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Cardiac and Intramuscular Metastases Following Nephroureterectomy for Metachronous Urothelial Carcinoma

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Corresponding Author: Chan Hiok Yang, e-mail: hiokyang@gmail.com**Financial support:** None declared**Conflict of interest:** None declared**Patient:** Male, 58-year-old
Final Diagnosis: Metastatic urothelial carcinoma
Symptoms: Right scapular lump • shortness of breath
Clinical Procedure: —
Specialty: Oncology • Radiology**Objective:** Rare disease**Background:** We present a case of metachronous cardiac and intramuscular metastases in a patient with a known history of radical nephroureterectomy for upper-tract urothelial carcinoma (UTUC).**Case Report:** A 58-year-old man had a history of metachronous renal pelvis urothelial carcinoma with prior left radical nephroureterectomy. He was also diagnosed with malignancy-associated deep vein thrombosis (DVT) and was on rivaroxaban. He presented at an oncology follow-up consult with shortness of breath and right scapular lump. CT scan revealed a soft-tissue mass at the surgical bed suspicious for local recurrence, as well as intracardiac hypodensities and intramuscular nodules in the right latissimus dorsi and right adductor muscles. The intracardiac hypodensities were located in the left atrial appendage and inter-atrial septum. Given that the patient had a history of DVT and in a pro-thrombotic state, differentials for the intracardiac densities included intracardiac thrombi or metastases. The intramuscular hypodensities were rim-enhancing. Given that the patient was on rivaroxaban, differentials included hematomas or metastases. As there was no overlying bruising and the lesions remained unchanged in size clinically, they were treated as metastases. The patient was treated with clexane but re-presented with worsening of shortness of breath and palpitations. CT scan showed increased size of intracardiac lesions, suggesting no response to anticoagulation, and therefore were likely metastatic in nature. He completed a 2-year course of IV pembrolizumab and was in complete remission.**Conclusions:** Our case highlights the importance of this clinically challenging scenario when patients with known malignancy and on anticoagulation present with cardiac or musculoskeletal symptoms. Though these patients are at risk of thrombus and haematoma, cardiac and intramuscular metastasis should be considered, as the prognosis is guarded.**Keywords:** Cardiac Imaging Techniques • Neoplasm Metastasis • Musculoskeletal Diseases • Carcinoma, Transitional Cell • Radiology**Abbreviations:** TURBT – transurethral resection of bladder tumor; CT TAP – CT thorax, abdomen and pelvis; TTE – transthoracic echocardiogram; TEE – transesophageal echocardiogram; UTUC – upper-tract urothelial carcinoma; BUC – bladder urothelial cancer**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/942864>

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Introduction

We present a case of metachronous cardiac and intramuscular metastases in a patient with a known history of radical nephroureterectomy for upper-tract urothelial carcinoma (UTUC). Bladder tumors account for 90-95% of urothelial carcinomas and are the most common malignancy of the urinary tract [1]. Upper-tract urothelial carcinoma (UTUC) accounts for 5-10% of urothelial malignancies and 10% of renal cancers [2,3]. Metachronous UTUC develops in 3-5% of muscle-invasive bladder urothelial cancer (BUC) after radical cystectomy [4]. Radical nephroureterectomy is considered the surgical standard of care for treating localized UTUC [5]. However, prognoses remain poor and local recurrence and/or distant metastasis often occur [4,6], with lung, liver, bone, and adrenal glands being common sites of metastasis [7,8]. Intramuscular metastasis account for less than 5% of urothelial metastases, and cardiac metastases are extremely rare [7]. To date, there has been no known case reported in the literature with both symptomatic cardiac and intramuscular metastases in metachronous UTUC and this can pose significant clinical challenges. We present a case of metachronous left renal pelvis urothelial carcinoma with multiple sites of metastatic disease – peritoneum, pulmonary, cardiac, and intramuscular.

Case Report

A 58-year-old man had a history of non-muscle-invasive BUC post elective transurethral resection of bladder tumor (TURBT) (histology – low-grade papillary urothelial carcinoma) in January 2020. It was not known if the patient underwent chemotherapy, as the whole course of treatment was conducted overseas. This was complicated by metachronous renal pelvis urothelial carcinoma (T3N0M0) for which laparoscopic left radical nephroureterectomy was performed in February 2021. There was no lymphovascular invasion; therefore, lymph node dissection was not performed. Final histology revealed high-grade papillary urothelial carcinoma. The surgical margins and left adrenal gland were not involved. Of note, he was diagnosed with malignancy-associated deep vein thrombosis of the left lower limb in May 2021 and was on rivaroxaban.

He presented at a routine oncology follow-up consult with a 1-month history of decreased effort tolerance, shortness of breath on exertion and a 2-week history of right scapular lump. There was no chest pain or history of trauma. Physical examination was unremarkable. His vitals were stable. Platelet count and coagulation panel were normal. He was not on any adjuvant treatment at the time of presentation as ongoing surveillance CT thorax, abdomen, and pelvis (CT TAP) prior to presentation revealed no evidence of local recurrence or metastatic disease. The last CT TAP was performed in June 2021. In view of his symptoms, CT TAP was performed 1 week later, in August 2021.

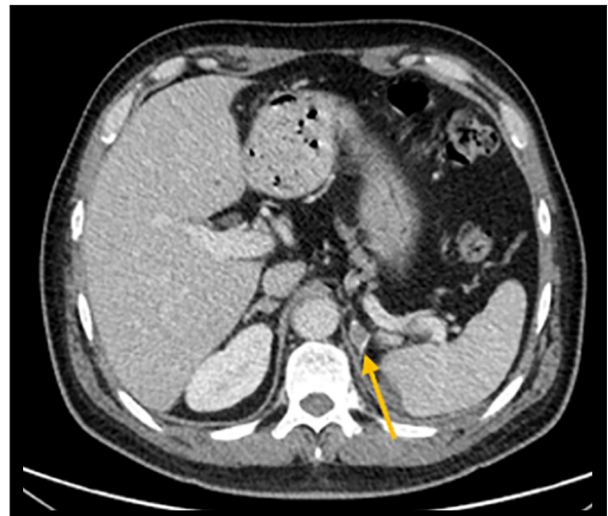


Figure 1. Local recurrence of urothelial carcinoma in left nephroureterectomy surgical bed. Non-enhancing soft-tissue hypodensity in left nephroureterectomy surgical bed (arrow), suspicious for local recurrence.

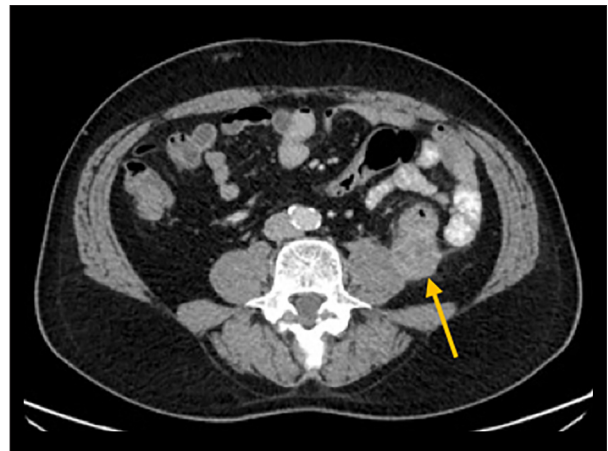


Figure 2. Peritoneal metastasis in a 58-year-old man. Heterogeneously-enhancing left flank nodule (2.3 cm, arrow) abutting the descending colon anteriorly and left psoas muscle medially, suspicious for peritoneal metastasis.

The CT TAP revealed a soft-tissue mass in the left nephroureterectomy surgical bed suspicious for local recurrence (**Figure 1**). There were new findings of bilateral pulmonary metastases, left lower paratracheal lymphadenopathy, left flank peritoneal metastasis (**Figure 2**), with the primary tumor presumably from left renal urothelial carcinoma given the local recurrence. There were also intramuscular mildly rim-enhancing nodules in the right latissimus dorsi (**Figure 3A**) and right adductor muscles (**Figure 3B**) and intracardiac hypodensities (**Figure 4A, 4B**).

The intracardiac densities were located in the left atrial appendage/left ventricle and another adherent to the inter-atrial

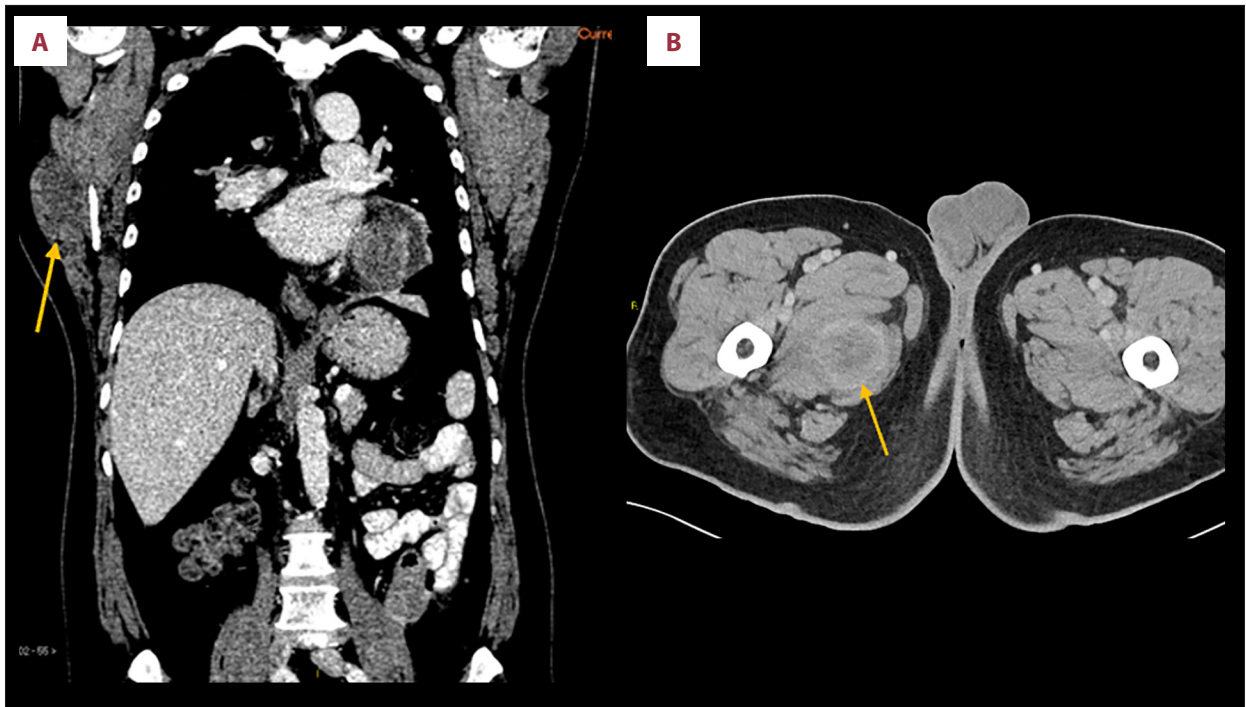


Figure 3. (A) Right latissimus dorsi intramuscular metastasis in a 58-year-old man. Right latissimus dorsi intramuscular ovoid hypodense lesion (arrow) abutting the scapula with faint rim enhancement, suspicious for intramuscular metastasis. (B) Right adductor intramuscular metastasis in a 58-year-old man. Right adductor intramuscular round hypodense lesion (arrow) with central hypodensity and rim enhancement, suspicious for intramuscular metastasis.

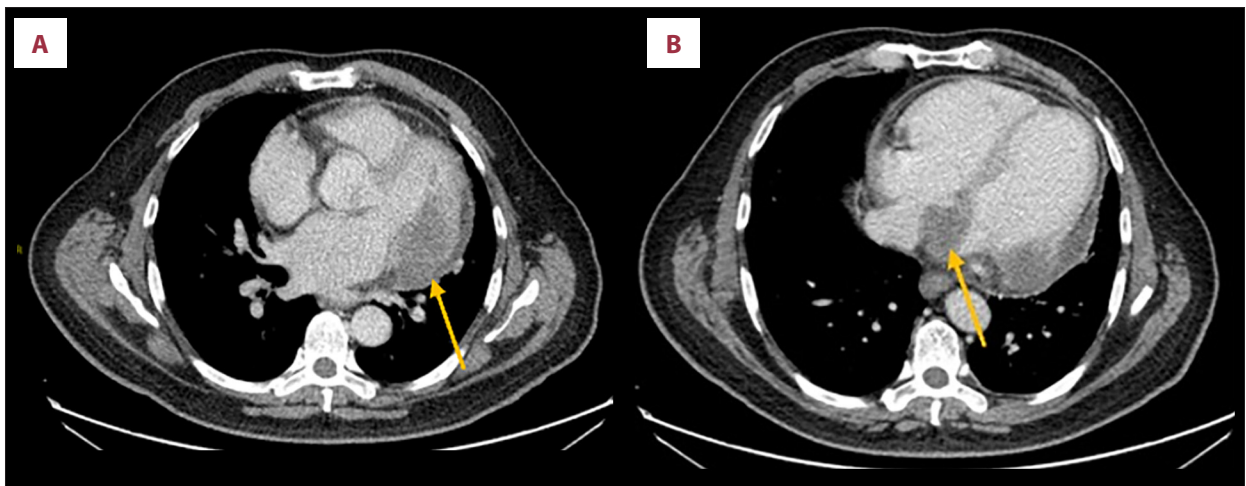


Figure 4. (A) Intracardiac metastasis in a 58-year-old man. Hypodense lesion (HU 45-50) involving the left ventricle (arrow, left image) and atrial appendage (HU 40-45) (arrow, right image) along the endocardium abutting the myocardium. (B) Intracardiac metastasis in a 58-year-old man. Inter-atrial septum nodular hypodense lesion extending into bilateral atria.

septum. The hypodensity attached to the left atrial appendage/left ventricle had a Hounsfield unit (HU) of 45-50, while the one adherent to the inter-atrial septum had a HU of 40-45. Given that the patient had a history of deep vein thrombosis and in a pro-thrombotic state, differentials for the intracardiac densities included intracardiac thrombi or metastases. The patient underwent a transthoracic echocardiogram (TTE)

for better anatomical correlation of intracardiac densities, but it was unable to clearly visualize the left atrial appendage due to its posterior location. There was no other significant abnormality seen on TTE. Transesophageal echocardiogram (TEE) or cardiac MRI was not performed as there would not be significant change in management given that he was already on anticoagulation.



Figure 5. (A, B) Companion case: right atrial thrombus induced by implanted venous access port insertion in a 41-year-old woman. Hypodense eccentric lesion (arrows) arising at the venous port tip within the right atrium abutting the right atrial wall.

The intramuscular masses in the right latissimus dorsi and right adductor regions were hypodense, mildly rim-enhancing, and not near vital neurovascular structures. Given that the patient was on rivaroxaban, differentials included hematomas or metastases. As there was no overlying bruising and the lesions did not change in size clinically, they were treated as metastases. The patient was also not interested in biopsy as stopping rivaroxaban for the procedure can worsen potential cardiac thrombus and known deep vein thrombosis.

The patient was treated with clexane but re-presented 3 weeks later with 2-3 days of fever, worsening of shortness of breath, decreasing effort tolerance, and palpitations. Physical examination was unremarkable. Electrocardiography revealed new-onset atrial flutter, possibly precipitated by the cardiac lesions. CT TAP was performed but no source of infection was noted. However, the intracardiac lesions had increased in size, suggesting that there was no significant response to anticoagulation and that they were likely metastatic in nature. Incidentally, there were new findings of peripancreatic peritoneal nodule and right adrenal nodule suspicious for metastases. He was treated for malignancy-associated fever and discharged well and stable. He was subsequently placed on a 2-year immunotherapy regimen with IV pembrolizumab 200 mg every 4 weeks after Tumor Board discussion. The patient was followed up closely with regular surveillance CT TAP and had complete remission by completion of immunotherapy.

Discussion

Cardiac Metastasis

In our literature review, we found that cardiac metastasis from renal cancer (encompassing all histological subtypes) have been reported to be intra-atrium [9,10], intra-ventricular [11,12], myocardial [13,14], endocardial [9], pericardial [15,16], or

involving multiple regions of the heart [9,14]. Cardiac metastasis can be asymptomatic or can present with life-threatening complications such as tamponade, outflow tract obstruction, arrhythmias, or valvular dysfunction [16-18]. Apart from routine transthoracic echocardiography, further imaging such as contrast-enhanced ultrasound, cardiac CT, cardiac MRI, or PET CT scan can be performed for further evaluation.

Differential Diagnosis – Cardiac Thrombus

There remains a clinical challenge when patients with metastatic disease present with cardiac lesions as they are at risk of developing both thrombus and metastasis, as in our case. We demonstrate a companion case of cardiac thrombus secondary to venous access port insertion in a patient with a known malignancy. A hypodense filling defect was seen in the right atrium near the catheter tip site and right-sided pulmonary artery emboli were noted. Though the lesion had a similar appearance as cardiac metastasis, its location at the catheter tip site in a patient with pulmonary embolism highly suggests cardiac thrombus (Figure 5). Based on location, lesions in the left atrial appendage in the setting of a patient with atrial fibrillation or left ventricle in a patient with ventricular dyskinesia favor thrombus [19,20]. On CT, cardiac metastasis appears as soft-tissue attenuation with heterogenous enhancement [20] while thrombus is of low attenuation and may demonstrate calcific foci when long-standing [19]. On MRI, cardiac metastasis generally demonstrates low T1-weighted signal, high T2-weighted signal with enhancement on first-pass perfusion [20,21], while a thrombus appears as a non-enhancing lesion with varied signal depending on age, although organized thrombus can have an enhancing rim [20,21]. Cardiac MRI is the optimal non-invasive imaging modality for differentiating thrombus and metastasis, as it is superior in tissue characterization [18,22]. However, cardiac MRI has its disadvantages such as lower temporal resolution, long acquisition times,

and inability to be performed in hemodynamically unstable patients [18]. On PET scan, cardiac metastasis is FDG-avid [18,22] while a thrombus is not. Another possible approach is to trial a course of anticoagulation treatment [18]; a thrombus would resolve or decrease in size while a metastatic lesion would remain the same or increase in size over time.

Intramuscular Metastasis

In our literature review, we found that intramuscular metastases from urothelial cancer have been reported most commonly in the iliopsoas [23], with other sites also reported, including the deltoid [24], rectus abdominis [25], adductors [25], sartorius [26], and gastrocnemius [27]. Intramuscular metastasis can present as localized pain but can also present as secondary to a compressive effect on surrounding structures [28]. Therefore, in patients with known or treated malignancy, any new-onset musculoskeletal swelling or pain should raise the suspicion of metastatic disease.

Differential Diagnosis – Intramuscular Hematoma

There remains a clinical challenge when patients are on anticoagulation, as a possible differential of an intramuscular mass would be a hematoma, as in our case. On CT, intramuscular metastases have varied patterns, but a hematoma may demonstrate a multicystic or fluid-fluid level [29,30]. On MRI, intramuscular metastasis demonstrates poorly defined margins, T1-weighted low/heterogeneous signal, T2-weighted high signal, restricted diffusion, heterogeneous or ring enhancement, or central necrosis with peritumoral edema [23,29]. On MRI, hematomas have variable T1-weighted and T2-weighted signals, depending on the age of blood products [31] and are typically non-enhancing, although rim enhancement can sometimes be seen [32]. On PET, intramuscular metastasis demonstrate focal and homogeneous avidity [29] while a hematoma may demonstrate a peripheral rim of FDG avidity [33,34]. Clinical examination and history of trauma would be prudent to evaluate the

likelihood of a hematoma as a differential. Serial imaging may be useful in demonstrating gradual resolution for hematomas with stable/increasing size for intramuscular metastasis [35,36].

Treatment and Prognosis

Palliative treatment is often the mainstay of treatment for symptomatic relief given the poor prognosis of cardiac and intramuscular metastases, especially if other widespread metastases are present. For cardiac metastasis, surgical debulking is indicated for treatment of complications such as embolism, outflow tract obstruction, tamponade, arrhythmia, or valvular dysfunction [37,38]. Chemotherapy and radiotherapy are utilized in patients who are contraindicated for surgery or as adjunct therapy with palliative debulking surgery to prevent local recurrence [39]. For intramuscular metastases, chemotherapy and radiotherapy can be administered for pain relief or reduction in mass effect from intramuscular metastases [26,27]. As patients often have widespread metastasis at presentation, surgery is only reserved for those with isolated soft-tissue metastases after a long disease-free interval.

Conclusions

Our case highlights the importance of being cognizant to this clinically challenging scenario when patients with known history of malignancy and on anticoagulation present with cardiac or musculoskeletal symptoms. Although these patients are at risk of thrombus and hematoma, cardiac and intramuscular metastasis should also be considered, as the prognosis is guarded.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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