Case Report

Pulmonary arteriovenous malformation and inherent complications with solitary lung nodule biopsy—literature overview and case report

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\textbf{A B S T R A C T}

Pulmonary arteriovenous malformation, also known as an arteriovenous fistula, is typically a congenital disease caused by structural deficiencies, particularly the lack of capillary wall development, leading to the abnormal dilation of the pulmonary capillaries. The majority of pulmonary arteriovenous malformation cases are associated with Rendu–Osler–Weber syndrome, also known as hereditary hemorrhagic telangiectasia. Pulmonary arteriovenous malformation rarely occurs due to chest trauma. Pulmonary arteriovenous malformations are long-lasting and often first diagnosed in adults. More than two-thirds of pulmonary arteriovenous malformation lesions are found in the lower lung lobe and the subpleural area, and the vast majority of cases present with the monofocal form. The initial diagnosis is often based on the identification of a solitary pulmonary nodule. However, a solitary nodule detected on chest computed tomography that is not correctly diagnosed as pulmonary arteriovenous malformation, even after intravenous contrast injection, can lead to the performance of a transthoracic biopsy. Biopsy of pulmonary arteriovenous malformations can lead to stroke occurrence, during which the patient often presents with severe pleural bleeding, which can have lifelong consequences if not immediately treated. We report a case of pulmonary arteriovenous malformation that was discovered incidentally in an adult patient.
Introduction

Congenital arteriovenous fistulas are also known as pulmonary arteriovenous malformations (PAVMs), which develop due to structural deficiencies that result in the abnormal dilation of pulmonary capillary walls during development. Approximately 35%-67% of PAVM cases are associated with Rendu–Osler–Weber syndrome, which is also known as hereditary hemorrhagic telangiectasia (HHT) and typically affects the skin and mucous membranes. In rare cases, PAVM can occur due to chest trauma or hepatopulmonary syndrome [1,2]. Although PAVM can develop during childhood, PAVM is typically first diagnosed in adults. More than two-thirds of cases are detected in the lower lung lobe, often in the subpleural area. Multisite arteriovenous catheterization occurs in 35% of cases, whereas bilateral PAVMs are detected in 10% of cases [1,3].

Two common types of PAVM can be detected on imaging: simple and complex. The simple form generally consists of a connection between a single pulmonary artery and one feeding vessel. The simple form is the most common form and accounts for the majority of PAVM cases. The complex form involves more than one pulmonary artery connecting to the PAVM sac and is very rare [1,4].

On radiographs, simple PAVMs commonly appear in the periphery, with a uniform, circular, oval, lobed, or zigzag-shaped opacity. The pulmonary veins draining the dilated sacs appear dilated and extend toward the hilum. The PAVM sac can expand slowly over a long period of time, but rapid enlargement can also occur [1,4,5].

On chest computed tomography (CT), PAVM typically appears as a smooth, well-margined, circular, or elliptical nodule and is almost always located in the subpleural region. An arteriovenous sac characterized by a chaotic plexus with a dilated pulse can appear as a lobed mass with wavy margins. In both cases, the feeding pulmonary artery and draining vein are dilated. When the PAVM sac is larger than 1-2 cm, the supplying artery is often easily discernible. In general, the incoming vessel diameter is usually half the PAVM sac diameter [1,5–7].

Spiral chest CT has high accuracy for evaluating the PAVM structure. In most cases, the findings are sufficient to diagnose PAVM, but contrast injection can be used to confirm the diagnosis. After contrast injection, the PAVM can be observed to rapidly absorb and clear the contrast agent, which tends to occur simultaneously with the contrast agent passing through the pulmonary artery and the right atrium [1,4,8,9].

PAVMs <2 cm in diameter that are detected on radiographs are typically asymptomatic. Simple PAVM is symptomatic in 35% of cases, a smaller proportion than symptomatic complex PAVM cases (85%). The PAVM usually produces a right-left shunt and often causes cyanosis, depending on the size of the shunt. The most common symptoms reported in patients with PAVM are dyspnea, palpitations, hemoptysis, and chest pain. Stroke can occur in association with polycythemia vera, and embolism through the PAVM from the systemic veins is very dangerous and can result in fatal complications. Contusions, tears, and pneumothorax are often the result of pulmonary hemorrhage. If left untreated, approximately 25% of PAVM patients experience severe symptoms, and 50% lead to fatal complications [1,9–11].

The treatment of PAVM can be simple, involving catheter occlusion using wire coil in fistulas with arterial diameters >3 mm. However, the recanalization of an arteriovenous catheter following wire coil occlusion is also common. Complex PAVM often presents with more symptoms than simple PAVM due to large shunt currents, and treatment is more difficult in complex cases due to the involvement of multiple afferent arteries [4,6,9,11]. For PAVMs that recanalize after embolization or in cases of complicated PAVMs, elective lung resection is often performed, which can often be performed using endoscopic video-assisted pneumonectomy techniques, which are widely used and more convenient than conventional resection surgeries [9,12–19].

PAVM diagnosis is not typically difficult when doctors suspect and are aware of this possibility during screening. The application of multisite CT with contrast injection can accurately detect most PAVM cases when the correct contrast agent dose and injection velocity are applied. When imaging is delayed by 20 seconds after contrast injection, the triple image of PAVM is often clear. If the intravenous contrast injection is not applied correctly (lack of drugs, slow injection velocity, incorrect scan parameters upon injection of intravenous contrast agent), PAVM can be misdiagnosed [1,10,12]. Isolated nodules are often biopsied, and the risk to patients is high when the biopsy needle pierces a PAVM, which can rapidly threaten the patient’s life, particularly if the biopsy is performed in facilities that are not equipped for emergency surgery.

We report a case of misdiagnosed PAVM to allow other clinicians to learn from our experience and provide guidance when encountering similar cases in the hopes of avoiding potentially dangerous outcomes and improving patient safety.

Case report

A 51-year-old woman was referred by a local hospital for examination and treatment at the National Lung Hospital due to the appearance of pleural effusion after a single pulmonary nodule biopsy was performed in the transthoracic lung under CT guidance.
The patient was healthy since childhood, rarely showed signs of respiratory infections, did not have a history of hemoptysis, nosebleeds, or bleeding in the skin and mucous membranes.

One month before visiting the local hospital, the patient developed a cough with little sputum, chest pain, and mild shortness of breath but no fever or hemoptysis. The patient received 2 doses of the coronavirus disease 2019 (COVID-19) vaccine, 4 months apart. Before admission to the clinic, the patient underwent a PCR test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with negative results. The local hospital performed a physical examination, chest X-rays, and basic tests. The chest X-ray is shown in Fig. 1.

Clinical examination at the local hospital revealed that the patient was thin, and the skin and mucous membranes were not pink. No evidence of edema, bleeding under the skin, or enlarged peripheral lymph nodes was detected. Auscultation of the right lung revealed poor ventilation, many crackles, and moist rales. Oxygen saturation (SpO₂) was 95%. Examination of the cardiovascular, digestive, and urinary systems showed no abnormalities.

The patient was tested twice for SARS-CoV-2, with negative results. A complete blood count and blood chemistry tests showed results within normal limits. The preliminary diagnosis was a right lung tumor.

The patient underwent a chest CT using a 16-row machine without intravenous contrast injection. The CT protocol was as follows: 130 kV, Xtube, 115 mA; slice thickness, 3 mm; window width (WW)/window length (WL), 1200/–800 (lung parenchymal window); and WW/WL, 350/50 (mediastinal window). Reconstruction was performed on 0.75-mm thin slices, and the images and detailed results are presented in Figs. 2 and 3.

The patient received consultation by qualified specialists at the local hospital, who concluded that follow-up was necessary for the solitary nodule in the right lung and recommended lung nodule biopsy under CT guidance.

The patient was subjected to coagulation tests, with results within normal limits. At that time, a transthoracic biopsy was performed under CT guidance. The biopsy needle hit the nodule, and 3 pieces of the specimen were removed. The case review from the local hospital revealed 2 hours after the biopsy, the patient underwent a chest X-ray, which revealed right pleural effusion. At that time, the patient had a stable pulse and blood pressure, and after 24 hours of follow-up by X-ray and ultrasound, the pleural fluid volume did not increase. The patient was treated with antibiotics at the hospital for 5 days and was re-evaluated before being released to outpatient status on the sixth day. The patient was released from the hospital and went home to await the pathology results. The conclusion of the local hospital was a right pleural bleeding complication associated with the performance of transthoracic biopsy. The degree of pleural bleeding was small, the bleeding had stopped, and no intervention was needed, as a small amount of blood will typically be absorbed over time without intervention. When discharged from the hospital, the patient experienced heaviness in the chest; however, the pathological results showed no malignant cells, so the patient endured this sensation with the hope of returning to normal. The patient self-monitored for 3 weeks, during which time the chest pain did not appear to decrease, and the patient began to experience fever. The patient then presented to our hospital for medical examination (in part due to complications associated with the COVID-19 epidemic, patients were reluctant to visit doctors unnecessarily).

When we received the patient, the patient described a high level of chest pain, cough, and difficulty breathing. We performed a chest X-ray at the patient’s bed. Detailed images and results are shown in Fig. 4.

Although the patient came to the clinic in an emergency condition, the patient’s hemodynamic status remained quite stable (heart rate 80 beats/min; blood pressure 110/80 mm Hg). We consulted the chest CT film from the local hospital, which the patient provided (as shown in Figs. 2 and 3), and considered the possibility of PAVM, which would suggest that the patient was experiencing late-onset hemorrhagic stroke after undergoing transthoracic biopsy 3 weeks prior to presentation at our hospital. We subjected the patient to a 64-slice CT scan with intravenous contrast. Detailed images and results are shown in Fig. 5.

Based on the strong enhancement of the right middle lobe nodule, we transferred the data for image processing. The volume rendering technique results clearly displayed PAVM. Details are shown in Fig. 6.

The patient underwent a right pleural puncture which revealed bloody fluid.

This case was diagnosed as PAVM, with late bleeding after the biopsy. Because the blood in the right pleural space has likely been present for a long time, the risks of infection and pleural deposit formation were high. Blood count, blood
chemistry, urine, and electrocardiogram examinations were rapidly performed, revealing normal results. The patient underwent cranial magnetic resonance imaging in case of multi-organ of arteriovenous malformations, which revealed normal results.

Summarizing all the data, we decided to operate on the patient, using video-assisted laparoscopic surgery to (1) perform the selective resection of the middle lobe parenchyma where the PAVM sac was located and (2) resolve pleural effusion.

The patient was operated on by a skilled thoracic surgery specialist. Images obtained during surgery are shown in Fig. 7.

The surgery was performed by creating a 5-cm skin incision at the fifth intercostal space in the right anterior axillary into the pleural space. The lungs were heavily attached to the chest wall, and the lungs were released from top to bottom. One trocar was placed in the seventh intercostal space in the middle axillary line (camera), revealing that the lungs were heavily attached to the chest wall, and the minor interlobar fissure was incomplete. The adhesions were removed, and the pleural deposits were entered, revealing a fovea with a thin shell containing pseudomembranous and red-pink fluid. Samples were obtained for microbiology analysis, and the pleura were peeled back, releasing the whole lung. The lungs were inflamed and sticky, with many proliferating blood vessels. Examination revealed a tumor-like form in the right middle lobe of the lung, approximately 3 × 3 cm in size, beating in time with the heart rate and purple in color. Dissection was performed, and the middle lobe was cut to remove the tumor, followed by closure with 3 staples. The pleural cavity was rinsed with warm 0.9% saline, verifying that the lung was well expanded, the apex was closed, and the bleeding was good. A drainage tube was placed, and the incision was closed according to anatomical layers. The patient was followed until full recovery. Dissection revealed the PAVM structure, and the specimens were sent for histopathological examination.

During the postoperative period, the patient underwent a routine chest X-ray twice. The detailed results are shown in Fig. 8.

The patient underwent a pleural ultrasound, which revealed no fluid in the pleural space on both sides. The ultrasound also confirmed pleural thickening.

The specimen mass was assessed by histopathology, and the results are detailed in Fig. 9.

**Discussion**

PAVM is an abnormal vascular connection between the pulmonary artery and the pulmonary vein. Most cases are con-
genital, and PAVMs often occur in patients with Rendu-Osler-Weber syndrome, also known as HHT. In rare cases, PAVM can be caused by hepatopulmonary syndrome or chest trauma [1–3,8,17]. Bronchiectasis has also been reported to cause PAVM, but this occurrence is very rare [6]. At the site of abnormal connections, a sac with an abnormal vascular structure is often generated, resulting in the development of a primarily left-right shunt. PAVMs rupture in 2%-8% of patients, particularly in those patients with coagulopathy or who are pregnant [1,2].

Once formed, PAVMs appear very similar to a tumor and are typically diagnosed as solitary pulmonary nodules [1–3]. PAVM is typically classified as either simple or complex. The simple form of PAVM is typically supplied by only one artery and one vein, whereas complex types involve 2 or more supplying arteries. When the PAVM sac ruptures, emergency embolization is often performed [3,4]. However, in cases in which the patient is allergic to embolization materials, particularly in cases of metal allergies, urgent surgical resection of the cystic lung should be prioritized [4]. The differential diagnosis of solitary pulmonary nodules in developed countries often relies on positron emission tomography/CT to determine the presence...
of possible malignancy, especially in patients with renal failure or allergies to contrast media [5].

The majority of PAVM cases are detected in adults, although the disease may develop during childhood [8,13,15]. When PAVM is detected in children, severe disease is often present, manifesting as cyanosis, difficulty breathing, and death in infants [8]. The evaluation, monitoring, and medical management strategies necessary for people with HHT require multispecialty medical facilities. In these subjects, after one arteriovenous malformation is detected, more are often detected in other organs, requiring comprehensive screening [19].

In reviewing the case we report here, we find many points that should be emphasized. From childhood until the onset of symptoms in middle age, the patient was completely healthy, with no evidence of classic PAVM symptoms in the patient's medical history. One month before presenting to the local hospital, the patient developed a cough with little sputum, chest pain, mild shortness of breath, with no fever or hemoptysis. None of these signs are specific for PAVM and are all commonly observed with respiratory tract infections. At the time, the patient had been fully vaccinated with 2 doses of the COVID-19 vaccine. The abnormality was clearly observed on both routine chest X-ray and CT, as the nodule was rather large (22 × 18 mm). The local hospital’s diagnosis of a solitary pulmonary nodule was correct, but the differential diagnosis was unsatisfactory. In middle-aged patients (a common age for the appearance of advanced lung cancer), the National Comprehensive Cancer Network (NCCN, 2021) recommends that solitary nodules larger than 15 mm should be evaluated by contrast-enhanced CT or positron emission tomography/CT. If the results suggest low-grade cancer, the patient should be scheduled to receive a low-dose CT scan every 3 months. If high-grade cancer is suspected, then a transthoracic biopsy or surgical excision is necessary; however, the local hospital did not follow these recommendations. The use of a contrast agent during chest CT greatly increases the probability of recognizing PAVM because most of these lesions strongly absorb contrast agents. The multifocal enhancement of this solitary nodule was quite typical of a PAVM. However, because PAVM is a rare disease, the clinicians at the local hospital likely had little experience with this entity, and they did not recognize this sign. The literature describes the possibility of pleural bleeding complications when performing a single nodule biopsy, which can present as either immediate bleeding after biopsy or delayed bleeding (several days to several weeks after biopsy). This patient presented with pleural bleeding immediately after the biopsy. In principle, the patient should have received a drainage tube to monitor the bleeding so that any increase in blood volume can be addressed immediately by surgery to address the cause of bleeding and remove the blood from the pleural space. The local hospital also failed to follow these recommended procedures. Instead, the patient went home while blood continued to flow into

Fig. 7 – Image of right middle lobectomy containing the PAVM sac and the postoperative specimen mass. (A, B) Exposing the middle lobe and the PAVM sac from the outside (yellow arrow). (C) Stapler apex image after middle lobe resection (white arrow). (D) Postoperative specimen mass clearly shows the pulmonary artery (green arrow), draining pulmonary vein (white arrow), and PAVM sac (yellow arrows).
Fig. 8 – Chest X-ray films from 5 and 7 days after surgery. (A) Postoperative radiograph on the fifth day showed right pleural thickening (yellow arrow) and air in the subcutaneous tissue of the right chest wall (red arrow). (B) Postoperative film on the seventh day showed right pleural thickening (yellow arrow) and only trace amounts of subcutaneous air in the right chest wall (red arrow). On both films, right pleural effusion was suspected.

Fig. 9 – Postoperative microscopic histopathology results. Template code: G22-0033. (A–D) Microscopic sections showed lung tissue (yellow arrows) exhibiting areas of thin and partially thick vascular channels of various sizes (black arrow), lined by endothelial cells and filled with red blood cells, surrounded by extensive intraalveolar hemorrhages (blue arrow) and focal areas of atelectasis. This area is in close proximity to the bronchus with a narrowed lumen (red arrow) and accompanying medium-sized arteries (green arrow) and predominantly closer to the thick pleural lining. Moderate plasmalymphocytic and hemosiderin macrophages are noted within the peribronchial and some alveolar spaces, indicative of the old bleeding area. No fibrocalcific nodules or evidence of chronic granulomatous disease was identified. No malignant cells were found. The conclusion was vascular abnormalities consistent with the vascular malformation of PAVM.
the pleural space, where it remained for up to 3 weeks. As a result, large amounts of blood pooled in the pleural space resulting in inflammation. Fortunately, the patient presented to our hospital in time for successful surgery, and this case was not fatal.

Finally, once PAVM is detected, the choice of treatment strategy is extremely important. In practice, both emergency and delayed management situations are likely to present for both simple and complex PAVM. In emergency situations (such as patients with moderate to heavy hemoptysis) due to ruptured PAVM, including those ruptured by biopsies, embolization should be the first approach. However, embolization is often a difficult technique to perform and can be highly risky because the catheterization of the right heart requires specialized equipment, experienced vascular interventionists, and a synchronous active resuscitation system. Therefore, the elective surgical resection of lungs presenting with PAVM (wedge resection), lobectomy, and bilateral surgery is becoming the strategy of choice in many countries. All surgeries use laparoscopic methods and modern Staplers, which shorten the surgery time (30-95 minutes) and reduce blood loss [7–9,12,14,19]. The case we reported was successfully treated with surgery, removing the section of the lung containing the PAVM sac and resolving the consequences of long-standing right pleural bleeding due to transthoracic lung biopsy. At present, the patient has returned to normal life and continues to be closely monitored by us.

Conclusion

We report a case of PAVM that was discovered incidentally; however, technical errors were made in the diagnostic approach. Through this report, we aim to highlight important points that should be learned. (1) Before conducting a transthoracic biopsy, regardless of the lesion, a chest CT should be performed with contrast injection. (2) When encountering a case presenting with isolated lung nodules, International Guidelines should be followed prior to biopsy (NCCN, Fleischer Society, ATS...). (3) When bleeding is detected in the pleural cavity after biopsy, this issue should be addressed completely (intubation of a drainage tube, monitoring, surgery) before the patient is discharged from the hospital. The idea that a small volume of blood in the pleural space does not need to be treated should be eliminated. (4) Doctors need to equip themselves with the minimum knowledge regarding the imaging features of a pulmonary PAVM to allow for accurate orientations regarding the diagnostic and treatment approaches required for this disease.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Authors’ contributions

Cung-Van C and Dinh-Van L contributed equally to this article as co-first authors. All authors read and approved final version of this manuscript.

Ethics approval

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of patient information in this article.

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