CLINICAL CASE OF THE MONTH

A 52-Year-Old Man with Back Pain

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CASE REPORT

A 52-year-old Vietnamese man was transferred to our hospital for further evaluation and care of suspected spinal osteomyelitis. He presented to an outside hospital two days earlier with a complaint of lower back pain for two months. The pain was dull and non-radiating, had become progressively worse with movement, and was occurring more frequently, preventing him from getting dressed in the morning. He denied any weakness, urinary incontinence, numbness, or tingling in any extremities. He also denied subjective fevers, chills, or sick contacts. On review of systems, he endorsed night sweats and looser fitting clothes over the past year, as well as two recent episodes of small-volume hemoptysis.

The patient reported no past medical history prior to admission to the hospital. He smoked one-to-two packs of cigarettes daily for 20 years, drank two seven-ounce beers every morning, and reported a remote history of occasional cocaine and marijuana use with last use of either 30 years prior to admission. He moved to the U.S. 35 years prior to admission and traveled back to Vietnam every year, with his most recent trip being one year ago. Since his arrival to the U.S., he worked as a shrimper, lived alone, and was able to perform his own activities of daily living. He had no history of homelessness, incarceration, or known tuberculosis exposure. Family history was positive for cerebrovascular accidents in his mother, father, and brother. He denied any surgical history. He had not seen a physician in several years and was not up to date on vaccinations or health care maintenance.

At the time of presentation to our hospital, the patient had a temperature of 98.3 °F, blood pressure of 156/90 mmHg, pulse of 90 per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 95% on room air. No murmurs, rubs, or gallops were appreciated on cardiac auscultation. The lungs were clear to auscultation bilaterally. The abdomen was non-tender to palpation, without rebound or guarding, and normoactive bowel sounds were present. A Murphy's sign and splenomegaly were not appreciated. The L2 lumbar spine region was tender in both the paraspinal and midline areas, and tenderness was exacerbated with exertional movement. The patient rated the pain a 7/10 in severity. Neurological exam revealed no focal deficits, with normal strength and sensation reported in all extremities.

The patient's white cell blood count was 8,800 cells/uL (normal range 4,500-11,000 cells/uL) with a normal differential. The hemoglobin was low at 11.8gm/dL (13.5 – 17.5 gm/dL) as was the hematocrit at 35%/L (40-51%/L). The patient was slightly hypochloremic at 95 mmol/L (normal range 96-110 mmol/L). Total protein was within normal limits, with a slightly decreased albumin at 3.3 g/dL (normal range 3.4-5.0 g/dL). Total bilirubin, alkaline phosphatase, and transaminase levels were all within normal limits. Urinalysis was positive for 2+ hematuria.

Imaging and lab results from the outside hospital were reviewed. MRI of the lumbar spine with contrast revealed diffuse enhancement of L2 with compression fracture (Fig. 1 A & B), as well as left hydronephrosis (not shown). Bone scan showed increased uptake in L2 and in the distal left clavicle. Urine cultures obtained at the outside hospital had grown *Enterococcus faecalis*. Given these results, the patient was continued on vancomycin and ceftriaxone for suspected spinal osteomyelitis and urinary tract infection.

Further review of the outside medical record revealed a chest radiograph report indicating bilateral lung base masses, which had been biopsied with results that were pending at the time of transfer. Computerized tomography (CT) scan of the abdomen and pelvis performed at the outside hospital showed left renal pelvis thickening and multiple masses in the liver. Because

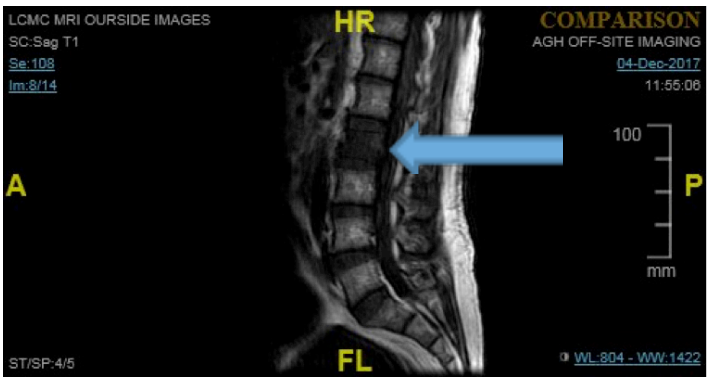

Figure 1A: T1 weighed MRI of lumbar spine from outside hospital revealing abnormality at L2

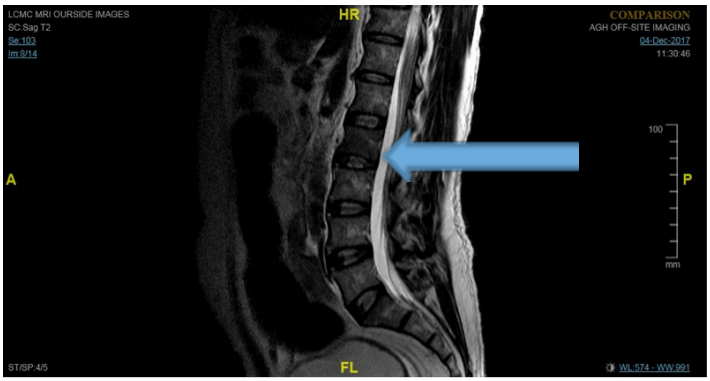

Figure 1B: T2 weighted MRI of lumbar spine from outside hospital revealing abnormality at L2

these additional findings were more suggestive of metastatic malignancy than infection, antibiotics were discontinued. Although suspicion for tuberculosis was low, evaluation for presence of tuberculosis in sputum was performed given the history of travel, weight loss, hemoptysis, and lung mass. This testing was negative. A CT scan of the chest to further evaluate the lung masses revealed a 3.8 cm right lower lobe pulmonary mass, additional pulmonary nodules, and an enlarged lower anterior mediastinal lymph node (Fig. 2). Although these findings appeared consistent with diffuse metastatic disease, a primary lung cancer with scattered metastatic sites could not be excluded. The initial lung mass biopsy results from the outside hospital became available and reported a suboptimal sample that contained necrotic tissue with clear cytoplasm suspicious for renal cell carcinoma.

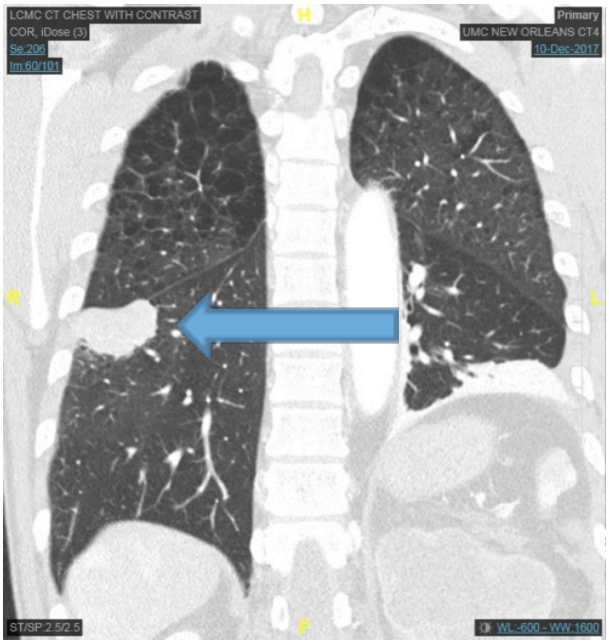

Figure 2: CT chest with contrast revealing mass within the right lung

An ultrasound of the kidneys and bladder revealed chronic severe left hydronephrosis with urothelial thickening in the left renal pelvis. Repeat CT scan of the abdomen and pelvis identified a possible urothelial malignancy. Follow-up CT urogram confirmed severe left-sided hydronephrosis with renal cortical thinning, suggestive of chronic obstruction, with an area suggestive of pathologic lymph nodes adjacent to the renal pelvis. Cystoscopy and ureteroscopy were performed, revealing a "Goblet sign" in the left distal ureter on retrograde pyelogram caused by a large papillary distal ureteral tumor (Fig. 3 A, B & C).[1] The tumor was biopsied, and noted to be a low grade, noninvasive papillary urothelial cell carcinoma.

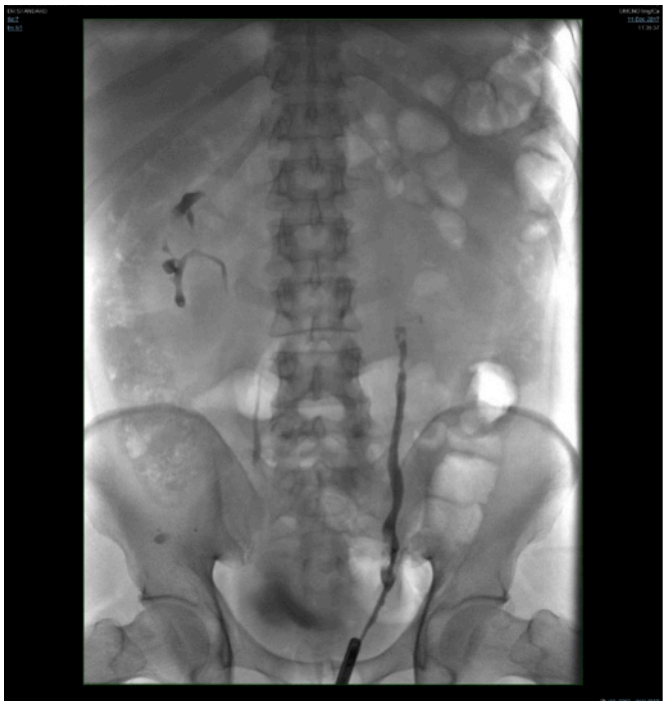

Figure 3A: Right ureteroscopy with normal findings

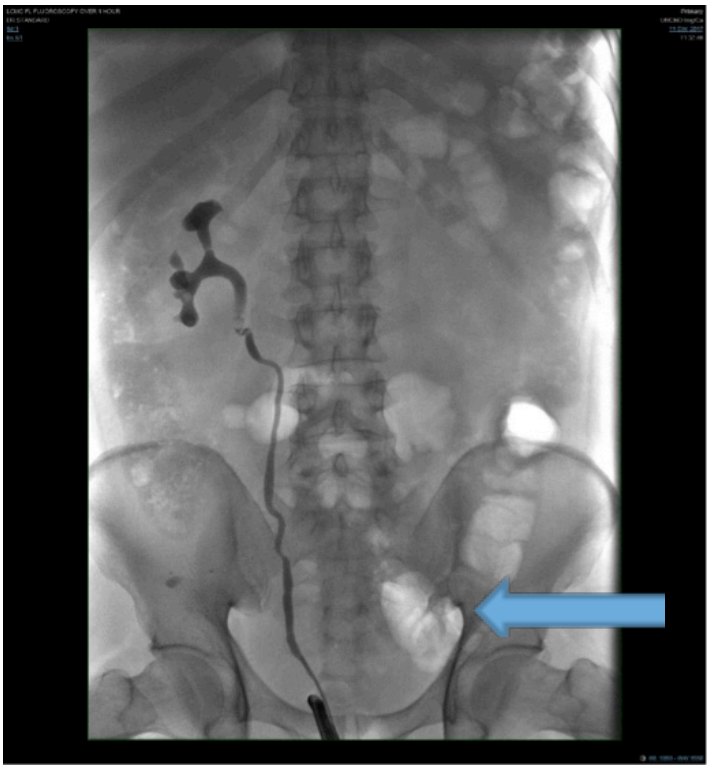

Figure 3B: Left lower ureteroscopy showing a "Goblet sign," or a cup-shaped dilated ureter classically associated with obstruction from urothelial cell carcinoma[1]

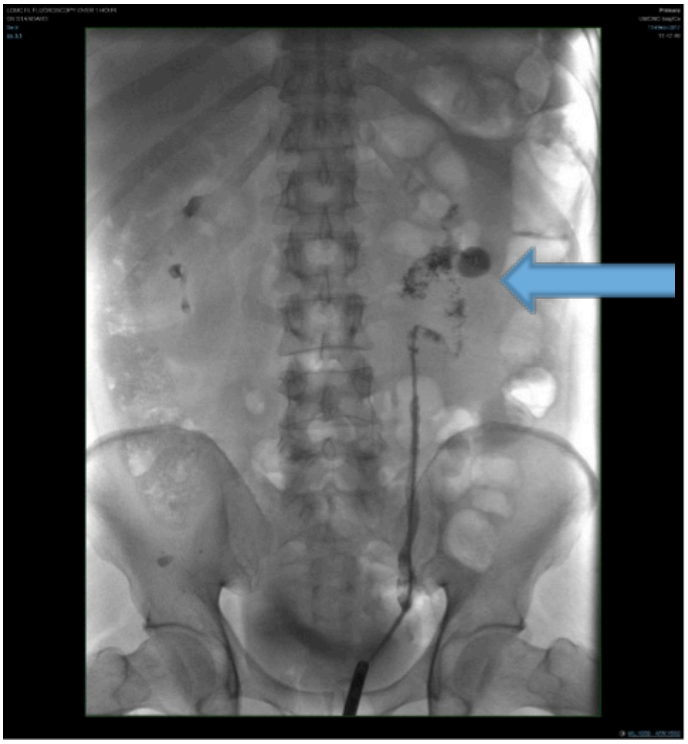

Figure 3C: Left upper ureteroscopy with evidence of renal pelvic mass

DISCUSSION

Back pain is a common presenting complaint. Investigating back pain in an individual such as our patient, who had not accessed the healthcare system in several years and had little known about his overall health, can be especially challenging. In this case, the patient's back pain was caused by metastatic cancer. The upper tract ureteral mass biopsy results were reported as a low grade, noninvasive urothelial cell carcinoma and the lung mass biopsy results were suspicious for clear cell type renal cell carcinoma, suggestive of two primary malignancies within the urinary tract. Synchronous urothelial cell carcinoma and renal cell carcinoma have been rarely reported, with about fifty cases of synchronous renal tumors documented in the literature.[2]

Urothelial cell carcinoma, also known as transitional cell carcinoma, includes cancers of the bladder, urethra, ureter, and pyelocaliceal cavities. Although it most commonly occurs in the bladder (90-95%), 5-10% present like in our patient as upper tract urothelial carcinomas. Upper tract urothelial carcinomas are more likely to be invasive at diagnosis (60% vs. 15-25% of bladder tumors), and are most likely to be found in male smokers aged 70-90 years of age.[3] The most common feature of upper tract urothelial carcinoma is microscopic hematuria (70-80%), although less common features include flank pain (20%) and lumbar mass (10%). Hydronephrosis and systemic symptoms are both associated with poorer outcomes.[3] CT urography is the preferred imaging modality because it has the highest diagnostic accuracy (0.67-1.0 sensitivity, 0.93-0.99 specificity) and should be the noninvasive imaging test of choice to assist in the diagnosis of upper tract urothelial cell carcinoma.[3,4]

Renal cell carcinoma accounts for the majority of kidney malignancies, with clear cell being the most common type in 80% of cases.[2,5] The classic triad of hematuria, abdominal mass, and flank pain occurs in less than 20% of patients diagnosed with renal cell carcinoma. The five-year survival rate with metastatic disease is 10%, and median survival is only eight months.[2,5] Similar to urothelial cell carcinoma, smoking tobacco is also associated with an increased risk of renal cell carcinoma. Genetic factors and an elevated BMI are other risk factors.[5]

In 2017, there were 3,630 new cases of cancer of the ureter or other urinary organs and 63,990 new cases of cancer of the kidney and renal pelvis.[6] Data from the Surveillance, Epidemiology, and End Results (SEER) database included 13,800 cases of upper-tract urothelial carcinoma from 1973-2005 and demonstrated an increase in incidence from 1.88-2.06 cases per 100,000 person-years with a relative increase in ureteral cancer (0.69-0.91) and a relative decrease in renal pelvic disease (1.19-1.15). Increasing age of the patient, metastatic disease, male gender, black race, and bilateral upper-tract urothelial carcinoma are all associated with decreased survival. Although improved imaging modalities have led to earlier diagnosis, over 40% of patients still present with metastatic disease.[7]

Two mechanisms have been proposed to describe the origin of urinary tract cancers. In the monoclonality hypothesis, a single

cell spreads throughout urothelial tract; in the field cancerization hypothesis, carcinogen exposure of the urothelial tract causes independent development of tumors at different cellular sites.[8] The field cancerization theory supports the development of synchronous or metachronous tumors at various sites. Tumors are considered synchronous if the interval between their discovery is less than or equal to six months and metachronous if the interval is more than six months.[9] Recently, there has been an increase in diagnosis of synchronous tumors, particularly in the genitourinary tract.2 Because our patient had not seen a physician in several years and had not had any previous imaging, it is unknown which tumor came first and the time interval between the two types of cancer that were diagnosed.

Because the patient's bone and liver metastases were not biopsied, it is unclear whether they resulted from an invasive urothelial cell carcinoma upstream of the ureteral biopsy, from renal cell carcinoma, or from another primary origin. Liver, lungs, and bone are three of the most common metastatic sites of urothelial carcinoma, and are three sites of metastasis in our patient.[10] Our patient had experienced two recent episodes of hemoptysis prior to discovery of his lung masses. Pulmonary symptoms of metastatic disease associated with urothelial cell carcinoma are primarily due to a cavitary lesion, pleural effusion, chylothorax, or endobronchial, pleural, or lymph node metastasis. Urothelial cell carcinoma frequently spreads through regional lymphatics, providing a route to the pulmonary system and causing symptoms such as cough, dyspnea, or hemoptysis.[11] Although bone metastases are usually associated with lung, prostate, and breast cancers, urothelial carcinomas are responsible for 4% of these and the spine remains its most common metastatic site outside of the pelvis.[10,12] Similarly, renal cell carcinoma frequently metastasizes to the lungs, bone, and liver, with lungs being the most common site.[13,14] However, one study found that 32% of patients with metastatic renal cell carcinoma developed bone metastases.[15] Bone metastases are mostly osteolytic and can cause fractures, which may require radiotherapy or surgical intervention.[13]

This case report reinforces the importance of conducting a thorough history, physical exam, and imaging work-up without anchoring on a previously made diagnosis. The patient was transferred with a primary diagnosis of spinal osteomyelitis accompanied by a lung mass, hydronephrosis, and urinary tract infection; this constellation of problems eventually proved to be related to metastatic cancer. This case also illustrates that patients who have not been medically evaluated for several years may have additional undiagnosed diseases and disorders. Lastly, although rare, patients can present with two distinct malignancies. Careful evaluation of symptomology, epidemiology, and biopsy results are necessary in order to determine the correct diagnoses.

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