ESC HEART FAILURE
ESC Heart Failure 2015; **2**: 204–207
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.12051

CASE REPORT

Non-thrombotic fatal pulmonary embolism with a 'rule-out' CT scan

Daniel Beug, Sigrun Friesecke, Stephan B. Felix and Klaus Empen*

Medizinische Klinik B, Universitätsmedizin, Greifswald, Germany

Abstract

We report on a 36-year-old woman suffering from metastasized breast cancer and severe dyspnoea owing to right heart failure. Symptoms and findings were highly suggestive of pulmonary embolism. In rare cases, pulmonary embolism is caused not by migration of venous thrombi but by emboli of other origin. Patients with cancer can suffer from non-thrombotic pulmonary embolism, either by (macroscopic) embolization of tumour mass or by microembolism also known as microscopic tumour microangiopathy. In patients with cancer with clinical presentation highly suggestive of pulmonary embolism, with echocardiographic findings confirming right ventricular dysfunction, and with negative CT angiography, pulmonary tumour microembolism should be considered as possible diagnosis.

Keywords Pulmonary embolism; Tumour embolism; Microembolism

Received: 09 February 2015; Revised: 28 May 2015; Accepted: 17 June 2015
**Correspondence to: Klaus Empen, Universitätsmedizin Greifswald, Sauerbruchstrasse, D-17475 Greifswald, Germany. Tel: + 49 3834 86 80500, Fax: + 49 3834 86 80502. Email: empen@uni-greifswald.de*

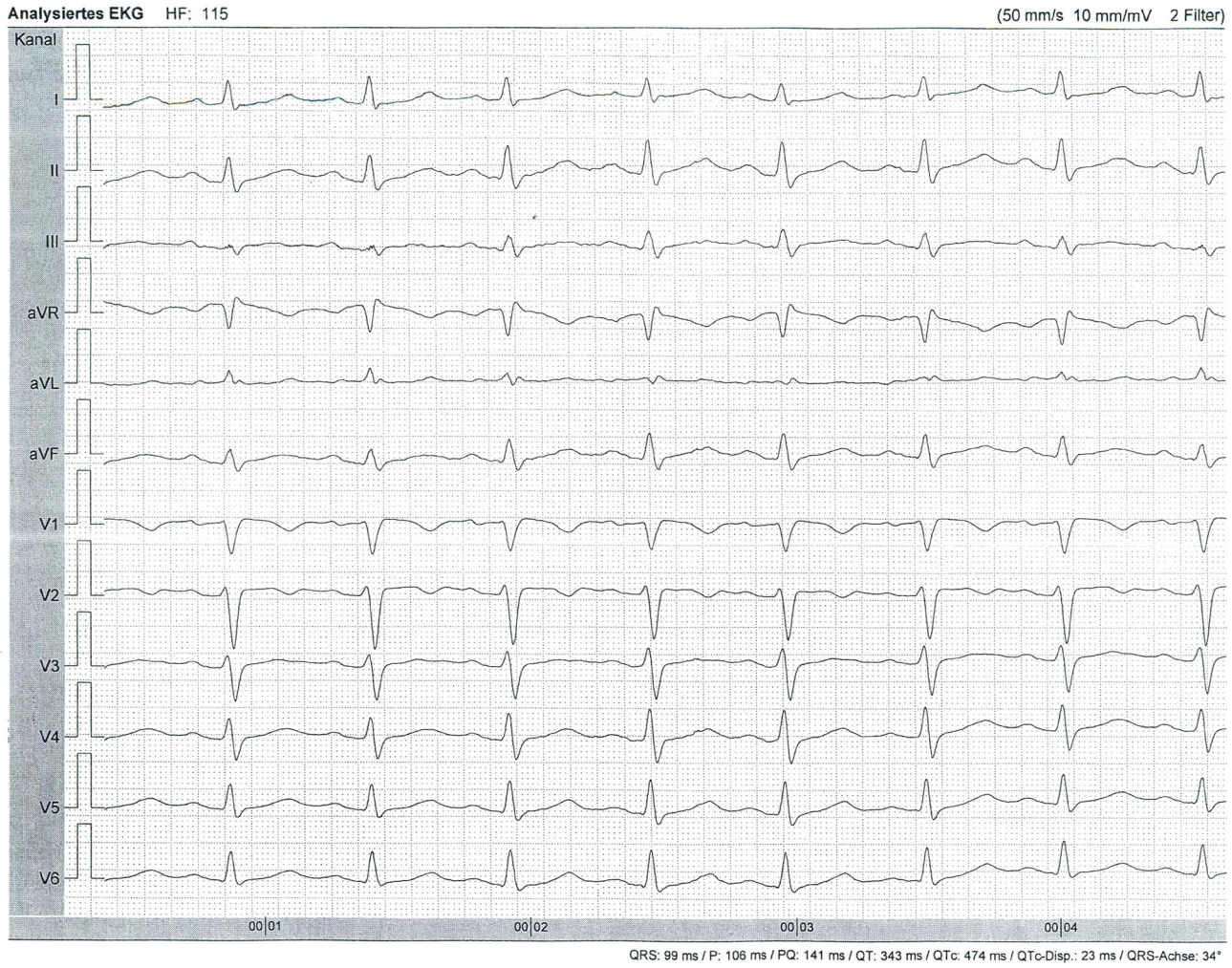
Case report

A 36-year-old woman was transferred to our intensive care unit owing to progressive dyspnoea and right heart failure. Previously, she had been treated for metastasized breast cancer in an oncological rehabilitation centre for 1 week. Two days before admission to our hospital, she had been referred to a local hospital as a result of worsening dyspnoea. ECG revealed sinustachycardia, sagittal axis type ($S_IS_{II}S_{III}$ pattern; *Figure 1*). Serial echocardiographies, performed at days 1 and 2 at the previous hospital, had revealed progressive dilation of the right ventricle (from 33 to 39 mm in the parasternal view) and pulmonary hypertension (estimated systolic pulmonary artery pressure 48 mmHg plus central venous pressure). Pulmonary embolism was suspected. As a result of heparin-induced thrombocytopenia in her medical history, anticoagulation with danaparoid sodium was begun. CT angiography did not confirm the suspected pulmonary embolism. However, this CT-scan revealed inhomogeneous density of the liver suggesting diffuse metastatic infiltration and multiple metastatic lesions of the vertebrae.

On admission to the ICU of our hospital, the patient was afebrile, suffered from tachycardia (110/min), and tachypnoea (24/min), while blood pressure was normal.

ECG revealed sinustachycardia, incomplete right bundle branch block, and a sagittal axis (S_IQ_{III} pattern, *Figure 2*). Troponin I level was only slightly elevated (0.2 μg/L, reference $<$0.1 μg/L), but NT-proBNP level was as high as 25337 ng/L (reference $<$125). Liver enzymes and bilirubin levels were only slightly elevated. Echocardiography revealed progressive right ventricle dysfunction—i.e. RV diameter larger than LV diameter from the apical four-chamber view (*Figure 3*), hypokinesia of the RV free wall, and progressive pulmonary hypertension—that was highly suggestive of acute cor pulmonale. On the basis of acute cor pulmonale and progressive pulmonary hypertension, inhalative iloprost was begun (5 μg every 2 h). Despite application of anticoagulation with danaparoid sodium, inhalative iloprost, and supportive intensive medical measures, the patient developed abrupt circulatory failure 6 h after admission to the ICU. Cardiopulmonary resuscitation was initiated immediately but proved futile and was terminated after 30 min. Establishing extracorporeal life support with the use of arteriovenous extracorporeal membrane oxygenation was not considered a therapeutic option because of the advanced stage of her cancer.

Figure 1 ECG 2 days before ICU admission.



Upon post-mortem examination, the liver had been largely replaced by metastases (*Figure 4*). Both lungs appeared haemorrhagic, but there was no macroscopic evidence of embolism in the great pulmonary arteries (*Figure 5*). Widespread tumour embolization to the small and medium pulmonary arteries became apparent only during microscopic examination of the lungs (*Figure 6*).

Discussion and conclusions

Although not uncommon in autopsy series of patients with cancer, and often disclosed as an incidental finding,[1] tumour embolism becomes clinically apparent in a minority of patients.[2] Tumour cells can invade the pulmonary vasculature by large tumour emboli, which occlude proximal pulmonary arteries; they become visible by CT angiography and during autopsy. The onset of dyspnoea in patients with macroscopic tumour emboli is usually sudden. On the other hand, tumour cells can invade the pulmonary microvasculature via lymphatic vessels (lymphangitic carcinomatosis) or through pulmonary blood vessels of intermediate or small size. In concordance with the most recent guidelines, we recommend naming this condition not microscopic tumour embolism[2] or pulmonary tumour thrombotic microangiopathy,[3] but more simply pulmonary tumour microembolism.[4] Pulmonary microembolism has almost exclusively been described in patients with adenocarcinoma, most often originating from the stomach, lungs, or breasts.[1–3] Patients with pulmonary tumour microembolism also suffer from dyspnoea,[2,3] but the onset is less rapid and the course more progressive than in patients with tumour macroembolism. In tumour embolism, the prognosis is poor. In the largest and most recent studies of patients with tumour microembolism published until now,[3] the median survival from the onset of symptoms was only 9 days.

DOI: 10.1002/ehf2.12051

Figure 2 ECG on ICU admission.

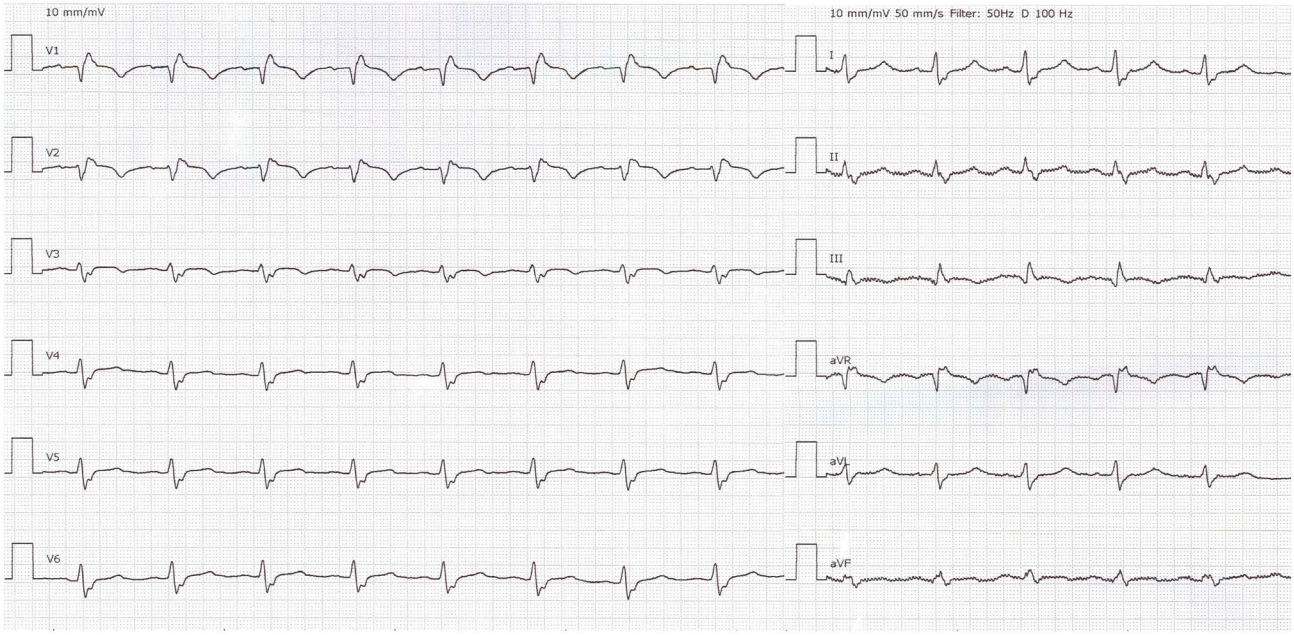
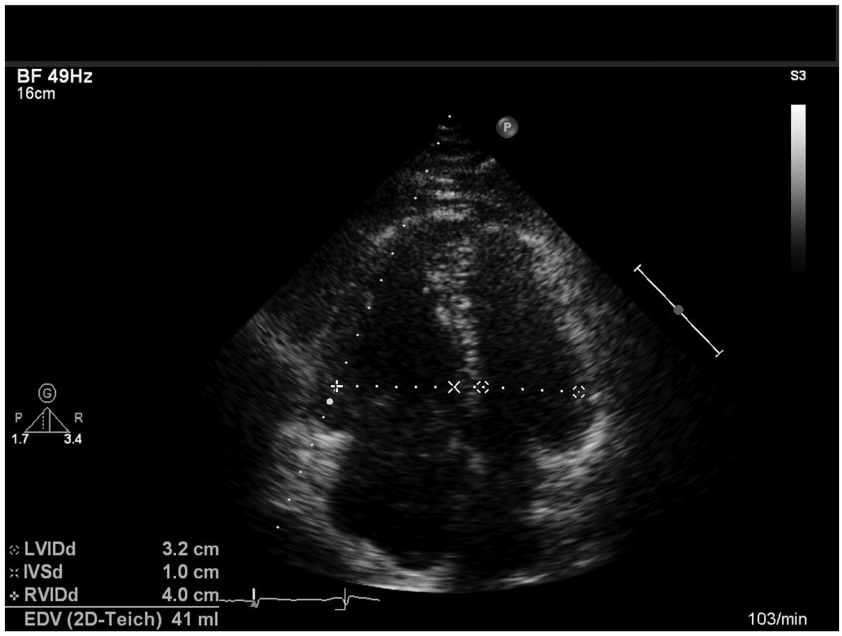


Figure 3 Transthoracic apical four-chamber view revealing right ventricular dilation.



DOI: 10.1002/ehf2.12051

Figure 4 Postmortal macroscopic view of the liver.

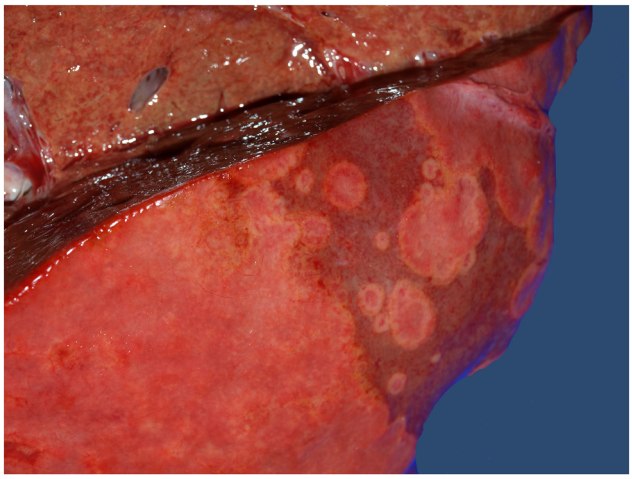


Figure 5 Postmortal macroscopic view of the lung.

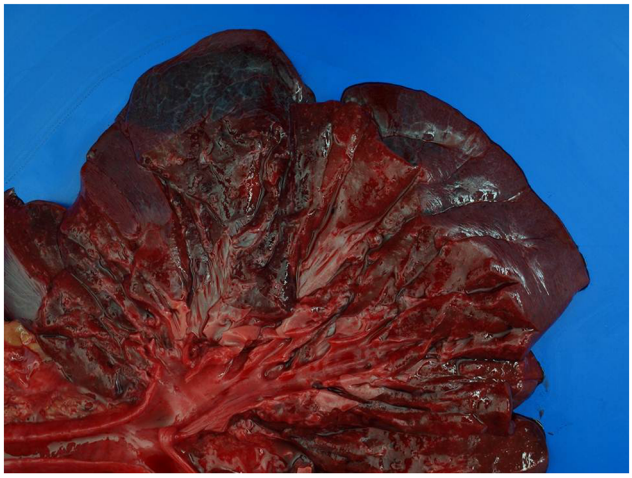
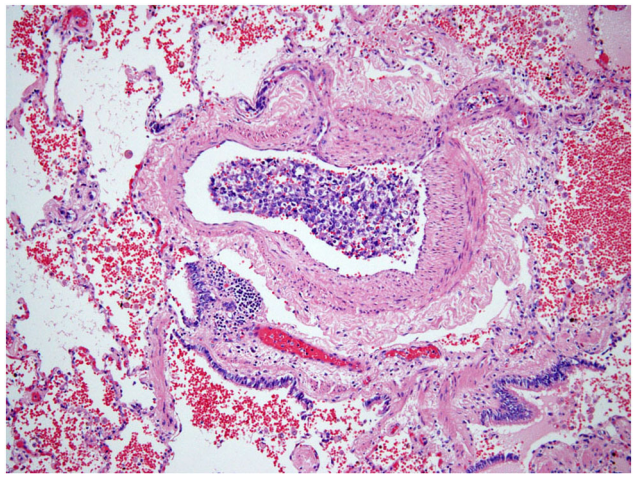


Figure 6 Histological examination of a lung specimen, hematoxylin-eosin staining, magnification 1:10.



Tumour microembolism is usually not demonstrable on CT angiography and is thus rarely diagnosed ante mortem. It is associated with poor prognosis, and there is no treatment of proven efficacy. In patients with cancer with clinical presentation highly suggestive of pulmonary embolism, echocardiographic findings confirming right ventricular dysfunction, as well as negative CT angiography, pulmonary tumour microembolism should be considered as possible diagnosis.

Conflict of Interest

None declared.

References

1. von Herbay A, Illes A, Waldherr R, Otto HF. Pulmonary tumor thrombotic microangiopathy with pulmonary hypertension. *Cancer* 1990; **66**: 587–592.
2. Roberts KE, Hamele-Bena D, Saqi A, Stein CA, Cole RP. Pulmonary tumor embolism: a review of the literature. *Am J Med* 2003; **115**: 228–232.
3. Uruga H, Fujii T, Kurosaki A, Hanada S, Takaya H, Miyamoto A, Morokawa N, Homma S, Kishi K. Pulmonary tumor thrombotic microangiopathy: a clinical analysis of 30 autopsy cases. *Intern Med* 2013; **52**: 1317–1323.
4. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, Gibbs JS, Huisman MV, Humbert M, Kucher N, Lang I, Lankeit M, Lekakis J, Maack C, Mayer E, Meneveau N, Perrier A, Pruszczyk P, Rasmussen LH, Schindler TH, Svitil P, Vonk Noordegraaf A, Zamorano JL, Zompatori M. Task Force for the D, Management of Acute Pulmonary Embolism of the European Society of C. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2014; **35**: 3033–3069, 3069a-3069k.