



CASE REPORT

Chronic thromboembolic pulmonary hypertension as a cause of dyspnoea in an older patient with a complex history

C.M. Kähler

ABSTRACT: A full diagnostic work-up for patients with pulmonary hypertension (PH) is vital. Classification and diagnosis of the underlying cause is important to ensure optimal management, but may be complicated by overlapping signs and symptoms. This case study describes how a full work-up identified chronic thromboembolic PH (CTEPH) as the cause of dyspnoea in a 68-yr-old male with a history of pulmonary embolism and an original diagnosis of chronic obstructive pulmonary disease. Key indicators included decreased tricuspid annular plane systolic excursion, increased Tei index and elevated systolic pulmonary artery pressure. Multi-slice spiral chest computed tomography and pulmonary angiography showed severe chronic thromboembolic pulmonary disease, both centrally and distally. Diffusing capacity of the lung for carbon monoxide was reduced and blood gas analysis revealed a wide alveolar–arterial oxygen pressure difference, which is typical of CTEPH. The patient was eligible for pulmonary endarterectomy according to established criteria. Residual PH after surgery was successfully managed with bosentan.

KEYWORDS: Chronic thromboembolic pulmonary hypertension, dyspnoea, pulmonary hypertension

A 64-yr-old male first presented in 2003 at a local chest hospital with exertional dyspnoea, following a pulmonary embolism in 2002 and a history of smoking. At that time, a computed tomography (CT) scan revealed pulmonary embolism mainly in the left lower lobe; transthoracic echocardiography showed a slightly reduced left ventricular ejection fraction (EF) and elevated pulmonary arterial pressure (P_{pa}) (table 1). He was hypoxic and hyperventilating, with low oxygen saturation. The patient was diagnosed with chronic obstructive pulmonary disease with hypoxaemia, and discharged; congestive heart failure was attributed to the low EF and the prior history of pulmonary embolism. Acenocoumarol, ramipril, carvedilol, oxygen and salbutamol were started. In 2007, he presented again at another local hospital with worsening dyspnoea; investigations showed increased P_{pa} , with similar EF and lung function to those at the first assessment (table 1).

The patient was subsequently reinvestigated by a specialist pneumology unit. Transthoracic echocardiography revealed decreased tricuspid annular plane systolic excursion (TAPSE; 1.4 cm) with

increased Tei index (1.61) and increased right atrial and ventricular dimensions, with estimated systolic P_{pa} of 70 mmHg (fig. 1). At this stage, forced vital capacity was 90% predicted, forced expiratory volume in 1 s was 76% pred (a ratio of 69%) and peak expiratory flow was 70% pred. Lung function tests and CT excluded emphysema, with normal total lung capacity and residual volume, and no hyperinflation. The patient's 6-min walk distance (6MWD) was 384 m. However, the diffusing capacity of the lung for carbon monoxide was reduced (59%), as is the case in ~20% of patients with idiopathic pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension (CTEPH) [1, 2]. Multi-slice spiral chest CT and pulmonary angiography showed severe chronic thromboembolic pulmonary disease, both centrally and distally (fig. 2). Doppler ultrasound revealed thrombosis of the vena poplitea up to the vena saphena magna on the left. Other investigations, including autoimmunity, sleep apnoea and HIV tests, were negative, although there was slight congestive hepatopathy. The patient was still hypoxic (arterial oxygen tension 56.4 mmHg) and hyperventilating (arterial carbon dioxide tension

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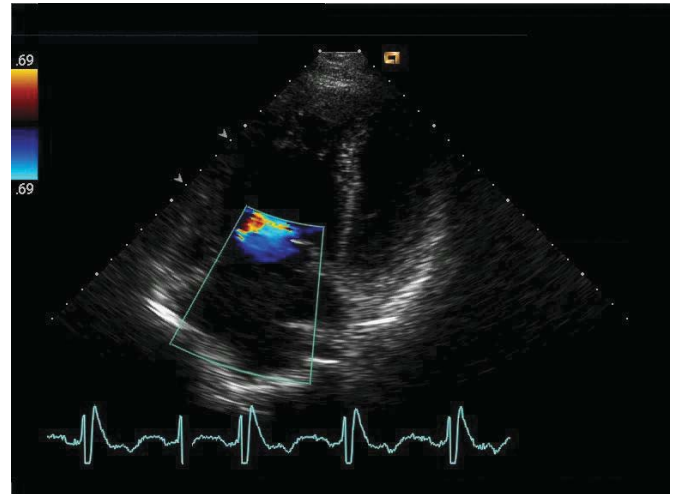
TABLE 1 Initial and secondary assessment prior to referral to specialist unit

	Initial assessment	Second assessment
Echocardiography		
EF %	45	50
TR grade	II	II
P_{pa} mmHg	45	70
Lung function		
FVC % pred	85	85
FEV1 % pred	78	72
FEV1/FVC %	69	69
PEF % pred	46	66
P_{a,O_2} mmHg	54.1	57.5
P_{a,CO_2} mmHg	30.9	30.6
pH	7.42	7.41
O_2 %	88	89

EF: ejection fraction; TR: tricuspid regurgitation; P_{pa} : pulmonary artery pressure; FVC: forced vital capacity; % pred: % predicted; FEV1: forced expiratory volume in 1 s; PEF: peak expiratory flow; P_{a,O_2} : arterial oxygen tension; P_{a,CO_2} : arterial carbon dioxide tension.

30.2 mmHg), with low oxygen saturation (89%) and blood pH of 7.41. Blood gas analysis revealed a wide alveolar–arterial oxygen tension difference of 45.2 mmHg, which is typical for patients with CTEPH [3]. Diagnosis was supported by right heart catheterisation (table 2).

The patient met the established criteria for pulmonary endarterectomy [4], including mean $P_{pa} \geq 25$ mmHg, ≥ 3 months of

**FIGURE 1.** Echocardiography image obtained during investigation by the specialist pneumology unit.

effective oral anticoagulation, evidence of surgically accessible thrombi, a beneficial relationship between pulmonary vascular resistance (PVR) and the anticipated thrombus mass, no comorbidities and no severe reduction in lung function. At $1,200 \text{ dyn}\cdot\text{s}\cdot\text{cm}^{-5}$, PVR was slightly higher than optimal (recommended $<1,000 \text{ dyn}\cdot\text{s}\cdot\text{cm}^{-5}$). The surgery was successful, and therapies including phenprocoumon, carvedilol, furosemide and salbutamol were started. Following surgery, N-terminal pro-brain natriuretic peptide concentrations declined from $\sim 5,000$ to $1,000 \text{ ng}\cdot\text{L}^{-1}$, and 6MWD increased to 479 m, with an improvement in World Health Organization functional class (from III to II).

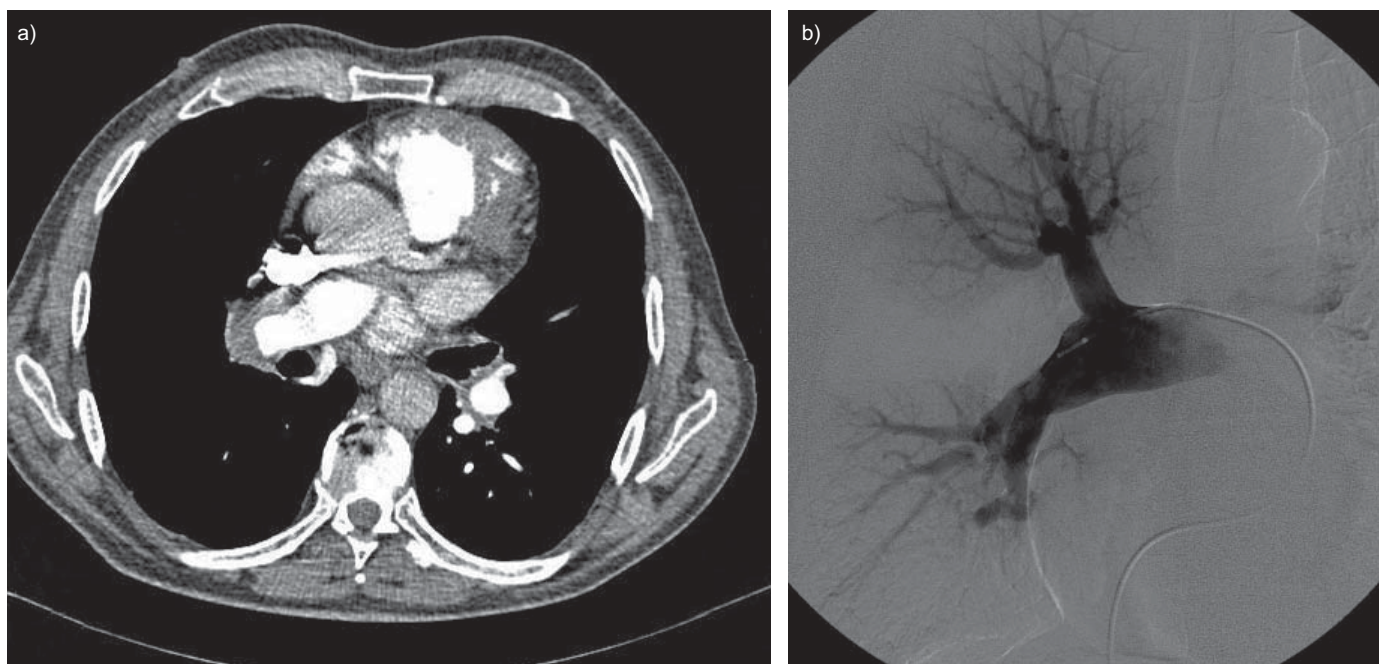
**FIGURE 2.** a) Multi-slice spiral chest computed tomography scan and b) pulmonary arterial angiography at diagnosis of chronic thromboembolic pulmonary hypertension.

TABLE 2 Right heart catheterisation at diagnosis of chronic thromboembolic pulmonary hypertension

Parameter	Value
\bar{P}_{pa} mmHg	58
P_{rv} mmHg	26
P_{ra} mmHg	20
\bar{P}_{pcw} mmHg	14
PVR dyn·s·cm ⁻⁵	1200
Cardiac output [#]	2.2

\bar{P}_{pa} : mean pulmonary artery pressure; P_{rv} : right ventricular pressure; P_{ra} : right atrial pressure; \bar{P}_{pcw} : mean pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance. #: measured using the Fick method.

However, although the surgery reduced mean P_{pa} (from 61 to 44 mmHg), it was still higher than that of the normal population, as was PVR (reduced from 1,200 to 514 dyn·s·cm⁻⁵). Similarly, the Tei index, although reduced from 1.61 to 0.67, was not within the normal range (≤ 0.4), and TAPSE was still abnormal (≤ 2 cm), having changed little from 1.4 to 1.3 cm. This indicated that, despite the surgery, there was residual pulmonary hypertension (PH) (fig. 3). To decrease the pulmonary pressure further, treatment with bosentan was initiated on a compassionate use basis and titrated to a final dose of 125 mg *b.i.d.* An increase in TAPSE (from 1.3 to 1.8 cm; approaching normal) and a decrease in Tei index (from 0.67 to 0.5; approaching normal) were observed following bosentan treatment. There was also a further improvement in 6MWD to 517 m. No further invasive assessments of haemodynamics were performed.

DISCUSSION

This case emphasises the importance of a full diagnostic work-up for patients with PH. Classification and diagnosis of the underlying cause of PH [5] is important, in order to ensure optimal management, but may be complicated by overlapping

signs and symptoms. While dyspnoea is a common clinical finding in PH, it is nonspecific; therefore, a correct diagnosis of patients presenting with breathlessness relies on a full diagnostic work-up. Echocardiography is a useful noninvasive technique in this respect, allowing estimation of baseline and follow-up P_{pa} , tricuspid regurgitation, and atrial and ventricular size and function. However, the correlation between calculated P_{pa} by echocardiography and that measured by right heart catheterisation is reported to be poor [6, 7]. TAPSE and Tei index are useful parameters of right ventricular function in pulmonary arterial hypertension (PAH) and assessment of these may be more accurate than echocardiography-calculated P_{pa} alone [8]. In addition, TAPSE and Tei index are predictors of survival [9, 10] and may, therefore, be more useful for assessing treatment responses than calculated P_{pa} alone.

The occurrence of CTEPH after a diagnosis of acute pulmonary embolism, although rare, is more common than previously thought, being estimated at 3.8% of all patients surviving an episode of symptomatic idiopathic pulmonary embolism within 2 yrs [11]. Depending on established eligibility criteria, pulmonary endarterectomy is the preferred approach for CTEPH patients, and may restore haemodynamics in 80% of cases [4]. However, as illustrated here, surgery does not always correct the PH; in a recent UK study, 35% of 198 patients had mean P_{pa} >25 mmHg and PVR >240 dyn·s·cm⁻⁵ after surgery [12]. Residual PH is the most important determinant of post-endarterectomy outcome, being associated with decreased survival [8]. In the UK study, patients who survived to 3 months after surgery, but had persistent PH, had a 3-yr survival of 94% [12]. In such cases of persistent PH, management options are currently limited; in a UK cohort, 18% of patients with persistent disease already received PAH-modifying therapies [12].

In this case study, the post-surgical residual PH was successfully treated with bosentan. Bosentan has previously shown promise for CTEPH patients, including those considered unsuitable for surgery and cases that have residual PH after surgery [13–16]. The response of the current patient also

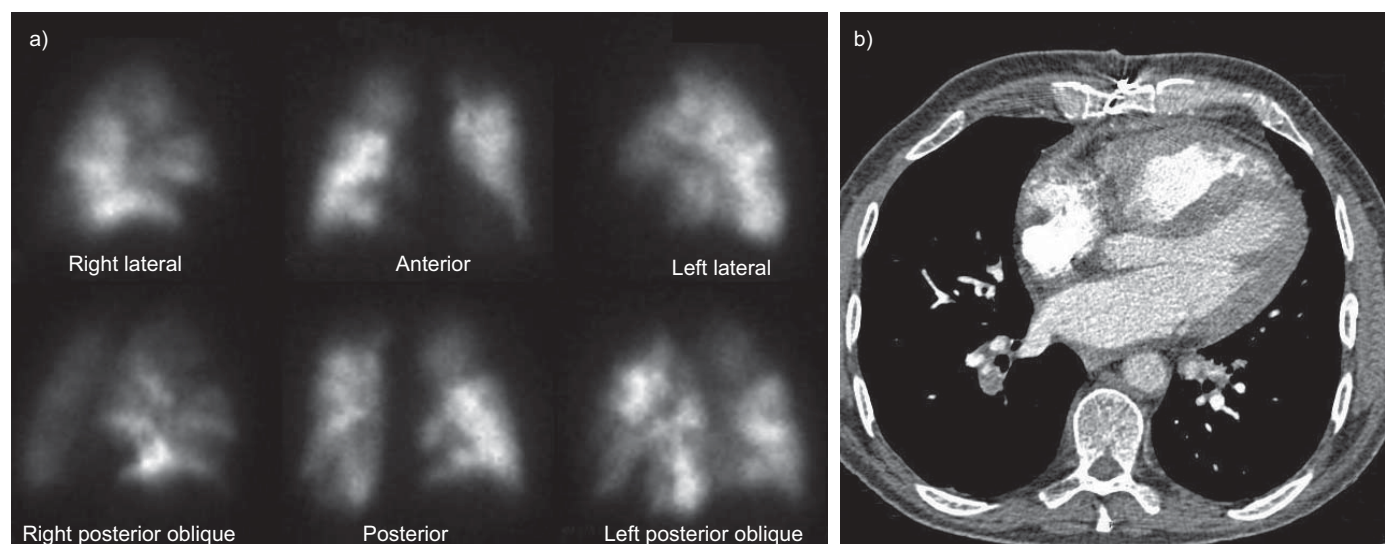


FIGURE 3. a) Lung perfusion (seated patient) and b) high-resolution computed tomography scans obtained after pulmonary endarterectomy.

suggests that bosentan may be of use for PH that persists despite surgery.

Conclusions

A full diagnostic work-up is required for patients with PH. Of those with CTEPH, candidates for pulmonary endarterectomy should be assessed against current eligibility criteria. The optimal management of inoperable cases of CTEPH is under evaluation and there are limited data describing the treatment of residual PH after surgery; however, there may be beneficial effects of novel targeted therapies, and further research is needed.

STATEMENT OF INTEREST

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