Paediatrica Indonesiana

p-ISSN 0030-9311; e-ISSN 2338-476X; Vol.61, No.3(2023). p.208-12; DOI: https://doi.org/10.14238/pi63.3.2023.208-12

Case Report

Pulmonary arteriovenous malformation as a cause of exercise intolerance in children: a case report

Pierluigi Morreale[1], Veronica Notarbartolo[2], Giancarlo Allegro[2], Mario G. Vallone[3], Francesca Finazzo[3], Vincenzo Antona[2], Maria F. Sanfilippo[1], Calogero Comparato[1]

Pulmonary arteriovenous malformations (PAVMs) in children are rare lesions characterized by abnormal low resistance vascular structures connecting a pulmonary artery to a pulmonary vein, resulting in an intrapulmonary right-to-left shunt. The insidious onset and variable signs and symptoms make diagnosis difficult, especially in children. PAVMs can be single or multiple, congenital or acquired, and up to 47-80% of cases are associated with hereditary hemorrhagic telangiectasia (HHT). **[Paediatr Indones. 2023;63:208-12; DOI: https://doi.org/10.14238/pi63.3.2023.208-12**].

Keywords: *pulmonary arteriovenous malformation;*

Pulmonary arteriovenous malformations (PAVMs) are direct communications between pulmonary arteries and veins without an intervening pulmonary bed. These lesions predominantly represent congenital malformations and can involve a large single sac or a plexiform mass of dilated vascular channels or consist of dilated and tortuous communications between a pulmonary artery and a venous tributary.[1] Although PAVMs are rare in children, they are important in the differential diagnosis of common pulmonary problems, such as hypoxemia, hemoptysis, and dyspnea on exertion. However, more than half of children diagnosed with PAVMs may be asymptomatic and their natural history in children remains largely unknown.[2] Guidelines for pediatric screening are not specific, reflecting the lack of scientific evidence on best practices. The aim of this case report was to emphasize the non-specific nature of the symptoms of PAVMs and how their diagnosis is often incidental , especially in childhood.

The case

The case was a 12-year-old female delivered via cesarean section for breech presentation, with a birth weight of 2,900 g; the first child of non-consanguineous parents. Her neonatal period was uneventful and her parents were seemingly healthy. At the age of 11 years, she experienced a fleeting episode of fever. A chest X-ray revealed increased density in the left upper lobe. Antibiotic therapy was prescribed until fever resolution. Later, the patient suffered from occasional headaches, nosebleeds, fatigue, and exercise intolerance. Mild oxygen desaturation (SpO_2 94%) was noted by her pediatrician and she was referred to our hospital. The family history was remarkable on the paternal line: her father's sister had pulmonary arteriovenous malformation (PAVM); her father had epistaxis and mucocutaneous telangiectasias; three of her father's other siblings also had epistaxis

From Unit of Pediatric Cardiology, A.R.N.A.S. Civico-Di Cristina-Benfratelli Hospital[1]Specialization School in Pediatrics, Department for the Promotion of Health, Mother and Child, Internal Medicine and Excellence Specialist "G. D'Alessandro," University of Palermo[2], Unit of Diagnostic Radiology, A.R.N.A.S. Civico-Di Cristina-Benfratelli Hospital[3], Palermo, Italy.

Corresponding author: Veronica Notarbartolo, A.R.N.A.S. Civico-Di Cristina-Benfratelli Hospital, Via dei Benedettini 1, Palermo, 90134. Telp. +39 0916666001; Email: veronicanotarbartolo@gmail.com.

Submitted March 31, 2021. Accepted June 27, 2023.

and headache; and a a cousin had telangiectasias on the lower lip and fingertips. There were few similar indications in the maternal line (**Figure 1**).

Upon presentation, the child's weight was 48 kg and height was 161 cm (body mass index 27.5 kg/m^2). On physical examination, a continuous 2/6 murmur with systolic reinforcement was best appreciated at the sub-clavicular border. The patient had no telangiectasias, clubbing, cyanosis, enlargement of the liver or edema in the lower legs; her extremities were not cold. Pulse oximetry showed oxygen saturation of 94% in room air. Laboratory tests showed a slight increase in red blood cells (RBC 5,580,000 u/L), Hb (16.4 g/dL) and hematocrits (46.8%), with normal mean corpuscular volume (84.2 fL). Abdominal ultrasound, as well as brain and abdominal CT scans, were negative. Her electrocardiogram showed a normal sinus rhythm with no ST-segment changes. Echocardiography showed normal left and right atria and normal ventricular size and function. Based on her clinical history and previous X-ray image which was suspicious of hereditary hemorrhagic telangiectasia (HHT),1 a bubble test was performed with shaken saline solution infused in the brachial vein. The result was a sudden moderate filling of the left atrium, with the appearance of microbubbles or microembolic signals (MES) a few seconds after their display in the right atrium (**Figure 2**).

Pulmonary CT angiography showed a voluminous PAVM in the apical and anterior segment of the left upper lobe, supplied by the apical segmental artery and by its sub-segmental branch draining into the left upper pulmonary vein, without interposed nidus. The maximum transverse diameter (TD) of the main afferent branch was 7.7 mm and of the sub-segmental branch was 2 mm. Further millimeter PAVM in the posterior basal segment of the left lower lobe was found (**Figure 3**).

The patient underwent percutaneous selective PAVM closure using a 12 mm Amplatzer occlusive system for the apical segmental branch and coil occlusion for the small subsegmental branch (**Figure 4**). At the examination one year after the procedure, the child was in good physical condition with normal oxygen saturation (SpO_2 98% in room air) without complaints of fatigue or exercise intolerance.

Discussion

Pulmonary arteriovenous malformations (PAVMs) in children are rare lesions characterized by abnormally low resistance vascular structures connecting a pulmonary artery to a pulmonary vein, bypassing the normal pulmonary capillary bed and resulting in an intrapulmonary right-to-left shunt.[3] It is the most common congenital pulmonary vascular anomaly, with an incidence of 1:2,600, and a female-to-male ratio of 1.5-1.8.[4] PAVMs can be single or multiple, congenital or acquired, and up to 47-80% of cases are associated with hereditary hemorrhagic telangiectasia

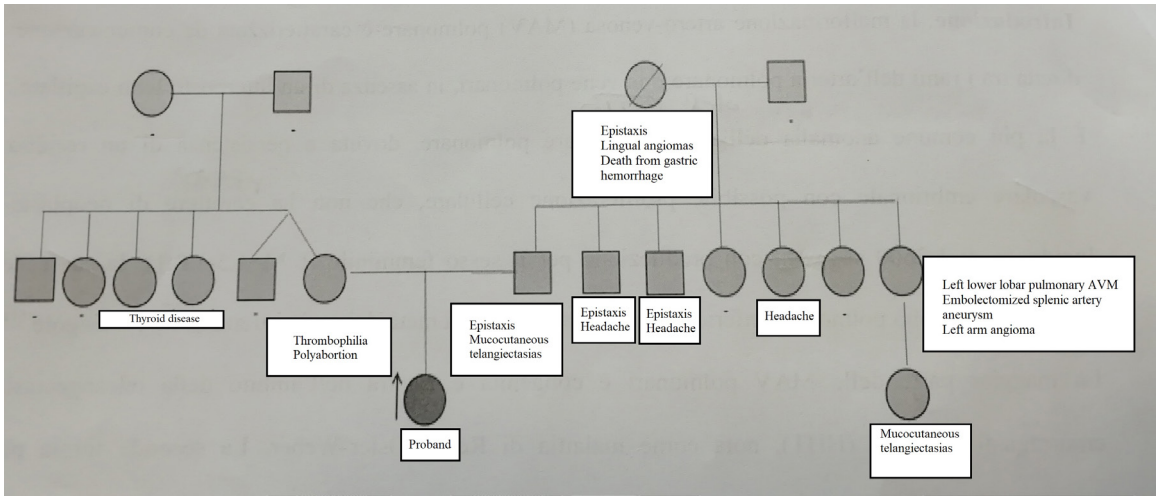

Figure 1. The family tree

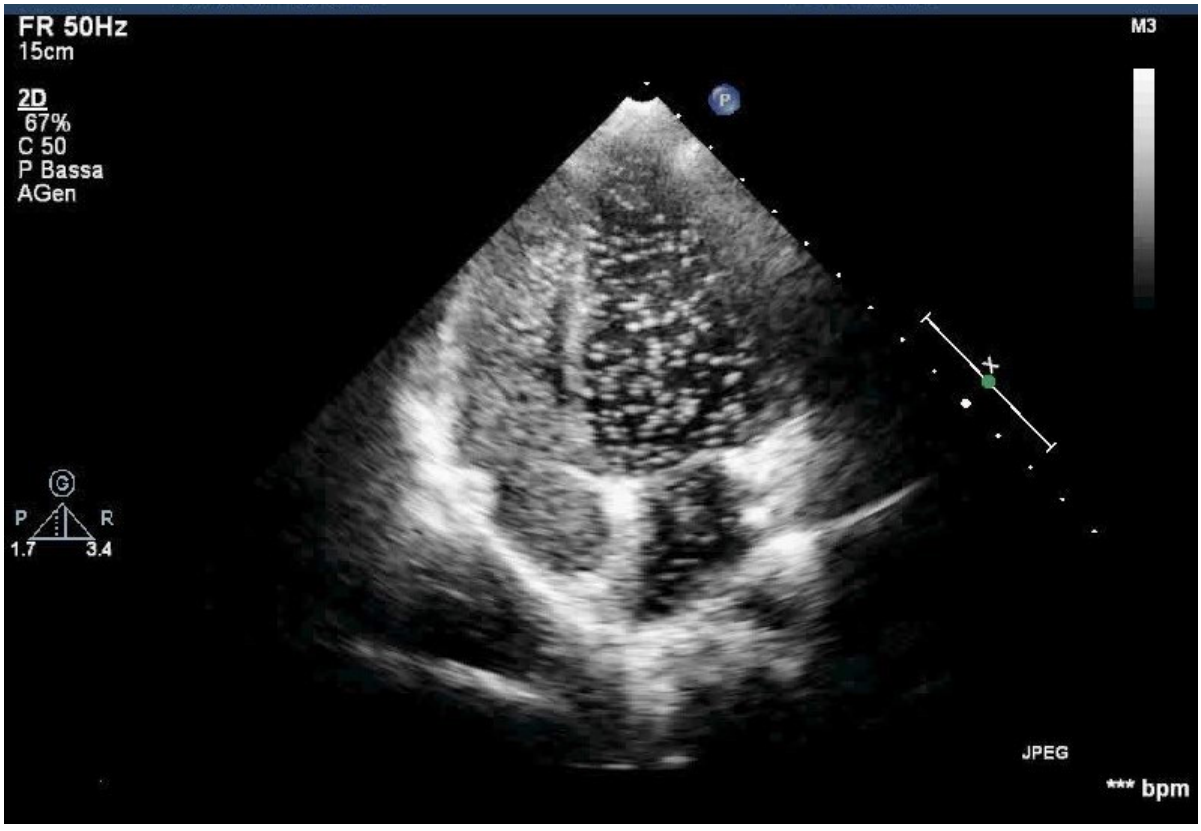

Figure 2. Bubble test on echocardiography showing sudden moderate filling of the left atrium, with the appearance of microbubbles (MES) a few seconds after their display in the right atrium

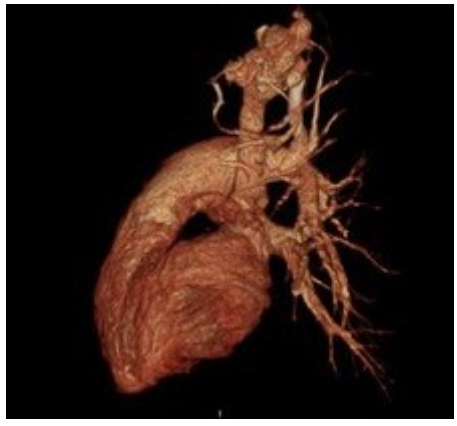

Figure 3. Contrast enhanced computed tomography image, showing voluminous PAVM in the apical and anterior segment of the left upper lobe, supplied by the apical segmental artery and by its sub-segmental branch draining in the left upper pulmonary vein, without interposed nidus.

(HHT), also known as Rendu-Osler-Weber disease.[5] The insidious onset and variable signs and symptoms such as dyspnea, hemoptysis, neurological symptoms, and cyanosis are present in only 15% of cases, making diagnosis difficult, especially in children.[6] Our patient represents a rare case of PAVM in the pediatric population.

From an embryological and anatomical point of view, the PAVM belongs to the second group of the Anabtawi classification.[7] As in most cases

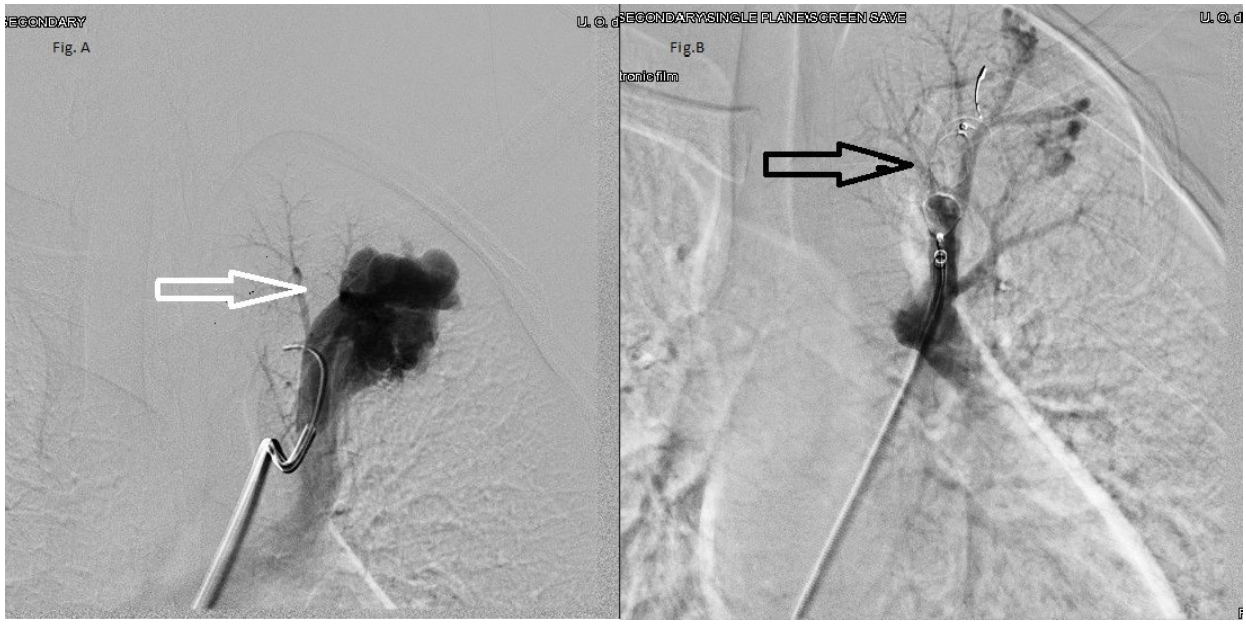

Figure 4. Pre- and post-device closure angiographic still frames of PAVMs in the apical and anterior segment of the left upper lobe. (A) shows preintervention angiography of the feeding arterial and draining venous vessels in the apical and anterior segment of the left upper lobe (white arrow). (4B) shows post-12 mm Amplatzer occlusive system device closure of the apical segmental branch with no residual shunting (black arrow).

described in the literature, our case had mild symptoms.4 It is well known that the share of the right-left shunt determines the clinical picture: if it is more than 20% of the cardiac systemic output, the resulting hypoxemia will cause varying degrees of dyspnea, cyanosis, digital clubbing, and compensatory polycythemia. In contrast, if the shunt constitutes less than 20% of the cardiac systemic output, symptoms may be non-specific, as in the case of our patient, or even absent.[4-7]

Neurological complications, including headache, ischemic stroke, and brain abscess occur in 15-50% of cases and are related to paradoxical embolism through the PAVM. Hemorrhagic complications due to AV rupture causing hemoptysis or hemothorax are rare.[7,8] None of these complications were observed in our patient, except occasional headache. At first, chest x-ray was suggestive of pneumonia or neoplasia, with a differential diagnosis of PAVM.[5-9] In suspected vascular extracardiac disorders resulting in right-to left shunts, a bubble test could be particularly useful, and desirable for its ease of execution, repeatability, and absence of complications. Pulmonary CT angiography, as widely described in the literature, is the diagnostic gold standard that confirmed the diagnosis, providing accurate anatomical data of the malformation. Most PAVM are located in the lower left lobe;[7] in our case, the AVM was instead located in the upper left lobe.

When a PAVM is diagnosed, it is important to exclude Rendu-Osler-Weber disease, along with the consequent burden of a higher rate of complications and poorer prognosis.[5-7] Rendu-Osler-Weber can be confirmed in the presence of at least three criteria among the following: epistaxis, multiple skin-mucosal telangiectasias, visceral lesions, cerebral and spinal AVM, pulmonary AVM, gastro-enteric telangiectasias, and family history (first-degree relative affected by HHT according to these criteria).[7] According to the Curaçao criteria,[1] the diagnosis of HHT disease is clinical; it is not necessary to perform genetic testing. In our patient, since three criteria were present, we did not perform any genetic testing according to the current guidelines.[1]

While epistaxis, the most common clinical manifestation in children, typically presents in childhood, telangiectasias can be found in puberty or adulthood or be completely absent.[7] In the presence of incomplete symptomatology, family history plays a central role for diagnosis, of which our case is an example. The patient's multi-generational family

history, at first considered irrelevant, in a subsequent reexamination highlighted the presence of two certain cases of HHT in the father and in a relative in the collateral line, and several cases of probable diagnoses in the paternal line. We can also assert, with a degree of certainty, that this case is a form of PAVM in a pediatric patient in the context of an HHT, probably of an autosomal dominant character, with incomplete penetrance on the paternal line. Nowadays, selective percutaneous occlusion represents the gold standard treatment of PAVMs, and can be carried out in symptomatic or asymptomatic cases with an afferent arteriole diameter of more than 3 mm with good results in terms of safety and efficacy.[10]

In conclusion, when evaluating symptoms of mild oxygen desaturation and exercise intolerance in children and adolescents, physicians should be aware of the possibility of PAVMs as a cause. Transthoracic contrast echocardiography is the screening test of choice for PAVM, with a sensitivity of up to 98.6%. Using only SpO_2 as a screening tool is not recommended due to its poor reproducibility and low sensitivity.1 Percutaneous occlusion is the treatment of choice for PAVMs and is a safe and effective procedure in the pediatric population.

Conflict of interest

None declared.

References

1. Saboo SS, Chamarthy M, Bhalla S, Park H, Sutphin P, Kay F, *et al.* Pulmonary arteriovenous malformations: diagnosis. Cardiovasc Diagn Ther. 2018;8:325-37. DOI: https://doi.org/10.21037/cdt.2018.06.01.
2. Mowers KL, Sekarski L, White AJ, Grady RM. Pulmonary arteriovenous malformations in children with hereditary hemorrhagic telangiectasia: a longitudinal study. Pulm Circ. 2018;8:2045894018786696. DOI: https://doi.org/10.1177/2045894018786696.
3. Feinstein JA, Moore P, Rosenthal DN, Puchalski M, Brook MM. Comparison of contrast echocardiography versus cardiac catheterization for detection of pulmonary arteriovenous malformations. Am J Cardiol. 2002;89:281-5. DOI: https://doi.org/10.1016/s0002-9149(01)02228-7.
4. Chang RK, Alejos JC, Atkinson D, Jensen R, Drant S, Galindo A, *et al.* Bubble contrast echocardiography in detecting pulmonary arteriovenous shunting in children with univentricular heart after cavopulmonary anastomosis. J Am Coll Cardiol. 1999;33:2052-8. DOI: https://doi.org/10.1016/s0735-1097(99)00096-0.
5. Shovlin CL. Pulmonary arteriovenous malformations. Am J Respir Crit Care Med. 2014;190:1217-28. DOI: https://doi.org/10.1164/rccm.201407-1254CI.
6. Rotondo E, Sgrazzutti L, Attanasi M, Petrosino MI, Chiarelli F, Di Pillo S. Quando policitemia e dispnea da sforzo non sono asma. Pneumologia Pediatrica. 2019;19:21-5.
7. Khurshid I, Downie GH. Pulmonary arteriovenous malformation. Postgrad Med J. 2002;78:191-7. DOI: https://doi.org/10.1136/pmj.78.918.191.
8. Wong HH, Chan RP, Klatt R, Faughnan ME. Idiopathic pulmonary arteriovenous malformations: clinical and imaging characteristics. Eur Respir J. 2011;38:368-75. DOI: https://doi.org/10.1183/09031936.00075110.
9. Sladden D, Casha A, Azzopardi C, Manchè A. A large pulmonary arteriovenous malformation causing cerebrovascular accidents. BMJ Case Rep. 2015;2015:bcr-2014207786. DOI: https://doi.org/10.1136/bcr-2014-207786.
10. Meek ME, Meek JC, Beheshti MV. Management of pulmonary arteriovenous malformations. Semin Intervent Radiol. 2011;28:24-31. DOI: https://doi.org/10.1055/s-0031-1273937.