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Between a rock and a hard place: Papillary renal cell carcinoma with synchronous lung adenocarcinoma

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Abstract

The simultaneous occurrence of two carcinoma is unusual and pose significant diagnostic and therapeutic challenges in differentiating a secondary lung malignancy from metastatic RCC. A 55-year-old male was diagnosed with Type 1 papillary RCC and underwent nephron-sparing surgery for a localized left renal tumor. On postoperative surveillance, a solitary right upper lobe lung nodule was detected. Histopathological evaluation of the lung lesion initially suggested metastatic RCC; however, immunohistochemistry (IHC) confirmed a separate primary lung adenocarcinoma (thyroid transcription factor-1 (TTF-1) positive, PAX8 negative) harboring *EGFR* mutations. The patient's RCC was organ-confined (pT1a) and managed surgically, while the lung adenocarcinoma was treated with targeted *EGFR* tyrosine kinase inhibitor therapy (Osimertinib). Radiologically and clinically, metastatic RCC can mimic a new primary lung cancer and vice versa, necessitating tissue diagnosis for accurate classification. IHC and molecular profiling were pivotal in distinguishing the two malignancies, directly influencing treatment choices. The RCC's favorable features (papillary Type 1, low grade, negative margins) portended an excellent prognosis with surgery alone, whereas identification of an actionable mutation in the lung adenocarcinoma enabled personalized systemic therapy. We discuss the rarity of synchronous RCC and lung cancer, the need for vigilance in such presentations, and provide a comparative overview of features differentiating metastatic RCC from primary lung adenocarcinoma.

Introduction

Renal cell carcinoma (RCC) accounts for roughly 3–5% of adult malignancies, with the lungs being the most frequent metastatic site.[1] The development of a second

primary lung cancer in an RCC patient, however, is exceedingly rare. Multiple primary malignant neoplasms (MPMNs) are defined as two or more distinct malignancies in the same individual and comprise fewer than 4% of all cancer cases.[2] If diagnoses occur simultaneously or within six months, they are considered synchronous cancers, whereas those arising sequentially are termed metachronous.[2]

The occurrence of RCC alongside a primary lung adenocarcinoma epitomizes the diagnostic dilemma of differentiating metastatic disease from a second primary tumor. Overlapping clinical and radiological features may blur the distinction.[3] Correct identification as a synchronous primary is crucial, as it fundamentally alters staging, prognosis, and treatment strategy.[3]

Case Report

A 55-year-old man presented with lower urinary tract symptoms of one month's duration. CT scan (May 2024) revealed a Bosniak category 4 solid-cystic lesion in the left kidney, a Bosniak category 1 cyst in the right kidney, prostatomegaly, and cystitis. Serum PSA was 6.99 ng/mL.

He underwent robot-assisted nephron-sparing surgery in May 2024. Pathology confirmed papillary RCC, Type 1, pT1a (2.5 cm, WHO/ISUP Grade 2). Margins were clear. IHC: CK7 and AMACR positive; CA-IX and 2SC negative; FH retained.

Follow-up chest CT (September 2024) showed a solitary 1.2 cm right upper lobe nodule. Biopsy revealed acinar carcinoma morphology. IHC: TTF-1 and napsin A positive, PAX8 and AMACR negative – confirming primary lung adenocarcinoma.

Molecular testing detected two sensitizing *EGFR* mutations (p.E709A, p.G719C) and CDKN2A loss. No RCC-specific mutations were seen.

At the multidisciplinary tumor board, RCC was deemed cured by surgery. Lung adenocarcinoma management was systemic therapy with Osimertinib (80 mg daily). After two months, the patient remains stable with no evidence of progression.

Discussion

This case demonstrates the complexity of distinguishing RCC metastasis vs synchronous lung cancer. Misclassification can lead to inappropriate therapy. RCC frequently metastasizes to the lung, but synchronous lung cancer, while rare, is well-documented.[4] (**Table 1**)

1. **Radiology:** Primary lung cancers are more likely spiculated; metastases are usually round/smooth. One study found spiculated margins in 47% of lung primaries vs ~5% of solitary metastases.[5]
2. **Pathology/IHC:** RCC metastases typically express PAX8, while lung adenocarcinomas are TTF-1/NapsinA positive.[3]
3. In our patient, actionable *EGFR* mutations permitted targeted therapy with Osimertinib. This agent has excellent CNS penetration and efficacy even in uncommon EGFR variants.[6]
4. **Rarity:** RCC patients have a 40% increased long-term risk of secondary malignancies, lung cancer among the most frequent.[7] Synchronous second primaries occur in ~3–6% of RCC cases.[8] Other reported associations include RCC with thyroid[4], squamous lung carcinoma, and prostate cancer.

Table 1: Distinguishing features of metastatic RCC vs primary lung adenocarcinoma

Feature	Metastatic RCC to Lung	Primary Lung Adenocarcinoma
Imaging	Multiple/round nodules	Often solitary; spiculated
Histology	RCC morphology	Acinar/papillary, mucin
IHC	PAX8+, AMACR+	TTF-1+, napsin A+
Molecular	RCC-specific (VHL, MET)	Lung drivers (*EGFR*, *KRAS*)
Management	RCC systemic therapy	NSCLC-specific therapy

This underscores the necessity of a multidisciplinary, individualized approach in managing such rare dual malignancies.

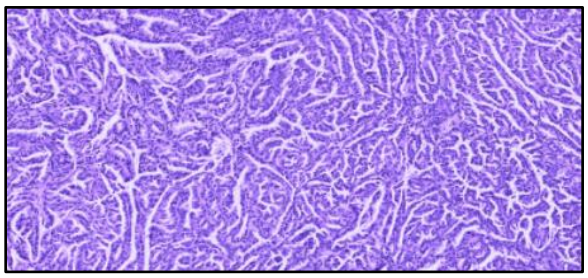

Figure 1: Renal histopathology

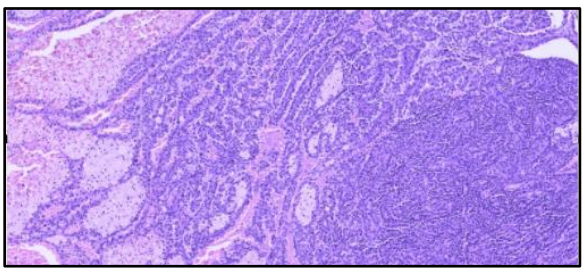

Figure 2; Lung biopsy

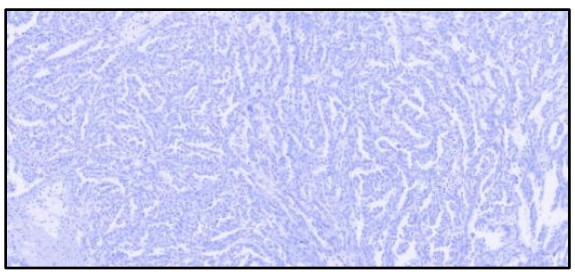

Figure 3: Pleural cytology

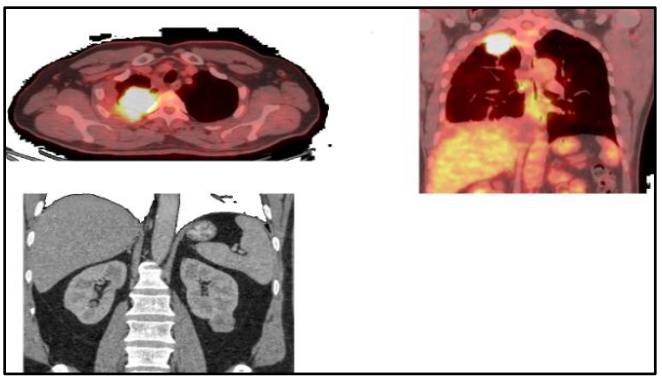

Figure 4: PETCT

Conclusion

The synchronous occurrence of papillary RCC and lung adenocarcinoma is rare but clinically significant. Careful histopathological and molecular evaluation is essential to avoid misclassification as metastasis. In this case, accurate diagnosis enabled curative RCC surgery and targeted lung cancer therapy, exemplifying the impact of precision oncology. Vigilance in follow-up is crucial, given the elevated risk of second primaries in RCC survivors.

Abbreviations: RCC – Renal Cell Carcinoma; IHC – Immunohistochemistry; EGFR – Epidermal Growth Factor Receptor; NSS – Nephron-Sparing Surgery; NSCLC – Non-Small Cell Lung Cancer

Source of Funding

None.

Conflict of Interest

None.

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