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Tumor-to-Tumor Metastasis: Lung Adenocarcinoma as a Recipient of Metastasis from Renal Cell Carcinoma: A Case Report

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Male, 67-year-old
Final Diagnosis: Lung adenocarcinoma
Symptoms: Abdominal pain
Medication: —
Clinical Procedure: Lobectomy
Specialty: Oncology • Pathology

Objective: Rare co-existance of disease or pathology

Background: The occurrence of metastasis from one neoplasm to another is known as tumor-to-tumor metastasis (TTM). It is a rare phenomenon in the natural history of any neoplasm, with approximately 100 cases reported in the literature to date. The lungs are the most frequent metastatic tumor donors and kidney cancer is the most common recipient. However, the opposite phenomenon (lung adenocarcinoma as a recipient of metastasis from renal carcinoma) has not been previously reported in the literature.

Case Report: We present the case of a man with a history of multiple neoplasms. He had a diffuse large B-cell lymphoma in 2006, a left papillary renal cell carcinoma (RCC) type 2 in 2006, and an acinar adenocarcinoma of the prostate in 2011. A follow-up computed tomography scan in July 2019 showed a suspicious lung nodule on the left upper lobe and a retroperitoneal hypermetabolic mass on the positron emission tomography scan. The lung nodule and retroperitoneal mass biopsies were consistent with a primary lung adenocarcinoma with a lepidic pattern and a metastatic RCC, respectively. In January 2020, he underwent a thoracoscopic left upper lobectomy and a mediastinal lymph node dissection. Histopathological evaluation revealed a 2-cm nodule composed of a lung adenocarcinoma with an intratumoral metastasis from a papillary RCC. To date, the patient has stable renal neoplastic metastatic disease and no locoregional recurrences of the lung adenocarcinoma.

Conclusions: Metastasis from one primary tumor to another primary tumor is an extremely unusual event. We report one of the first cases of an RCC metastasis to a primary lung adenocarcinoma.

Keywords: Carcinoma, Renal Cell • Case Reports • Lung Neoplasms • Neoplasm Metastasis

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/932012

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Background

Tumor-to-tumor metastasis (TTM) is a rare event, which consists of the metastasis from one primary tumor to another synchronous or metachronous primary tumor. In these cases, lung cancer is the most frequent metastatic tumor donor and kidney cancer is the typical recipient, while the opposite phenomenon (lung adenocarcinoma as a recipient of metastasis from renal carcinoma) has not been previously reported in the literature [1,2]. We present the case of a man with a history of papillary renal carcinoma with a pulmonary nodule identified in his follow-up examination. The initial lung biopsy showed a lung adenocarcinoma; however, the histopathological analysis of the left upper lobectomy was consistent with a metastatic papillary renal carcinoma to a lung adenocarcinoma.

Case Report

A 67-year-old man with a history of smoking was diagnosed with a diffuse large B-cell lymphoma in 2006. The initial stage was IVB due to bone marrow involvement and the International Prognostic Index risk was intermediate/high. He received 6 cycles of R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) with complete response to the treatment and without relapse at the date of publication of this paper. In the same year (2006), a left papillary renal cell carcinoma (RCC) was diagnosed (type 2, Fuhrman grade 3-4, stage III by pT3N0M0, according to the American Joint Committee on Cancer [AJCC], 6th edition); therefore, he underwent a radical nephrectomy by laparoscopy. During the subsequent clinical and imaging follow-ups, a third primary tumor was diagnosed in 2011 (stage I acinar adenocarcinoma of the prostate, pT2AN0M0, Gleason 3+3 score 6, initial prostate-specific antigen 7.6 ng/ml [AJCC, 7th edition]). He underwent a radical prostatectomy and an extended lymphadenectomy; he has had no relapse to date. In 2015, he had an isolated left para-aortic lymph node relapse that required a lymphadenectomy with a complete resection, and the pathological anatomy was compatible with a papillary renal cell carcinoma type 2 metastasis. Given the absence of measurable disease at another site, he was followed up every 3 months. The follow-up computerized tomography (CT) scan in 2018 identified a nonspecific pulmonary nodule in the central aspect of the left upper lobe, which was left (untreated) in observation status. In July 2019, this pulmonary nodule showed 21 mm of mixed solid and ground-glass components and it had increased in diameter by 19% compared to the 2018 CT scan. Micronodules of up to 5 mm in diameter were observed in both lung fields (**Figure 1**). A positron emission tomography computed tomography (PET-CT) scan showed nodules and micronodules with soft tissue density. Some of them had high metabolic activity; they were located in both lung fields, and

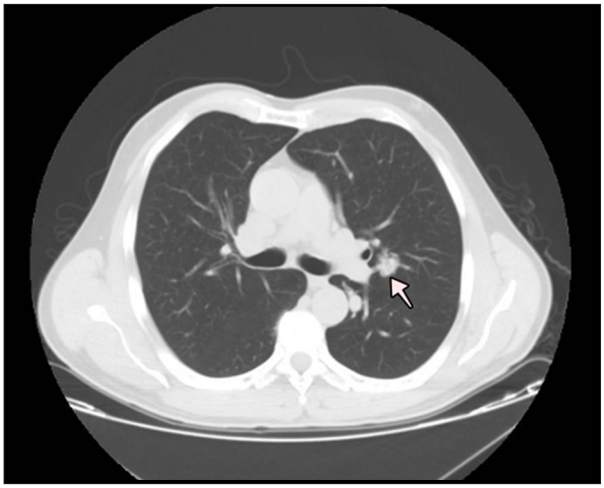

Figure 1. A thoracic computed tomography scan showing a pulmonary nodule with mixed solid and ground-glass opacity (21-mm diameter), located in the central aspect of the left upper lobe.

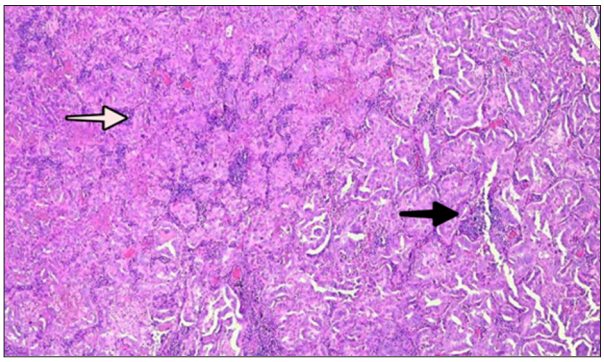

Figure 2. The moderately differentiated lung adenocarcinoma displayed a 40% solid (white arrow) and 60% acinar (black arrow) pattern (hematoxylin and eosin stain, 4× magnification).

were compatible with metastatic involvement. A left para-aortic hypermetabolic adenopathy, which was a hypermetabolic mass that infiltrated the left psoas minor muscle and another hypermetabolic focus in the left posterior muscle wall of the retroperitoneum, were suggestive of metastatic involvement. Biopsies of the pulmonary nodule and the retroperitoneal mass were performed. The pulmonary nodule biopsy was compatible with a primary pulmonary adenocarcinoma with a lepidic pattern, and the retroperitoneal mass biopsy revealed a papillary adenocarcinoma compatible with a primary renal tumor.

In January 2020 he underwent a left upper lobectomy and mediastinal lymph node dissection by thoracoscopy. The histopathological evaluation of the left upper lobe found a larger 2.0×1.5 cm nodule composed of a lung adenocarcinoma (**Figure 2**) with an intratumoral metastasis (0.2-cm diameter) from a papillary RCC (**Figure 3A, 3B**).

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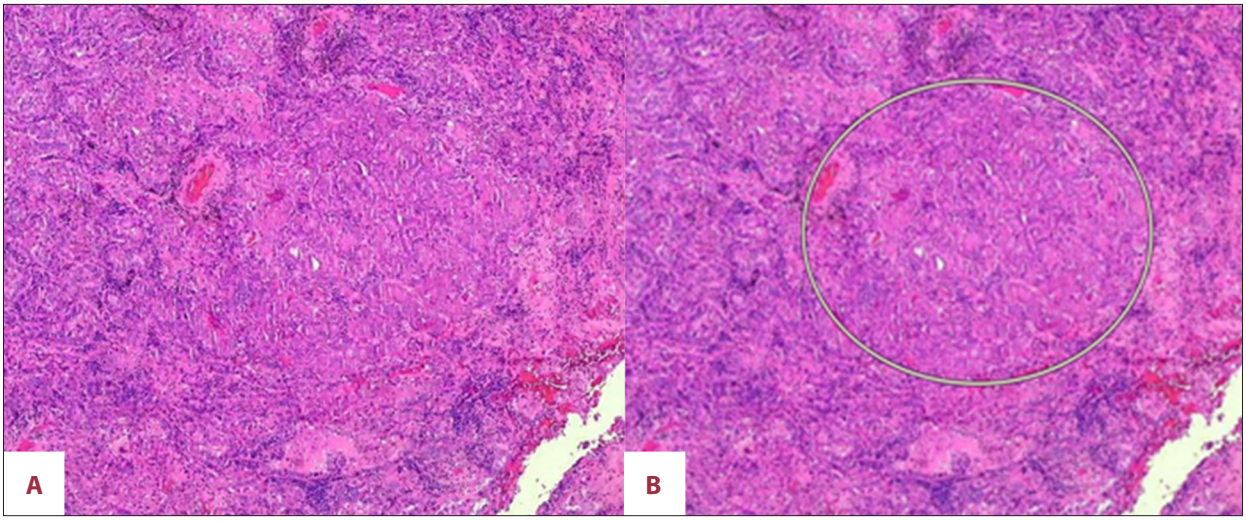

Figure 3. (**A**) Intratumoral metastasis of the papillary renal cell carcinoma type 2 measuring 0.2×0.2 cm, surrounded by a lung adenocarcinoma. (**B**) The circle encloses the intratumoral metastasis (hematoxylin and eosin stain, 10× magnification).

Immunohistochemistry markers showed positivity for CKAE1/AE3 in the lung cancer (**Figure 4A**) and RCC (**Figure 4B**), and CK7 positivity in the lung cancer (**Figure 4C**) and RCC (**Figure 4D**). Napsin A was positive in the lung adenocarcinoma (**Figure 4E**) and negative in the RCC (**Figure 4F**). The thyroid transcription factor (TTF-1) was positive in the lung adenocarcinoma (**Figure 4G**) and negative in the RCC (**Figure 4H**). The RCC was positive for the RCC marker (**Figure 5A**), CD10 (**Figure 5B**), and PAX8 (**Figure 5C**).

A second smaller nodule (1.0×0.5 cm) was found to be metastasized from the RCC. The lung adenocarcinoma was staged as pT1bN0M0R0 IA2 (AJCC, 8th edition) with no adverse risk factors observed in the histopathologic analysis; therefore, no adjuvant treatment was offered. The renal cancer was considered to be low risk on the International Metastatic RCC Database Consortium scale. However, metastatic progression with a high tumor burden led to some symptoms, including pain and weight loss; therefore, he underwent systemic therapy with sunitinib in April 2020.

In September 2020, CT images of the chest and abdomen revealed stable neoplastic disease. Sunitinib therapy had to be suspended due to progressive dyspnea, which resolved after the sunitinib was discontinued. At this time, cardiovascular studies, including transthoracic echocardiography, and an ischemia induction test showed normal results. In October 2020, although the retroperitoneal disease was stable, it was generating significant pain; therefore, a urologic oncologist performed a palliative resection. At the last follow-up visit in November 2020, he was asymptomatic and a PET-CT scan revealed stable neoplastic disease. Based on a joint decision with his oncologist, the patient is under close observation with no active treatment. In search of a possible hereditary cancer, a germline mutation-testing panel of 105 genes was carried out using next-generation sequencing (NGS, MiSeq System, Illumina Sequencing Technology, San Diego, CA, USA); however, it did not show any alteration. The patient gave informed consent for the publication of this case report.

Discussion

The presentation of a metastasis from one primary tumor to another (TTM) is a rare phenomenon in the natural history of any neoplasm. Since the initial description of TTM by Berent in 1902, >100 cases have been reported in the literature [1-3]. Campbell et al (1969) proposed the criteria for a true TTM as the existence of ≥2 primary neoplasms, the recipient tumor must be a true neoplasm, and the evidence of the second metastatic neoplasm with invasion or growth in the host tumor should not be due to contiguous growth (the latter event is known as a collision tumor) [3]. The present case meets all these criteria.

From the cases described in literature, RCC is the most frequent recipient tumor in up to 65% of cases, and lung and breast carcinomas are usually the donors' [1]; however, other types of tumors in different combinations have been described as causes of TTM [1,3-5]. In contrast, in the present patient, the lung cancer was the recipient site and RCC was the metastatic donor, which is a phenomenon not yet described in the literature to the best of our knowledge.

Several theories can explain the reasons for an occurrence of TTM. Paget et al (1889) proposed the theory of 'soil and seed,' in which a tumor develops owing to the presence of a fertile microenvironment (soil) where the tumor (the seed) can

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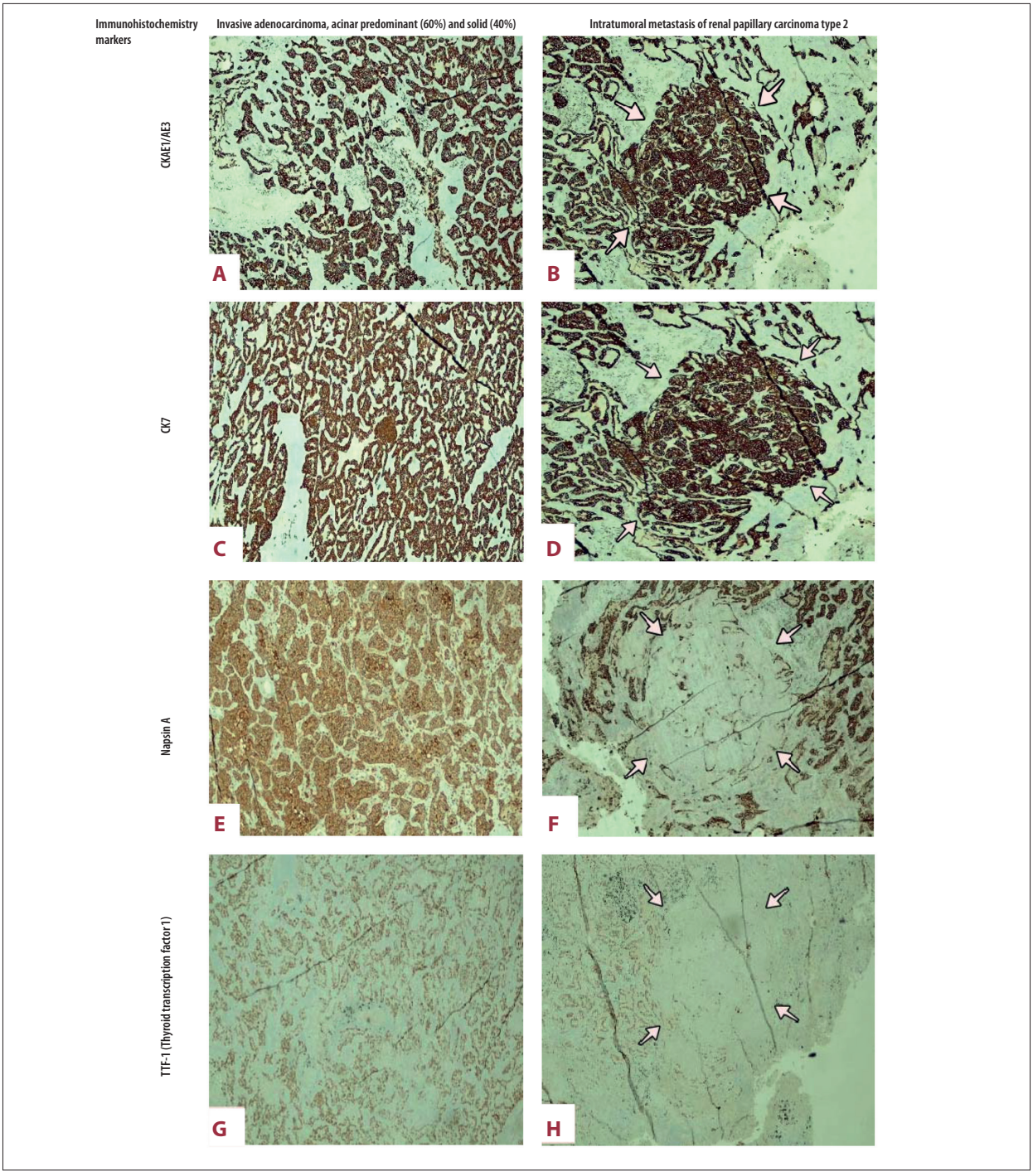

Figure 4. Immunohistochemical studies with positivity for CKAE1/AE3, CK7, Napsin A, and thyroid transcription factor 1 (TTF-1) in the acinar (60%) and solid (40%) lung adenocarcinoma. Positivity for CKAE1/AE3 and CK7, and negativity for Napsin A and TTF-1 for the metastasis from the papillary renal cell carcinoma (RCC) type 2 metastasis (arrows indicate intratumoral RCC metastasis): (**A**) CKAE1/AE3 in the lung adenocarcinoma (CKAE1/AE3 stain, 4× magnification). (**B**) CKAE1/AE3 in the intratumoral metastasis of the papillary RCC type 2 (CKAE1/AE3 stain, 10× magnification). (**C**) CK7 in the lung adenocarcinoma (CK7 stain, 4× magnification). (**D**) CK7 in the intratumoral metastasis of the papillary RCC type 2 (CK7 stain, 10× magnification). (**E**) Napsin A in the lung adenocarcinoma (napsin A stain, 4× magnification). (**F**) Napsin A in the intratumoral metastasis of the papillary RCC type 2 (napsin A stain, 10× magnification). (**G**) TTF-1 in the lung adenocarcinoma (TTF1 stain, 4× magnification). (**H**) TTF-1 in the intratumoral metastasis of the papillary RCC type 2 (TTF-1 stain, 10× magnification).

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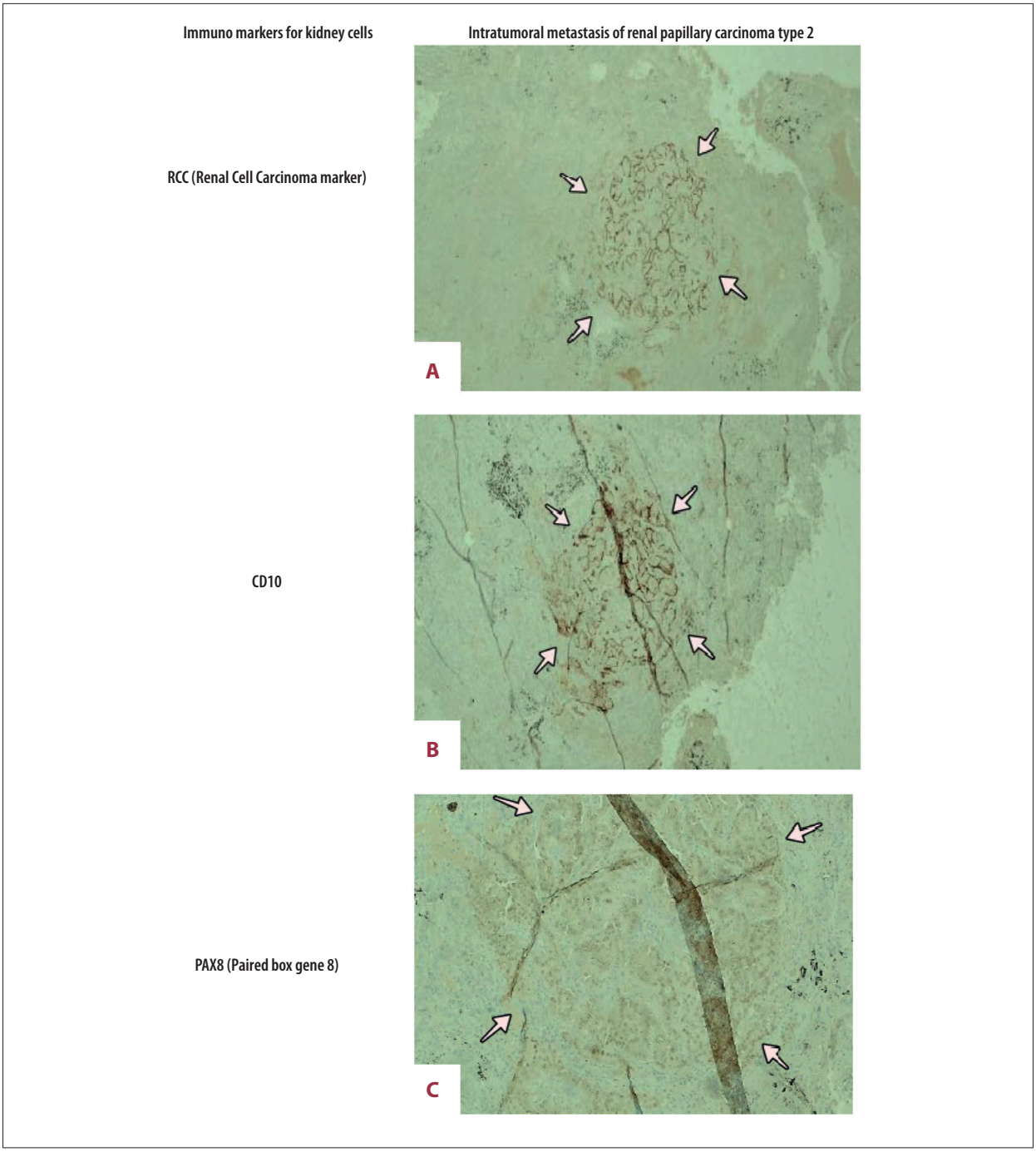

Figure 5. Immunomarkers for kidney cells: Positivity in the intratumoral metastasis of the papillary renal cell carcinoma (RCC) type 2, negativity in the periphery corresponding to the lung adenocarcinoma (arrows indicate intratumoral RCC metastasis): (**A**) RCC marker (RCC stain, 4× magnification). (**B**) CD10 (CD10 stain, 4× magnification). (**C**) Paired box gene 8 (PAX8 stain, 40× magnification).

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proliferate [6]. On the other hand, Ewing et al (1928) described a 'mechanical' theory, where the site compromised by metastasis depends on the quantity of viable tumor cells delivered to the target organ. The specificity of this metastatic involvement can be related to other anatomical considerations, including vascularization and location [7].

The lungs are the second most frequent site for metastatic involvement by extra-thoracic tumors, and they are affected in up to 54% of cases. RCC metastases are present in up to 30% of patients, and the lungs, in addition to non-regional lymph nodes, are probably the most frequently involved organs (70%) [8,9].

RCC is a good receptor for lung cancer metastasis due to the high renal blood volume, and high lipid and glycogen content of the RCC; however, the reasons for the reverse phenomenon, as occurred in our patient, are unclear [1,2,3,6]. One possible hypothetical explanation is the inflammatory microenvironment of the lung adenocarcinoma, which can potentially attract and host metastatic RCC tumor cells, as seen in the case of metastasis of an RCC to the oral cavity after tooth extraction (in wounds) [10].

Another aspect to highlight in this case is the possibility of the presentation of synchronous primary pulmonary tumors in patients with a history of renal cancer. In a case series of 151 patients with pulmonary metastatic RCC, 2% of the patients had synchronous non-small cell lung carcinoma. However, no cases of TTM were reported in this case series [11].

The close follow-up of the present patient due to his oncological history influenced the timely diagnosis of the TTM and resulted in the curative management of his lung adenocarcinoma.

Conclusions

Metastasis from a malignant tumor to another primary tumor is a rare event. Possible explanations for this phenomenon are scarce, and include some anatomical considerations (the high blood-flow volume of the lungs and kidneys), an advantageous microenvironment of the primary tumor that can host metastatic tumor cells, and the patient's characteristics, including a personal history of multiple synchronous or metachronous tumors. TTM usually represents a diagnostic challenge, which demands a careful pathological study to ensure a precise diagnosis and appropriate treatment.

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Department and Institution Where Work Was Done

Department of Clinical Oncology, National Cancer Institute, Bogotá, Colombia.

Conflicts of Interest

None.

Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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