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CLINICAL VIGNETTE

Eisenmenger Syndrome: A Potential Complication of Small VSDs

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Abstract

Eisenmenger syndrome (ES) is the process in which a long-standing left-to-right cardiac shunt caused by a congenital heart defect is eventually reversed into a cyanotic right-to-left shunt.[1] ES associated with small VSDs is rare but crucial to recognize.[2]

We report a 31-year-old female with WHO Diagnostic Group 1: pulmonary arterial hypertension associated with congenital heart diseases, and known small VSD with ES, who completed heart and lung transplantation.

Background

Pulmonary arterial hypertension (PAH) is a common complication among patients with congenital heart disease (CHD).[3,4] In the presence of an unrepaired left-to-right shunt, the pressure of the pulmonary circulation leads to vascular remodeling, resulting in a progressive rise in pulmonary vascular resistance and right ventricular overload.[5] Despite growing evidence supporting use of PAH therapies in PAH associated with CHD (PAH-CHD) population, mortality remains high. Three percent of patients with small or moderate VSD defects, ≤1.5 cm in diameter will develop Eisenmenger syndrome.[2] We present a patient with severe PAH and a small VSD, who was referred to transplantation due to inadequate response to PAH therapy and Eisenmenger syndrome.

Case

A 31-year-old female, with WHO Diagnostic Group 1: pulmonary arterial hypertension associated with congenital heart diseases, and unrepaired Ventricular septal defect (VSD) presents with worsening dyspnea.

The patient grew up in the Philippines and was monitored regularly for known VSD. At age 13, she was hiking up a mountain in Thailand and felt short of breath and her mother noticed her lips were blue. On return to home in the Philippines she was diagnosed with idiopathic pulmonary arterial hypertension by Echocardiogram. She moved to Australia for further care and started treatment with Bosentan. At age 15 years she transferred her care to Stanford and was stable on oral sildenafil and subcutaneous Treprostinil pump for 8 years. At this time, her 6-minute walk test (6MWD) was 1501 feet. Echocardiogram revealed RV with moderate dilation, and right ventricular hypertrophy with moderate reduction of RV function. RA showed no dilation, and a small membranous VSD. Right Heart Catheterization revealed PVR (pulmonary vascular resistance) = 18.4.

The patient transferred to school in Israel for five years and was lost to follow-up. In the interim, was hospitalized for two weeks with pulmonary hemorrhage. The patient still reports bleeding with hemoptysis and dyspnea at exertion. Her 6MWD and SpO2 were stable. Her RHC was similar in terms of PAP and Qp:Qs compared to the prior RHC, but her PVR (25.5) was significantly worse compared with 15 years prior. Echocardiogram revealed a small peri membranous VSD with bidirectional shunting. There was worsening right ventricular enlargement with marked systolic dysfunction. Estimated RVFAC = 18%. Moderate RVH. New onset of mild to moderate TR with an estimated RVSP of 102 mmHg (RAP = 5 mmHg). The patient was placed on the transplant list for heart and lung a few months later and completed transplantation five years later.

Discussion

This case raises several important issues in the management of patients with PH associated with congenital heart disease (CHD). This highlights changes in management strategies for these patients regarding screening of CHD in developing countries and potential indications for transplant in PAH-CHD.

CHD screening in developing countries

CHD in developing countries is typically diagnosed late due to lack of access to healthcare, and lack of data and knowledge regarding CHD.[6] Lack of data on prevalence of congenital malformations at birth is due to limited diagnostics, poor epidemiological data, and absence of birth defect registries.[7] Late diagnosis of CHD in conjunction with lack of expertise for timely repair of cardiac defects results in further development of PAH. Late presentation and diagnosis is also due to poor health literacy and lack of healthcare access. There is also a lack of CHD awareness in health workers, leading to misdiagnosis and inappropriate counseling.[8] Enhancing education of healthcare providers, providing proper diagnostic tools, and increasing access is key to improving CHD screening in these populations.

Indicators for transplant in PAH-CHD

An argument has been raised about the impact of hemoptysis on mortality in PAH-CHD. Studies have reported a mortality rate of 3% to 11.4% in patients with PAH-CHD presenting with hemoptysis.[9-11] The reported decrease in fatal hemoptysis in PAH-CHD over the past decades may be explained by improvement in clinical understanding, medical management, and interventional techniques for pulmonary vascular disease. Nevertheless, one could argue that recurrent hemoptysis may reflect disease progression that requires the escalation of treatment and an early referral for transplantation assessment.[12]

Conclusion

A small VSD can contribute to the development of PAH and even ES. Special attention should be given to improving CHD screening in developing countries to avoid late diagnosis and disease progression. It is important to monitor for indicators of disease progression such as hemoptysis for early referral to transplantation.

REFERENCES

1. **Basit H, Wallen TJ, Sergent BN**. Eisenmenger Syndrome. 2023 Feb 13. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 29939577.
2. **Simonneau G, Galiè N, Rubin LJ, Langleben D, Seeger W, Domenighetti G, Gibbs S, Lebrec D, Speich R, Beghetti M, Rich S, Fishman A**. Clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2004 Jun 16;43(12 Suppl S):5S-12S. doi: 10.1016/j.jacc.2004.02.037. PMID: 15194173.
3. **D'Alto M, Mahadevan VS**. Pulmonary arterial hypertension associated with congenital heart disease. *Eur Respir Rev*. 2012 Dec 1;21(126):328-37. doi: 10.1183/09059180.00004712. PMID: 23204121; PMCID: PMC9487226.
4. **Kempny A, Hjortshøj CS, Gu H, Li W, Opotowsky AR, Landzberg MJ, Jensen AS, Søndergaard L, Estensen ME, Thilén U, Budts W, Mulder BJ, Blok I, Tomkiewicz-Pająk L, Szostek K, D'Alto M, Scognamiglio G, Prokšelj K, Diller GP, Dimopoulos K, Wort SJ, Gatzoulis MA**. Predictors of Death in Contemporary Adult Patients With Eisenmenger Syndrome: A Multicenter Study. *Circulation*. 2017 Apr 11;135(15):1432-1440. doi: 10.1161/CIRCULATIONAHA.116.023033. Epub 2016 Dec 15. PMID: 27979875.
5. **Dimopoulos K, Wort SJ, Gatzoulis MA**. Pulmonary hypertension related to congenital heart disease: a call for action. *Eur Heart J*. 2014 Mar;35(11):691-700. doi: 10.1093/eurheartj/eht437. Epub 2013 Oct 29. PMID: 24168793.
6. **Mocumbi AO, Lameira E, Yaksh A, Paul L, Ferreira MB, Sidi D**. Challenges on the management of congenital heart disease in developing countries. *Int J Cardiol*. 2011 May 5;148(3):285-8. doi: 10.1016/j.ijcard.2009.11.006. Epub 2009 Nov 22. PMID: 19932516.
7. **Bode-Thomas F**. Challenges in the Management of Congenital Heart Disease in Developing Countries [Internet]. *Congenital Heart Disease - Selected Aspects*. InTech; 2012. Available from: http://dx.doi.org/ 10.5772/27273.
8. **Leblanc JG**. Creating a global climate for pediatric cardiac care. *World J Pediatr*. 2009 May;5(2):89-92. doi: 10.1007/s12519-009-0019-0. Epub 2009 Jul 9. PMID: 19718529.
9. **Schuuring MJ, van Riel AC, Vis JC, Duffels MG, van Dijk AP, de Bruin-Bon RH, Zwinderman AH, Mulder BJ, Bouma BJ**. New predictors of mortality in adults with congenital heart disease and pulmonary hypertension: Midterm outcome of a prospective study. *Int J Cardiol*. 2015 Feb 15;181:270-6. doi: 10.1016/j.ijcard.2014.11.222. Epub 2014 Dec 13. PMID: 25535690.
10. **Ntiloudi D, Apostolopoulou S, Vasiliadis K, Frogoudaki A, Tzifa A, Ntellos C, Brili S, Manginas A, Pitsis A, Kolios M, Karvounis H, Tsioufis C, Goudevenos J, Rammos S, Giannakoulas G; CHALLENGE investigators**. Hospitalisations for heart failure predict mortality in pulmonary hypertension related to congenital heart disease. *Heart*. 2019 Mar;105(6):465-469. doi: 10.1136/heartjnl-2018-313613. Epub 2018 Sep 29. PMID: 30269081.
11. **Cantor WJ, Harrison DA, Moussadji JS, Connelly MS, Webb GD, Liu P, McLaughlin PR, Siu SC**. Determinants of survival and length of survival in adults with Eisenmenger syndrome. *Am J Cardiol*. 1999 Sep 15;84(6):677-81. doi: 10.1016/s0002-9149(99)00415-4. PMID: 10498138.
12. **Arvanitaki A, Diller GP**. The use of pulmonary arterial hypertension therapies in Eisenmenger syndrome. *Expert Rev Cardiovasc Ther*. 2021 Dec;19(12):1053-1061. doi: 10.1080/14779072.2021.2021069. Epub 2021 Dec 27. PMID: 34958619.