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Deep venous thrombosis as the single sign of unexpected metastatic urinary tract cancer in a patient with a history of cutaneous melanoma: A case report

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ABSTRACT

INTRODUCTION: Cancer is a recognized risk factor of venous thromboembolism (VTE) as it induces a prothrombotic state through various mechanisms of activation of coagulation. Recognizing occult cancer as a risk factor is equally important. In patients with no known thromboembolic risk factors, utilizing PET/CT as a screening tool may be considered in order to reveal occult malignancy associated with otherwise unexplainable VTE.

METHODS: This case report has been reported in line with the SCARE criteria.

PRESENTATION OF CASE: We describe a case of deep venous thrombosis of the lower leg as the single sign of metastatic urinary tract cancer. The patient had a history of cutaneous melanoma but no thromboembolic risk factors. Following treatment for deep venous thrombosis, the patient was referred directly to the plastic surgery department for further examination including PET/CT due to suspicion of metastatic melanoma.

DISCUSSION: Screening for occult cancer in patients with unprovoked VTE has so far not been shown to benefit survival. As new treatments emerge, significant improvement in prognosis might be expected with early diagnosis of occult cancer and initiation of treatment. Thus an open mind should be kept towards utilizing advanced diagnostic tools such as PET/CT to screen for occult cancer in patients presenting with unprovoked VTE.

CONCLUSION: This case highlights the importance of considering all possible causes and utilizing targeted diagnostic tools when assessing a patient with seemingly unprovoked deep venous thrombosis. A whole-body PET/CT scan ultimately proved significant in revealing occult metastatic cancer of a completely different origin than expected.

1. Introduction

The thromboembolic risk associated with cancer has been described for several specific malignancies including bladder cancer [1] and breast cancer [2,3] but only rarely for metastatic melanoma [4,5], and to our knowledge not for cutaneous melanoma.

Other known thromboembolic risk factors include immobilization, trauma, major surgery, pregnancy, obesity, certain drugs, advancing age, some hematological disorders, congenital coagulation factor abnormalities and more.

Both circulating tumor cells and solid tumors may exhibit procoagulant properties.

The presence of circulating tumor cells in peripheral blood has been shown in a prospective study by Mego M et al. [2] to exhibit a positive association with elevated plasma D-dimer levels in primary breast cancer, indicating a potential role for activation of the coagulation cascade by circulating tumor cells. A retrospective study by Mego M et al. [3] showed a direct association between circulating tumor cells and increased risk of deep venous thrombosis (DVT) in patients with metastatic breast cancer.

Studies so far have found associations between venous thromboembolism (VTE) and certain native properties of cancer cells as both direct activators of the coagulation cascade, and indirect activators by stimulating the prothrombotic potential of other cells.

There are several mechanisms involved and considered to be responsible for a hypercoagulable state in malignancy. It has been shown that constant expression of Tissue Factor (coagulation factor III) and Cancer Procoagulant (CP) protein by cancer cells, expression by cancer cells of fibrinolytic molecules, and cancer cell release of microparticles and cytokines can induce thrombosis [6,7]. Furthermore direct physical interaction between cancer cells and normal

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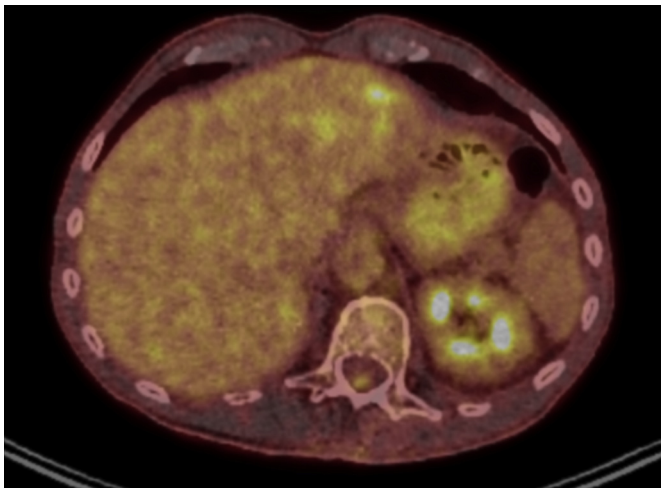

Fig. 1. PET-positive tumors in the liver.

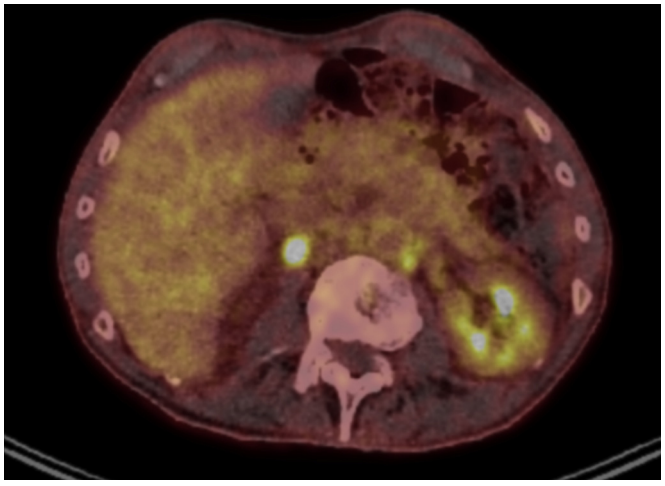

Fig. 2. PET-positive lymph node next to the inferior vena cava.

cells has been shown to result in localized clotting activation and platelet aggregation, and leukocyte-release of procoagulant cytokines [8].

We describe a case from a university hospital, which highlights the importance of utilizing targeted diagnostic tools when assessing the cause of VTE in a patient with no known risk factors of VTE.

The patient's history of cutaneous melanoma was the single piece of information prompting further examination, and a whole-body PET/CT scan ultimately proved vital in revealing an occult metastatic cancer, which furthermore was of a completely different origin than expected.

2. Methods

This case report has been reported in line with the SCARE criteria [9].

3. Presentation of case

A 78 year old retired, caucasian male was admitted to the medical emergency department by his general practitioner with measurable swelling and pain of the left lower leg developed over the course of a few days prior to admission. He was on oral Alendronate therapy following a high velocity femur fracture four years earlier, had a minor use of pipe tobacco, but was otherwise healthy and had no family history of thrombosis.

Blood tests and an ultrasound scan of the left lower leg were performed, and the patient was subsequently diagnosed with a DVT of the popliteal vein with an elevated Fibrin D-dimer plasma-level of 1.06 FEU mg/L (FEU: Fibrin Equivalent Units; normal value: <0.5 FEU mg/L).

Antithrombotic treatment with oral Rivaroxaban was commenced and the patient was discharged the day after for routine follow-up at the local anticoagulation clinic, and referred to the plastic surgery department for further examination due to suspicion of metastatic melanoma from cutaneous melanoma treated four years earlier.

Following examination at the plastic surgery outpatient clinic where no clinical signs of metastatic melanoma were found, the patient underwent a whole-body ^{18}F-FDG PET/CT scan, which revealed several areas suspicious of malignancy in both liver lobes (Fig. 1), in the mediastinal and retroperitoneal lymph nodes (Figs. 2 and 3) and in the long biceps tendon of the right shoulder.

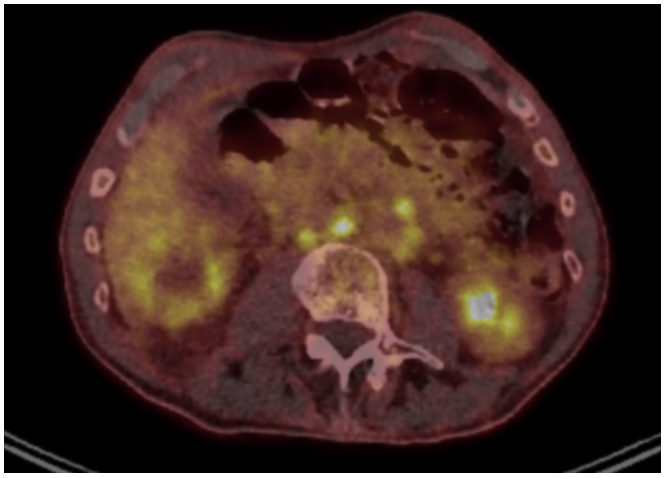

Fig. 3. PET-positive lymph nodes surrounding the abdominal aorta.

An ultrasound guided needle biopsy of the liver lesions unexpectedly revealed metastatic carcinoma cells of urothelial origin. Through further diagnostic testing and surgery by the urology department, the patient was eventually diagnosed with non-invasive papillary urothelial cancer of the bladder and urothelial carcinoma located at the right ureter ostium of the bladder.

Four years prior to the DVT the patient was diagnosed with cutaneous melanoma on the left leg. Histological examination showed a superficially spreading melanoma, Clark level 3, Breslow thickness 1.87 millimeters, containing more than one mitosis per square millimeter in the dermis, and showing signs of regression but no ulceration.

The melanoma was treated with wide local excision, and sentinel lymph node biopsy from the left inguinal region revealed no regional metastases. During the follow-up course the patient was not diagnosed with further melanoma and never experienced any general or specific symptoms of cancer or DVT.

Five months following excision of the melanoma and left-side inguinal sentinel node biopsy, the patient presented with a palpable mass in the left inguinal region, but had no discomfort or general symptoms of disease. The mass was removed and revealed a varicose vein with a thrombus and no signs of malignancy on histological analysis.