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Case Report

Isolated pulmonary artery choriocarcinoma masquerading as pulmonary embolism diagnosed by endovascular biopsy ^{☆,☆☆,★}

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ABSTRACT

Pulmonary arteries may rarely be involved by primary and secondary tumors. Clinical and imaging features mimic those of PE making it challenging to diagnose. Choriocarcinoma is a malignant germ cell tumor, typically in the female genital tract. Rarely, they can present as PA thrombus. Female patients with a history of a molar pregnancy, ectopic pregnancy, abortion or in this case a miscarriage, are at a higher risk of gestational trophoblastic disease which can manifest in this way, albeit this is rare.

In this report we describe the case of a 52-year-old female who presented with a 1 month history of worsening dyspnea and pleuritic lower thoracic pain. A diagnosis of pulmonary embolism (PE) was confirmed on CT pulmonary angiogram, with a large volume thrombus in the left pulmonary artery (PA). She failed to improve on standard anticoagulation therapy and was found to have a raised beta-human chorionic gonadotropin of >100,000. This leads to an extensive malignancy work-up. The only pertinent finding was that of increased fluorodeoxyglucose (FDG) accumulation in the PA thrombus. Endovascular biopsy of the thrombus was performed, and the patient was diagnosed with choriocarcinoma of the PA.

This case highlights the importance of further investigation in patients failing to respond to anticoagulation therapy for PE. It also illustrates the role of interventional radiology in obtaining histological diagnosis in patient's presenting with PA tumor thrombus.

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Abbreviations: CTPA, computed tomography pulmonary angiogram; CT-AP, computed tomography abdomen pelvis; PE, pulmonary embolism; PA, pulmonary artery; HCG, human chorionic gonadotropin; OGD, oesophago-gastro-duodenoscopy; BSO, bilateral salpingo-oophorectomy; FDG, fluorodeoxyglucose; VATS, Video assisted thoracoscopic surgery; IHC, Immuno-histo-chemistry; EBUS-TBNA, endobronchial ultrasound and transbronchial needle aspiration; ECMO, extracorporeal membrane oxygenation.

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Background

The pulmonary vasculature may rarely be involved by primary and secondary tumors. The most common primary tumors of the pulmonary arteries are poorly differentiated sarcomas [1]. Clinical and imaging manifestations may mimic those of pulmonary embolism which can make the diagnosis challenging. Secondary involvement of pulmonary arteries and veins can be due to direct invasion from primary or secondary lung malignancy or due to tumor emboli (e.g. renal cell carcinoma) [1,2].

Choriocarcinoma is a rare aggressive and highly malignant germ cell tumor, which can be gestational and, less commonly, non-gestational. It accounts for less than 0.1% of primary ovarian neoplasms and less than 1% of testicular tumors being pure choriocarcinoma [3]. There are wide regional variations; In Europe and North America it affects approximately 1 in 40,000 pregnancies and 1 in 40 hydatidiform moles, whereas in South-East Asia it is as high as 9.2 in 40,000 [3]. It typically displays vascular invasion and subsequent haematogenous spread. Up to 75% of patients have pulmonary metastases at the time of diagnosis [4].

This case report highlights the role of interventional radiology in diagnosis of malignant pulmonary embolism.

Case report

A 52-year-old female presented to the emergency department with a 1-month history of worsening dyspnoea and lower thoracic pleuritic pain. Her past medical history was relatively unremarkable, with no history of cardiac or pulmonary disease and she was a lifelong non-smoker. She had no identifiable risk factors for venous thromboembolism. Her obstetric history was gravida 4, para 2. She had 2 uncomplicated pregnancies and 2 miscarriages at 5 and 7 years previously, both of which were managed conservatively without any complications. She was perimenopausal at the time of presentation but had no active issues requiring hormone replacement therapy. She had no other gynecological history.

Her examination was unremarkable and there were no signs of a deep vein thrombosis. Her initial blood work, chest X-ray, and electrocardiogram were normal apart from a persistent sinus tachycardic and an elevated D-dimer (over 5 times the upper limit of normal). CT pulmonary angiogram (CTPA) was performed which demonstrated bilateral pulmonary emboli with a large burden of clot in the proximal left sided pulmonary arteries (Fig. 1). She subsequently commenced oral Apixaban, 5 mg twice a day and was discharged with a plan for outpatient clinical review.

She returned to hospital 2 weeks later with worsening symptoms, despite reporting full compliance with medication. A repeat CTPA revealed extension of clot with associated pulmonary infarcts. She was commenced on a higher dose of anticoagulation (enoxaparin 1.25 mg/kg twice a day) under the guidance of coagulation specialists and she was admitted for further investigation. Her blood work-up during this admission revealed a Beta-HCG of >100,000 mIU/mL. She also

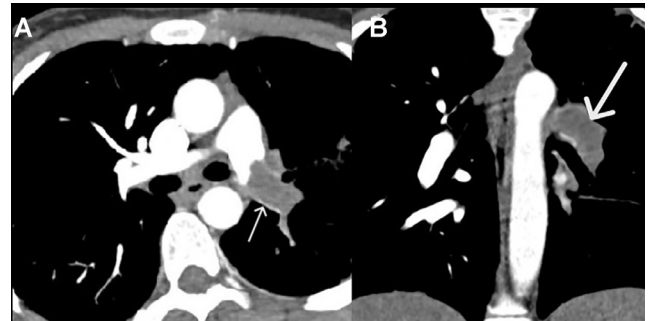


Fig. 1 – (A) Axial CTPA. Large volume thrombus in the left main pulmonary artery (white arrow). (B) Coronal CTPA through the same level further demonstrating the extensive thrombus in the left main pulmonary artery (white arrow).

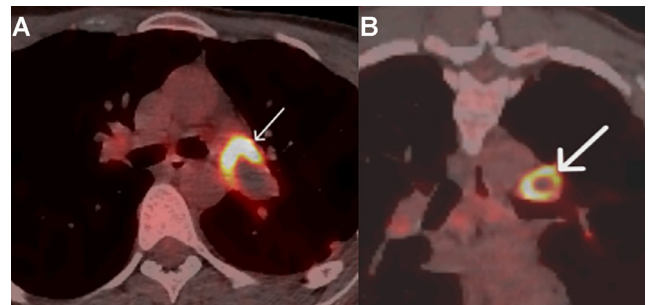


Fig. 2 – (A) Axial ^{18}F -FDG PET/CT fused. Thrombus in the left main pulmonary artery which is intensely FDG-avid at its proximal aspect concerning for tumor thrombus. (B) Coronal ^{18}F -FDG PET/CT fused at the same level demonstrating intensely FDG-avid thrombus.

developed per vaginal bleeding during the treatment which led to an extensive radiological malignancy work-up including completion CT imaging of her abdomen and pelvis and an MRI pelvis which were unremarkable apart from features suggesting adenomyosis. She underwent hysteroscopy with biopsy and laparoscopy with BSO, which revealed a benign endocervical polyp but otherwise no pathology. Furthermore, MRI brain, pituitary, and upper abdomen were performed as was an OGD, all of which were normal. Due to ongoing clinical concern for un-identified malignancy, it was at this point that a PET-CT was performed which demonstrated abnormal intense FDG accumulation with the pulmonary artery thrombus with no other sites of FDG-avid disease (Fig. 2).

Subsequently she underwent interventional radiology pulmonary artery catheter angiogram. Venous access was obtained via the right common femoral vein. A pulmonary artery flush catheter was placed in the main pulmonary artery and angiogram confirmed a large filling defect in the left main pulmonary artery. Then an 80 cm 8-French braided arrow sheath (Super Arrow Flex, Arrow International LLC) was inserted into the left main pulmonary artery. Through this sheath a 5.5 French endovascular biopsy forceps (biopsy forceps, cordis) was inserted and multiple tissue samples were obtained from the thrombus (Fig. 3).

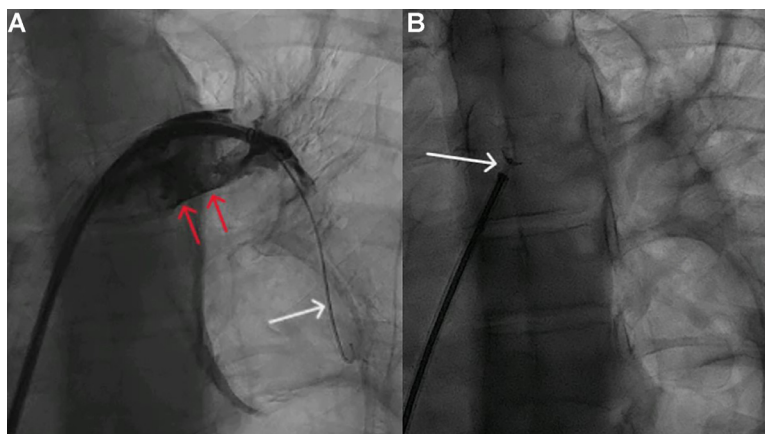


Fig 3 – (A) Fluoroscopic image. Wire passed through the thrombus (white arrow) with a catheter over the wire. Extensive filling defects in the left pulmonary artery consistent with thrombus (red arrows). (B) Fluoroscopic image. Biopsy forceps in position and open (white arrow) ready to biopsy the thrombus.

Histopathological analysis confirmed the thrombus was consistent with malignant choriocarcinoma.

Following diagnosis, she was seen urgently by oncology and started on an appropriate chemotherapy regimen of Etoposide, Methotrexate, Dactinomycin, Cyclophosphamide, and Vincristine every 2 weeks until hCG normalizes, with a plan to continue then for an additional 8 weeks. At the time of writing, her HCG levels had normalized and repeat imaging has the tumor thrombus is reducing in size.

Discussion

Choriocarcinoma causing pulmonary artery thrombosis with an absence of choriocarcinoma detected elsewhere is extremely rare. As a result, these tumors are often diagnosed inaccurately as thromboembolism. While choriocarcinoma presenting as a pulmonary embolism is rare, it should be considered in woman of fertile age presenting with similar symptoms and a serum or urine Beta-HCG should be measured [5].

The underlying pathophysiology remains unclear. Autopsies performed on 10 woman who died after delivery or abortion found trophoblasts in the pulmonary artery of ninety percent of the woman, suggesting that it may be caused by malignant transformation of normal trophoblasts that entered the pulmonary artery at the time of the gestational event. Others have hypothesized that it may represent metastases from an undetected trophoblastic disease which has undergone spontaneous regression in a phenomenon known as “burn-out”, specific to choriocarcinoma [5,6].

Diagnosis of PA malignancy can be challenging due to the symptomatology and imaging findings being identical to that of thromboembolic disease. Useful non-invasive imaging methods including CTPA, MRI and in particular PET-CT can help distinguish PA malignancy from pulmonary thromboembolism. On CTPA, malignant thrombus is more likely to fill the proximal lumen or expand the vessel. Obviously, thrombus extending beyond the vessel wall is highly suggestive. On MRI, tumor

embolism demonstrates increased gadolinium enhancement when compared to bland emboli. On ^{18}F -FDG PET/CT tumor thrombus will demonstrate increased FDG uptake with the additional advantage that it can help identify a distant primary source and other sites of metastatic disease [1,2,5,7].

However, the ultimate diagnosis often remains unclear when based on imaging alone, and obtaining pathological specimens is essential to guide treatment. Obtaining specimens of pulmonary artery lesions can pose a challenge. CT-guided transthoracic biopsy is one option, however given the location it poses the high risk of bleeding. Endobronchial ultrasound and transbronchial needle aspiration (EBUS-TBNA) is another option which allows better visualization of the tumor and blood flow via doppler ultrasonography, however due to increased pulmonary artery pressure and resultant bronchial artery hypertrophy, there is also a high risk of bleeding [2,8,9].

Endovascular biopsy including forceps biopsy and catheter aspiration has been used to make a treatment diagnosis for PA tumors, which has been shown as both effective and safe in multiple studies.

A retrospective study examined 22 such patients who underwent one or both procedures. They found a diagnostic accuracy of 91%. Of the 15 patients who underwent both, they found forceps biopsy to be far superior in terms of technical success of obtaining diagnosis: 93.3% vs 6.7%. Furthermore, there were no acute or fatal complications. This does, however, require extensive training in PA catheterization and ability to use forceps of a considerable size to obtain appropriate samples [2,8,9].

In terms of treatment options, they can be subdivided into emergency treatment and long-term treatment. In the immediate, Anti-coagulation is typically started. The use of extracorporeal membrane oxygenation (ECMO) in PA choriocarcinoma has been described as a bridge to circulatory collapse and provide time to reach the diagnose and start appropriate treatment [10]. Embolectomy, open or endovascular, can be used in the immediate treatment and as a planned surgical intervention in conjunction with chemotherapy. Choriocarcinoma tends to respond well to chemotherapy and with timely treatment, complete remission is possible [3].

Conclusion

This case demonstrates the importance of further investigation where pulmonary emboli are failing to respond to appropriate anticoagulant therapy. It also highlights the role of interventional radiology in diagnosing these rare tumors.

Ethical approval and consent to participate

Formal ethics approval was not required as per our institutions standard guidelines. Informed consent was obtained from all individual participants included in the study.

Availability of data and materials

Not applicable.

Author contributions

SD: Writing- original draft, writing- review and editing, supervision, project administration, conceptualization, image acquisition and labelling. RK: Writing- original draft, writing- review and editing, and conceptualization. NMCE: Writing- original draft, writing- review and editing, conceptualization and image acquisition.

Patient consent

Consent for publication was obtained for every individual person's data included in the study.

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