Case Report

Pulmonary Circulation

Chronic thromboembolic pulmonary hypertension following long-term peripherally inserted central venous catheter use

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Abstract

A 36-year-old woman presented with recurrent pulmonary emboli (PE) despite oral anticoagulation. She was a type I diabetic with severe gastroparesis requiring insertion of multiple long-term peripherally inserted central catheters (PICC) over a 10-year period. Imaging at presentation demonstrated a PICC-associated mobile mass in the right atrium and signs of pulmonary hypertension (PH). She was thrombolyzed and fully anticoagulated, and diabetic management without PICC strongly recommended. PH persisted, however, and she developed chronic thromboembolic pulmonary hypertension (CTEPH), for which successful pulmonary endarterectomy (PEA) surgery led to symptomatic and hemodynamic improvement. This was the first case of CTEPH reported related to long-term PICC use outside the setting of malignant disease, and a novel observation that the PEA specimen contained multiple plastic fragments. Long-term PICC placement increases the risk of CTEPH, a life-threatening, albeit treatable, complication.

Keywords

Chronic thromboembolic pulmonary hypertension, diabetes, pulmonary endarterectomy

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Case description

A 36-year-old woman presented with sudden onset breathlessness. She had type I diabetes diagnosed at the age of five years, with debilitating gastroparesis requiring partial gastric bypass surgery at the age of 15 years. Debilitating nausea symptoms necessitated increasing use of intravenous cyclizine, with little benefit from oral anti-emetics. Difficult venous access prompted repeated insertion of long-term peripherally inserted central catheters (PICC) over a 10-year period before the onset of dyspnea.

At initial assessment, computed tomography pulmonary angiography (CTPA) demonstrated acute pulmonary embolism (PE) within the left pulmonary artery, for which the direct oral anticoagulant rivaroxaban was initiated. Three months later, she developed World Health Organization (WHO) functional class (FC) III breathlessness, with additional PE confirmed on CTPA, despite rivaroxaban and therapeutic anti-Xa levels. Transthoracic echocardiography demonstrated signs of pulmonary hypertension (PH). She was switched to warfarin and referred to her regional PH center for suspected chronic thromboembolic pulmonary hypertension (CTEPH).

Clinical examination revealed a left basilic vein PICC and signs of PH without right ventricular (RV) failure. Ventilation-perfusion scanning confirmed large unmatched bilateral segmental perfusion defects in upper and lower lung lobes. Repeat CTPA revealed chronic remodeling of the previously noted left pulmonary artery thrombus and reduced perfusion in most lobar and segmental vessels of

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both lower lobes, with a new filling defect in a segmental branch of the right upper lobe. Anti-phospholipid antibodies, connective tissue disease antibodies, lower limb ultrasonography, and a malignancy screen were negative. Six-minute walk distance (6MWD) was reduced (190 m), with oxygen desaturation from 99% to 78% on air. Echocardiography estimated a systolic pulmonary artery pressure (PAP) of 63 mmHg with impaired RV function. A right atrial thrombus (20×12 mm) was noted, attached to the PICC line, confirmed on cardiac magnetic resonance imaging. Despite intravenous heparin, the thrombus doubled in size (45 mm) after seven days. Thrombolysis with intravenous alteplase was administered, followed by PICC line removal, which precipitated acute chest pain, breathlessness, and hypoxemia. Subsequent CTPA and a ventilation-perfusion scan revealed new perfusion defects in the right middle lung lobe and lingula, indicating a new embolic episode. After stabilization in intensive care, she was converted to long-term low molecular weight heparin (with factor Xa monitoring to ensure therapeutic levels) due to presumed malabsorption of oral anticoagulants secondary to gastroparesis and/or previous gastric bypass. Long-term oxygen therapy was also initiated.

At three months, right heart catheterization showed a raised PAP of 54/18/32 mmHg (systolic/diastolic/mean), cardiac output 2.7 L/min^{-1} via thermodilution and raised pulmonary vascular resistance (7.8 Wood units). She was in WHO FC III, with no change in 6MWD. She was initiated on sildenafil monotherapy and referred for pulmonary endarterectomy (PEA) surgery. Meanwhile, she re-presented with recurrent PE following insertion of a new PICC contrary to advice. She was thrombolyzed but deteriorated locally, with WHO FC IV symptoms, now bed-bound and requiring increasing supplemental oxygen, with clinical and echocardiographic evidence of RV failure. She was accepted for transfer to Royal Papworth Hospital for urgent PEA. To avoid further use of PICC, the patient was weaned from intravenous cyclizine and started on buccal prochlorperazine and dispersible ondansetron for control of nausea symptoms. PEA surgery was successful, with removal of Jamieson type 2 disease bilaterally, with hemodynamic and clinical improvement. She was now in WHO FC II, with 6MWD now at 339 m without oxygen desaturation. Unusually, there was evidence of blackish material visible on the macroscopic surgical specimen (Fig. 1a). Further microscopic analysis (Fig. 1b–e) showed evidence of chronic thromboembolism with the black foreign material seen in segmental pulmonary artery casts, highly suggestive of plastic fragments. There was no evidence of microbiological staining or growth on prolonged culture. At one-year follow-up, she was in WHO FC II, with maintained 6MWD and no evidence of persistent PH.

Discussion

This case describes the first non-malignancy related case of PICC-associated CTEPH, with foreign body (plastic fragments) accumulation within the thrombotic surgical specimen.

CTEPH is a specific cause of PH due to the formation of chronic thrombi within the pulmonary arteries, usually following a known venous thromboembolic episode, despite three months of effective anticoagulation.[1] This causes obstruction to pulmonary blood flow in the occluded vessels

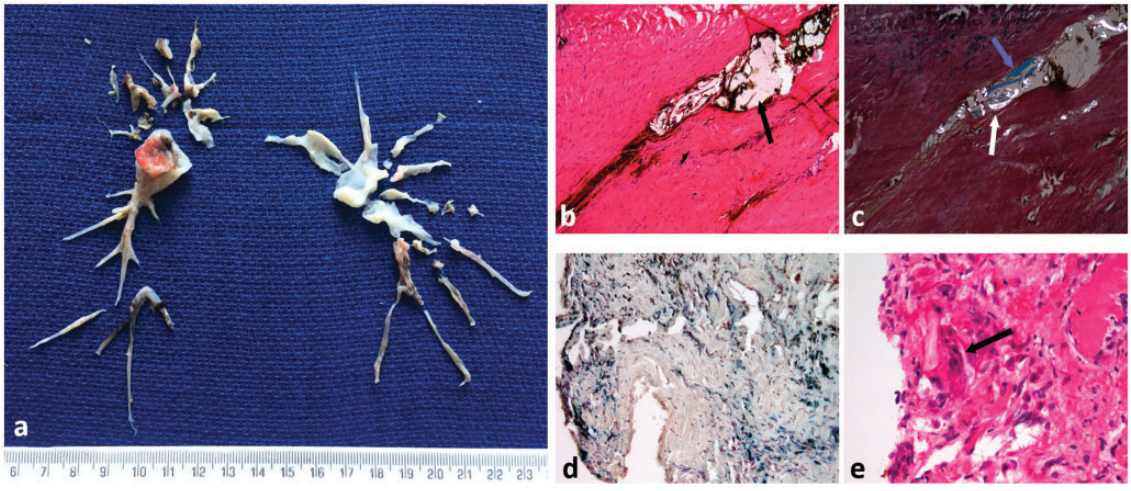

Fig. 1. Macroscopic and microscopic pulmonary endarterectomy specimens. (a) Gross specimen of pulmonary endarterectomy casts. The casts consist mainly of very fine distal branches containing some blackish material along with some thicker yellow proximal organizing thrombus. (b) Dense luminal fibrosis with black pigment and colorless, transparent material (arrow; hematoxylin and eosin stain [H&E], 100×). (c) Some of the foreign material is polarizable (white arrow) and some stains blue on the elastic van Gieson stain (blue arrow; 100×). (d) Some of the pigment stains blue on a Perl's stain indicating hemosiderin, but most of the pigment is not hemosiderin (200×). (e) In places, the foreign material elicits a macrophage giant cell reaction (arrow; H&E, 400×).

and idiopathic pulmonary arterial hypertension-like pulmonary vascular remodeling in smaller non-occluded vessels.[2] Both mechanisms lead to breathlessness symptoms, elevated PAPs, and, if untreated, RV failure and poor prognosis. The primary treatment for CTEPH is PEA.[3]

Prevention of CTEPH via recognition and management of risk factors is key. These include hypercoagulable disorders,[3,4] cancer, chronic inflammatory disorders, hypothyroidism, previous splenectomy, previously infected ventriculo-atrial shunts for the treatment of hydrocephalus, infected pacemaker leads, and indwelling venous catheters.[1,5,6]

Deep vein thrombosis (DVT) related to PICC line use has been described in intensive care unit (ICU) patients and cancer patients receiving chemotherapy.[1,7,8] For example, PICC-related upper limb DVT was detected by ultrasound in ~60% of ICU patients;[9] in a recent study of 490 cancer patients, 5.5% developed local PICC-related thrombus and 5.3% developed distant venous thrombosis (in some rare cases including PE), despite anticoagulation.[8]

CTEPH related to PICC use has been described in a single series of cancer patients. Natali et al. published 17 cases of CTEPH with prior port-a-cath lines between 2006 and 2010, where the interval between port-a-cath insertion and CTEPH onset was 5.6 ± 4.0 years. Eight patients underwent PEA, with clinical and hemodynamic benefit in most cases. All port-a-caths were removed and staph epidermidis was cultured in 30% of specimens,[10] suggesting an important role for chronic line infection. We did not, however, clearly demonstrate chronic line infection in our case.

We report the first non-malignant case of CTEPH related to PICC line use, and for the first time demonstrate plastic material with a giant cell response within the surgical specimen. It is likely that repeated endothelial injury, inflammation (and possibly chronic line infection) contributed to thrombus formation, which we showed was closely associated with plastic fragments from the line. This case is unusual in the longevity of PICC line use; however, it raises awareness of the serious associated risk of CTEPH, given the prevalence of PICC use for many indications.

Conflict of interest

The author(s) declare that there is no conflict of interest.

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