Refractory sciatica could be a sign of malignancy:
A unique case presentation
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ABSTRACT
Renal cell carcinoma is one of the highly aggressive tumors and notorious for late presentations. It is associated with high morbidity and mortality. Renal cell carcinoma is known for rare metastatic sites. In clinical practice, it is often important not to anchor to a particular diagnosis but rather revisit and reevaluate entire history and clinical examination. We describe a case of metastatic renal cell carcinoma that was initially treated as sciatica and later found to have advanced debilitating malignancy. Internal medicine physicians should be able to recognize one of the rare metastatic sites of renal cell carcinoma and understand the importance of imaging studies if patient has persisting sciatica symptoms without improvement.
KEYWORDS: Oncology, renal cell carcinoma, soft tissue metastasis, skeletal muscle metastasis, refractory sciatica

INTRODUCTION
Renal cell carcinoma (RCC) represents about 90% of all kidney neoplasm. Twenty to twenty-five percent (20–25%) of the patients initially present with advanced disease and around 5% present with a single metastatic site.1 RCC is the sixth most common malignancy in men and the eighth most common malignancy in women in the United States. The incidence of RCC rose by 1.6% per year between 2002 and 2011 with 63,920 new cases and 13,860 deaths anticipated in 2014.14 Making a diagnosis of metastatic RCC to the skeletal muscle is challenging, because the site is unpredictable, in addition to it being rare. Furthermore, cases of metastasis arising long after nephrectomy have been reported. In this clinical vignette, we will discuss about a unique presentation of RCC.

CASE PRESENTATION
A 48-year-old male with no significant past medical history presented to the primary care clinic with two months of radiating pain down the right leg and which was treated as sciatica and piriformis syndrome in another facility. He came to our primary care clinic for a second opinion. He reported that pain was much worse in severity and that he had developed fever, night sweats and chills in the last 2 weeks. He recalled significant weight loss of 10 pounds in the last 4 months, malaise and severe painful ambulation. He felt very stressful and was not able to concentrate in his job. The pain was severe enough to restrain him from working and he was on medical leave. Recently he was able to feel that his right gluteal region was abnormal compared to his left. He stopped smoking in 2005 after 20 years of smoking. He had no history of trauma or intramuscular injections. His mother had a history of transitional cell carcinoma of the right kidney.

On exam, his temperature was 98.4 degree Fahrenheit, blood pressure was 120/78mm hg and oxygen saturation was 99% in room air. Physical exam was significant for systolic murmur in left second intercostal space. He was found to have ill defined, firm, warm, immobile and mildly tender mass in the right iliac bone and gluteal region. Other systemic exam was unremarkable.

Complete blood count showed hematocrit of 38.5%, basic chemistry profile was normal. C-reactive protein was elevated to 150mg/dl, Erythrocyte sedimentation rate was elevated to 88 mm/hr. CT scan of abdomen and pelvis revealed right renal mass of 5 cm in the lower pole and a large osteolytic lesion of right sacral and iliac bones. In addition, there was a 10 x12 cm infiltrating mass in the piriformis and gluteal muscles consistent with metastatic disease. CT scan of the chest showed a sclerotic lesion in the upper sternal body. CT scan guided biopsy of the right gluteal mass showed metastatic renal cell carcinoma of clear cell type. (Figures 1-3)

Patient underwent radical nephrectomy and subsequently received immunotherapy with Interleukin-2 and later received palliative radiotherapy. During this period he was hospitalized multiple times for lethargy and failure to thrive. He was also started on pazopanib for progressive disease.

DISCUSSION
RCC is a tumor known for its unusual presentations and high rate of metastasis.1 The most common sites of RCC metastases are the lung (50%), lymph nodes (35%), liver (30%), bone (30%) and adrenal glands (5%).1, 2 Possibly the first case of skeletal muscle metastasis originating from an RCC was reported in 1979.2 Presentation of RCC as a solitary metastasis in the skeletal muscle is very unusual and poorly documented site of metastasis.2 Atypical presentations and distant metastasis are characteristic of RCC.3, 2
RCC rarely spreads to the skeletal muscle, with a reported percentage of only 0.4%.\(^1\)

Even after surgical removal of tumor late recurrence is a possibility. McNichols et al demonstrated that 11% of metastatic RCC cases occurred more than 10 years after the initial diagnosis, even after complete resection.\(^9\)

Renal cell carcinoma accounts for approximately 3% of all adult tumors and about one-third of cases present as metastasis either as initial presentation or late complication. Because of complex lymphatic drainage and early hematogenous spread atypical presentations and distant metastasis remain characteristic of RCC.\(^6\)

Despite its rich blood supply and large surface area, the skeletal muscle is a rare site of metastasis.\(^2\) The mechanism involved in metastasis to the skeletal muscular tissue is not well understood. However, the presence of protease inhibitors in the basement membrane inhibiting cell invasion, increased lactic acid levels and acidic environment interfering with tumor cell growth were described as possible causes.\(^3\) However, detection of metastases to the skeletal muscle is difficult because of the painless nature of the tumors and their small size.\(^1\) Other differentials for soft tissue mass are rhabdomyosarcoma, angiosarcoma and hemangioma.\(^2\)

Better knowledge of prognostic and predictive factors could improve the management of metastatic renal cell cancer (RCC) by identifying those patients at a higher risk of death or disease progression. The most commonly used prognostic scores are the Memorial Sloan-Kettering Cancer Center score and the recent Heng risk score for patients receiving targeted therapies.\(^8\)

More than a decade ago, immunotherapy with cytokines was the standard treatment for metastatic RCC (mRCC). Subsequently, targeted agents such as vascular endothelial growth factor tyrosine kinase inhibitors (VEGF-TKIs) and inhibitors of mammalian target of rapamycin (mTOR) showed significantly improved responses and progression-free survival (PFS). These agents were also relatively well tolerated, thereby changing the treatment paradigm for metastatic RCC.\(^14\)

Extrapulmonary metastases may benefit from surgery; the presence of multiple visceral metastases is not a contra-indication. Surgery for RCC-related metastases may provide favourable long-term results and should not be contraindicated for recurrent disease when complete resection may be achieved.\(^12\) Forthcoming studies should analyze the role of the lymphatic system and the biology of metastatic cells in order to clarify the pattern of spread of RCC metastases.

This case illustrates one of the unique presentations of RCC and demonstrates the rare skeletal muscle metastasis of RCC. According to several European orthopedic association guidelines, conservative management is recommended for six to eight weeks and imaging is indicated if no improvement occurs.\(^15\) So imaging is indicated in case of red flag signs and persistent symptoms of more than six to eight weeks.
References


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