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Hybrid Procedural Management of Multiple Pulmonary Arteriovenous Malformations In A Patient With Hereditary Hemorrhagic Telangiectasia: A Case Report

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Abstract:
Hereditary Hemorrhagic Telangiectasia (HHT) is an autosomal dominant disorder characterized by vascular malformations, including Pulmonary Arteriovenous Malformations (PAVMs), which can lead to serious complications such as dyspnea and hemorrhage. This report features a 37-year-old woman with HHT and multiple PAVMs. The diagnosis was established through physical examination, laboratory tests, and thoracic multislice computed tomography (MSCT). A hybrid management approach was applied, including embolization and thoracotomy. The patient underwent successful embolization of the inferior segment, followed by thoracotomy to overcome procedural difficulties. After the intervention, the patient's symptoms improved significantly, with no recurrence. Management of complex PAVMs may require a combination of methods, including embolization and surgery. The importance of early detection and adaptive management in HHT patients is expressed, given the high risk of complications. Embolization is the primary treatment for PAVMs, but in complex cases, surgical intervention is required. This study emphasizes the importance of a hybrid management approach and early detection in preventing serious complications in HHT patients, as well as the need for the development of better clinical guidelines for the management of PAVMs.

Keywords: Hereditary Hemorrhagic Telangiectasia, Pulmonary Arteriovenous Malformations, Embolization Therapy, Hybrid Procedural Management, Case Report, Vascular Malformations

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INTRODUCTION

Hereditary Hemorrhagic Telangiectasia (HHT), also known as Osler-Weber-Rendu Syndrome, is an autosomal dominant disorder characterized by vascular malformations in mucocutaneous and visceral tissues, resulting in direct connections between arterioles and venules without intervening capillaries (McDonald & Stevenson, 2021). Patients with Hereditary Hemorrhagic Telangiectasia (HHT) often develop telangiectasia and Arterial Venous Malformation (AVMs) in various organs, which can lead to various serious complications. The importance of this study is in understanding the clinical impact of this condition. By studying cases of HHT, researchers can identify risk factors and complications that may arise, and formulate more effective management strategies (Meier et al., 2018).

The prevalence of HHT increased from 6.1 to 12.1 per 100,000 persons, with the greatest percentage increases observed among patients aged 18 to 29 years and those older than 60 years (Ferry et al., 2020). Diagnosis of HHT relies on not only by clinical detection using the Curaçao criteria, but also using genetic testing to identify the affected genes (Viteri-Noël et al., 2022). Genetic mutations that have been identified include ENG, ACVRL1/ALK1, and MADH4/SMAD4 (Kritharis et al., 2018).

Pulmonary arteriovenous malformations (PAVMs) are the most common manifestation of AVMs in HHT, rarely occurring sporadically outside of this syndrome. Approximately 15–50% of HHT patients have PAVMs. Pulmonary Arteriovenous Malformation (PAVM) can be asymptomatic or present with symptoms such as exertional dyspnea, palpitations and fatigue, especially in patients with Hereditary Hemorrhagic Telangiectasia (HHT). PAVM is more common in HHT patients due to genetic involvement that affects the formation and regulation of blood vessels, which can lead to the formation of abnormal connections between arteries and veins. The main risks faced by patients with PAVMs are stroke or embolism, which can result from irregular blood flow and blood clots, requiring proper medical monitoring and intervention to prevent serious complications (Girit et al., 2020).

Although currently there is no definitive treatment, the treatment approach of HHT is aimed at decreasing the amount of hemorrhage and minimizing complications. Meanwhile, the main goals in managing PAVM are to minimize embolic complications, prevent and treat hemorrhage from PAVM rupture, and improve functional capacity by reducing shunt-related hypoxemia (Narsinh et al., 2013).

We present a 37-year-old woman with HHT and multiple PAVMs, presenting with persistent weakness, recurrent nosebleeds, and exertional dyspnea. The patient underwent physical examination, blood tests, X-ray, echocardiography, and thoracic multislice computed tomography (MSCT). Embolization and thoracotomy was performed in this patient.

RESEARCH METHODS

A 37-year-old woman came to our facility with a chief complaint of persistent weakness lasting one month, exacerbated over the past week. Weakness was not alleviated by food or rest and worsened with activity. Additionally, she reported episodes of sudden, unexplained nosebleeds since childhood, which stopped spontaneously. Additionally, she experienced exertional dyspnea unaffected by dust, weather, or allergens. There was no history of limb weakness, jaundice, trauma, surgery, malignancy or prior heart, lung, or kidney disease. The patient was a passive smoker, frequently exposed to cigarette smoke. She had chronic anemia and had received multiple blood transfusions over the past two years with no significant improvement.

Physical examination revealed anemic conjunctiva and bilateral crackles with minimal wheezing. Laboratory tests showed severe anemia (Hb 3.6 g/dL, Hct 14%), normal leukocytes at 5.3 x 109/L, platelets at 516 x 109/L with normal renal and hepatic function. Peripheral blood smear showed microcytic hypochromic erythrocytes. A chest X-ray (CXR) revealed cardiomegaly, pulmonary edema, and a solitary nodule in the right paracardium, as shown in figure 1. Echocardiography showed left ventricular concentric remodeling with good contractility (ejection fraction 69%) and normal diastolic function and valves.

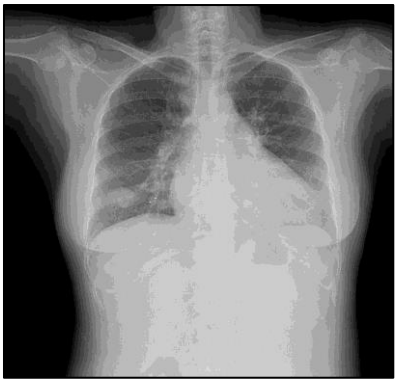

Figure 1. CXR showed cardiomegaly, pulmonary edema, and a solitary nodule in the right paracardium

A thoracic multislice computerized tomography (MSCT) scan revealed a solid mass with spiculated edges in the apicoposterior segment of the left upper lobe, accompanied by a pneumonic reaction and multiple lymphadenopathies in the mediastinum, bilateral axilla, and supraclavicular regions. The scan also showed multiple nodules in the right lung field, left pleural effusion. Based on these findings, a preliminary diagnosis of a suspicious right lung tumor was made. The patient received symptomatic treatment and anemia correction with packed red cells (PRC) transfusion and was discharged upon symptom improvement. However, she returned repeatedly with similar complaints, mainly weakness and nosebleeds. A planned bronchoscopy was postponed due to frequent nosebleeds.

Given the recurrent symptoms, a thoracic MSCT angiography was performed. Figure 2 revealed multiple vascular lesions in the right lung (inferior lobe, laterobasal segment, and middle lobe, medial segment) with tortuous appearance forming nodes receiving arterial supply from the segmental branch of the right pulmonary artery and draining into the segmental branch of the right pulmonary vein, consistent with pulmonary arteriovenous malformations (AVMs). Additional findings included multiple lymphadenopathies in the mediastinum, bilateral axillary regions, and bilateral supraclavicular regions, as well as cardiomegaly.

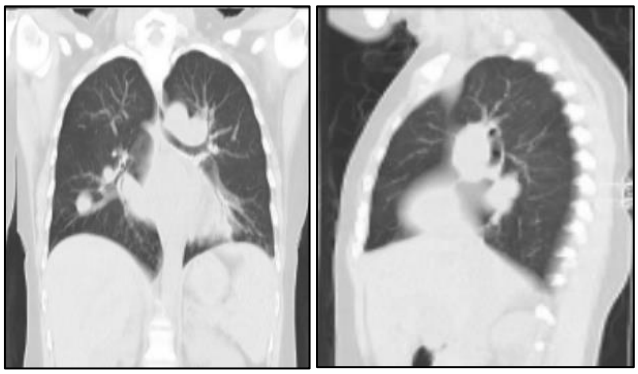

Figure 2. Subsequent MSCT angiography of the patient confirmed multiple PAVMs

Based on these findings, the patient's diagnosis was confirmed with hereditary hemorrhagic telangiectasia (HHT) with multiple PAVMs. Immediate embolization was planned, and the first embolization was successfully performed on the laterobasal segment of the inferior lobe under general anesthesia in December 2023. The patient was discharged with improved symptoms and a second embolization on the medial segment of the middle lobe was planned for April 2024. However, this procedure was unsuccessful due to the difficult position for intervention. Subsequently, a thoracotomy was planned and performed one month later. Successful double ligation of the medial segment AVM was done. The patient was then treated in the ICU for four days and discharged in good condition six days post-surgery. Post-procedure, the patient's condition significantly improved, with no recurrence of weakness or nosebleeds.

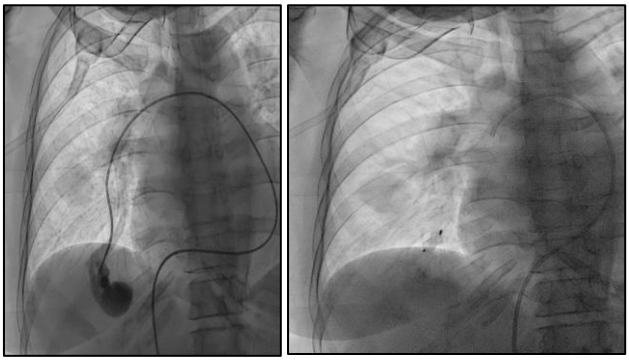

Figure 3. Left: The PAVM located in the inferior lobe, laterobasal segment. Right: Embolization procedure of the PAVM.

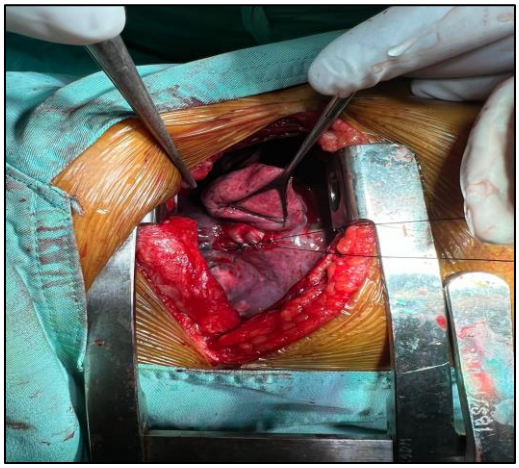

Figure 4. Surgery of the double ligation of the medial segment AVM.

RESULTS AND DISCUSSION

This case report highlights the complexity of multiple PAVMs necessitating a hybrid procedural management in a 37-year-old HHT woman. PAVMs are abnormal direct vascular communications between pulmonary arteries and veins which bypass capillary beds to create low-resistance, high-flow continuous intrapulmonary right-to-left shunts (Girit et al., 2020). PAVMs are highly associated (70% or more) with the autosomal dominant disorder HHT (Majumdar & McWilliams, 2020). The relationship between the endothelium and affected genes in HHT is based on the regulation of angiogenesis by ENG and ACVRL1, a process in which the pathways of endothelial cell migration and proliferation are crucial, which can affect the formation and function of the blood vessels (Zarrabeitia et al., 2017). ENG mutations are more commonly associated with PAVMs with larger shunts (58%) than ACVRL1 mutations (18%) (Tellapuri et al., 2019). These mechanisms can develop the classical triad of PAVMs : cyanosis, polycythemia and clubbing (Girit et al., 2020).

Symptoms of the PAVM depend mostly on size and less on number of the lesions. Solitary PAVM smaller than 2 cm are most commonly asymptomatic; whereas bigger lesions may present with symptoms (Shovlin et al., 2017). Dyspnea is frequently reported as a symptom, but it can be challenging to distinguish from symptoms caused by other aspects of HHT, such as iron deficiency anemia, high-output heart failure due to extensive intrahepatic shunting, or venous thromboembolism (VTE) (Meier et al., 2018). Palpitations, fatigue can also be seen, meanwhile cyanosis and clubbing are less likely to occur (Saboo et al., 2018). In our patient, symptoms varied from fatigue to dyspnea.

Paradoxical septic emboli and stroke can be developed from PAVMs, since the blood passing through a PAVM does not engage in alveolar gas exchange, which lowers the oxygen levels in the blood returning to the left heart. Additionally, this blood does not undergo the essential process of physical filtration, which can cause thrombi and other blood-borne substances to enter the systemic circulation (Shovlin et al., 2017). Hence, prompt and early screening and detection is important to reduce the mortality and morbidity in patients.

There were some screening tests that were carried out in this patient. An inexpensive first line imaging, easily available modality, a chest x-ray, was used as the first imaging diagnostic tools in our patient. However, x-ray has low sensitivity for the detection of small sized PAVMs and is not specific in and various differential diagnosis of lung nodules needs to be excluded. Therefore, another imaging test was performed. Thorax CT is recommended for imaging PAVMs characterized by serpentine or clearly defined nodular masses. In this patient, a chest MSCT angiography was performed. Our patient's final diagnosis was confirmed through chest MSCT angiography.

The feeding artery for most of the PAVMs arises from the pulmonary arteries but rarely can be from the systemic arteries, such as the intercostal, phrenic, bronchial and internal mammary arteries (Saboo et al., 2018). PAVM angioarchitecture is classified as simple or complex (Majumdar & McWilliams, 2020). Simple PAVMs are the most common lesion, almost 80% of the cases are classified as simple PAVMs (Lee & Hyun, 2022). This type is supplied by a single segmental pulmonary artery, connected through a bulbous, aneurysmal, non-septated communication with one or more draining veins, where the draining veins are generally 1–2 mm larger than the feeding arteries. On radiological imaging of a simple PAVM, a lobulated peripheral nodule or well-defined rounded image will be obtained. PAVMs can be established if there is a connection between the nodule and both of arteries and veins that supply it (Saboo et al., 2018).

Complex PAVMs are rarer cases, namely around 10 to 20% of all PAVM cases. Complex PAVMs are defined by a lesion that is supplied by two or more feeding arteries which are connected to two or more draining veins. The connections in the complex types could be circular or divided into multiple small interconnecting vessels (Saboo et al., 2018). Apart from that, there is a type that occurs less frequently in less than 5% cases, namely diffuse PAVMs (Chamarthy et al., 2018). Diffuse PAVMs are a subtype of complex PAVMs, where in this case there is involvement of all segments involving at least one lobe of the lung and sometimes affecting the entire lung or more widely than multiple PAVMs (Ferry et al., 2020). Patients with diffuse PAVMs will be more at risk of hypoxemia, hemoptysis and neurological complications. This classification is important to determine endovascular interventions (Saboo et al., 2018).

The goals of PAVMs management are to minimize embolism complications, prevent and manage bleeding due to PAVMs rupture, and increase lung functional capacity by reducing shunt-related hypoxemia (Meier et al., 2018).

The standard treatment for PAVMs is embolization, this can increase oxygen content and reduce the risk of embolism. In this procedure there is still a possibility of recanalization and reperfusion in around 25% of cases. This condition can happen when not all the supplying arteries are embolized. However, if all the supplying arteries can be closed, the sac will regress within 6 months (Salibe-Filho et al., 2023). Indications for this procedure are PAVMs with a feeding artery diameter (FAD) ≥2 mm, and technically feasible, PAVMs with symptomatic symptoms regardless of size, or atypical cases but there is PAVMs reproduction on cross-sectional imaging with suggestive symptoms (Chamarthy et al., 2018). The most common failure of this procedure is due to arterial recanalization, but it can also be due to collateral perfusion from the supplying pulmonary artery branches or systemic perfusion (Meier et al., 2018).

Apart from that, in cases of complex or multiple PAVMs, where embolization with a catheter is not possible, surgery can be performed. Surgical treatment is rarely carried out, but in some cases, it is possible that surgical therapy is the only definitive therapy that can be carried out. Lung transplantation can also be performed in certain cases, for the sake of the patient's survival. In addition, it is also recommended that PAVMs patients receive prophylactic antibiotics, antibiotics must be given 1 to 2 hours before the procedure and another dose should be taken after the procedure (Salibe-Filho et al., 2023).

CONCLUSION

Embolization is the primary treatment for pulmonary arteriovenous malformations (PAVMs), but in some cases, such as complex PAVMs, this procedure may not be feasible or may fail, requiring alternatives such as surgery. From this case study, we recommend that clinical practice pays attention to the importance of early detection and management of PAVMs in patients with Hereditary Hemorrhagic Telangiectasia (HHT) to prevent serious complications. In addition, a hybrid management approach, which combines embolization and surgical intervention, may be considered for patients with similar conditions. However, this study has limitations, including a limited number

of patients and a relatively short duration of follow-up. Further research is needed to explore the long-term effectiveness of various treatment approaches for PAVM in HHT patients, as well as to identify risk factors that may affect treatment outcomes. Thus, the results of this study are expected to contribute to the development of better clinical guidelines for the management of PAVM in patients with HHT.

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