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An Uncommon Incidence of Pulmonary Hypertension Associated With Neurofibromatosis Type 1: A Case Report

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Abstract

Pulmonary hypertension (PH) is often a difficult condition to diagnose, since it occurs insidiously and is a diagnosis of exclusion. Patients with neurofibromatosis type 1 (NFT1) have been associated with severe exacerbations of PH. To our knowledge, less than 20 cases of PH in NFT1 patients have been reported. However, the severity of presenting symptoms requires physicians to be aware of this association and pursue the appropriate diagnostic workup. In our report, we present a 54-year-old NFT1 patient who presented with worsening dyspnea secondary to PH, which was being treated with trepostanil and macitetan. She required a right heart catheterization to assess her pulmonary artery pressures (which remained elevated). She was placed on tadalafil in addition to trepostanil and macitetan and noted significant resolution of her symptoms. Further studies are required to explore the association between PH and NFT1 and examine the efficacy of triple therapy with endothelin receptor antagonists, phosphodiesterase 5 inhibitors, and parenteral prostanoids in the initial treatment of PH in the aforementioned patient population.

Keywords

pulmonary hypertension, neurofibromatosis type 1

Introduction

To our knowledge, there are less than 20 documented cases of pulmonary hypertension (PH) occurring in patients with neurofibromatosis type 1 (NFT1). Although the association is still very much being explored, it appears that NFT1 patients initially present with rapidly worsening symptoms of PH, such as dyspnea with minimal physical activity. Prompt recognition is required in order to pursue appropriate diagnostic workup, such as echocardiography and right heart catheterization, as well as initiation of appropriate medical therapy.

Case Presentation

We present a 54-year-old female with past medical history most significant for NFT1, PH, breast cancer treated previously with chemotherapy and radiation therapy, who presented from home with worsening dyspnea and chest pain.

Our patient was diagnosed with PH 3 months prior to the current admission. She had a transthoracic echocardiogram (TTE) performed at that time which showed a severely dilated right-sided chambers along with severe tricuspid regurgitation. The estimated right ventricular systolic pressure was 101 mm Hg. A right heart catheterization revealed a pulmonary artery pressure of 87/37 mm Hg and a mean pressure of 55 mm Hg. She was treated with trepostanil infusion at 45 ng/kg/min and was discharged to home on macitetan 10 mg daily, furosemide 20 mg twice daily, and spironolactone 25 mg daily.

Past surgical history was significant for bilateral mastectomy and hysterectomy. She denied cigarette smoking, alcohol use, or recreational drug use.

During her admission, our patient stated that her symptoms started 3 days prior to presentation. Her symptoms of dyspnea were progressive to a point where she was unable to walk around her house. She attested to chest pain that accompanied the dyspnea, which was left sided, constant, and nonradiating. She denied weight loss, and did not have a history of HIV, venous thromboembolism, or pulmonary embolism.

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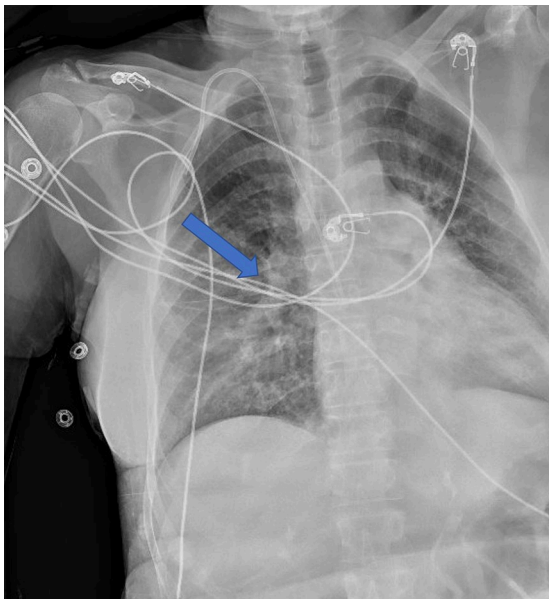

Figure 1. Chest radiography showed prominent pulmonary arteries, concurrent with pulmonary hypertension.

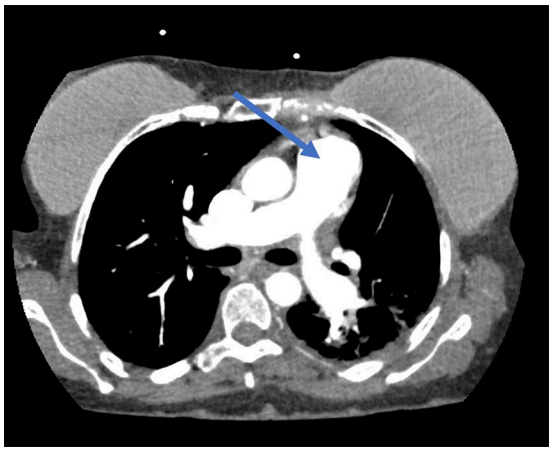

Figure 2. Computed tomography angiography of the thorax and a prominent pulmonary trunk (arrow).

In the emergency department, she was noted to have a blood pressure of 92/72 mm Hg (concurrent with her baseline), heart rate of 114 beats per minute, respiratory rate of 25 breaths per minute, and an oxygen saturation of 84% on room air. Physical examination showed a woman in acute respiratory distress, with tachycardia, tachypnea, and 1+ bilateral lower extremity pitting edema. Her initial troponin was noted to be <0.01 ng/dL. Chest radiography (Figure 1) showed prominent pulmonary arteries, consistent with PH. Computed tomography angiography (CTA)

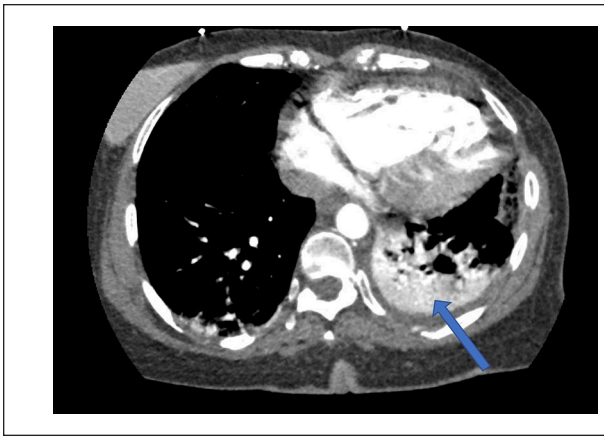

Figure 3. Computed tomography scan showing lung windows with left-sided pleural effusion (blue arrow).

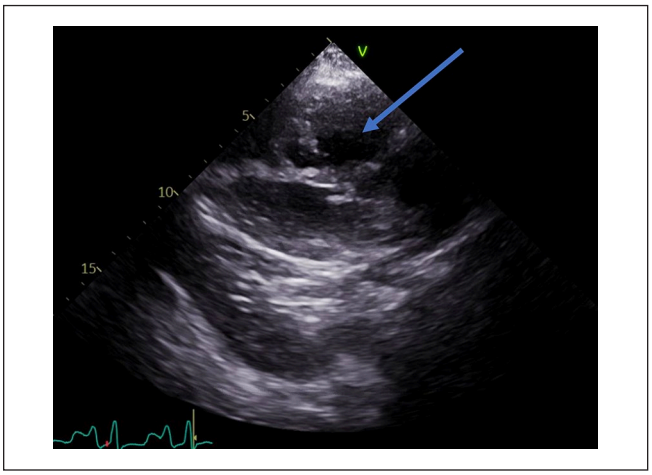

Figure 4. A transthoracic echocardiogram was performed, which showed an ejection fraction of 65% to 70%, enlarged right ventricle (arrow) with decrease right ventricular systolic function, and moderate tricuspid regurgitation.

of the thorax (Figure 2) showed a small pleural effusion and a prominent pulmonary trunk, likely secondary to increased pressure in the pulmonary system. A TTE (Figure 3) was performed, which showed an ejection fraction of 65% to 70% along with an enlarged right ventricle with decreased right ventricular systolic function and moderate tricuspid regurgitation (Figure 4). She was continued on her home dose of furosemide and spironolactone.

A right heart catheterization was performed during this admission showed a right atrial pressure of 6 mm Hg, right ventricular pressures of 74/10 mm Hg, pulmonary artery pressure of 73/25 mm Hg with a mean pulmonary artery pressure of 47 mm Hg, and pulmonary capillary wedge pressure of 10 mm Hg.

Our patient was restarted on all her home medications in addition to tadalafil 20 mg daily. Her symptoms improved drastically, and she was discharged from the hospital.

Discussion

PH can be divided into 5 subclasses according to the World Health Organization (WHO) classification. Of these, group V is considered to be PH in the setting of unclear multifactorial mechanisms, such as in the setting of neurofibromatosis type 1.[1]

The clinical features of PH are insidious in onset and may initially consist of fatigue and generalized weakness. As the disease progresses, patients may complain of signs and symptoms of right-sided heart failure, including bilateral pedal edema, abdominal swelling, and syncope. Chest radiography and chest computed tomography could show enlargement of the pulmonary trunk and arteries, as well as bilateral pleural effusions.

The initial step in diagnosis would be pursuing a TTE, which would reveal a pulmonary artery systolic pressure >35 mm Hg in young adults or >40 mm Hg in older adults. A right heart catheterization is required for the confirmation of the diagnosis of PH.

The management of PH is very extensive. Patients who are asymptomatic can be placed on vasodilator monotherapy, usually phosphodiesterase 5 inhibitors (PDE5I). Patients who are unable to climb a flight of stairs, walk 2 blocks, or experience limitations of daily activities would require an endothelin receptor antagonist (ERA) and a PDE5I.[2] Patients who are unable to carry out any physical activity require parenteral prostenoids, such as intravenous epoprostanol or trepostanil in addition to an ERA or a PDE5I.

Less than 20 cases of PH have been reported in patients with NFT1. In addition to being aware of this association, health care providers must be aware of the sudden decline in function due to PH in this population. Our patient initially presented with shortness of breath and was tried on macitetan (ERA) and trepostanil (parenteral prostanoid). However, within the course of just 2 months, she began experiencing worsening dyspnea and fatigue with minimal physical activity prompting hospitalization and initiation of tadalafil, a PDE5I. Given a PCWP (pulmonary capillary wedge pressure) of 10 mm Hg on right heart catheterization, the likelihood of this presentation belonging to WHO group II (PH secondary to heart failure) was low. It was important to rule out PH secondary to WHO group II, since the initiation of vasodilators would be contraindicated. A computed tomography scan of thorax did not show any inherent lung disease, nor pulmonary emboli, making WHO groups III and IV less likely. Several other cases document similar PH exacerbations in patients with NFT1 who showed improvement after the initiation of PDE5I's, which drove the decision to initiate tadalafil in our patient.[3-7] Currently, there is minimal data to support the use of vasodilators in the management of WHO group V PH.[7] Since pulmonary venous involvement is implicated in group V PH, the use of pulmonary vasodilators is not standard of care. However, our patient did show improvement with pulmonary vasodilators. Further studies are necessary to assess the efficacy of starting triple therapy with PDE5I, ERA, and parenteral prostanoids in order to decrease hospitalization and improve quality of life.

There are several other cases that have tried different modalities to manage PH in NFT1. Atrial septostomy was found to be successful in managing PH in one study.[8] Additionally, another study was able to demonstrate a decrease in pulmonary artery systolic pressure on repeat right heart catheterization after the initiation of sorafenib, a tyrosine kinase inhibitor.[9]

Conclusion

The diagnosis of PH can be difficult to make, until symptoms and signs of right-sided heart failure develop. In patients with NFT1, symptoms of dyspnea and fatigue should prompt health care providers to pursue a diagnostic work up for PH, including a right heart catheterization. Further studies are required to assess the efficacy of initially starting a triple therapy regimen consisting of parenteral prostanoids, PDE5Is, and ERAs in NFT1 patients diagnosed with PH (regardless of WHO subclass presentation), in order to avoid rapid exacerbation of the disease.

Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient for their anonymized information to be published in this article.

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References

1. Frost A, Badesch D, Gibbs JSR, et al. Diagnosis of pulmonary hypertension. *Eur Respir J*. 2019;53:1801904.
2. Galiè N, Barberà JA, Frost AE, et al; AMBITION Investigators. Initial use of ambrisentan plus tadalafil in pulmonary arterial hypertension. *N Engl J Med*. 2015;373:834-844.

3. Gumbiene L, Petrulioniene Z, Rucinskas K, et al. Pulmonary hypertension: a fatal complication of neurofibromatosis type 1. *Respir Care*. 2011;56:1844-1848.
4. Carrascosa MF, Larroque IC, Rivero JLG, et al. Pulmonary arterial hypertension associated with neurofibromatosis type 1. *BMJ Case Rep*. 2010;2010:bcr0520102961.
5. Chaddha U, Puscas I, Prosper A, et al. 63-year-old woman with neurofibromatosis type 1 and pulmonary hypertension with worsening hypoxemia. *Chest*. 2017;152:e89-e93.
6. Rojas M, Mubarik A, Henderson EA, et al. Pulmonary arterial hypertension: a rare yet fatal complication of neurofibromatosis type 1. *Respir Med Case Reports*. 2019;27:100832.
7. Jutant EM, Girerd B, Jaïs X, et al. Pulmonary hypertension associated with neurofibromatosis type 1. *Eur Respir Rev*. 2018;27:180053.
8. Giannakoulas G, Savvoulidis P, Grosomanidis V, Mouratoglou SA, Karvounis H, Hadjimiltiades S. Atrial septostomy and disease targeting therapy in pulmonary hypertension secondary to neurofibromatosis. *BMC Pulm Med*. 2016; 16:175.
9. Tamura Y, Ono T, Sano M, Fukuda K, Kataoka M, Satoh T. Favorable effect of sorafenib in a patient with neurofibromatosis-associated pulmonary hypertension. *Am J Respir Crit Care Med*. 2012;186:291-292.