Renal Cell Carcinoma Presenting as Pleural Effusion

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ABSTRACT

Renal cell carcinoma is well-known for its propensity to present in unusual ways, and renal cell carcinoma presenting as pleural effusion is extremely rare. Pleural effusion secondary to renal cell carcinoma constitutes only about 1% to 2% of all malignant pleural effusions. We report the case of a 34-year-old man with no significant past medical or surgical history who presented in the Emergency Department with dyspnea. Chest x-ray demonstrated right-sided pleural effusion; computed tomography (CT) reported right-sided effusion in the pleura with suspicious mass in the upper border of left kidney. CT-guided pleural tap was performed and cytology was positive for vimentin and common acute lymphocytic leukemia antigen (CD10), leading to the diagnosis of primary renal cell carcinoma presenting as unilateral pleural effusion. While lungs are the common site of metastasis, the presentation of renal cell carcinoma as pleural effusion or pleural metastasis without lung involvement is rare.

INTRODUCTION

There are several systemic and pulmonary disorders that can lead to pleural effusion. Pleural effusion can also develop secondary to underlying malignancy of solid organs such as breast and lung.[1] The involvement of pleura in renal cell carcinoma is not very common; it has been reported in about 12% of the autopsies of patients with metastatic renal cell carcinoma, even though the lung is one of the most common sites of metastasis.[1] However, the presentation of renal cell carcinoma as pleural effusion is uncommon and little is reported in the literature. Metastasis to the pleura, along with pleural effusion, is a late event in the course of malignancy.[1]

Renal cell carcinoma may spread by direct invasion, lymphogenous spread, or direct hematonegenous dissemination.[1] The exact mechanism of pleural metastases or the development of pleural effusion is not known; however, the mechanism is thought to be via lymphatics or through vertical plexus of veins.[1]

Expected 5-year survival of a person with renal cell carcinoma in Stage I is as high as 95%.[1] However, patients who develop metastatic disease have a 5-year survival rate of only 29% to 54%, if metastases are resectable.[1]

Renal cancers have been called "the internist's tumor" and are among the great mimics in medicine because they present with systemic symptoms unrelated to the kidney cancer, such as hypertension (secondary to elevated renin levels),[2] hypercalcemia (PTHrP), polycythemia (erythropoietin), eosinophilia, leukemoid reactions, Cushing's syndrome (ACTH), fever or wasting syndromes, and Stauffer's syndrome (reversible hepatic dysfunction after primary tumor removal).[2]

CASE PRESENTATION

A 35-year-old man with recently diagnosed hypertension presented to our Emergency Department with the symptoms of fever, cough, chills, chest pain, and shortness of breath worsening with any position except when leaning forward. He was last observed to be asymptomatic 4 weeks prior. Hypertension was diagnosed

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Figure 1. Complex Cystic Mass on the Upper Pole of Left Kidney, Measuring 7.9 x 7.0 cm

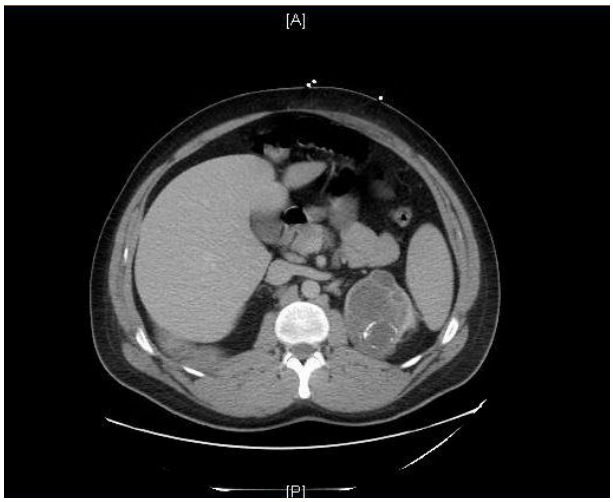
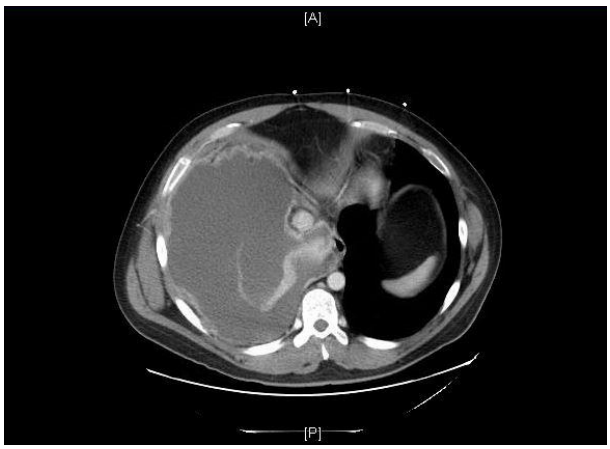


Figure 2. Computed Tomographic Scan of Chest Showing Right-Side Pleural Effusion Along With Generalized Thickening of Right Pleural Reflections



about 3 months prior at the primary care clinic. He had no significant past medical, surgical, or family history. There was no history of cigarette smoking or use of alcohol or illicit drugs.

The patient described a 4-week history of progressively worsening right-sided chest discomfort, along with shortness of breath and some productive cough with yellowish sputum. He denied having any pulmonary symptoms, and did not complain of any headache, dizziness, lightheadedness, chest or abdominal pain, bowel or bladder symptoms, loss of consciousness, or recent trauma.

On physical examination, he was febrile and toxic looking, with low grade fever of 99.2º F and tachycardia. Chest examination revealed dullness of right-sided chest wall upon percussion and reduced breath sounds at the right lung base on auscultation, negative for rales or wheezing. Complete blood count, comprehensive metabolic panel, and prothrombin time/international normalized ratio were all unremarkable. Chest X-ray reported subpulmonic pleural effusion with mild atelectasis of the right lung and elevation of right hemidiaphragm. At this point, several differentials were taken into consideration, including infectious etiology (parapneumonic effusion, empyema), trauma (chylothorax), and possible underlying malignancy (lymphoma, bronchogenic carcinoma).

Computed tomographic (CT) scan of the chest showed right-sided pleural effusion with generalized thickening of right pleural reflections, along with atelectasis of the right middle lobe and right lower lobe. Interestingly, a complex cystic mass on the upper pole of left kidney was found on the last slice of chest CT, measuring 7.9 x 7.0 cm in size (Figure 1).

The patient's initial clinical presentation was highly suspicious of an underlying infection, and he was admitted to the hospital. Initial management was started with empirical intravenous antibiotics. However, the chest CT reporting large pleural effusion and suspicious cystic renal mass guided attention towards malignancy (Figure 2). The patient underwent diagnostic thoracentesis, and about 2,800 ml of serosanguinous fluid was removed. Pleural fluid pathology reported reactive-appearing mesothelial cells. These atypical cells were checked for multiple tumor markers and were found positive for Vimentin and CD10, raising the suspicion of renal cell carcinoma. CT abdomen and pelvis showed a separate mass on the upper pole of left kidney with negative lymph nodes, leading to the diagnosis of stage IV renal cell carcinoma (T2a, N0, M1). The patient's recently diagnosed hypertension may also have been related to the underlying renal cell carcinoma not picked up earlier.

Cancer management was started with surgical removal of the tumor, leading to left-sided nephrectomy with negative margins. Most patients with advanced renal cell carcinoma (metastatic) are treated with molecular targeted therapies, including agents directed at the molecular target of rapamycin (mTOR) pathway (temsirolimus) or vascular endothelial growth factor receptor inhibitors (sunitinib, bevacizumab).[3]

After the surgical treatment, chemotherapy options were discussed with the patient. He refused high-dose interleukin-2 therapy due to side-effect profile but agreed on temsirolimus. He showed minimum response to the treatment regimen and continued to develop recurrent right-sided pleural effusions managed by right thoracoscopy. Pleural biopsy proved parietal pleura neoplasm consistent with renal cell carcinoma. Chemical pleurodesis was later done for the recurrent pleural effusions. High-dose interleukin-2 therapy was started, but the tumor showed increased growth after 2 rounds of interleukin-2 therapy. Axitinib, a tyrosine kinase inhibitor, was started. The tumor advanced rapidly, and CT chest reported extensive intrathoracic neoplasm, with massive extrathoracic tumor extending around the posterior thorax. Radiation therapy was given to the chest wall. Unfortunately, the patient's health deteriorated and he expired few days later.

DISCUSSION

While lung is the most common metastatic site for renal cell carcinoma, metastasis solely to the pleura without the involvement of lung parenchyma is very rare.[2] There are only few (about 4-5) case reports published to date that document the pleural metastasis as initial presentation of renal cell carcinoma. Most of these cases have been reported from Europe and Japan. A study by Ohnishi et al, documents a case of a 66-year-old man who presented with dyspnea and was found to have multiple mesothelioma-like pleural masses along with effusion in the left pleural space.[4] There were no pulmonary lesions.[4] Tumor markers from pleural effusion came back positive for cytokeratinin-19. Abdominal CT reported renal cell carcinoma mass in right kidney. The patient was treated with pleurodesis and right-sided nephrectomy. Pleural lesions showed dramatic improvement after nephrectomy.[4] Our case, however, differs in terms of resolution of the pleural tumors. Although our patient remained adherent to the treatment course and tolerated his treatment well, he did not show any response to chemotherapy, immunotherapy, or pleurodesis. Other case reports by Taylor et al,[5] Kataoka et al,[6] and Chow and Eckhardt,[7] have reported the case of metastatic renal cell carcinoma with similar presentation, that of worsening dyspnea and fatigue.

Renal cell carcinoma accounts for 90% to 95% of malignant neoplasms arising from the kidney.[2] The classic triad of hematuria, abdominal pain, and a palpable mass is present in ≤10% of cases.[2,4,8] While the lungs are the most common sites of metastasis, the presentation of renal cell carcinoma as pleural effusion is very rare. Pleural effusion secondary to renal cell carcinoma constitutes only 1% to 2% of all the malignant pleural effusions.[6] In most of the cases, pleural effusion is found in the diagnosed cases of renal cell carcinoma.[5] Our case, however, is unique because pleural effusion was the initial presentation of the renal cell carcinoma. Other uncommon presentations include cutaneous metastases in the form of scalp skin nodules, demyelinating neuropathy, numb-chin syndrome, and panhypopituitarism.[9]

Renal cell carcinoma often metastasizes to lung parenchyma. Pleural metastases have been described but are commonly secondary to underlying pulmonary metastases. One study reported about 12% of 1,451 patients with renal carcinoma had pleural metastases at autopsy, but no single patient had isolated pleural metastasis.[6,10]

CONCLUSIONS

The presentation of renal cell carcinoma as pleural effusion and isolated pleural metastasis without the involvement of lung parenchyma is very rare. It is important to keep the differentials broad in patients with unilateral pleural effusion. Newly diagnosed hypertension in younger patients also requires closer follow-up and thorough workup to elucidate the cause of elevated blood pressure.

Acknowledgements: Ethical approval for this case report was obtained from the institutional review board. The patient is deceased and family was not reachable.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. Hofmann HS, Neef H, Krohe K, Andreev P, Silber RE. Prognostic factors and survival after pulmonary resection of metastatic renal cell carcinoma. *Eur Urol.* 2005;48(1):77-81. doi:10.1016/j.eururo.2005.03.004

2. Kiely JM. Hypernephroma – the internist's tumor. *Med Clin North Am.* 1966;50(4):1067-1083.

3. Agarwal A, Sahni S, Iftikhar A, Talwar A. Pulmonary manifestations of renal cell carcinoma. *Respir Med.* 2015;109(12):1505-1508. doi:10.1016/j.rmed.2015.10.002

4. Ohnishi H, Abe M, Hamada H, et al. Metastatic renal cell carcinoma presenting as multiple plural tumours. *Respirology.* 2005;10(1):128-131. doi:10.1111/j.1440-1843.2005.00652.x

5. Taylor DR, Page W, Hughes D, Varghese G. Metastatic renal cell carcinoma mimicking pleural mesothelioma. *Thorax.* 1987;42(11):901-902.

6. Kataoka M, Yata Y, Nose S, Yasuda K, Ohara T. Solitary pleural metastasis from renal cell carcinoma: a case of successful resection. *Surg Case Rep.* 2015;1(1):36. doi:10.1186/s40792-015-0039-z

7. Chow L, Eckhardt S. Sunitinib: from rational design to clinical efficacy. *J Clin Oncol.* 2007;25(7):884–896.

8. Renshaw AA, Richie JP. Subtypes of renal cell carcinoma. Different onset and sites of metastatic disease. *Am J Clin Pathol.* 1999;111(4):539-543.

9. Gharabaghi MA. Clinical Spectrum of Patients with Renal Cell Carcinoma. In: Amato RJ, ed. Emerging Research and Treatments in Renal Cell Carcinoma. Iran: InTechOpen; 2012:229-244. https://www.intechopen.com/books/emerging-research-and-treatments-in-renal-cell-carcinoma/clinical-spectrum-of-patients-with-renal-cell-carcinoma. Accessed October 23, 2018.

10. Saitoh H. Distant metastasis of renal adenocarcinoma. *Cancer.* 1981;48(6):1487-1491.

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