A case of Multiple Unilateral Pulmonary arteriovenous Malformation Relapse: Efficacy of embolization treatment

Keywords: Pulmonary arteriovenous Malformations (PAVMs), Embolization, Unilateral fistula, Angio-CT Scan.

1 Introduction

Pulmonary arteriovenous Malformations (PAVMs) are a rare vascular alteration with an overall incidence estimated to be approximately two to three per 100,000 population. PAVMs are abnormal communications between the pulmonary arteries and veins, which bypass the pulmonary capillary bed resulting in an extracardiac right-to-left (R-L) shunt. The majority of patients with PAVMs have an hereditary hemorrhagic telangiectasia (HHT), an autosomal dominant vascular disorder also known as Osler-Weber-Rendu Syndrome [2]. The remaining cases are idiopathic, however other causes associated to infections, trauma and Fanconi Syndrome have been described [1]. Diagnosis of PAVMs is not straightforward, as symptoms are common to other cardiovascular and respiratory diseases, related to both individual and environmental factors including cigarette smoking [3-17]. The major clinical manifestations are hypoxemia, dyspnea and cyanosis, the severity of which depend upon the extent of lesions. Serious morbidity and mortality are largely related to complications including paradoxical embolization causing cerebrovascular ischemic events or cerebral abscesses; migraine and hemothorax have also been reported. PAVMs are described according to their anatomical characteristics. Approximately 85% of PAVMs are simple, where the arterial supply arises from one or more branches of a single segmental pulmonary artery [18]. Most of the remainder are complex PAVMs which have multiple arterial feeder vessels from more than one pulmonary segment, while a smaller percentage of PAVMs are diffuse with disseminated involvement of multiple pulmonary segments [19]. The diagnosis of...
PAVMs is often made as a result of a chest X-ray or a chest CT scan which is more accurate in differential diagnosis and extension of PAVMs. On chest X-ray, the classic sign of PAVMs is a well-defined round or oval nodule or mass. Additional noninvasive methods to assess PAVMs are quantitative right-to-left shunt studies (100% oxygen method or radionuclide perfusion scanning) and contrast echocardiography. Pulmonary angiography is generally now reserved for post-diagnosis therapeutic purposes [1,3,20]. The fistula-type PAVMs have a feeding artery directly connected to a draining vein, with an intervening single aneurysmal sac while, less commonly, PAVMs are plexiform with a multiseptated aneurysm or a cluster of vascular channels. In the past, symptomatic PAVMs were treated surgically but since the introduction of embolotherapy, percutaneous trans-catheter embolization with coils has significantly decreased the rate of complications [19,21]. According to the International HHT Guidelines, PAVMs should be embolised preventatively to decrease the risk of complications irrespective of symptomatology [22].

2 Case Report

We report a rare case of an 18 year old female with severe respiratory failure caused by Multiple unilateral pulmonary artero-venous fistula. The patient was admitted to the Department of Cardio-Thoracic and Respiratory Science at the Second University of Naples with progressive shortness of breath that had gradually worsened during the previous two month period. Family history was negative for both genetic and cardiovascular diseases. In 2010, following an episode of haemoptysis, the patient underwent an angio-CT scan which revealed marked dilation of bronchial arteries in the right lung as well as dilatation of venous branches approaching superior and inferior pulmonary veins, leading to a diagnosis of artero-venous shunt of right lung with alveolar hemorrhage, involving the majority of the inferior right lobe and lateral segment of median lobe. The patient, then, underwent selective angiography and embolization of the AV fistula using the Gianturco method. Until 2013, the patient was clinically stable, with follow up angio-CT scans showing no disease progression. In 2014 the patient presented with severe dyspnea and was admitted to hospital for assessment. On examination she was found to be dyspnoeic at rest with marked cyanosis and finger clubbing. Oxygen saturation on air was 83-84% and blood gas analysis showed pO2: 50 mmHg and pCO2: 33 mmHg with little improvement demonstrated on administration of high flow oxygen. Thoracic angio CT scan, cranial and maxillofacial CT, echocardiogram and abdominal ultrasound were carried out to exclude Rendu-Osler Syndrome. The thoracic angio-CT scan showed the presence of Multiple Artero-Venous Fistulas (MAVFVs) of Right Upper Lobe (RUL) and Right Lover Lobe (RLL) with an increase of pulmonary venous caliber compared to left lung field; a marked increase of right bronchial artery caliber and its branches was also observed in addition to an aneurismatic dilatation of 1 cm not previously detected; Web-like appearance was evident in the superior segment of RUL (Figure 1). Pulmonary angiogram, carried out before the embolization procedures, confirmed the presence of MAVFs involving the superior and inferior lobes of the right lung; aortography showed the presence of a systemic-pulmonary bridge arising from the thoracic aorta towards the right lung. Percutaneous trans-catheter embolization (TCE) was successfully performed using 8 Amplatzer Vascular Plug IV (St. Jude Medical, Saint Paul - Mn, USA) devices, as well as inserting 2 Amplatzer Vascular Plug IV (St. Jude Medical, Saint Paul - Mn, USA) devices within the systemic-pulmonary bridge (Figure 2). These procedures resulted in a clinical and functional respiratory improvement. Within 90 days, a progressive stabilization of blood gas parameters was achieved. Thoracic angio-CT scan carried out six months post-embolization showed a substantial normalization of the arteriovenous morphology within the right lobes without bronchial pseudo aneurysm; enlargement of some vessels of ventral segment of RUL and few peripheral MAVFs persisted at the level of the superior segment of the RLL (Figure 3).

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors’ institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from all individuals included in this study.

3 Discussion

Our case confirms that patients with PAVMs require lifelong clinical, radiological and cardio-respiratory function assessments as recanalization and collateralization may recur after embolization therapy. We have shown that percutaneous TCE is effective and safe for the treatment of disease relapse. Diagnosis of PAVMs may be intriguing as clinical, physiopathological and radiological characteristics may mimic other cardio-respiratory diseases arising from different cellular and biomolecular pathways [1,3,23-40]. Percutaneous TCE is recognized as the gold standard...
Figure 1: Thoracic angio-CT scan at admission shows: presence of multiple AV Fistulas of RUL and RLL, increase of pulmonary venous and right bronchial artery and its branches caliber associated to aneurismatic dilatation of 1 cm. Web-like appearances are evident in the superior segment of RUL. Transversal (a) and Coronal (b) view.

Figure 2: Embolization procedures using the Amplatzer Vascular Plug IV (8 devices) as well as insertion of Amplatzer Vascular Plug IV (2 device) within the systemic-pulmonary bridge.

Figure 3: Thoracic angio-CT after embolization. Transversal (a) and Coronal (b) view.
for treatment of PAVM due to its efficacy and safety in reducing the risk of paradoxical embolism and other complications associated with PAVM [61-65]. Major indications for treatment are prevention of neurological complications, including stroke and cerebral abscess from paradoxical embolism, improvement in exercise tolerance, reduction in migraine prevalence, and prevention of lung hemorrhage [1,3]. Advantages over surgical intervention include it being less invasive and easy to repeat, although collateralization and revascularization over time have to be taken into account. Regardless of symptoms, any PAVM with a feeding artery of ≤ 3 mm in diameter detected by CT scan should be considered for therapy using this technique. During embolization, the supplying artery immediately preceding the PAVM is the target for occlusion just proximal to the aneurysmal sac. It is important to achieve an embolization as distal as possible in the feeding artery to avoid occluding branches supplying normal adjacent lung. The choice of embolization device depends on the vascular anatomy of the patient and the practice preference of the operator. A variety of materials are used to embolize PAVMs, depending on the size and complexity of the vessels. In general, PAVM with feeding artery diameters of between 3 and 9 mm are treated with balloons or coils, whereas those with diameters > 8 mm may be treated with either coils alone, an overinflated balloon impacted within a nest of coils, or with vascular plugs. Magnetic resonance-compatible steel or platinum coils are used in the majority of cases. Depending on the anatomy of the specific PAVM, other techniques may be employed. For example, if the neck of the feeding vessel is particularly large or wide, the aneurysm sac may be packed. The deployed coils are designed to coil within the vessel lumen and carry microfibers that activate platelets to generate an occluding platelet plug, whereas Amplatzer vascular plugs and balloon devices provide direct obstruction to vascular flow.

4 Conclusions

Our case describes a relapsing multiple MAVFs within the right lung in an 18 year old woman. The monolaterality of the malformation excludes Rendu-Osler Syndrome; etiopathogenesis remains unknown, although the young age at presentation suggests a miopragia of the vessel walls as possible cause of the vascular malformation. As relapses are not infrequent in PAVMs, patients should undergo regular clinical and radiological assessment. Embolization is effective in the treatment of relapsing disease.

Conflict of interest statement: Authors state no conflict of interest

References

[1] Cartin-Ceba R, Swanson KL, Krowka MJ. Pulmonary arteriovenous malformations Chest 2013 Sep;144(3):1033-44.
[2] Bayrak-Toydemir P, Mao R, Lawin S, Mc Donald J. Hereditary hemorrhagic teleangectasia: an overview of diagnosis and management in the molecular era for clinicians. Genet Med 2004; 6:175-91
[3] Shovlin CL., Pulmonary arteriovenous malformations. Am J Respir Crit Care Med. 2014 Dec;190(11):1217-28.
[4] Mazzarella G, Iadevaia C, Guerra G, Rocca A, Corcione N, Rossi G et al.: Intralobar pulmonary sequestration in an adult female patient mimicking asthma: a case report. Int J Surg. 2014; 12(Suppl 2):S73-7.
[5] Cattaneo F, Guerra G, Parisi M, Lucariello A, De Luca A, De Rosa N et al.: Expression of Formyl-peptide Receptors in Human Lung Carcinoma. Anticancer Res. 2015 May;35(5):2769-74.
[6] Corbi G, Bianco A, Turchiarelli V, Cellurale M, Fatica F, Daniele A et al.: Potential Mechanisms Linking Atherosclerosis and Increased Cardiovascular Risk in COPD: Focus On Sirtuins. Int J Mol Sci. 2013 Jun 17;14(6):12696-713.
[7] Cattaneo F, Guerra G, Parisi M, De Marinis M, Tafuri D, Cinelli M et al.: Cell-surface receptors transactivation mediated by g protein-coupled receptors. Int J Mol Sci. 2014 Oct 29;15(11):19700-28.
[8] Mazzarella G, Bianco A, Catena E, De Palma R, Abbate GF. Th1/Th2 lymphocyte polarization in asthma, Allergy 2000; 55(Suppl. 61):6-9.
[9] Esposito V, Lucariello A, Savarese L, Cinelli MP, Ferraraccio F, Bianco A et al.: Morphology changes in human lung epithelial cells after exposure to diesel exhaust micron sub particles (PM₁₀) and pollen allergens. Environ Pollut. 2012 Dec;171:162-7.
[10] Mazzarella G, Esposito V, Bianco A, Ferraraccio F, Prati MV, Lucariello A et al.: Inflammatory effects on human lung epithelial cells after exposure to diesel exhaust micron sub particles (PM₁₀) and pollen allergens. Environ Pollut. 2012 Feb;161:64-9.
[11] Mazzarella G, Lucariello A, Bianco A, Calabrese C, Thanassoulas T, Savarese L et al.: Exposure to submicron particles (PM1.0) from diesel exhaust and pollen allergens of human lung epithelial cells induces morphological changes of mitochondria tonofilaments and rough endoplasmic reticulum. In Vivo. 2014 Jul-Aug;28(4):557-61.
[12] Mazzarella G, Ferraraccio F, Prati MV, Annunziata S, Bianco A, Mezzogiorno A et al.: Effects of diesel exhaust particles on human lung epithelial cells: an in vitro study. Respir Med. 2007 Jun;101(6):1155-62.
[13] Grella E, Piacco G, Caterino U, Mazzarella G. Respiratory function and atmospheric pollution. Monaldi Arch Chest Dis. 2002 Jun-Aug;57(3-4):196-9.
[14] de Laurentis G, Parisi D, Melck D, Montuschi P, Maniscalco M, Bianco A et al.: Separating Smoking-Related Diseases Using NMR-Based Metabolomics of Exhaled Breath Condensate. J Proteome Res. 2013 Mar 1;12(3):1502-11.
[15] Vatrella A, Montagnani S, Calabrese C, Parrella R, Pelaia G, Biscione GL et al.: Neuropeptide expression in the airways of COPD patients and smokers with normal lung function. J Biol Reg Homeost Ag 2010 Oct-Dec;24(4):425-32.

[16] Moccia F, Dragoni S, Cinelli M, Montagnani S, Amato B, Rosti V et al.: How to utilize Ca2+ signals to rejuvenate the reparative phenotype of senescent endothelial progenitor cells in elderly patients affected by cardiovascular diseases: a useful therapeutic support of surgical approach? BMC Surg 2013 Oct 8;13(Suppl 2):S46.

[17] Moccia F, Guerra G. Ca2+ Signalling in Endothelial Progenitor Cells: Friend or Foe? J Cell Physiol. 2015 Aug 6. doi: 10.1002/jcp.25126. [Epub ahead of print]

[18] White RI Jr, Pollak JS, Wirth JA. Pulmonary arteriovenous malformations: diagnosis and transcatheter embotherapy. J Vasc Interv Radiol 1996; 7: 787–804.

[19] Faughnan ME, Lui YW, Wirth JA, Pugash RA, Redelmeier DA, Hyland RH et al.: Diffuse pulmonary arteriovenous malformations: characteristics and prognosis. Chest 2000; 117: 31–38.

[20] Brunese L, Greco B, Setola FR, Lassandro F, Guarracino MR, De Rimini M et al.: Non-small cell lung cancer evaluated with quantitative contrast-enhanced CT and PET-CT: net enhancement and standardized uptake values are related to tumour size and histology. Med Sci Monit. 2013 Feb 7;19:95-101.

[21] Gupta P, Mordin C, Curtis J, Hughes JM, Shovlin CL, Jackson JE. Pulmonary arteriovenous malformations: effect of embolization on right-to-left shunt, hypoxemia, and exercise tolerance in 66 patients. Am J Roentgenol 2002; 179: 347–352.

[22] Faughnan ME, Palda VA, Garcia-Tsao G et al. International guidelines for the diagnosis and man-agement of hereditary hemorrhagic telangiectasia. J Med Genet 2011; 48: 73–87.

[23] Fryer AA, Spiteri MA, Bianco A, Hepple M, Jones PW, Strange RC et al.: The -403 G-->A promoter polymorphism in the RANTES gene is associated with atopy and asthma. Genes Immun. 2000 Dec;1(8):509-14.

[24] Spiteri MA, Bianco A, Strange RC, Fryer AA. Polymorphisms at the glutathione S-transferase GSTP1 locus. A new marker for bronchial hyperresponsiveness and asthma. J Med Genet 2000 Apr;37(5):1803-7.

[25] Gupta P, Mordin C, Curtis J, Hughes JM, Shovlin CL, Jackson JE. Pulmonary arteriovenous malformations: effect of embolization on right-to-left shunt, hypoxemia, and exercise tolerance in 66 patients. Am J Roentgenol 2002; 179: 347–352.

[26] Brunese L, Greco B, Setola FR, Lassandro F, Guarracino MR, De Rimini M et al.: Non-small cell lung cancer evaluated with quantitative contrast-enhanced CT and PET-CT: net enhancement and standardized uptake values are related to tumour size and histology. Med Sci Monit. 2013 Feb 7;19:95-101.

[27] Gupta P, Mordin C, Curtis J, Hughes JM, Shovlin CL, Jackson JE. Pulmonary arteriovenous malformations: effect of embolization on right-to-left shunt, hypoxemia, and exercise tolerance in 66 patients. Am J Roentgenol 2002; 179: 347–352.

[28] Vatrella A, Montagnani S, Calabrese C, Parrella R, Pelaia G, Biscione GL et al.: Neuropeptide expression in the airways of COPD patients and smokers with normal lung function. J Biol Reg Homeost Ag 2010 Oct-Dec;24(4):425-32.

[29] Moccia F, Dragoni S, Cinelli M, Montagnani S, Amato B, Rosti V et al.: How to utilize Ca2+ signals to rejuvenate the reparative phenotype of senescent endothelial progenitor cells in elderly patients affected by cardiovascular diseases: a useful therapeutic support of surgical approach? BMC Surg 2013 Oct 8;13(Suppl 2):S46.

[30] Moccia F, Guerra G. Ca2+ Signalling in Endothelial Progenitor Cells: Friend or Foe? J Cell Physiol. 2015 Aug 6. doi: 10.1002/jcp.25126. [Epub ahead of print]

[31] White RI Jr, Pollak JS, Wirth JA. Pulmonary arteriovenous malformations: diagnosis and transcatheter embotherapy. J Vasc Interv Radiol 1996; 7: 787–804.

[32] Faughnan ME, Lui YW, Wirth JA, Pugash RA, Redelmeier DA, Hyland RH et al.: Diffuse pulmonary arteriovenous malformations: characteristics and prognosis. Chest 2000; 117: 31–38.

[33] Brunese L, Greco B, Setola FR, Lassandro F, Guarracino MR, De Rimini M et al.: Non-small cell lung cancer evaluated with quantitative contrast-enhanced CT and PET-CT: net enhancement and standardized uptake values are related to tumour size and histology. Med Sci Monit. 2013 Feb 7;19:95-101.

[34] Gupta P, Mordin C, Curtis J, Hughes JM, Shovlin CL, Jackson JE. Pulmonary arteriovenous malformations: effect of embolization on right-to-left shunt, hypoxemia, and exercise tolerance in 66 patients. Am J Roentgenol 2002; 179: 347–352.

[35] Faughnan ME, Palda VA, Garcia-Tsao G et al. International guidelines for the diagnosis and man-agement of hereditary hemorrhagic telangiectasia. J Med Genet 2011; 48: 73–87.

[36] Fryer AA, Spiteri MA, Bianco A, Hepple M, Jones PW, Strange RC et al.: The -403 G-->A promoter polymorphism in the RANTES gene is associated with atopy and asthma. Genes Immun. 2000 Dec;1(8):509-14.

[37] Spiteri MA, Bianco A, Strange RC, Fryer AA. Polymorphisms at the glutathione S-transferase GSTP1 locus: a novel marker for bronchial hyperresponsiveness and asthma. J Med Genet 2000 Apr;37(5):1803-7.

[38] Gupta P, Mordin C, Curtis J, Hughes JM, Shovlin CL, Jackson JE. Pulmonary arteriovenous malformations: effect of embolization on right-to-left shunt, hypoxemia, and exercise tolerance in 66 patients. Am J Roentgenol 2002; 179: 347–352.

[39] Brunese L, Greco B, Setola FR, Lassandro F, Guarracino MR, De Rimini M et al.: Non-small cell lung cancer evaluated with quantitative contrast-enhanced CT and PET-CT: net enhancement and standardized uptake values are related to tumour size and histology. Med Sci Monit. 2013 Feb 7;19:95-101.

[40] Faughnan ME, Lui YW, Wirth JA, Pugash RA, Redelmeier DA, Hyland RH et al.: Diffuse pulmonary arteriovenous malformations: characteristics and prognosis. Chest 2000; 117: 31–38.

[41] Gupta P, Mordin C, Curtis J, Hughes JM, Shovlin CL, Jackson JE. Pulmonary arteriovenous malformations: effect of embolization on right-to-left shunt, hypoxemia, and exercise tolerance in 66 patients. Am J Roentgenol 2002; 179: 347–352.

[42] Faughnan ME, Lui YW, Wirth JA, Pugash RA, Redelmeier DA, Hyland RH et al.: Diffuse pulmonary arteriovenous malformations: characteristics and prognosis. Chest 2000; 117: 31–38.

[43] Gupta P, Mordin C, Curtis J, Hughes JM, Shovlin CL, Jackson JE. Pulmonary arteriovenous malformations: effect of embolization on right-to-left shunt, hypoxemia, and exercise tolerance in 66 patients. Am J Roentgenol 2002; 179: 347–352.

[44] Faughnan ME, Lui YW, Wirth JA, Pugash RA, Redelmeier DA, Hyland RH et al.: Diffuse pulmonary arteriovenous malformations: characteristics and prognosis. Chest 2000; 117: 31–38.

[45] Gupta P, Mordin C, Curtis J, Hughes JM, Shovlin CL, Jackson JE. Pulmonary arteriovenous malformations: effect of embolization on right-to-left shunt, hypoxemia, and exercise tolerance in 66 patients. Am J Roentgenol 2002; 179: 347–352.
patients with pulmonary arteriovenous malformations. Am Rev Respir Dis. 1990;142(2):420-425.

[43] Pollak JS, Saluja S, Thabet A, Henderson KJ, Denbow N, White RI Jr. Clinical and anatomic outcomes after embolotherapy of pulmonary arteriovenous malformations. J Vasc Interv Radiol. 2006;17(1):35-44.

[44] Hsu CC, Kwan GN, Thompson SA, Evans-Barns H, van Driel ML. Embolisation therapy for pulmonary arteriovenous malformations. Cochrane Database Syst Rev. 2015 Jan 29;1:CD008017