

Trousseau's Syndrome in a Patient with Advanced Pancreatic Cancer: A Case Report

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Abbreviations:

DVT: Deep vein thrombosis; PE: Pulmonary embolism; VTE: Venous thromboembolism; LMWH: Low molecular weight heparin; UFH: Unfractionated heparin

Keywords:

Trousseau's syndrome; Thromboembolism; Pancreatic cancer

1. Abstract

1.1. Background

Trousseau's syndrome was first described in 1865, by Armand Trousseau, as migratory superficial thrombophlebitis forewarning of visceral malignancy [1].

This syndrome is well known, partly because Armand Trousseau not only described it, but also diagnosed the syndrome on himself two years later secondary to gastric cancer [2].

The clinical presentation of cancer-associated thrombosis includes Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), chronic Disseminated Intravascular Coagulation (DIC) and arterial thrombosis. Venous thromboembolism, the most frequent clinical presentation of this syndrome, includes both DVT and PE [3, 4].

Herein we present the case of a 48-year-old female with this condition to increase awareness of this unusual entity.

2. Case Presentation

A 48-year-old female with unremarkable medical history presented to the hospital with the chief complaints of swelling of both lower extremities and concomitant unintentional weight loss appeared on January 2021. She had no other systemic symptoms. No serious comorbidities detected. All hematological investigations were within normal limits. The patient did not have previous similar attack and family history for similar illness was negative. On the outpatient setting duplex ultrasound showed bilateral femoropopliteal DVT, Low Molecular Weight Heparin (LMWH) was initiated. Assignment

to abdominal CT was performed, but the patient did not admit to scheduled examination.

One month later she presented to emergency department with complain on progressive dyspnea, severe swelling of both legs and acute pain in the left lower extremity lasting for 4 days. Critical left limb ischemia with gangrene of the midfoot and I, II, III finger was diagnosed.

Laboratory blood results upon admission showed HGB 9.6g/dl, WBC 27.4 x 10⁹/L, RBC 3.46x 10⁶/L, PLT 136 x10⁹/L, GFR 41ml/min, bilirubine 9.7mkmol/l, INR 1.16, prothrombine 72%. D-dimer was positive and SARS-CoV-2 (COVID-19) testes were negative.

CT of thoracic and abdominal cavity as well as CT angiography of both legs performed.

Lower leg CT angiography showed right popliteal artery complete occlusion (Figure 1).

Abdominal contrast enhanced CT showed hypoattenuating mass in pancreatic body and tail region with hyper vascular peripheral rim (Figure 2). Multiple, bilobar liver metastases with hypoattenuating central part and hypervascular peripheral rim and secondary hepatomegaly were found on abdominal CT. Ascites also present (Figure 3). There were also evidences of right renal artery embolus (Figure 4).

Bilateral, symmetrical, predominantly perihilar interlobular septal thickening with alveolar filling was found on chest CT (Figure 5). In addition, segmental and sub segmental bilateral pulmonary thromboembolism was detected (Figure 6).

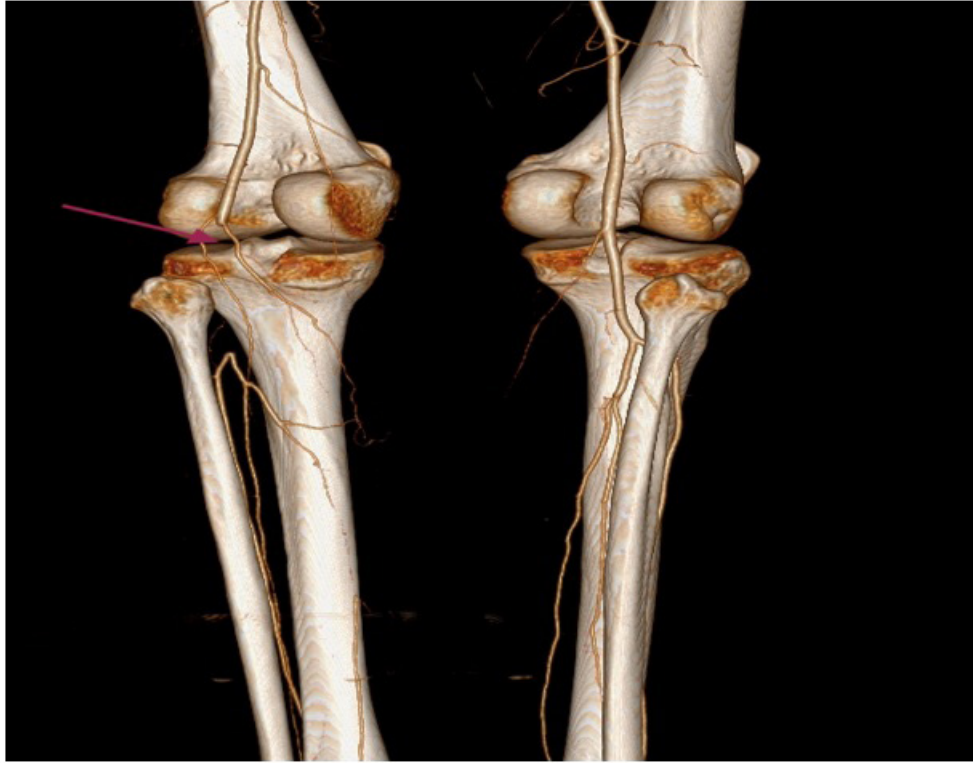


Figure 1: Symptomatic popliteal artery occlusion with preserved flow in other lower limb arteries and no signs of atherosclerosis raised suspicion for distal thrombembolism of popliteal artery. (Red arrow)



Figure 2: Abdominal contrast enhanced CT showed hypoattenuating mass in pancreatic body/tail region with hypervascular peripheral rim. (Red arrow).

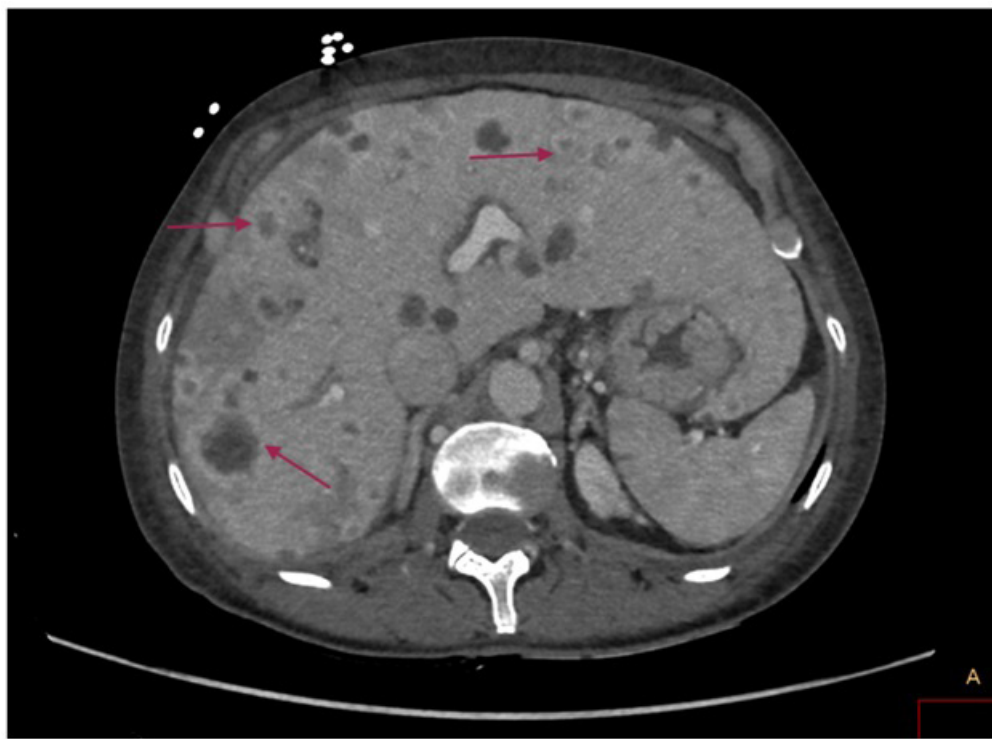


Figure 3: Multiple, bilobar liver metastases with hypoattenuating central part and hypervascular peripheral rim and secondary hepatomegaly were found on abdominal CT .(Red arrow). Ascites also present.



Figure 4: Renal artery subocclusion. Subocclusive filling defect detected also in renal artery suggesting showering thrombembolism. (Red arrow).

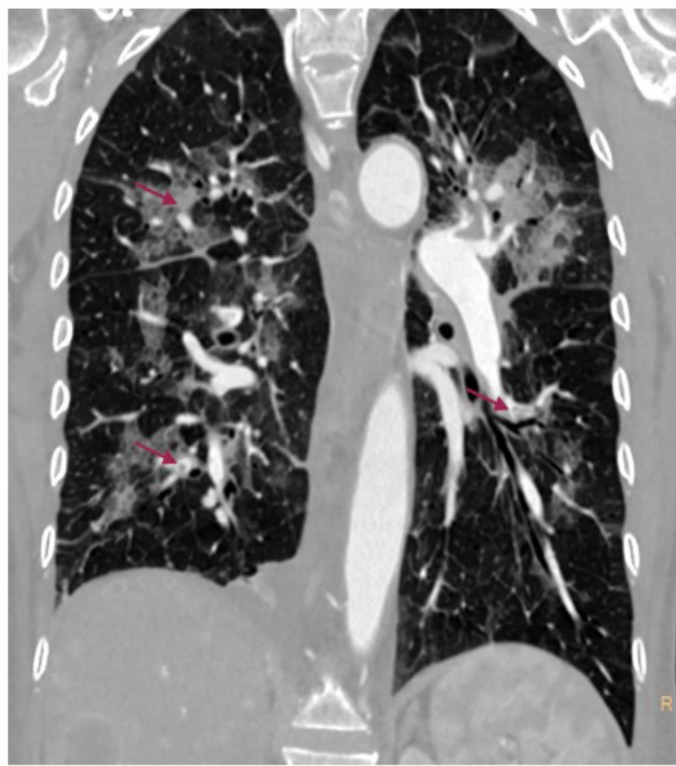


Figure 5: Lymphangitic carcinomatosis. Chest CT showed bilateral, symmetrical, predominantly perihilar interlobular septal thickening with alveolar filling. (Red arrows).



Figure 6: Segmental/ subsegmental pulmonary thromboembolism. (Red arrow)

Lower limbs color Doppler sonography showed evidence of thrombosis in the left popliteal artery, bilateral iliofemoral deep vein. Echocardiography showed EF 58%, tachycardia, severe regurgitation of mitral valve. There was also evidence of mitral and aortic valve vegetations, pathognomonic to endocarditis, and pulmonary hypertension.

Despite poor general status open thrombectomy from left popliteal artery performed, nevertheless peripheral puls was not achieved due to coexisting thrombosis of crural arteries. Acute cardio surgery or

TAVI was not possible due to poor general status and progressive sepsis due to gangrene of the left lower limb. On the third day after admission despite antibacterial treatment patient developed septic shock and her vital functions withered leading to death five days after admission.

3. Discussion

Thrombotic events represent the second leading causes of death in cancer patients, after cancer itself [5]. The clinical presentation of cancer-associated thrombosis includes Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), and arterial thrombosis. The most frequent clinical presentation of cancer-associated thrombosis is Venous Thromboembolism (VTE). It is reported to occur in 4–20% of cancer patients [6]. The common primary tumor sites identified at the time of VTE diagnosis are the lungs (17%), pancreas (10%), colon and rectum (8%), kidneys (8%) and prostate (7%) [7].

In 1977 Sack et al, summarized the essential clinical, pathophysiologic, and therapeutic features of Trousseau's syndrome. [8] Despite its well-described features, however, Trousseau's syndrome may be difficult to diagnose in individual cases with occult malignancy especially when the first presentation is solitary embolus or thrombotic episode.

According to Callander and Rapaport research [3], the hypercoagulability of Trousseau's syndrome mostly stems from the exposure of tissue factor (thromboplastin) from tumor cells to the circulating blood.

Based on guidelines which published by the National Comprehensive Cancer Network (NCCN) [9] and the American Society of Clinical Oncology (ASCO) [10] for the management of cancer patients with acute VTE, the initial therapy is generally the same, irrespective of whether cancer is present or not. The initial treatment modalities for cancer-associated thrombosis include Low Molecular Weight Heparin (LMWH), unfractionated heparin (UFH) and fondaparinux. LMWH is generally preferred because it does not require blood test monitoring and hospitalization. [11] Additionally, a meta-analysis of randomized controlled trials found that, compared with UFH, LMWH was associated with a statistically significant reduction in mortality after 3 months of treatment [relative risk = 0.71; 95% confidence interval (CI) = 0.52–0.98] without an increased risk of bleeding [12].

Our patient had episode of acute DVT as a heralding sign of cancer, because of lack of accompany symptom without further imaging investigations she has been discharged from emergency department and treated as outpatient with LMWH. Four weeks later despite receiving therapeutic dose of LMWH, she presented with acute ischemia in the lower limb, accompany with evidence of emboli in other organs including lung. Her clinical situation considered as recurrent emboli secondary to possible malignancy and underwent detailed chest and abdominal imaging.

One of the most challenging findings in our presented case were

lung lesions. Chest CT revealed bilateral, symmetrical, predominantly perihilar interlobular septal thickening with alveolar filling. Although non-massive segmental and subsegmental bilateral pulmonary thromboembolism was also detected but the infiltration was not typical to infarction pneumonia. Viral pneumonia including COVID-19 excluded based on laboratory tests results and lack of characteristic imaging findings of COVID, therefore the finding was interpreted as lymphatic carcinomatosis which can be found in adenocarcinoma patients with hematogenous spread. Lymphangitis carcinomatosa is the malignant infiltration and inflammation of lymphatic vessels secondary to the metastatic spread of malignancy from a primary site. Pulmonary lymphangitis carcinomatosa diagnosis is associated with a poor prognosis: approximately half of patients die within two months of their first respiratory symptoms and three weeks from admission to hospital [13].

Our patient has the misfortune to have concomitant endocarditis with mitral and aortic valve vegetation which caused severe mitral valve dysfunction. Despite poor general status open thrombectomy from left popliteal artery performed, which was unsuccessful. Acute cardiac surgery was not possible due to poor general status and progressive sepsis secondary to gangrene of the left lower limb and finally she died five days after admission.

Overall Trousseau's syndrome is a constellation of multiple thromboembolic events occur in patients with cancer. Based on this definition, besides clinical and imaging findings especially characteristic lesion in pancreas accompany with liver and lung metastases and also recurrent vascular emboli, the presented case fulfilled all necessary diagnostic criteria of Trousseau's syndrome.

4. Conclusions

Trousseau's syndrome is a constellation of multiple thromboembolic events occur in patients with cancer. Although for patients with acute VTE, the initial therapy is generally the same, irrespective of whether malignancy is present or not but compared with patients without malignancy, this type of patients has increased tendency of major bleeding owing to the cancer itself. It is also well-known that thrombosis in cancer is frequently recurrent.

Our experience with this case showed the necessity of detailed investigation and admission of patients with recurrent vascular events, in times where hospitals and staff are still overwhelmed by COVID-19 Patients.

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