

CASE REPORT

Delayed Presentation of Metastatic Renal Cell Carcinoma as an Arteriovenous Malformation Mimicking Vascular Tumour of the Forearm

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Introduction: The development of metastatic renal cell carcinoma (RCC) many years after a nephrectomy is not common but has been reported. A metastasis appearing as a hypervascular tumour, mimicking an arteriovenous malformation (AVM), is a highly unusual phenomenon, with a biopsy required for diagnostic confirmation. Surgery is an option for a solitary metastatic lesion amenable to complete excision, with proven survival benefits. However, widespread metastatic disease carries a very poor prognosis, and is best treated with systemic agents such as anti-angiogenic drugs or tyrosine kinase inhibitors.

Report: A 58 year old man developed an AVM mimicking a vascular tumour within his left brachioradialis muscle 10 years after a nephrectomy for RCC. Ultrasound and magnetic resonance imaging did not reveal any suspicious features of the vascular lesion.

The lesion was successfully removed surgically, and was later proven histopathologically to be metastatic RCC. Further imaging showed widespread metastatic disease, and the patient survived only 15 months after receiving tyrosine kinase inhibitor therapy.

Discussion: This case report aims to highlight a few important points: RCC metastases may be hypervascular, mimicking an AVM. A long disease free interval does not necessarily exclude recurrence or metastasis, as in this case, therefore long term surveillance is recommended. A high index of suspicion must be maintained to avoid delay in treatment, and biopsy of any suspicious lesion for histological examination is mandatory, albeit after many years of cancer remission. Whole body imaging with computed tomography or positron emission tomography computed tomography may detect clinically occult recurrence or metastases, and is important to guide further treatment.

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INTRODUCTION

Renal cell carcinoma (RCC) is the most common cancer of the kidney, and accounts for about 2% of adult malignancies. Unusual manifestations of metastatic RCC can be a diagnostic conundrum.¹ The time period between the initial diagnosis of a localised cancer to development of stage 4 disease can be highly variable.² Therefore, these patients will require long term and vigilant follow up for early detection of recurrence or spread.³ Localised metastatic lesions can be removed surgically, as this has been shown to

improve survival.⁴ While multiple new therapies for metastatic disease continue to be discovered, overall survival remains limited once distant disease has developed.⁵

CASE REPORT

A 58 year old man presented with a slow growing mass on the left forearm. It appeared two years prior to presentation. He experienced no pain or limitations in activities. There was no preceding trauma, and there were no complaints of skin changes. His past surgical history was significant for a radical left nephrectomy done 10 years previously for RCC (clear cell type, Fuhrman nuclear grade 2). Routine annual surveillance was negative for local recurrence or distant metastases. On physical examination, there was a solitary swelling on the volar aspect of the proximal left forearm, measuring approximately 4 cm in length and 3 cm in diameter. The overlying skin was normal.

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It was not tender, with a smooth surface. The mass appeared to be pulsatile, and was compressible, with immediate refill. There was no thrill or bruit. Ultrasound revealed a solitary, heterogeneous, ovoid intramuscular lesion with increased signal on colour Doppler. Subsequent magnetic resonance imaging showed a well defined fusiform lesion with heterogenous signal intensity within the left brachioradialis muscle (Fig. 1). Intense enhancement was seen post-gadolinium administration. Areas of flow void were also seen, which suggested the possibility of a fast flowing vascular malformation. There was no marked surrounding oedema to indicate surrounding muscular infiltration. From the imaging, it was concluded that although there was a possibility of it being a hypervascular mass, as the features of the lesion were more benign in nature, a fast flow vascular malformation was more likely. Excision of this lesion was performed under general anaesthesia. Intra-operatively there was a benign looking lesion, with a smooth surface, encapsulated by a thick fibrous wall (Fig. 2). It measured 4 cm in length by 2 cm in diameter by 1.7 cm in thickness. It was pulsatile and compressible, with immediate refilling with blood. The main

feeding vessel was seen to arise from the recurrent radial artery. The entire lesion was removed successfully, after ligation of its feeding branches. Recovery from the operation was uneventful. Surprisingly, histopathological examination of the specimen was consistent with metastatic RCC (Fig. 3). An urgent staging computed tomography scan showed widespread metastatic disease in the vertebrae and lungs. Oncology referral was sought, and tyrosine kinase inhibitor therapy was initiated. Unfortunately, the disease progressed; with development of symptomatic metastases to the brain, and the patient died 15 months post-operatively.

DISCUSSION

RCC accounts for 2%–3% of all cancers globally. There is a male predominance, and it usually presents in the older age group, with a peak incidence seen between 60 and 70 years. The majority of RCCs are of the clear cell type, accounting for up to 90% of cases.⁴ It is notoriously well known for being able to spread to many different and sometimes unusual locations.^{2,3,6,7} An analysis of > 11 000 patients



Figure 1. Magnetic resonance imaging. (A) T1 weighted sagittal image of a heterogeneously iso- to hyperintense intramuscular ovoid lesion, with flow voids noted peripherally (white arrow) suggestive of either a possible fast flow vascular malformation or vessels supplying a vascular lesion. (B) Axial short tau inversion recovery image, showing a heterogeneously hyperintense lesion; again, flow voids suggestive of vessels are seen adjacent to it (white arrow). No significant perilesional oedema is present to suggest surrounding muscular infiltration. (C) Post-gadolinium T1 weighted fat saturated sagittal image demonstrating intense lesional enhancement, similar to the gadolinium enhanced vessel (white arrow). This suggests either a hypervascular lesion or a fast flow vascular malformation (note the adjacent flow voids, as in A and B).

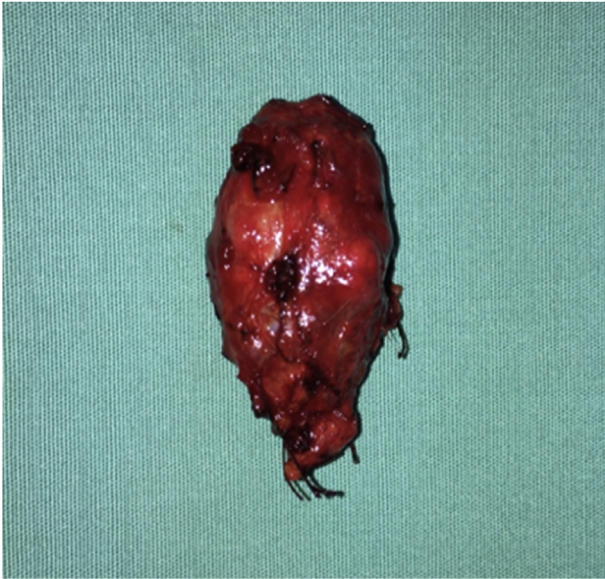


Figure 2. Intra-operative specimen of the ovoid, arteriovenous malformation mimicking a vascular tumour, excised from the left brachioradialis muscle. The main feeding vessel was seen to arise from the recurrent radial artery (intra-operatively).

recorded the most common sites of spread to be the lung, bone, lymph nodes, liver, adrenal glands, and brain.⁷ RCC has also been known to recur many years after treatment, with one author reporting skeletal muscle metastasis 19 years after a radical nephrectomy.² Generally, the spread of any type of cancer to skeletal muscle is a rare occurrence.^{8,9} With RCC, skeletal muscle metastasis occurs in < 1% of patients, having only been described in case reports.^{2,8}

To the authors' knowledge, metastatic RCC presenting as an AVM mimicking hypervascular tumour of the forearm has never been reported. Chan and Wolfe reported a case of metastatic RCC appearing as a large AVM like vascular tumour in the thigh, 12 years after a radical nephrectomy for clear cell carcinoma.⁶ Lohiya *et al.*,³ in their experience, excised a large hypervascular mass from the posterior aspect of patient's thigh, which was eventually confirmed to be metastasis from a primary RCC diagnosed 11 years earlier. Another report, by Albandar *et al.* in 2017, described a patient who presented with brain metastasis associated with an AVM.¹⁰

To understand the aetiopathogenesis of this extremely rare entity, the highly vascular nature of RCC has been analysed. RCC itself is a very vascular tumour, with mutations in the von Hippel-Lindau (*VHL*) gene frequently found.⁴ This mutation, when present, may lead to abnormalities of angiogenesis. High levels of hypoxia inducible factor 1 α signalling pathway proteins and vascular endothelial growth factor have been found in patients with metastatic disease, and this could possibly explain the development of AVM mimicking tumours during the disease course.¹⁰

In this case, it is important to note that as 10 years had passed since the patient's cancer diagnosis, the appearance of a benign appearing vascular lesion on the forearm did not raise any alarms. As the lesion was small and amenable to excision in its entirety, surgery was performed immediately without pre-operative histology. In retrospect, the importance of biopsy to confirm the diagnosis, prior to embarking on further treatment, is acknowledged. However, given the highly vascular nature of the tumour, haemorrhage poses a serious risk and should be approached with caution.

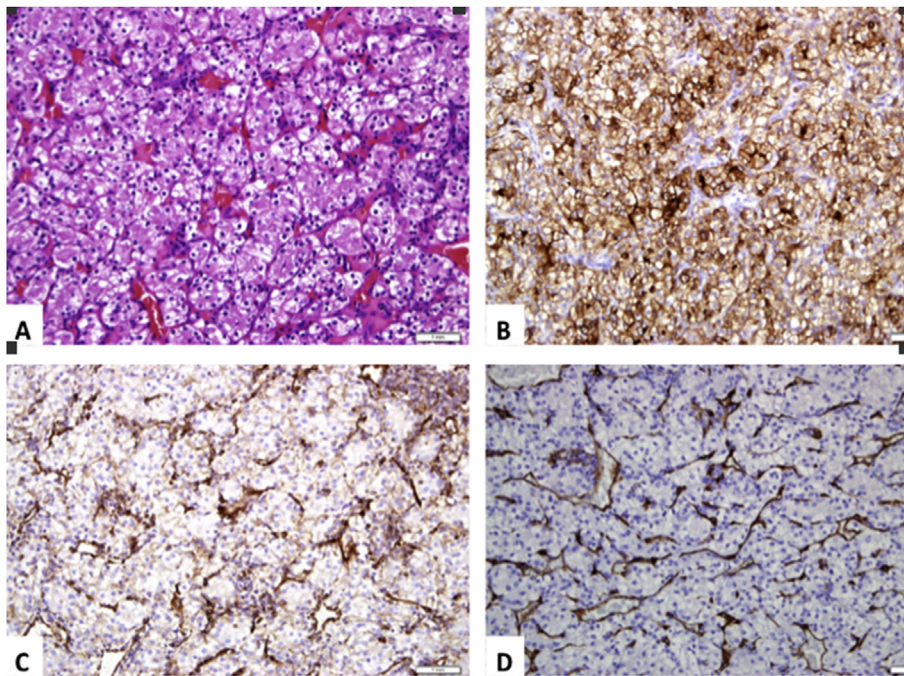


Figure 3. Histopathology images. (A) Malignant clear cells in acinar pattern interspersed with numerous thin walled vessels. (B, C) Immunohistochemistry staining showed malignant cells with positivity for CD10 and vimentin. (D) CD34 highlights the blood vessels.

Excision of localised metastatic disease can be performed and is beneficial in terms of prolonging survival.⁴ For widespread disease, survival was previously estimated to be one year, when the main treatment option was immunotherapy with agents such as interleukin-2 and interferon- α . There have been advances in therapy for metastatic RCC since 2005. Survival can now be prolonged to over two years with the use of anti-angiogenic drugs and tyrosine kinase inhibitors.⁵ This is an area of ongoing research with promising results.

CONCLUSION

RCC has the potential to metastasise, sometimes following a long disease free interval. Owing to the highly vascular nature of the original tumour, metastatic lesions can also appear as hypervascular lesions, sometimes mimicking an AVM, and leading to confusion in the diagnosis. Management should include a prompt biopsy in the presence of suspicious lesions, identification of other sites of metastatic disease, and either resection of localised disease or targeted therapy for widespread disease.

CONFLICT OF INTEREST

None.

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