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CASE REPORT

Pleural cavitations and pneumothorax following axitinib therapy in metastatic renal cell carcinoma: A case report

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Abstract

Background: Tumor cavitation and pneumothorax are uncommon yet serious complications of antiangiogenic therapies. These risks are particularly significant in patients with metastatic renal cell carcinoma (mRCC). Axitinib, a selective inhibitor of vascular endothelial growth factor receptors (VEGFRs), is generally used as a second-line treatment for mRCC. However, rare cases of lung metastases with cavitary lesions and pneumothorax have been reported after the use of axitinib. Therefore, we decided to report one of these rare cases.

Case presentation: A 46-year-old male with mRCC developed pleural cavitations and secondary pneumothorax after starting axitinib therapy. Despite intensive management, his condition worsened with recurrent pneumothorax, ultimately leading to sepsis and multiorgan failure.

Conclusion: This case underscores the potential risks of tumor cavitation-induced pneumothorax in patients receiving axitinib. Close radiological monitoring and timely intervention are essential for reducing morbidity and mortality in such cases. Clinicians should remain vigilant for this rare but serious complication during axitinib therapy.

KEYWORDS

renal cell carcinoma, lung metastasis, axitinib, cavitation, pneumothorax

INTRODUCTION

Renal cell carcinoma (RCC) originates in the renal cortex and accounts for 80%–85% of primary kidney tumors. Classic symptoms include flank pain, blood in the urine, and an abdominal mass [1]. Advances in systemic therapies have improved patient outcomes; however, metastatic disease remains a significant challenge [2].

RCC most commonly spreads to the lungs, affecting 50%–60% of cases [3]. It typically presents as solitary or multiple lung nodules, which can be misdiagnosed as primary lung tumors [4]. Metastases may involve the lung parenchyma, pleura, or even the endobronchial region [5, 6].

Axitinib, a selective inhibitor of vascular endothelial growth factor receptor (VEGFR)–1, –2, and –3, has shown promising efficacy in metastatic renal cell carcinoma (mRCC) treatment [7, 8]. By disrupting angiogenesis, it slows growth and progression of the tumor. However, this mechanism can also induce tumor necrosis, leading to cavitation and an increased risk of pneumothorax [9].

Pulmonary metastases from RCC can present in various forms, including nodular lesions, pleural involvement, and endobronchial spread [10]. Although pleural metastases are rare, cases without accompanying lung involvement have been reported [11, 12]. In some instances, pleural metastases develop years

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after nephrectomy, highlighting the unpredictable nature of RCC progression [13].

Recognizing and monitoring pulmonary complications in patients receiving VEGFR inhibitors is critical [14]. This case illustrates the risks of tumor cavitation and pneumothorax associated with axitinib therapy.

TABLE 1 Timeline of clinical events and treatment steps.

Date	Events
03/2019	Diagnosed with right RCC during routine hypertension screening
05/2019	Underwent right nephrectomy
08/2020	Lung metastases detected
09/2020	Pazopanib initiated
02/2021	Disease progressed; switched to nivolumab
04/2021	Received 12-day radiotherapy to the lungs
26/04/2021	Last dose of nivolumab (4th cycle)
14/05/2021	Thorax computed tomography (CT): infection and radiotherapy-induced changes, ground-glass opacities, and multiple pleural metastases

CASE PRESENTATION

A 46-year-old male, working as an electrician, had a history of hypertension. He was married, and his spouse assisted in his care. In May 2019, he was diagnosed with a right renal mass and underwent radical nephrectomy. Pathological examination confirmed clear cell RCC, with an early-stage classification.

By August 2020, routine imaging revealed multiple bilateral lung metastases. Pazopanib was initiated but failed to control disease progression. As a result, nivolumab was started in February 2021 (Table 1). However, new metastases based on the pleura were detected in April 2021, leading to a switch to axitinib (5 mg twice daily (BID)).

In July 2021, he presented to the emergency department with acute dyspnea, pleuritic chest pain, and fatigue. On examination, he had decreased breath sounds and reduced chest expansion on the right side. Oxygen saturation was mildly reduced, and laboratory tests showed elevated white blood cell counts, indicating inflammation. A chest X-ray examination revealed bilateral pneumothorax with cavitated lung metastases (Figure 1).

The patient was admitted and started on broad-spectrum intravenous antibiotics due to suspected

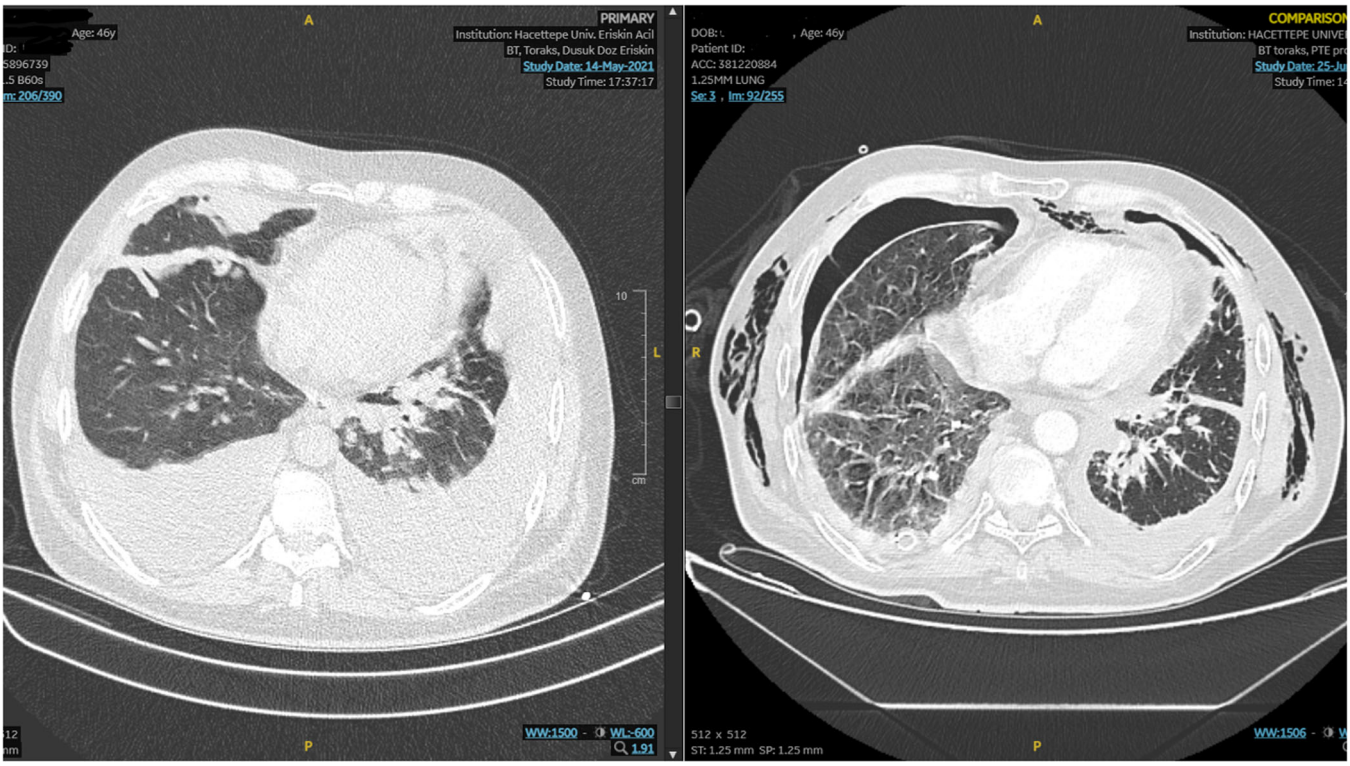

FIGURE 1 Bilateral pleural metastases predominantly seen on the right lung before axitinib treatment (left) and pneumothorax developing following cavitation of metastatic areas in response to axitinib treatment (right).

infection. A chest tube was inserted, relieving symptoms initially. However, pneumothorax recurred a week later, necessitating prolonged drainage. Imaging confirmed extensive tumor necrosis with cavitation. Over the following weeks, he developed sepsis and multiorgan failure, leading to his passing 1 month later.

DISCUSSION

Tumor cavitation due to antiangiogenic therapy is a recognized but often neglected phenomenon. VEGFR inhibitors, including axitinib, promote tumor necrosis by reducing vascular supply, which may lead to cavitation [9]. This structural weakening of metastatic lesions, especially near the pleura, predisposes patients to spontaneous pneumothorax [9, 15].

Several reports have documented the link between VEGFR inhibitors and pneumothorax [11]. In one case, a 56-year-old male on axitinib developed recurrent pneumothorax due to cavitated lung metastases [9]. Additionally, a case reported a patient with mRCC and pulmonary nodules who developed bilateral secondary spontaneous pneumothorax during sunitinib treatment [16]. Similarly, osimertinib, another tyrosine kinase inhibitor (TKI), has been associated with severe bilateral pneumothorax in lung cancer patients [17].

Pleural metastases from RCC are rare but clinically significant [11, 12]. Unlike parenchymal lung metastases, pleural involvement often manifests with effusions and nodular thickening, mimicking mesothelioma [13]. Some researchers propose that RCC metastasizes to the pleura via hematogenous spread, bypassing lung involvement [11].

Managing these complications requires a multifaceted approach. Clinicians should exercise caution when prescribing VEGFR inhibitors for patients with subpleural metastases. Early detection through serial imaging and timely intervention can help mitigate adverse events. In some cases, dose adjustments or switching to alternative therapies may be necessary [18].

CONCLUSION

Axitinib is an effective second-line therapy for mRCC, but it poses a risk of tumor cavitation and pneumothorax. This case emphasizes the importance of proactive monitoring and prompt management of pulmonary complications. Future research should explore predictive markers to identify patients at higher risk for cavitation-related adverse events.

AUTHOR CONTRIBUTIONS

Feride Yılmaz: Conceptualization; methodology; writing original draft. **Serkan Yaşar**, **Figen Demirkazık**, **Zafer Arık:** Investigation; writing original draft. **Mustafa Erman:** Supervision; project administration; writing original draft. All authors approved the final manuscript.

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The authors have nothing to report.

CONFLICTS OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Ethical approval was not required for this study in accordance with local and national guidelines. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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