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Case report

Gastrocnemius acrometastasis from muscle-invasive urothelial bladder carcinoma: A case report[☆]

Mohd Zulkimi Roslly, M.D.^{*}, Aida Widure Mustapha Mohd Mustapha, M.D., Isa Azzaki Zainal, M.D.

Department of Radiology, Faculty of Medicine, Hospital Canselor Tunku Muhriz, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

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ABSTRACT

Urinary bladder carcinoma is a common malignancy worldwide. The metastatic disease to distant organs including lung, liver, and bone is well established. However, metastasis to below-knee-level; also known as acrometastasis is a rare occurrence and occurs approximately 0.1% of all bone metastases. It is standard of care to obtain a contrast enhanced computed tomography scan of the chest, abdomen, and pelvis for pretreatment planning, primary staging, and post treatment disease surveillance. This makes the occurrence of acrometastasis harder to detect and may only manifest clinically in advance disease. We report a case of 55 years old gentleman treated as muscle-invasive bladder urothelial carcinoma, presented with chronic left knee pain, and imaging demonstrating tumor in the left knee region. Histopathologic study shows features of metastatic disease from urinary bladder carcinoma to the left gastrocnemius muscle. The attending physician should raise the suspicion of metastatic disease if the patient with known malignancy presented with new soft tissue lesion elsewhere in the body.

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Introduction

Urinary bladder neoplasm is a common entity account for 2%–6% of all tumors, ranked 4 in United States as the most common malignancy [1]. It can arise from any layer of the bladder wall and is divided into 2 distinct forms: Epithelial or non-

epithelial. Epithelial-based neoplasm being the most common histopathologic class and the urothelial carcinoma accounts for 90% of them. Bladder urothelial carcinoma invasion into the adjacent structures is well established, including prostate, vagina, uterus, and pelvic wall. This tumor commonly spreads to the pelvic lymph nodes, lung, liver and bone [2].

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^{*} Corresponding author.

E-mail address: p90915@siswa.ukm.edu.my (M.Z. Roslly).

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According to the latest AJCC Staging Manual 8th edition of urinary bladder carcinoma, the presence of distant metastasis (M1 stage) is subdivided into 2; M1a and M1b which includes distant nodal and non-nodal metastatic disease. All cancers staging is based on the contrast enhanced computed tomography (CECT) scan of the thorax, abdomen, and pelvis to ascertain the advancement of the disease. If the distant metastasis occurs beyond the CT coverage area, it will be missed out, and possibly thought to be a different pathology.

Case summary

Mr. MY, 55 years old man with past medical history of diabetes, hypertension, paroxysmal atrial fibrillation, and chronic kidney disease. He initially presented with painless frank hematuria for 2 months' period. Abdominal examinations were unremarkable. Cystoscopy showed posterior bladder wall tumor measuring 5 cm in diameter. Biopsy performed during cystoscopy revealed infiltrating urothelial carcinoma; high-grade pT2 (AJCC 8th ed). He was then subjected for trans-urethral resection of bladder tumor (TURBT) and subsequent CECT of the thorax for staging purpose and further evaluation.

CECT thorax, abdomen, and pelvis performed a month later showed no evidence of distant metastasis. However, patient had a prolonged stay in hospital for post-operative complications including anastomotic leak, rectal perforation, and intraabdominal abscess collection. He was discharged after nearly 3 months' hospital admission. Serial CECT performed during the hospital stay revealed no evidence of residual or metastatic disease.

Upon follow up 7 months' later, patient was noted to have lower back pain and elevated serum calcium levels. Bony metastasis was suspected but re-staging CECT showed no evidence of local recurrence or distant metastasis. However, 2 months' later patient started complaining of left knee pain and swelling. Fig. 1.

Ultrasound of the left lower limb was performed (Fig. 2). It showed an oval shaped, heterogenous, intramuscular hypoechoic lesion within the proximal part of left lateral gastrocnemius muscle measuring $2.0 \times 3.2 \times 3.9$ cm. Presence of peripheral vascularity on color Doppler. Impression of soft tissue tumor as a differential diagnosis was made. He was then subjected for MRI of the left lower limb to ascertain the diagnosis.

MRI of the left knee (Fig. 3) revealed an ill-defined enhancing soft tissue lesion within the proximal part of lateral gastrocnemius muscle. It is isointense on T1WI, heterogeneously hyperintense on T2WI and measures $2.5 \times 4.3 \times 4.2$ cm (AP x width x height). The mass is associated with edema and enhancement of the surrounding gastrocnemius muscle which could represent inflammatory edema or infiltration. The adjacent proximal fibula marrow displays moderate hyperintensity on T2WI with enhancement post contrast. Aggressive primary soft tissue tumor and metastatic foci were the differential diagnosis at that point of time.

Core-needle biopsy of the left leg mass was performed and the histologic findings showed malignant cells arranged in sheets and trabeculae surrounded by desmoplastic stroma.



Fig. 1 – Radiograph of left tibia-fibula showing lytic destructive bone lesion at proximal fibula (arrow).

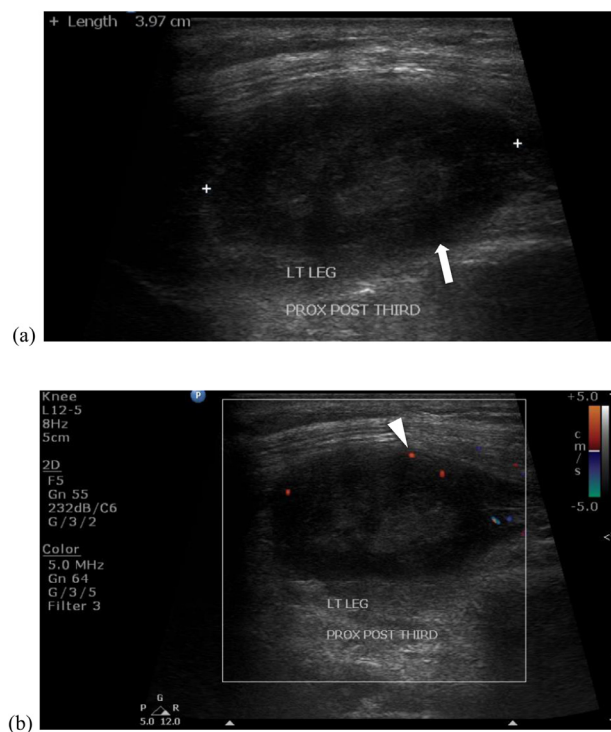


Fig. 2 – (A) Heterogenous, hypoechoic, intramuscular mass at proximal third of the gastrocnemius muscle (arrow). (B) Patchy areas of peripheral vascularity within the mass (arrowhead).

Immunohistochemistry staining shows positivity to CK7 and CK20 (Fig. 4). The diagnosis of metastatic carcinoma from urinary bladder was made.

Subsequently the patient was subjected to radiotherapy of the left leg mass. He was doing well at home and able to ambulate with limping. He is currently under urology follow up for the primary and metastatic disease.

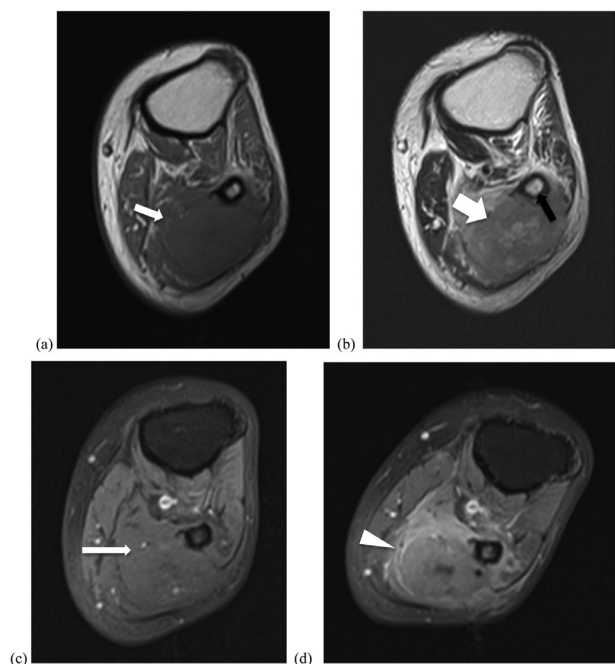


Fig. 3 – (A-D) MRI images showing ill-defined left gastrocnemius intramuscular mass. (A) T1W image shows the mass (arrow) demonstrates isointense signal. (B) T2W image demonstrate heterogeneously hyperintense signal mass (thick arrow) with associated proximal fibula marrow hyperintensity (arrowhead) suggestive of edema. (C) T1W fat-saturation (FS) sequence shows intermediate intensity (black arrow) and heterogeneous enhancement on T1W FS post-gadolinium sequence (arrowhead).

Discussion

Malignant neoplasm of urinary bladder is one of the most common urological conditions worldwide. In United States alone, approximately 70,980 new cases were diagnosed with approximately 20% mortality rate [1].

Histologically, according to a local study done by Christopher and co-worker in 2010, transitional cell or urothelial carcinoma is the commonest type. [3] This is coherent with a larger cytologic study by Rabbani in 2000 [4] which showed transitional cell constitutes 90% of all bladder malignancy. The rest of cytologic subtypes contribute to less than 10%; namely squamous cell carcinoma and adenocarcinoma.

Bladder carcinoma is known to metastasis and according to Taher et.al in 2006 [5], the most frequent site of metastases of TCC is to lymph nodes (51%-88%), lung (36%-40%), bone (22%-37%) and adrenal glands (6%-21%). According to Nagao and co-workers, the less-frequent metastatic sites from urothelial carcinoma include the pleura, brain, and skin. [6]. Even though muscles constitute approximately 50% of cardiac output and body mass, they constitute a rare site of metastases from distant primary lesions. [6,7].

Older study by Mulsow in 1943 [8] postulated that the rarity of skeletal muscle metastasis is attributed to several factors. These factors that resist the metastatic deposits include muscle motion and mechanical tumor destruction, inhospitable muscle pH, and the muscle's ability to remove tumor by production of lactic acid.[8] Thus Seung et al. in 2011 concluded that metastatic disease to skeletal muscle tends to be found in advanced-stage neoplasms. The largest muscles, such as the erector spinae, psoas, and gluteal are the most common sites of metastatic involvement. [7]

Few reports of acrometastasis have been published in literature including metastatic disease to the tibia and foot. However, up to our knowledge, no cases have been reported with metastatic disease to the calf muscle. In our case, patient is known to have urothelial carcinoma of the bladder and presented with new musculoskeletal pain nearly a year later. However, in some series, few patients came in with skeletal muscle pain as an initial presentation of urothelial carcinoma. Seung et.al reported a case of left sartorius muscle metastasis from urothelial carcinoma in which muscular pain was the initial presentation [7]. This is also compatible with several other studies that skeletal muscle metastatic lesions are painful.

In imaging workup, the lesion can be found as incidental findings or as a presenting symptom [6]. However, subclinical skeletal muscle metastasis has a tremendous number as

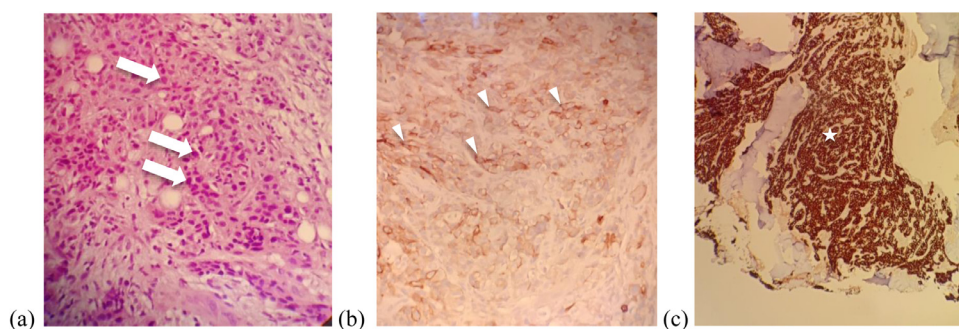


Fig. 4 – (A) The magnification view (100 x) of Hematoxylin and Eosin (H&E) staining showing malignant cells (white arrows) arranged in sheets and trabecular. (B) Magnification view (100 x) of immunohistochemistry staining shows positivity to CK20 (arrowheads). (C) Magnification view (40x) of the malignant cells show strong positivity to CK7 immunohistochemistry staining (star).

found by Pickren (1976) in a large post mortem study. [9] He found that out of 5,298 people who died of malignancies, 6% ($n = 298$) had involvement of the anterior chest wall or abdominal wall musculature and 13% ($n = 666$) had diaphragmatic musculature involvement. In our case, the painful, and swollen knee clinically leads to further imaging studies. The initial Roentgenologic study shows no obvious abnormality and retrospectively, very subtle periosteal reaction is seen in proximal fibula. Ultrasound in our patient shows a well-defined hypoechoic lesion in the proximal lateral part of gastrocnemius muscle, which demonstrates vascular flow. There have not been many reports published in literature on ultrasound features of metastatic disease involving the skeletal muscle. Our sonographic findings are similar to the case reported by Seung et al in which his patient had metastatic lesion in left sartorius muscle.

On magnetic resonance imaging, the lesion appears intermediate signal on T1-weighted image and heterogeneously hyperintense on T2-weighted image. It is enhanced in heterogeneous fashion with evidence of adjacent proximal fibula marrow involvement. Similar to the case reported cases by Seung (2011), the MRI findings of the metastatic lesion demonstrate T1W signal hypointensity and T2W hyperintensity. Despite these consistent findings, MRI features of muscular metastasis are concluded to be non-specific and not pathognomonic for urothelial metastasis. [10]

The skeletal muscle metastasis in urothelial bladder carcinoma is usually present in a patient with advance disease and having a poorer prognosis than another distant metastasis. [7,11] Pretorius et. al. had 87% of patients with evidence of widespread metastatic disease at the time of detection of muscular lesions. [12] This fact is against our case in which patient does not have evidence of another metastasis. Nabi et al. reported that the mean survival rate for patient with urothelial bladder carcinoma with skeletal muscle metastasis was 8 months' following chemotherapy. [11] Our patient is still under follow up after a year of skeletal metastasis was made.

Conclusion

We report a case of muscular-invasive urothelial bladder carcinoma with acrometastasis to left gastrocnemius muscle. The metastatic deposit in the gastrocnemius muscle was missed for 2 months' after the initial complaint of leg pain and raised serum calcium. Because of surveillance CECT for malignancy only covering the thorax, abdomen, and pelvis, the occurrence

of metastatic disease beyond the coverage area easily can be missed like in our case. In patients with a known malignancy, particularly with advanced disease, any new swelling or pain in the skeletal muscles should raise the suspicion of metastatic disease. Prompt assessment by biochemical, radiological, and cytologic means should be done.

Patient consent

The informed and written consent obtained from the patient prior to submission of this case for publication.

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