Er6]: Give reference.

Commented [Er7]: Give reference.

Commented [Er8]: Give Reference.

Commented [Er9]: Plagiarized from: https://www.sciencedirect.com/topics/nursing-and-health-professions/artery-intima-proliferation
Suggestion: Paraphrase and Rewrite

Commented [Er10]: Give reference.

Commented [Er11]: Give reference.

Commented [Er12]: Plagiarized from: https://erj.ersjournals.com/content/46/4/1178
Suggestion: rewrite text

Commented [Er13]: Give Reference for this.

right heart chambers with D-shaped interventricular septum can indicate impaired right heart function. Fractional area changes of the RV and tricuspid annular plane systolic excursion (TAPSE) can estimate RV function (2, 3). Exercise testing by a six-minute walk test can be used to measure degree of functional impairment. In PPH exercise capacity correlates with right atrial pressure, pulmonary arterial pressure, and cardiac index (3). Cardiac catheterization is necessary to establish PAH, mPAP ≥ 25 mm Hg, PAWP ≤ 15 mm Hg, and PVR > 3 Wood units ~~is~~ are suggestive of PAH (2, 3, 6). Inhaled NO, intravenous epoprostenol, or adenosine can be used to determine vasoreactivity (2, 3). Cardiac magnetic resonance imaging (CMR) can be used to evaluate RV function, pulmonary vascular bed, and myocardium. CMR remains the gold standard in estimating RV size and function as it has better spatial resolution, and freedom from acoustic window (2). Proliferating cell nuclear antigen (PCNA) is an intranuclear protein and has a role in DNA repair and replication. Anti-PCNA antibodies are considered a rare but highly specific marker for SLE (4, 5). These antibodies are seen in approximately 2-6 % of patients with SLE, little is known about the clinical relevance of a positive anti-PCNA test, and remains a scope for further research (4, 5).

Commented [Er14]: Give reference.

Commented [Er15]: Give reference.

Conclusion

Differentiation of Pulmonary hypertension from primary pulmonary artery hypertension in young can be quiet confusing. Many patients remain underdiagnosed for PPH as many patients are considered to be having PH secondary to structural heart diseases causing delay in diagnosis and treatment. ~~Overall~~ The overall effect is the progression of disease leading to high morbidity and mortality in younger patients by diagnosing them as Eisenmenger syndrome and giving only palliative care considering the irreversible nature of PAH. Every patient presenting with suspicion of pulmonary hypertension should undergo a complete workup to facilitate early diagnosis and treatment.

References

1. Memet B, Ginzler EM. Pulmonary manifestations of systemic lupus erythematosus. Semin Respir Crit Care Med. 2007 Aug;28(4):441-50. doi: 10.1055/s-2007-985665. PMID: 17764061.
2. Memon HA, Park MH. Pulmonary Arterial Hypertension in Women. Methodist Debakey Cardiovasc J. 2017 Oct-Dec;13(4):224-237. doi: 10.14797/mdcj-13-4-224. PMID: 29744015; PMCID: PMC5935282.
3. Haworth SG. Pulmonary hypertension in the young. Heart. 2002 Dec;88(6):658-64. doi:10.1136/heart.88.6.658. PMID: 12433912; PMCID: PMC1767475.
4. Vermeersch P, De Beeck KO, Lauwerys BR, et alAntinuclear antibodies directed against proliferating cell nuclear antigen are not specifically associated with systemic lupus erythematosusAnnals of the Rheumatic Diseases 2009;68:1791-1793.
5. Satoh M, Vázquez-Del Mercado M, Chan EK. Clinical interpretation of antinuclear antibody tests in systemic rheumatic diseases. Mod Rheumatol. 2009;19(3):219-28. doi: 10.1007/s10165-009-0155-3. Epub 2009 Mar 10. PMID: 19277826; PMCID: PMC2876095.
6. Xia YK, Tu SH, Hu YH, Wang Y, Chen Z, Day HT, Ross K. Pulmonary hypertension in systemic lupus erythematosus: a systematic review and analysis of 642 cases in Chinese population. Rheumatol Int. 2013 May;33(5):1211-7. doi: 10.1007/s00296-012-2525-y. Epub 2012 Sep 16. PMID: 22983159; PMCID: PMC3632720.