

Case Report of Renal Cell Carcinoma Presenting to Urgent Care with Indolent Back Pain: A Wolf in Sheep's Clothing

Urgent Message: Although back pain is often due to benign etiologies, symptoms of progressive pain, weakness, and near syncope in one patient ultimately led to a diagnosis of renal cell carcinoma.

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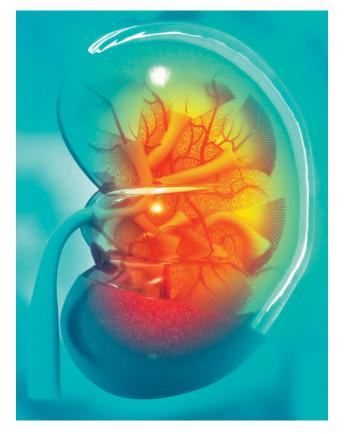
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Abstract

Introduction: Back pain is a common complaint in the urgent care and is most commonly due to benign etiologies. This case report details a patient with back pain and multiple primary care provider (PCP) visits who ultimately was diagnosed with renal cell carcinoma (RCC) after being seen in urgent care (UC) and referred to an emergency department (ED).

Clinical presentation: A 41-year-old man with a history of hypertension presented multiple times to his PCP and the ED with low back pain (LBP). He denied any saddle anesthesia or urinary retention or incontinence. His physical exam revealed normal spinal range of motion, lower extremity strength, sensation, and deep tendon reflexes (DTR). Distal pulses were strong and symmetric. The patient did have tenderness in the paraspinal musculature on the left side down to the level of the left iliac crest.

Case resolution: The patient presented to an urgent care



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for his 5th episode of seeking care when the low back pain had progressed with bilateral back and lower extremity pain, weakness, and near syncope. He denied fevers, urinary incontinence or retention, and dysuria. With his symptoms progressing and the recent history of multiple PCP visits, the UC clinician determined that the patient should be referred to an ED for further evaluation.

Conclusion: In the ED, additional history revealed 25 pounds of unintentional weight loss. A computed tomography (CT) scan of the abdomen and pelvis was obtained which demonstrated findings consistent with metastatic cancer. Subsequent evaluation revealed the primary cancer to be renal cell carcinoma. Unfortunately, the patient died of complications of this diagnosis soon thereafter.

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Introduction

ack pain is a nearly universal human experience with a 50-80% lifetime prevalence in adults.¹ The differential diagnosis of low back pain is broad, but can be divided functionally into 2 categories: mechanical (eg, strain, spasm, fracture, degenerative disc disease, etc.) and non-mechanical etiologies (eg, epidural abscess, psoas abscess, primary or metastatic malignancy, abdominal aortic aneurysm, etc.).² Approximately 23% of the world's adult population suffers from chronic LBP, which explains why it is such a common presenting complaint in a variety of medical settings such as primary care, UC, and the ED.³ The following case serves to illustrate that renal cell cancer may present in an innocuous fashion simply as painless hematuria, back pain, or weight loss.

Clinical Case

Excerpts in quotations are from actual documentation, and identifying details have been omitted to protect patient privacy. Less relevant elements are redacted for brevity.

Primary Care Office: Day 1

■ History of Present Illness (HPI): "The patient is a

41-year-old male with a past medical history of hypertension, hyperlipidemia, and tobacco use disorder who initially presents with a 3-week history of LBP. States that he injured his back while on vacation, and the pain is now interfering with his daily activities. Patient denies any urinary/stool incontinence or saddle paresthesia."

- Physical Exam: "Lumbar paraspinal muscle spasm and tenderness."
- Lumbar Spine X-ray: "No acute fracture or subluxation." "A [corticosteroid] injection was administered during the office visit and the patient was prescribed a [corticosteroid] oral taper, cyclobenzaprine, and hydrocodone/acetaminophen."
- Diagnosis: "Lumbosacral strain"

Emergency Department: Day 14

- **HPI:** "The patient presents to the ED for left sided lumbar back pain...He denies any radiation of the pain, numbness, tingling, weakness, bowel, or urinary incontinence."
- Physical Exam: "Full range of motion of the lower extremities and the lumbar spine, intact plantar flexion, and dorsiflexion of the feet bilaterally against resistance, no sign of foot drop, intact distal neuro-vascular response, and 2+ DTRs in the patellar reflexes bilaterally. There is tenderness in the paraspinal musculature on the left side down to the level of the left iliac crest."
- Diagnosis: The ED clinician determined that there was no indication for imaging at this time and assigned a diagnosis of "musculoskeletal back pain."
- Treatment: The patient was treated symptomatically again, receiving intramuscular (IM) ketorolac and a skeletal muscle relaxant. He was discharged with instructions to "continue NSAIDs [non-steroidal anti-inflammatory drugs] and muscle relaxants and to follow up with his PCP."

Primary Care Office: Day 21

- HPI: "Reports no new symptoms aside from his persistent back pain."
- Physical Exam: His physical exam showed persistent paraspinal tenderness, and his neurologic exam of the lower extremities was normal.
- **Treatment:** He was given another ketorolac injection and his hydrocodone/acetaminophen prescription was refilled.

Primary Care Office: Day 26

■ HPI: The patient was seen by his PCP's colleague for

an urgent follow-up visit due to his progressive symptoms. "Now complains of left upper and lower quadrant abdominal pain associated with constipation, fevers, and chills. He denies any urinary symptoms."

- Physical Exam: "Abdomen is soft, nondistended... positive tenderness in the left lower quadrant area. Back without CVAT [costovertebral angle tenderness]."
- **Diagnosis:** At this visit, the patient was diagnosed with "mild diverticulitis" due to a "history of diverticulosis" and was prescribed oral antibiotics.

Urgent Care: Day 30

- **HPI:** The patient presents to UC for bilateral back and lower extremity pain, weakness, and near syncope. "He denies any fevers, chills, urinary incontinence or retention, dysuria, or frequency."
- Physical Exam: Alert and oriented. Lungs clear to auscultation bilaterally. Heart: regular rate and rhythm without murmurs, rubs, gallop. Abdomen: soft and nontender, without rigidity, rebound, guarding. Back: normal appearance, no tender to palpation, no costovertebral angle tenderness. Nontender midline spine.
- Medical Decision Making: "Concern for multiple visits and associated near syncope without confidence that this is musculoskeletal." At this time and with the recent history of the patient's multiple visits to his PCP, the provider determines that the patient needs to be transferred to the ED for further evaluation and management.

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Diagnosis and Discussion

Among the most pressing questions on patients' and clinicians' minds when evaluating patients with acute or subacute low back pain surrounds imaging. As most causes of acute LBP are mechanical and self-limited, consensus statements and guidelines generally recommend against imaging in the absence of "red flags" in the history and physical (eg, American College of Radiology appropriateness criteria).⁴

Among the red flag risk factors that are important to screen for in patients' histories are a personal or family history of certain cancers (eg, breast, prostate, lung, kidney, or multiple myeloma), factors associated with an increased risk of spinal infection (eg, history of injection drug use, spinal instrumentation, or immunosuppression), prolonged glucocorticoid steroid use, significant trauma, osteoporosis, or advanced age (concern for vertebral compression fracture). It is similarly important to recognize red flag symptoms as well, such as new-onset urinary retention, fecal incontinence, saddle anesthesia, or objective neurologic deficits of the lower extremities that may suggest cauda equina syndrome (CES).5 While a presumptive initial diagnosis of mechanical LBP or lumbar strain is often appropriate at an initial visit, an expanded differential is prudent in cases with severe and progressive LBP, as was the case with this patient.

Lumbar X-Ray in Nontraumatic LBP

A lumbar x-ray (XR) was ordered at the initial PCP visit, however, plain films are specifically *not* recommended in non-traumatic acute LBP. The American College of Physicians (ACP) and the American Pain Society have jointly published guidelines with a "strong" recommendation for appropriate imaging in patients with acute LBP. This recommendation specifically states:^{6,7}

- 1. In patients with non-specific low back pain, providers should not routinely obtain imaging.
- Diagnostic imaging should be obtained in patients with progressively worsening or severe neurologic symptoms, or when, based on history and physical, a serious condition is suspected.
- 3. In patients whose treatment outcome will change and who are candidates for epidural steroid injections and surgery, diagnostic imaging should be performed either with magnetic resonance imaging (MRI) (preferred) or CT.

The term "diagnostic imaging" encompasses multiple modalities, most notably XR, CT, and MRI. However, when selecting the imaging test of choice, it is critical that the appropriateness of the modality in narrowing the differential diagnoses of concern should trump convenience and availability of the imaging study. While XR is generally more widely available in UC settings, it lacks sufficient sensitivity to exclude many time-sensitive etiologies of LBP.⁴

Prevalence Of Cancer And Other Serious Causes Of LBP In Primary Care

To date, there have not been studies describing the

prevalence of various etiologies of LBP in the UC setting. However, a prior study in the primary care setting showed the prevalence of low back pain due to cancer was only 0.7%. Other important causes of LBP were also rare in this population with compression fractures occurring in 4% and spinal infections in only 0.01%.8 Prevalence of these serious causes of back pain was unsurprisingly higher when ED populations were studied with the rate of cancer related LBP as high as 2.1%.9 In the case presented, it would have been relevant to have inquired about unexplained weight loss and failure for pain to improve after 1 month, as this may have provided clues to the possibility of a more serious cause of the patient's back pain.¹⁰

Initial Management of Non-Specific Acute Low Back Pain

In the case presented, the patient was prescribed both oral corticosteroids and opioids at the initial PCP visit. Multiple randomized controlled trials of ED patients from the last decade have shown that neither the addition of opioids nor corticosteroids improves short and medium term outcomes for patients with non-specific low back pain beyond what is observed with the use of acetaminophen and NSAIDs. 11,12 However, an article published in 2021 did highlight the added efficacy and safety of patient participation in active interventions such as multidisciplinary rehabilitation, pilates, and yoga. Prescribing such interventions for patients with acute low back pain was also shown to be cost effective.13 In the case presented, evidence does not support the initial management and treatment recommendations. In such situations, this unfortunately common pattern of prescribing may complicate care and/or delay definitive diagnosis.

Clinical Case Conclusion **ED Visit: Day 31**

The patient presented to the ED for ongoing back pain. He was afebrile, and vital signs were otherwise normal.

HPI: "Patient presents with complaint of an aching sensation in both of his legs. He does not have any current gluteal or lower extremity paresthesias and no urinary incontinence or retention. He has had back pain for the last 3 weeks and has had medications from his primary care physician. Initially had some numbness, but that is now resolved. He has never used intravenous drugs. No complaint of fever. He does have a history of diverticulitis or diverticulosis, he is not sure which. Also, he denies any dysuria or urinary frequency, blood in the urine. Yesterday he felt generalized weakness and like his blood

pressure was low. When he stood up, he fell down onto the right gluteal area but there were no other injuries. No complaint of vomiting and diarrhea. No blood in the stool. Social history: Smoker, has not drank alcohol for 1 month, no history of intravenous drugs. Pain Scale: 10."

"The classic triad of RCC presentation involves hematuria, flank pain, and a palpable abdominal mass, but this triad is only present in 9% of cases."

- Physical Exam: "Back: Normal appearance, does have pain with palpation musculature right low back and upper gluteal area but no midline pain with palpation. Straight leg raise test is negative to 45 degrees ×2. Strength 5/5 flexion extension bilateral lower extremities, patellar DTRs 2+ and equal ×2. Neurovascular status intact. No evidence of urinary incontinence" The ED clinician ordered bloodwork, and his complete blood count (CBC) revealed normocytic anemia and thrombocytosis. Of note, normocytic or microcytic anemia precedes the diagnosis of renal cell carcinoma in 29-88% of patients with advanced disease.14 The patient's complete metabolic panel (CMP) showed hyponatremia and elevated alkaline phosphatase (AP). Urinalysis (UA) was orange and turbid, and the urine dip was positive for protein, large blood, and trace leukocyte esterase (LE).
- **Treatment:** The patient underwent a CT scan of the abdomen and pelvis without contrast with a primary consideration for renal colic as a diagnosis. However, the CT instead demonstrated a 6 cm solid mass on the superior pole of the left kidney, consistent with primary RCC. Incidentally, multiple lung nodules were noted on the visualized portions of the lungs, which were suggestive of pulmonary metastases. Multiple low-attenuation liver lesions, diffuse abdominal adenopathy, and lytic lesions of the pelvis and spine were also seen, which represented additional sites of metastases. The patient was subsequently admitted to the hospital, and urology and oncology services were consulted. However, the patient declined rapidly and died of hypoxic respiratory failure secondary to the significant pulmonary metastasis while receiving hospice care.

Discussion of Metastatic Renal Cell Carcinoma

Epidemiology

There are approximately 80,000 new cases of RCC diag-

nosed in the US annually. RCC occurs twice as often in males and has an overall 18% mortality rate. The average age of diagnosis is between 65-74 years of age, though rarely seen in patients younger than 45.15 The risk factors with the clearest association for RCC include smoking, obesity, chronic kidney disease, hypertension, family history. Additionally, exposure to chemicals such as trichloroethylene and certain medications (eg, NSAIDs) may play a role in certain cases. 16

Genetic and Hereditary Risk Factors

RCC risk is influenced significantly by genetics as well as family or personal history of other kidney disease or RCC itself. Having a first-degree relative with a history of RCC is present in 2-4% of RCC cases. Additionally, genetic syndromes like von Hippel-Lindau syndrome, hereditary leiomyomatosis and renal cell cancer syndrome, Birt-Hogg-Dubé syndrome, polycystic kidney disease, and hereditary papillary renal cell carcinoma syndrome predispose patients to the disease.¹⁷

Clinical Manifestations

The classic triad of RCC presentation involves hematuria, flank pain, and a palpable abdominal mass, but this triad is only present in 9% of cases. Additionally, the presence of this triad suggests advanced disease. ¹⁸ Other clinical manifestations may include hypertension, fevers, unexplained weight loss, or night sweats, but these symptoms vary with the stage, location, and size of tumor. ¹⁹

Additionally, less common findings can offer clues to the diagnosis of RCC if detected. For example, scrotal varicoceles can occur in up to 11% of males with RCC due to the obstruction of the gonadal vein at the intersection with the renal vein. If the inferior vena cava is involved, it can lead to lower extremity swelling and pulmonary emboli.20 Paraneoplastic symptoms, due to ectopic production of hormones such as erythropoietin (EPO), parathyroid related peptide (PTHrP), gonadotropins, renin, can also occur.21 Anemia, when present, can be severe and will most often present as anemia of chronic disease.²¹ However, erythrocytosis can also be observed due to inappropriate EPO secretion which occurs in 1-5% of patients with advanced cancer.14 Hypercalcemia can result from a variety of mechanisms including lytic bone metastases, production of PTHrP, and increased synthesis of prostaglandins.

RCC will frequently have no symptoms in the early stages of the disease. In fact, RCC is often incidentally discovered during imaging studies done for other reasons. Incidental RCC discovery has increased over recent years due to the increased utilization of advanced imaging overall.²²

Evaluation

RCC may be considered in the differential of patients presenting with hematuria. In such cases, it is important to collect pertinent medical, social, and family history, including risk factors for RCC, such as smoking, chronic kidney disease, family history of kidney cancer, and previous exposure to radiation or industrial chemicals. The extent of hematuria and presence of back or flank pain, unintentional weight loss, and other constitutional symptoms can also be documented. Pertinent physical exam maneuvers include palpation of the abdomen and flanks for masses. An abdominal mass is an uncommon finding.²³

Common laboratory studies include screening CBC, CMP, and UA. Imaging studies which can be considered include CT, MRI, or ultrasound.

"RCC is often incidentally discovered during imaging studies done for other reasons."

Pathophysiology

RCC is characterized by dysplasia that originates in the lining of tubules within the kidney. These abnormal cells will form solid tumors that grow, invade nearby tissues and organs, and eventually metastasize. Under a microscope, RCC is characterized by the presence of clear, pale cells (clear cell RCC), which account for about 75-85% of all cases. Other less common subtypes of RCC include papillary (10-15%), chromophobe (5-10%), oncocytic (3-7%), and collecting duct (very rare).²⁴ Each subtype has distinct cellular and genetic features that can affect the prognosis and treatment of the disease. In addition to the tumor cells, the pathology of RCC may also involve changes in the surrounding kidney tissue, such as inflammation, fibrosis, and blood vessel abnormalities. These changes can contribute to the progression and spread of the tumor and may also affect the function of the kidney.

Treatment

The treatment of RCC depends on the cancer's stage, location and size of the tumor, and the overall health and functional status of the patient. The main treatment considerations include surgery, radiation, and cytotoxic chemotherapy and/or immunotherapeutic agents. Sur-

gery can be curative at an early stage, and a partial or radical nephrectomy is the first line treatment for RCC in early stages of disease.²⁵ It is preferred in patients with Stage I-III. Radiation can be used adjunctively to treat symptomatic patients or in Stage IV RCC. Targeted therapy can also be used in combination with immunotherapy or molecular therapy.

Screening

Screening for RCC is generally not recommended as it has not been shown to be effective in reducing mortality except in patients with risk factors such as a strong family history or high-risk genetic syndrome.²⁴ It is important to note, though, that these screening tests can yield false-positive results, leading to unnecessary diagnostic procedures and patient anxiety. A detailed and informative discussion about risks and benefits should occur in patients deemed at an increased risk.²⁵

Summary

- When patients present repeatedly for the same undifferentiated complaint, an expanded differential is critical. For back pain specifically, an expanded differential should include malignancy as well as other time sensitive diagnoses (eg, epidural compression syndrome, pancreatitis, or aortic pathology).
- Renal cell cancer may present with painless hematuria, back pain, unexplained anemia, and weight loss.
- Screening for RCC has not been shown to be effective in the general population, however, it is important to consider the presence of risk factors such as family history, smoking history, male gender, and occupational exposures when determining which patients may warrant additional evaluation.
- As is the case with most cancers, morbidity and mortality are reduced with earlier diagnosis, therefore, UC patients will be best served if UC clinicians keep RCC in their differential for patients with hematuria and/or back pain.

Ethics Statement

Informed consent was not obtained as patient had died in the interval time period. Identifying details have been modified to protect the patient's privacy.

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