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REVIEWER'S REPORT

Manuscript No.: IJAR-57834

Title: Renal metastasis of bronchial squamous cell carcinoma

Recommendation:
Accept after minor revision

Rating	Excel.	Good	Fair	Poor
Originality		✔,		
Techn. Quality		✔,		
Clarity	✔,			
Significance	✔,			

Reviewer Name: Abdul Haseeb Mir

Detailed Reviewer's Report

The manuscript titled **"Renal metastasis of bronchial squamous cell carcinoma"** documents a clinically significant and unusual case of secondary renal involvement stemming from primary non-small cell lung cancer (NSCLC). While the kidney represents the fifth most common site for distant malignant metastases in the human body, clinically diagnosed cases remain notably rare due to their characteristically asymptomatic presentation during early stages.

The scope of this case report details the diagnostic timeline and therapeutic management of a 62-year-old male patient, a chronic smoker with a 35 pack-year history, who initially presented with a multi-month history of dry cough and systemic decline. The clinical course was uniquely marked by the subsequent onset of gross hematuria and lower back pain, which prompted an expansive diagnostic evaluation that ultimately uncovered a widespread, advanced stage of malignancy.

The diagnostic investigation outlined in the study highlights the critical integration of multi-modal radiologic imaging and histopathological analysis:

- **Radiological Findings:** Initial chest radiographs demonstrated right lower lobe basithoracic atelectasis. A subsequent chest computed tomography (CT) scan revealed a significant right mediastinal-pulmonary mass accompanied by background emphysema. Cross-sectional abdominal-pelvic CT imaging identified a contrast-enhancing left renal mass along with secondary hepatic nodules, establishing multi-organ involvement.
- **Bronchial Biopsy and Profiling:** Direct bronchoscopy revealed a distinct necrotic nodule at the entrance of the right lower lobe bronchus. Pathological examination confirmed squamous cell

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carcinoma. This was corroborated by an immunohistochemical (IHC) profile showing positive nuclear staining for $p40$ and negative expression for Thyroid Transcription Factor-1 ($TTF\text{-}1$).

- **Renal Biopsy and Metatastic Confirmation:** An ultrasound-guided biopsy of the left renal mass was performed to differentiate between a primary renal cell carcinoma and a secondary lesion. The IHC analysis of the renal tissue demonstrated positive expression for $GATA3$, $p63$, $p40$, $PAX8$, and $CD10$, while remaining negative for Cytokeratin 20 ($CK20$) and Cytokeratin 7 ($CK7$), successfully confirming an epidermoid bronchial origin.

The discussion section provides an analytical overview of solitary versus widespread renal metastatic disease. Autopsy series suggest a subclinical incidence of renal metastases ranging from 2.36% to 12.6% in terminal malignancies. However, the paper notes that when an isolated renal lesion is identified, the primary underlying source is most frequently located in the lungs, followed by the colorectum, breast, soft tissues, and thyroid gland.

The core scholarly contribution of this manuscript lies in its clear demonstration of the potential overlap in IHC markers during complex oncological staging. Specifically, the positive expression of renal-associated transcription factors (such as $PAX8$ and $CD10$) inside a biopsy that simultaneously expresses classic squamous markers ($p40$ and $p63$) underscores the absolute necessity of using comprehensive staining panels. Because distinguishing primary renal tumors from atypical metastases is difficult using radiology alone, this case emphasizes utilizing extensive tissue profiling to prevent misdiagnosis and avoid unnecessary nephrectomies in a disseminated disease setting.

Suggestions for Improvement

- **Organize the Narrative Framework with Standard Academic Headings:** The main text should be structured using standard, clear subheadings to improve overall scannability. Divide the manuscript into clear sections, such as **"Introduction," "Case Description," "Pathological and Immunohistochemical Analysis," "Discussion,"** and **"Conclusion."**
- **Incorporate a Visual Diagnostic and Staging Roadmap:** Add a sequential flowchart mapping the patient's diagnostic journey. The roadmap should trace the clinical progression from initial respiratory symptoms to chest X-ray findings, bronchoscopic biopsy, subsequent abdominal CT discovery of the renal mass, and the final clarifying ultrasound-guided core biopsy.
- **Introduce a Comparative Immunohistochemical Staging Matrix:** Include a comprehensive reference table contrasting the typical IHC expression profiles of primary renal cell carcinoma against metastatic bronchial squamous cell carcinoma. This matrix should clearly display

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expected results for markers like $p40$, $p63$, $TTF\text{-}1$, $PAX8$, $CD10$, $CK7$, and $CK20$ to guide differential diagnoses.

- **Elaborate on the Conflict of Dual-Positive Lineage Markers:** Expand the clinical discussion regarding the co-expression of $PAX8$/$CD10$ (typically indicative of renal lineage) alongside $p40$/$p63$ (indicative of squamous differentiation) in metastatic tissue. Provide a clear biochemical or literature-based explanation clarifying whether this represents entrapped non-neoplastic renal parenchyma or true aberrant tumor expression.
- **Provide Quantifiable Radiographic and Laboratory Parameters:** Enhance the clinical presentation by incorporating specific tumor measurements (in centimeters) for the right mediastinal mass, the left renal cortex lesion, and the secondary hepatic nodules. Additionally, state the patient's total white blood cell count, hemoglobin levels, and quantified estimated glomerular filtration rate (eGFR) alongside the provided serum values.
- **Detail the Post-Diagnostic Palliative Care Plan and Follow-up Timeline:** Expand the final therapeutic section to specify the exact palliative chemotherapy regimens selected by the multidisciplinary board. Clarify whether platinum-based doublets or targeted immunotherapies were used, and provide the patient's clinical outcome or survival status at the final follow-up evaluation.
- **Standardize In-Text Citation Typographical Formatting:** Revise the manuscript's in-text citations to eliminate non-standard formatting, such as raw parentheses enclosing numerical digits. Standardize all citations to follow a uniform journal style, such as Vancouver or AMA superscript formats.
- **Rectify Missing Bibliographic Metadata in the References Section:** Conduct a thorough review of the final reference list. Ensure that incomplete citations—such as entries 1, 3, 6, 9, and 11—are thoroughly updated to include all missing academic metadata, including complete co-author lists, formal journal volume and issue numbers, explicit page ranges, and active Digital Object Identifiers (DOIs).

Recommendation for Publication

I recommend this manuscript for **publication with major revision**. The case report addresses a clinically important scenario where metastatic non-small cell lung cancer mimics a synchronous primary renal malignancy, which can easily confuse diagnostic staging. The documentation of the biopsy tissue and the mixed IHC profile provides an excellent educational warning for oncology and pathology teams.

However, to meet international indexing standards, the author must restructure the text into formal academic subsections, provide deeper context on the contradictory $PAX8$/$p40$ co-expression, add an

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organized reference matrix, and thoroughly correct the formatting of the text citations and incomplete bibliography. These modifications will significantly elevate the clinical utility and scientific rigor of the paper.