

Case report

## Recurrent pulmonary embolism in a patient with renal tumor

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### ABSTRACT

Venous thromboembolism is one of the main causes of sudden death in hospitalized patients. Among the classical risk factors involved, cancer occupies a special place. Up to 20% of oncological patients will develop a VTE episode, and in 10% of them, it will be a direct cause of death. In the case presented below, incidental pulmonary embolism and renal tumor were diagnosed at the same time, and there was an event of embolism despite optimal antithrombotic treatment. Such a scenario of complications may correlate with a clinically advanced stage of cancer, and may be associated with a poorer prognosis, requiring an individualized therapeutic management.

**Key words:** pulmonary embolism, thrombosis, renal tumor, heparin, vena cava filter, clear cell carcinoma

## INTRODUCTION

Venous thromboembolism (VTE) that takes the form of pulmonary embolism (PE) is the cause of up to 30% of sudden deaths in patients hospitalized for internal diseases, and 11% of deaths in patients treated for cancer [1]. Altogether, VTE is the second most common cause of death in cancer patients [2]. In the general population, its incidence is 100–200 cases/100.000 persons/year [3]. As for the general population, a number of VTE risk factors have been determined, making it possible to estimate the risk of PE or deep vein thrombosis (DVT). The most significant classical risk factors include: immobility, surgery, trauma, oral contraception and hormone replacement therapy. Cancer patients constitute a population that is especially exposed to the risk of VTE, and in particular those who suffer from hematological malignancies, lung cancer, gastrointestinal cancer, kidney or brain tumors, as well as those who undergo chemotherapy [4].

VTE is often diagnosed only incidentally, when performing imaging tests aimed at diagnosing or monitoring the progression of a neoplastic disease. Up to 20% of cancer patients are affected by the condition [5]. The high VTE rates in oncological patients, and a potentially lethal course of the disease, require special diagnostic vigilance, in particular in patients with additional VTE risk factors.

## CASE DESCRIPTION

A previously healthy 52-year-old patient was transferred to the CMKP Department of Pulmonary Circulation, Thromboembolic Diseases and Cardiology from a district hospital in another town due to acute pulmonary embolism and left kidney tumor. The patient had been on anti-coagulation treatment for 5 days with unfractionated heparin (UFH), and upon admission her condition was average and hemodynamically stable. Laboratory test results revealed elevated inflammatory parameters (PCT 0.23 ng/mL, CRP 28.11 mg/dL [N < 0.5]) that persisted throughout the treatment, despite the antibiotics administered, and with sterile blood and urine cultures. Additional findings included anemia (Hgb 8.9 g/dL) and a high concentration of NT-proBNP (N-terminal B-type natriuretic peptide) – 624 pg/mL, indicating cardiac overload. Echocardiogram revealed signs of right heart pressure overload, with the tricuspid pressure gradient (TVPG) reaching up to 52 mmHg (fig. 1), and reduced pulmonary acceleration time (AcT) of 72 ms (fig. 2). Compression ultrasonography (CUS) of lower limb veins was additionally performed, revealing a previously undiagnosed thrombosis in the right femoral vein, occluding 90% of the lumen, and in the left popliteal vein, involving 50% of the vessel lumen.

FIGURE 1.  
Retrograde flow through the tricuspid valve, measured with CWD (continuous-wave Doppler), TVPG measurement.

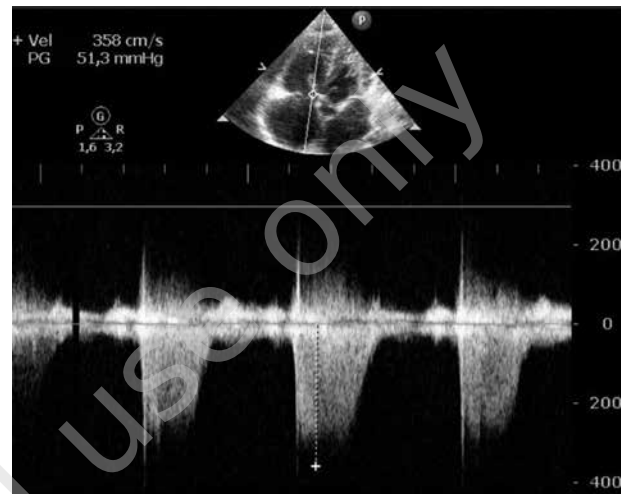
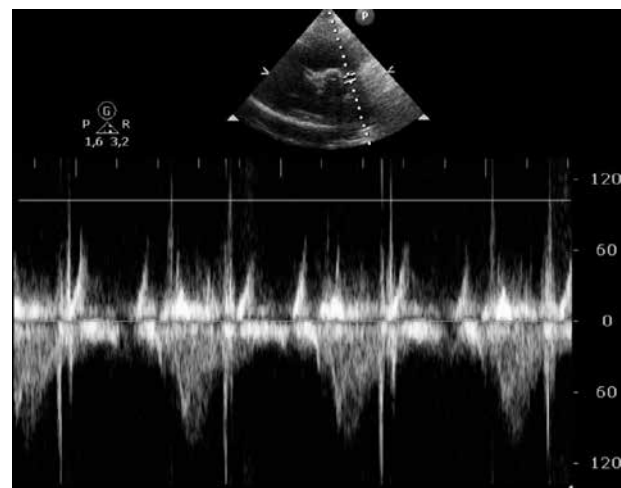


FIGURE 2.  
Flow through the pulmonary valve in PWD (pulse-wave Doppler). AcT measurement.



Due to persisting signs of cardiac overload in the consecutive echocardiograms as well as no clinical improvement despite the administered UFH anticoagulation therapy, it was decided that the patient would undergo a chest angio-CT. The CT scan revealed another episode of PE. The findings included the previously absent thrombi, involving the left pulmonary artery, an area corresponding to pulmonary infarction, and fluid within the left pleural cavity (fig. 3, 4). Abdominal angio-CT revealed thrombosis involving both common iliac veins, reaching down to the inferior vena cava (IVC), as well as a kidney tumor sized 41 × 45 mm (fig. 5).

Due to the patient's stable hemodynamic condition, it was decided that UFH therapy would be continued for 12 days, main-

FIGURE 3.

Chest angio-CT. Thrombi present in the right pulmonary artery and its ramifications.



FIGURE 4.

recurrent episode of pulmonary embolism. Presence of thrombi in the left pulmonary artery, fluid in the pleural cavity and parenchymal lesions corresponding to pulmonary infarction.



FIGURE 5.

Left kidney tumor.



taining therapeutic levels of the activated partial thromboplastin time (aPTT). The patient's condition was stable, but her body temperature remained elevated, which is why antibiotic therapy

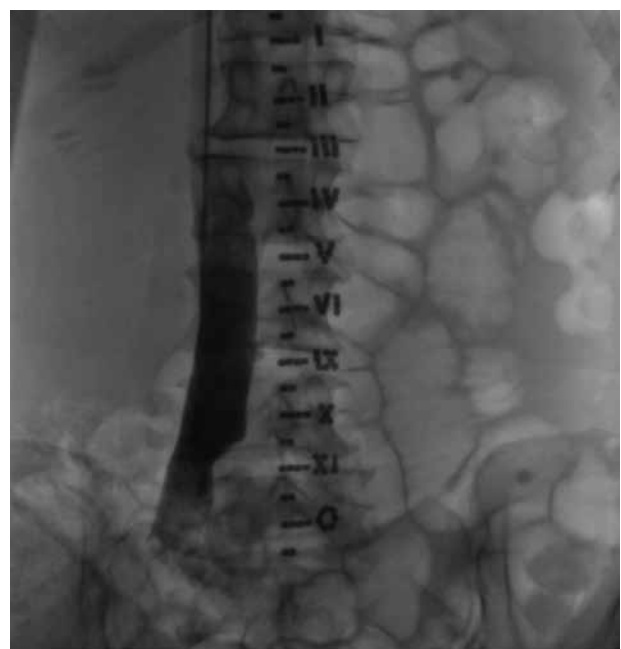
was initiated, involving piperacillin and tazobactam plus ciprofloxacin. Nearly 2 weeks into the anticoagulation treatment, a follow-up echocardiogram revealed a reduction in TVPG to 31 mmHg, and AcT normalization (108 ms). High-resolution computed tomography (HRCT) additionally revealed a regression of the inflammatory lesions in the left lung.

An interdisciplinary case conference (cardiologist, anesthesiologist, urologist and oncologist) resulted in a decision on total left-sided nephrectomy. The arguments behind the decision included a shorter duration of surgery and lower risk of cardiovascular complications as compared with tumorectomy. In light of the persistent DVT and the necessity to discontinue anticoagulation therapy in the perioperative period, as well as in light of the earlier episode of pulmonary embolism while on anticoagulation therapy, an inferior vena cava filter (IVCF) was implanted for perioperative protection of the pulmonary vascular bed.

Before IVCF implantation, cavography was performed, revealing a thrombotic left common iliac vein (fig. 7). The patient had a retrievable *Option Elite IVC* filter implanted below the renal vein ostia. The patient was operated on under general anesthesia, and there were no complications. Subsequently, she was started back on anticoagulation therapy with low molecular weight heparin (enoxaparin), initially at a reduced dose of 40 mg/24 h, followed by the dose of 1 mg/kg/24 h. The previously reported elevated body temperature receded, and the inflammatory markers went down. After a few days at the ICU, followed by a short stay at the urology floor, the patient was discharged from the hospital.

FIGURE 6.

Cavography: free flow of contrast in the right common iliac vein; thrombotic left vein from the bifurcation of the inferior vena cava.



The subsequent histopathology test revealed a poorly differentiated (Fuhrman 4, pT3, Nx, Mx, R0) clear cell renal cell carcinoma (CCRCC) with areas of sarcomatoid and papillary features, and with necrotic foci. The tumor did not infiltrate the surrounding tissues or renal vein.

## DISCUSSION

CCRCC is a unique type of cancer. Its special immunological character is manifested in its resistance to chemo- and radiotherapy, and a frequently emerging fever. The elevated body temperature is found in over 11% of RCC patients, and in over 4% of them it may be the sole manifestation of malignancy [6]. When treating metastatic disease or local CCRCC recurrence, interferon and cytokines were used in the past, while presently molecular targeted drugs are administered, targeting the molecular pathways associated with angiogenesis, i.e. tyrosine kinase inhibitors (TKIs) as well as serine/threonine kinase inhibitors (mTOR) and immunotherapy. One of the recently registered new drugs is nivolumab, a human monoclonal antibody directed against the immunoregulatory receptor PD-1 [7, 8].

In the case presented above, abdominal CT was performed twice, without revealing enlarged lymph nodes, which does not exclude the presence of metastatic cells in them, though.

The patient received anticoagulation therapy in accordance with the binding ESC (*European Society of Cardiology*) standards [8]. Nevertheless, there was a recurrent episode of pulmonary embolism, most probably as a result of migration of thrombus from deep veins. IVC filters are indicated in such cases [9]. In the above described case, a retrievable IVC filter was implanted, which may safely be removed transvenously, following a completed treatment, and with no further indications for anticoagulation therapy [10, 11].

Prognosis of renal cell carcinoma RCC patients is assessed based on the SSIGN score (*Stage, Size, Grade and Necrosis*) [12]. The patient's score was 8, which classifies her as a high-risk patient, with the estimated 5-year survival rate of 21% [13]. Oncological follow-up of the RCC patient involves chest and abdomen CT repeated every 6 months in the first 2 years, with subsequent test intervals determined on a case by case basis, depending on the patient's clinical status [12]. Following resection, median time to relapse is 1.9 years [15].

An additional factor that directly affects patient prognosis is recurrent pulmonary embolism. In cancer patients on antico-

agulation therapy the risk of recurrent pulmonary embolism or major bleeding is 3–6 times higher than in the non-cancer population [13].

Treatment of acute VTE and chronic anticoagulation therapy is different in cancer patients from that administered in patients without malignancies. Low molecular weight heparins (LMWHs) are preferred over the first 6 months of treatment. Such management is associated with a lower risk of VTE recurrence or hemorrhagic complications as compared with vitamin K antagonists (VKAs) [16]. Afterwards, the patient may be switched over to oral VKAs or anticoagulation drugs may be discontinued, if the neoplastic disease in question is believed to be cured, and if there are no other indications for anticoagulant therapy.

A simultaneous diagnosis of VTE and cancer is associated with a high probability of significant clinical advancement of the tumor, often with the presence of distant metastases [17]. It results both from the high thrombogenicity of the primary tumor and its metastases as well as with the release of pro-thrombotic factors by the mutated cells. Additionally, the tumor stage itself is responsible for the higher risk of VTE. Stage G3–4 tumors are associated with a higher risk of thromboembolic complications than stage G1–2 lesions [18].

In a general population of patients with idiopathic PE, where it is not possible to identify the classical VTE risk factors, cancer will be diagnosed in up to 10% of the patients, over the first year of follow-up in most of the cases. However, extended diagnostics, including whole body imaging scans (PET, MRI, CT), does not result in a better prognosis in that group of patients. Hence, it is not recommended to perform extended imaging diagnostics on a routine basis. Instead, what is promoted is in-depth clinical monitoring [19, 20].

## CONCLUSIONS

Cancer patients are exposed to an especially high risk of thromboembolic complications, which are usually associated with poor prognosis. Decisions on anticoagulation therapy, followed by anti-cancer treatment, require a case by case approach.

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Jarosław Kępski: 70%; Sebastian Szmit: 20%; Marcin Kurzyna: 10%.

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The paper complies with the Helsinki Declaration, EU Directives and harmonized requirements for biomedical journals.