Pulmonary embolism a possible incidental finding in computer-tomography evaluation of patients with urological neoplasms

Cristina Dumitrescu¹,3, Ioana G. Lupescu¹,3, I. Sinescu²,3

¹ Department of Radiology, Medical Imaging and Interventional Radiology of Fundeni Clinical Institute, Bucharest
² Center for Uronephrology and Renal Transplantation of Fundeni Clinical Institute, Bucharest
³ University of Medicine and Pharmacy “Carol Davila” Bucharest, Romania

Abstract

Introduction: Cancer patients undergo more frequently CT examinations for oncologic purpose than other patients. With the newly technique of multislice computer tomography (MSCT) there is an increase in the discovery of incidental pulmonary embolism in oncological population.

Material and method: Retrospective database imaging study using the key words “pulmonary thromboembolism” in the period September 2004 until October 2014. The patients have been explored with monoslice and multislice CT with the advantages of MSCT acquisitions with thinner slices and shorter time of scanning.

Results: During the 10 years retrospective study period, 20 urological cancer patients were identified with PE. The mean age was 62.6 years with male gender prevalence but with younger age debut in females. All patients had active cancer renal cell carcinoma, urothelial carcinoma - renal or bladder, prostatic and adrenal adenocarcinoma. Most patients had advanced-stage disease at the time of PE diagnosis or long-term active cancer. The CTA discovered in the majority, incidental PE and other medical causes explaining the mimicking signs of PE and made an emboli burden evaluation.

Conclusions: The PE was found in preoperative and in early postoperative periods, or in long-term active cancer. Contrast enhanced MSCT or CT-angiography represent valuable tool to detect incidental PE such scenario being the most frequently encountered in our study. CTA of PE in oncological patients is similar in appearance as PE in non-oncological patients but the differentiation with tumor emboli may be challenging.

Keywords: incidental pulmonary embolism, urological cancer, multislice-CT, CT-angiography

Correspondence: Ioana Lupescu
Fundeni Clinical Institute, Radiology, Medical Imaging and Interventional Radiology Department
Sos Fundeni, nr. 258, sect.2, Bucharest
Phone: 0212750700
E-mail: ilupescu@gmail.com
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Introduction

Oncological patients are undergoing CT examinations more frequently for neoplasm survey, over time, than patients with other pathologies. With the newly technique of multislice computer tomography (MSCT) there is an increase in the discovery of incidental pulmonary embolism in oncologic population.

Material and method

Retrospective study in the radiology database archive using the key words “pulmonary thromboembolism” (“PE) in the period September 2004 until October 2014. The patients have been scanned with monoslice CT between 2004-2009 and multislice CT with 16 rows in 2009-2014 or 64 slice CT in 2013-2014 intervals. The advantages of MSCT acquisitions are thinner slices and shorter time of scanning.

Results

Out of the 592 patients included in our retrospective study, 114 were oncologic patients, 84 of them examined between January 2013 and October 2014. From all oncology patients, 20 were with urological cancers, the renal cell carcinoma being on the first place (12 patients). The other urological cancers were: urothelial upper tract carcinomas (3 cases), urinary bladder carcinoma (1 case), prostatic adenocarcinomas (3 cases) and adrenal carcinoma (1 case). The ratio male/female was 16/4 with a mean age of 62,61 years.

We have encountered three scenarios:
1. patients with clinical suspicion of PE unconfirmed on CT angiographic (CTA) scanning (9 cases);
2. patients with incidental PE at CTA (8 cases);
3. patients with clinical suspicion of PE confirmed at CTA (3 cases).

The clinically suspected PE episode was at CTA imaging acute in 1 case, after arterial embolization of renal cell carcinoma remitted under low molecular weighted heparin therapy and chronic in 2 cases, with long term renal cell carcinoma and urothelial carcinoma of the bladder. The incidental PE appearance at CTA was: acute, in 1 case when the CT examination has been made for the diagnostic purpose of a renal cell carcinoma with tumoral thrombus into the inferior vena cava and the right atrium, in 1 case was in a chronic phase, in a context of long-term follow-up of an prostate adenocarcinoma and in 6 cases it was in a subacute state. The emboli burden was classified in two groups the first with “saddle embolus” found in 1 case and the second with lobar, segmental or subsegmental location in the other 10 cases. The location of the emboli was most frequently at the pulmonary bas, bilateral (6 cases), on the right side (four cases) and on the left side (2 cases). The lung parenchyma changes were found in 2 patients as an infarct in a long-term follow-up of a prostatic adenocarcinoma case and “perfusion oligemia” in the acute PE case.

In the incidental PE group there were: 3 cases of Grawitz tumor with inferior cava and right atrium tumor extension and 1 urothelial renal carcinoma with pulmonary metastases and multiple adenopathy at their first hospital admission, 2 renal cell carcinoma cases with PE after surgery and 2 cases of renal cell carcinoma and 1 prostatic adenocarcinoma with PE under chemotherapy and hormone therapy. In the third group of patients with concordance between clinical suspicion and CTA findings of PE there has been one massive PE after renal cell carcinoma embolization and two into the course of their cancers with a chronic appearance of PE. In the first group the ACT did refute the diagnosis of PE but has confirmed other causes which have explained the patients symptoms in 5 cases: - 2 with pneumonia, -1 with metastases, -1 with small pleural fluid collection and -1 case with miliary infiltrates. The PE was associated with advanced form of disease with direct tumor extension in the inferior cava vein, renal vein and right atrium in the preoperative period (Fig. 1), in early post-operative state after arterial embolization, and later in the long-term evolution in renal cell carcinoma. In the cases of upper tract urothelial carcinoma (Fig. 2) PE was associated with either with advanced tumor (stage IV) or in patients who underwent nephrectomy or during the follow-up of the disease. All cases of prostatic adenocarcinoma and bladder urothelial carcinoma developed PE after 2 years from the initial tumor discovery. In the only case with adrenal carcinoma the PE was detected at the moment of the tumor diagnosis.
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Discussions

Some studies have reported a 7 times increased risk of venous thromboembolic events (VTE) in patients with cancer compared with those without (1). Active cancer accounts for almost 20% of all new VTE events occurring in the community (2). The risk of venous thrombosis and PE varies by cancer type and is especially high among patients with pulmonary, pancreatic, gastric, adenocarcinomas with unknown origin in particular the mucin producing tumors (3). In the present study renal cell carcinoma was on top, with a different distribution than those found in various articles of literature, which probably is owing to the specific pathology in our hospital. In fact there are studies that placed on top the central nervous system cancer (4). In the male patients, the clear cell renal carcinoma was found in younger ages between 45 and 62 and prostatic adenocarcinoma and urothelial carcinoma in older between 67 and 76 years. In the female cases, renal cell carcinoma was found in the ages from 37 until 56, the adrenal carcinoma at 28 years and urothelial renal carcinoma above 70 years. The PE had the same distribution in male and female with no predilection for gender.

Incidental discovery of PE in cancer patients by CTA scanning is a reality accepted and extensively debated in terms of clinical impact of the symptomatic versus asymptomatic PE. In literature emerges more clearly the equivalence between incidental and symptomatic PE in terms of impact on prognosis and therapeutic approach. Both forms are causing a poor prognosis and imposing similar anticoagulant therapy as in PE in noncancerous population, but its duration is not yet clearly established, several authors proposing treatment indefinitely (5, 6).

More likely there are several factors that contribute to the low sensitivity of clinical diagnosis - clinical diagnosis was generally on empirical criteria one, and not based on Wells or simplified Geneva criteria for suspected pulmonary embolism, - some of the symptoms that would raise suspicion of thromboembolism such as dyspnea, pleuritic pain type, cough are nonspecific and may occur secondary to the underlying disease or as side effects to chemotherapy. Pulmonary embolism should be suspected in cancer patients by the appearance of a single symptom even minor (7). Additionally the D dimer test is not very helpful because cancer patients get into intermediate or high risk groups according to Wells probability clinical scores and the only scenario that may exclude thromboembolism is the association between low clinical probability and a negative D dimer (8). In the present study the D dimer testing was isolated.

The PE in patients with renal cell cancer was analyzed in several respects in a small number of studies with following conclusions: there is an increased risk of preoperative venous thromboembolism in patients with renal cell carcinoma and tumor thrombus but the occurrence of PE does not predict poor postoperative outcome and there is higher risk of venous thromboembolism in renal cell carcinoma patients with resid-

Fig. 1 Pulmonary embolism in a 37 y female with a renal cell carcinoma (T3cN1Mx): CTA evaluation axial plane (a, d), coronal plane reformat (b,c) right renal tumor involving the upper pole (arrow) with tumoral extension into the right renal vein, IVC, right atrium and common iliac veins (star); curoic thrombus in the left renal vein; pulmonary “saddle embolus” (arrow) and obstructive embolus in the distal right lobar artery (arrowhead) and right pleural effusion (oval).

Fig. 2 Pulmonary embolism in a 70y, female with left renal pelvis urothelial carcinoma. Coronal reformats (a,c), and axial plane (c,d) after MSCT acquisition with iv contrast in arterial (a), venous (b) and excretory phase (c): diffuse mass involving the calices and the left renal pelvis (arrowhead), adenopathies (star), homogeneous enhancement of IVC and left renal vein (thick and empty arrows) and right pulmonary embolus minimally attached to the vessel wall (arrow); high resolution CT using a pulmonary window (d): pulmonary metastasis (black arrow).
ual tumor thrombus (9,10). Regarding this matter, the discussion is still open and there is a need for further research studies.

In our study, 2 recently examined cases, one with renal cell carcinoma and inferior cava vein, left renal vein and right atrium tumor extension and one with upper urothelial tract carcinoma with metastatic extension, had a good postoperative outcome with a three month uneventful surveillance (the period passed after surgery removal of the tumors).

Classically, acute PE on CTA scans is characterized by four distinct criteria’s: 1. spontaneously hyperdense thrombus; 2. complete arterial occlusion with dilatation of the affected vessel; 3. incomplete arterial occlusion with thrombus surrounded by the contrast; the thrombus adherent to the wall and; 4. eccentric thrombus connecting at an acute angle to the wall of the vessel. The signs of chronic PE on CTA are: 1. complete arterial occlusion with lumen reduction; 2. incomplete occlusion with thrombus located peripherally connected with vascular wall in an obtuse angle; 2. thickened vessel wall and reduced external diameter by thrombus recanalization; 3. organized adherent thrombus with a band or web appearances. There may also be changes in the lung parenchyma secondary to impaired perfusion as lung infarction with the initial appearance of “groundglass” infiltrate evolving toward alveolar syndrome plated on pleura, triangular in shape with the top toward the hilum and in the end as restitutio ad integrum or scarring. “Olighemia perfusion” appears as translucent pulmonary hypoperfusion areas and decrease number pulmonary vessels alternating with normal parenchyma areas, which looks opaque like “groundglass”. In the acute phase there may be signs of acute pulmonary hypertension with dilatation of the right cavities and in the chronic phase there may be signs of chronic pulmonary hypertension and systemic or bronchial collateral circulation (11,12,13).

In our study, the prevalence of CTA signs pointed towards the subacute phase in most of the cases with the thrombus, in the process of organizing partially attached to the vessel wall but with no changes of the lumen diameter. The embolic burden of the vascular bed was framed in a broad spectrum from isolated involvement of a segmental branch to the location in main pulmonary arteries with subsequent inferior extension. The majority of patients presented with bilateral location of the PE, mainly basal. We did find in 1 case the “saddle thrombus”. According to some authors the presence of “saddle emboli” compete to worsening prognosis, over 80% of patients dying in the first year after the episode of PE (14).

In the present study, there are a small number of patients who benefited from systematic CTA scanning for PE follow-up which does not allow a proper statistical analysis on the type of evolution of TEP under anticoagulation therapy.

It is widely accepted that PE in oncology patient represents an event with poor prognosis and higher risk of recurrence rate under anticoagulant treatment than in the non-oncology population. To what extent can CTA scanning surprise PE recurrence is difficult to assess in the context of low sensibility of clinical diagnosis additionally with greatly reduced sensitivity and specificity of D dimer test. On the other hand on CTA it is difficult to distinguish between recurrent emboloc event and residual chronic emboli which may persist in 20%-40 % of cases (15,16,17).

The main differential diagnosis must be done with arterial tumor emboli (18). There are two ways that tumor cells reach the pulmonary arterial system, either as isolated cells, which can undergo a process of destruction or do localize in the capillary system and give rise to parenchymal lung metastases either aggregate together forming tumor emboli who come to settle in arterial vessels of similar caliber to their size. The pulmonary damage is classified in types: 1. large tumor emboli in located in lobar and segmental arterial branches, 2. lymphatic spread 3. microscopic tumor emboli with damage to arteries and arterioles 4. a combination of the three variants (19,20,21).

According to literature microscopic arterial tumor emboli frequency identified at autopsy is approximately 2.6%-24% (22,23) and radio-imaging examinations are negative in this situation. CTA may reveal: 1. a large tumor emboli located in the main trunk, which causes lobar and segmental filling defects that may mimic pulmonary embolism or 2. smaller emboli located in subsegmentary territory where it produces vascular dilatation evolving in time to beaded aspect of the vessel or diameter increase (24) and 3. small emboli affecting lobular arteries with “tree in bud” appearance (25,26). Like pulmonary thromboembolism, tumor emboli in the pulmonary vasculature do not enhance with contrast, making the differential diagnosis possible only on their evolution under anticoagulant therapy. Tumor emboli remain stationary or grow in size (27). In the literature there are some especially case reports about pulmonary tumor embolism in renal cell carcinoma in patients with inferior cava tumor thrombus (28,29).
Conclusions
1. Contrast enhanced MSCT or CTA represent a valuable tool in detecting incidental PE in patients with urological neoplasms, such scenario being the most frequently encountered in our study.
2. The PE was found in the preoperative and in the early postoperative periods or in long-term of active cancer.
3. CTA proofs to be helpful in outlining other pulmonary changes with medical impact in patients with clinical suspicion for PE.
4. CTA in oncology patients with PE has similar findings as PE in non-oncological patients but the differentiation with tumor emboli may be challenging.
5. The evaluation of the embolic burden of the pulmonary vasculature is important in stratifying the prognosis.

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