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Metastatic RCC Presenting as an AVM Mimicking Hypervascular Tumor of the Distal Lower Extremity: A Case Report

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Abstract

Renal cell carcinoma (RCC) is the dominant type of renal malignancy and while it commonly metastasizes to the lungs, liver, bones, and brain, skeletal muscle metastasis (SMM) is rare. Due to the highly vascular nature of RCC, cases of hypervascular RCC SMM may mimic an arteriovenous malformation (AVM). This poses a considerable diagnostic hurdle as these two pathologies drastically differ in both treatment and prognosis. To our knowledge, there are only 4 reported cases of metastatic RCC presenting as an AVM mimicking hypervascular skeletal muscle tumor. We report a case of a patient with a history of RCC who achieved remission following nephrectomy, but 11 years later developed a hypervascular metastasis to the hallucis longus muscle which mimicked an AVM. Our case emphasizes the need for vigilant surveillance and suspicion of late-onset skeletal muscle metastases in RCC patients, even after a lengthy disease-free period. We also discuss the role and limitations of imaging modalities in distinguishing an AVM from a highly vascular RCC SMM and highlight the crucial role of tissue biopsy in confirming the diagnosis.

Keywords: *Renal cell carcinoma, skeletal muscle metastasis, late recurrence, calf*

1. Introduction

Renal cell carcinoma (RCC) is the prevailing form of renal malignancy and represents approximately 3% of all adult malignancies in the United States (Jemal). It typically metastasizes to the lung (50%), lymph nodes (35%), liver (30%), bone (30%) and adrenal glands (5%) (Hanno),[1] and rarely to the skeletal muscle. In the literature, metastases have been reported to occur anywhere from months up to 21 years after nephrectomy, highlighting the importance of long-term surveillance. Specifically, metastases to skeletal muscle may present a diagnostic challenge by mimicking an AVM, which has a significantly different treatment course and prognosis.

2. Case Description

A 67-year-old male with past medical history of T3aNx clear cell renal carcinoma status post left radical nephrectomy and adrenalectomy in 2012, presented 11 years later with a 4-month history of a right lateral calf mass. Ultrasound of the region showed a lobulated hypoechoic intramuscular structure measuring up to 5.5 cm in the posterior and lateral aspect of the distal right leg concerning for a soft tissue sarcoma (Fig. 1a). Follow-up MRI revealed a 2.9 x 6.0 x 8.8 cm enhancing mass located predominantly within the flexor hallucis longus muscle with extension into the peroneus longus muscle. The lesion appeared T1 isointense to muscle and had a few foci of slight T1 hyperintense signal (Fig. 2a) and T2 hyperintense signal with internal flow voids (Fig. 2b). It also noted multiple serpiginous vessels originating and arising from the enhancing mass (Fig. 1b). These findings were most suspicious for a vascular lesion, such as an arteriovenous malformation. Core biopsy of the lesion showed a richly vascular epithelial neoplasm composed of nests of polygonal cells with clear cytoplasm and central ovoid nuclei most consistent with metastatic renal cell carcinoma, clear cell type. Histochemical analysis of the tumor cells was positive for AE1/3, CAM5.2, CAIX (diffuse membranous staining) and Pax-8 consistent with metastasis from RCC. Subsequent computed tomography (CT) of the chest, abdomen and pelvis demonstrated metastatic lesions in bilateral

lungs, pancreatic tail/splenic hilum, right kidney and adrenal gland (Fig. 3). Bone scan revealed no evidence of bony metastasis, though the scan did reveal uptake corresponding to the right upper quadrant mass and right calf mass. The patient was subsequently started on immunotherapy and a tyrosine kinase inhibitor. Repeat CT chest, abdomen and pelvis 3 months after initiation of therapy revealed an essentially stable exam.

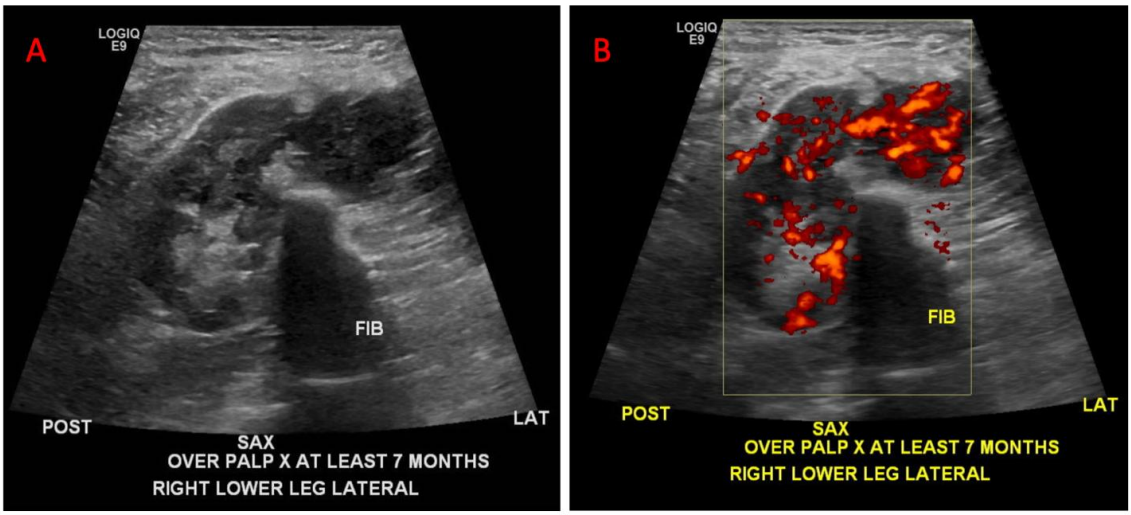

Figure1. (A) *Ultrasound of the region showed a lobulated hypoechoic intramuscular structure measuring up to 5.5 cm in the posterior and lateral aspect of the distal right leg concerning for a soft tissue sarcoma.* ***(B)*** *Color Doppler: There appeared to be multiple serpiginous vessels with rapid internal flow arising from the mass suggestive of a vascular lesion.*

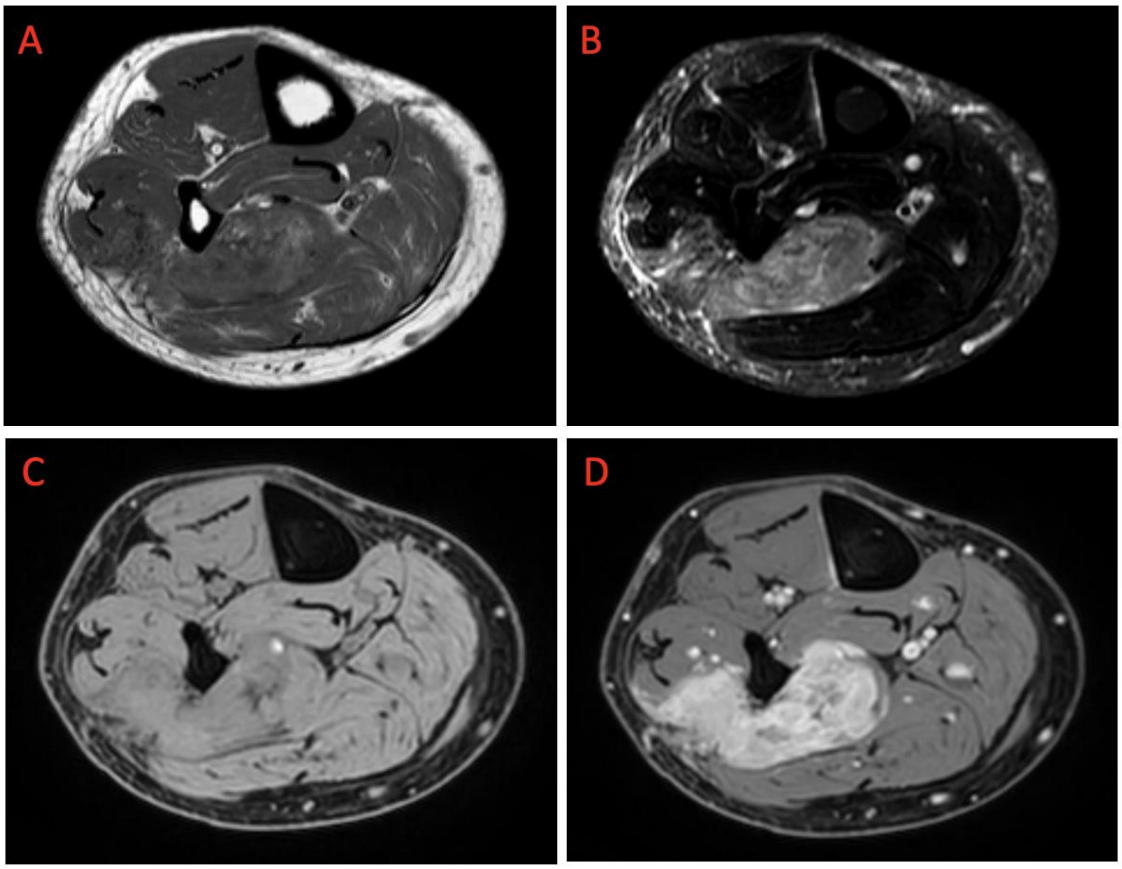

Figure2. *Axial MR images.* ***(A)*** *T1: Large mass in the flexor hallucis longus muscle extending into the peroneus longus muscle is relatively isointense to the surrounding muscles with few foci of slight T1 hyperintense signal.* ***(B)*** *STIR: Heterogenously hyperintense mass to the adjacent muscle.* ***(C, D)*** *T2: Enhancing mass with hyperintense signal and internal flow voids.*

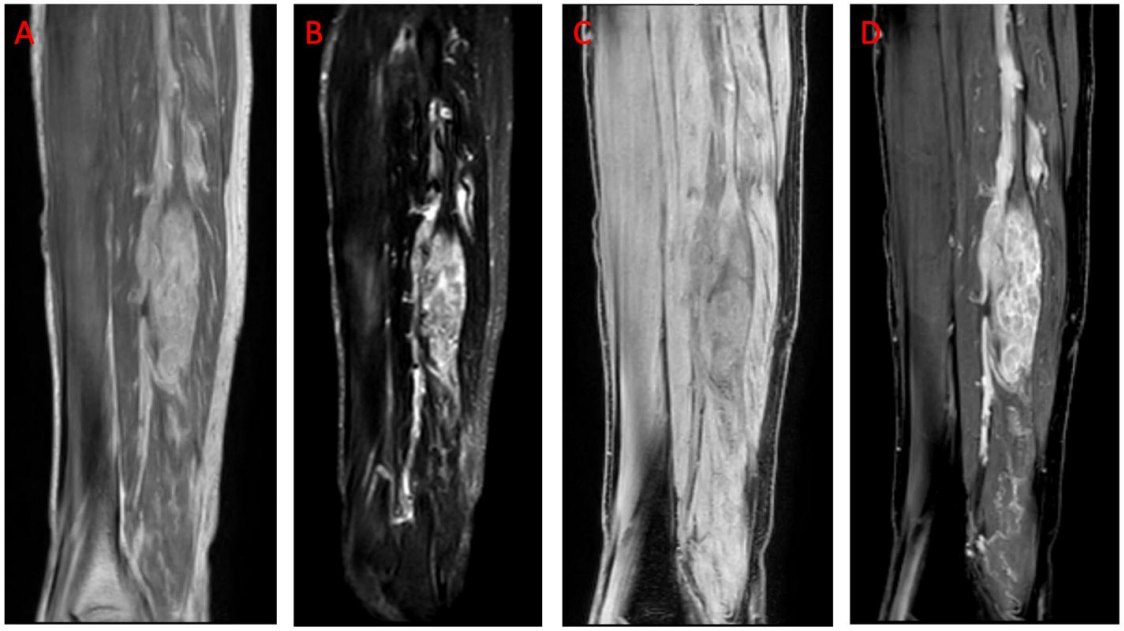

Figure3. *MR imaging. (**A**) Sagittal T1-weighted: Large mass in the flexor hallucis longus muscle extending into the peroneus longus muscle at the posterior and lateral aspect of the distal right leg. The mass is relatively isointense to the surrounding muscles with few foci of slight T1 hyperintense signal. **(B)** STIR: Heterogenously hyperintense mass to the adjacent muscle. **(C, D)** Sagittal T2-weighted: Enhancing mass with hyperintense signal and internal flow voids.*

3. DISCUSSION

RCC typically metastasizes to the lung (50%), lymph nodes (35%), liver (30%), bone (30%) and adrenal glands (5%).[1] Skeletal muscle metastases from RCC are extremely uncommon, occurring in less than 1% of patients and mainly reported in case reports.[2] SMM has occurred anywhere from months up to 21 years after initial radical nephrectomy.[3] A study published by Sun et al. in 2022 noted that there were a total of 41 published cases of RCC SMM.[3] Of the 41 cases, 49% of the SMM were located in the limbs.[3] The rarity of SMM can be attributed to factors such as the high vascularity of muscles, resistance to angiogenesis due to lactic acid production, inhibitory factors like free radicals and skeletal muscle-derived factors, and the absence or scarcity of specific receptors in muscles affecting RCC metastasis potential.[3]

Metastasis of RCC in soft tissues typically appears as a solitary mass[4] and can be difficult to distinguish from a primary skeletal muscle tumor. The presence of pain is highly indicative of metastasis rather than a typically painless, primary soft tissue tumor such as a sarcoma.[4] However, patients with SMM from RCC are typically asymptomatic in the early stages. Symptoms appear as the metastases grow larger, causing local pain, swelling, and/or a palpable mass,[3] as was observed in our patient.

Unusual manifestations of metastatic renal cell carcinoma (RCC), particularly to the skeletal muscle, can pose a diagnostic challenge. To our knowledge, there are only a handful of reported cases of metastatic RCC presenting as an AVM mimicking hypervascular skeletal muscle tumor. These cases are in the form of case reports and describe tumors in the forearm[2] and thigh.[5,6] RCC is known to be a very vascular tumor, often containing a mutated version of the von Hippel-Lindau (VHL) gene.[7] This mutated gene promotes abnormal angiogenesis through high expression levels of hypoxia-inducible factor-1α protein and VEGF expression, resulting in hypervascular metastatic tumors that may mimic an AVM.[7]

Late recurrence, occurring more than 10 years after curative nephrectomy, represents one of the uncommon characteristics of RCC occurring at a rate between 4.3-11%.[8] The highest risk of recurrence is observed during the initial 5 years following nephrectomy, with the majority of recurrences happening within 3 years.[9] The cause of late recurrence has been attributed to factors such as decreased host immunity and hormonal changes, which may trigger tumor growth.[10]

Radiologically, SMM appear as a hypervascular mass often with high signal intensity on T2-weighted MR.[11] Color Doppler imaging often

detects a high-frequency doppler shift in multiple malignant musculoskeletal tumors, which can aid in distinguishing a SMM from a benign tumor.[11] In addition, SMM often exhibit small feeding vessels that are thought to form in response to tumor-induced oxygen deprivation.[12] Surov et al. reported that on ultrasound, SMM were typically hypoechoic and on PET/CT, muscular metastases appeared as focal hypermetabolic lesions.[13] In our case, the MRI features of iso-hypointense signal on T1, flow voids, and contrast enhancement in combination with US showing a hypoechoic lesion with serpiginous vessels with internal flow were suggestive of an AVM. However, lack of significant intralesional fat characterized by T1 hyperintensity and lack of phleboliths (commonly seen in slow flow AVMs) were suggestive of a mass rather than an AVM. As evidenced by our case, biopsy is necessary to distinguish skeletal muscle metastases (SMM) from RCC and pathology is the gold standard.

In terms of surveillance of metastatic RCC, recent studies have reported that FDG-PET/CT are equivocal to other imaging modalities. Survival time of RCC with skeletal muscle metastasis ranged from 3 months up to 8 years.[3] Metastasectomy is the mainstay treatment for patients with localized disease.[14] If metastatic disease is widespread, as in the case of our patient, systemic treatment with targeted therapy, immunotherapy or chemotherapy provides potential survival benefit.[14] Detecting recurrence or metastatic burden at an early stage may increase the likelihood of a positive response to systemic therapy.

4. Conclusion

We present a rare case of a hypervascular RCC skeletal muscle metastasis that was discovered 11 years after nephrectomy and mimicked an AVM on imaging. Our case highlights the importance of surveillance and maintaining a high index of suspicion for late-onset skeletal muscle metastases that may initially mimic an AVM, even in RCC cases with a long disease-free interval. Additionally, we describe the crucial role of tissue biopsy in establishing a definitive diagnosis given the imaging similarities between an AVM and hypervascular RCC SMM.

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