

Metastatic Clear Cell Renal Carcinoma Presenting as Lymphadenopathy and Parotid Nodules After 11 Years: A Case Report

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ABSTRACT

Background: Clear cell renal carcinoma (ccRCC) rarely metastasizes to the head and neck region. When it does, such cases are diagnostically challenging due to the overlap with primary tumors in those regions.

Case Presentation: We report the case of a 66-year-old man with a history of ccRCC treated by partial nephrectomy in 2014. In 2022, he underwent parotidectomy for a benign cystadenoma. In 2025, he presented with cervical lymphadenopathy and parotid nodules. MRI revealed lymphadenopathy in level 2A and three nodules suspected of malignancy. Selective neck dissection and histopathological evaluation (Figure 1) confirmed metastatic ccRCC. Immunohistochemistry supported the diagnosis with CK7, CK18, and GATA3 positivity, and ruled out alternate origins.

Conclusion: This case illustrates an uncommon metastatic presentation of ccRCC, highlighting the critical role of immunohistochemistry (Figure 2) and thorough clinical history. Awareness of such atypical metastatic patterns is essential for accurate diagnosis and appropriate treatment.

Keywords: Clear Cell Renal Carcinoma; Metastasis; Parotid; Lymphadenopathy; Case Report

Abbreviations: ccRCC: Clear Cell Renal Carcinoma; SGs: Salivary Glands; SGTs: Salivary Gland Tumors; FNA: Fine-Needle Aspiration; VEGF: Vascular Endothelial Growth Factor; HGIPN: High-Grade Prostatic Intraepithelial Neoplasia; ENT: Ear Nose and Throat

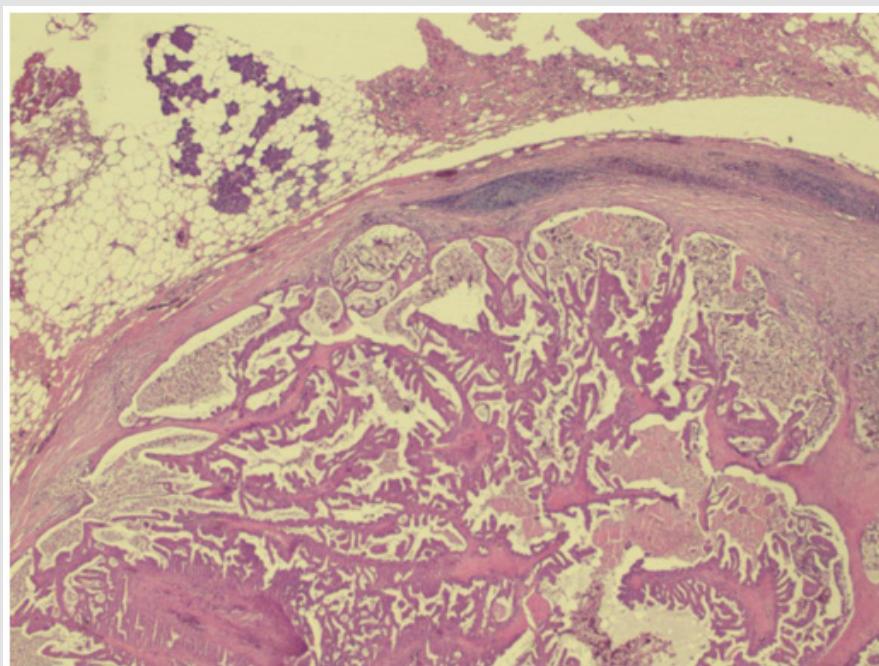


Figure 1: Photomicrograph showing salivary gland with metastasis (H and E, x25).

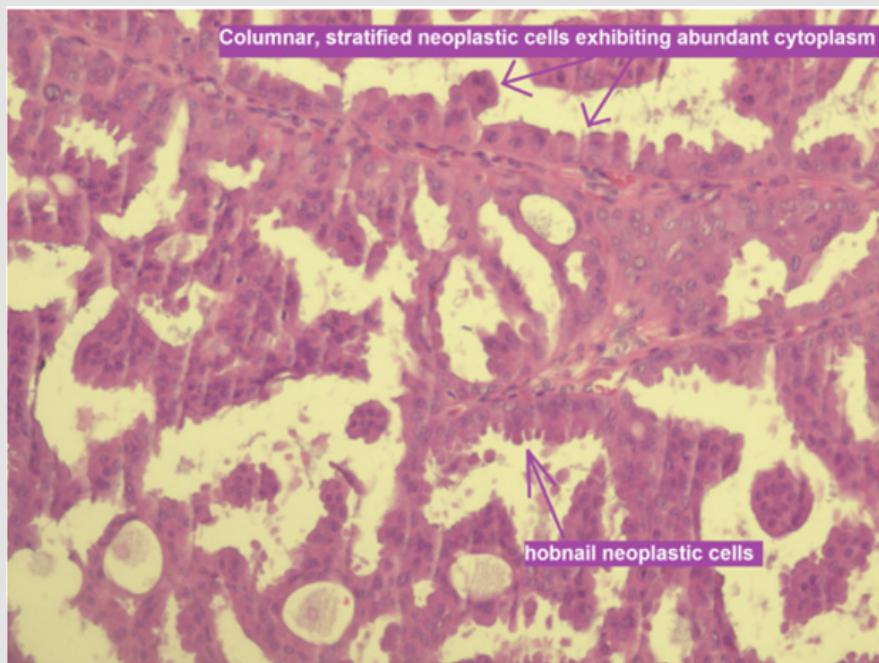


Figure 2: Photomicrograph stained with H and E, x200.

Introduction

Clear cell renal cell carcinoma (ccRCC) is the most common histological subtype of renal malignancies, accounting for approximately 75% of all renal cell carcinomas (RCC). It typically affects older adults and is characterized by high vascularity and an unpredictable metastatic pattern. While metastases to the lungs, liver, and bones are common, involvement of the head and neck region is highly unusual, especially in the absence of more widespread disease [1,2]. Distant metastasis to the salivary glands (SGs) is an uncommon event, most frequently associated with primary skin malignancies. Metastatic involvement occurs in only 1–4% of all salivary gland tumors (SGTs). Besides skin cancers, primary tumors of the breast, lung, kidney, and prostate can also metastasize to the SGs. Renal cell carcinoma (RCC), arising from the proximal renal tubular epithelium, is the seventh most common cancer in the world and is notable for its prolonged asymptomatic course and high metastatic potential in advanced stages [3]. The classic triad of RCC symptoms—hematuria, flank pain, and palpable mass—is present in only about 10% of cases. Approximately 18% of patients have metastases at diagnosis and more than half develop metastases during follow-up post-nephrectomy. The lungs, bones, lymph nodes, liver, adrenal glands and brain are the most common metastatic sites.

Head and neck metastases are rare (8–14%), with the thyroid gland being the most frequently involved in this region [4,5]. RCC is known to metastasize to unusual sites, including the salivary glands. Metastases to the SGs from RCC counts for roughly 0.1% of all SG metastatic tumors, with the parotid gland being the most commonly affected [6]. Reports of ccRCC metastasizing to the parotid gland and

cervical lymph nodes are exceptionally rare. This atypical presentation can pose diagnostic challenges, particularly when it occurs many years after initial curative treatment. We present a unique case of ccRCC that recurred as isolated nodal and parotid involvement over a decade after nephrectomy, emphasizing the importance of long-term follow up.

Case Presentation

A 66-year-old male with a history of clear cell renal carcinoma diagnosed in 2014 (Figures 3 & 4), initially treated with a left partial nephrectomy. The tumor was classified as Fuhrman grade 2, ISUP grade 1, staged T1N0M0L0V0R0. In 2022, he was diagnosed with a left parotid cystadenoma and subsequently underwent a superficial left parotidectomy with preservation of the facial nerve. His medical history is notable for multiple allergies, including myalgin, morphine, trachium, ciprinol, penicillin, and MRI contrast agents. Additionally, he has a history of ischemic cardiomyopathy. In 2025, the patient referred to the Oral and Maxillofacial Surgery Clinic II Cluj-Napoca with a progressively enlarging, painless swelling on the left side of the neck. Physical examination identified lymphadenopathy at level 2A, along with three nodules—two intraparotid and one infraparotid—raising suspicion for malignancy. MRI imaging confirmed lymphadenopathy at level 2A, round lymph node with a short axis of 17mm and the presence of the three nodules, one within the parotid gland about 7 mm diameter and two below the parotid gland about 17 mm respectively 12 mm diameter. (Figure 5) The patient's oncologic history, combined with cardiovascular comorbidities (ischemic cardiomyopathy) and multiple allergies, make this case a complex case for general anaesthesia and postoperative management.

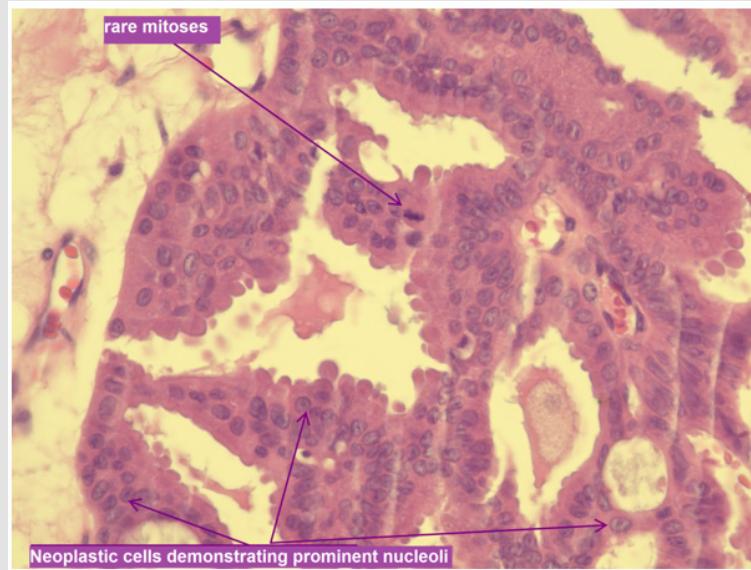


Figure 3: Photomicrograph stained with H and E, x400.

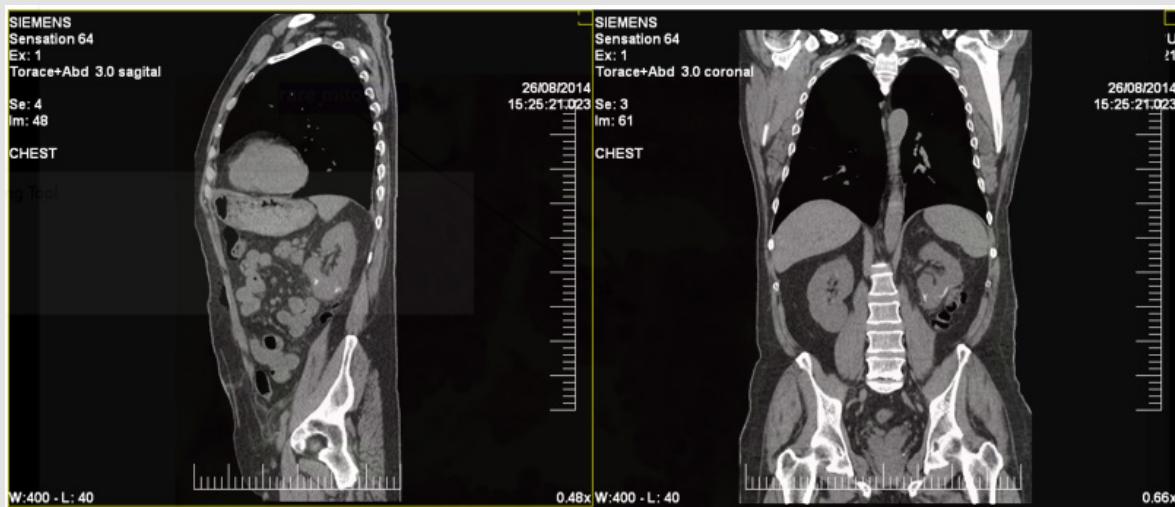


Figure 4: Sagittal and coronal views of a CT scan demonstrating a solid renal mass at the lower pole of the left kidney, measuring approximately 37 x 35 x 31 mm. (2014).

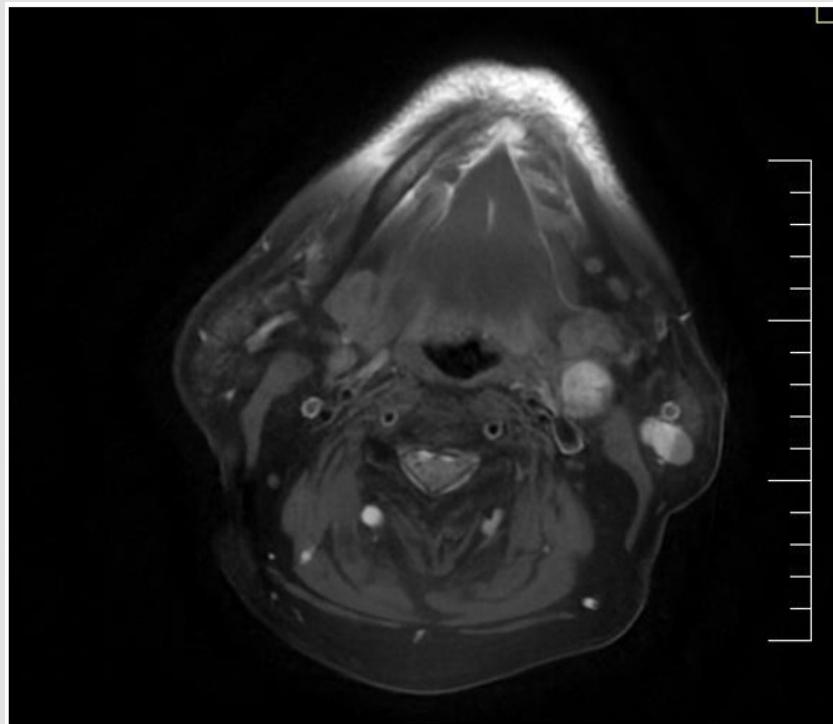


Figure 5: Axial MRI images demonstrate a left level IIa laterocervical lymphadenopathy, round shape, with a short-axis diameter of 17 mm and heterogeneous internal structure, showing areas of T1 fat-saturated hyperintensity. The imaging features are suspicious for malignancy.

Additionally, his active smoking and alcohol use likely contributed to a delay in diagnosis, as early symptoms were initially attributed to lifestyle-related gland inflammation. Given the high clinical and radiologic suspicion of malignancy, the multidisciplinary team elected to proceed directly with a selective neck dissection, foregoing fine-needle aspiration (FNA), to allow for simultaneous diagnostic tissue sampling and therapeutic intervention. Histopathological analysis proved critical in establishing the diagnosis. Notably, PAX8 expression—commonly present in primary renal tumors—was absent, a finding that may occur in metastatic lesions or poorly differentiated tumors.

Diagnostic Workup

Selective neck dissection was performed on the left side, along with excision of the nodules. Histopathological examination confirmed metastatic clear cell renal carcinoma. Immunohistochemical staining results:

Stage 1:

- CK7: Intensely positive (Figure 6)
- p63: Weakly positive
- AMACR: Weakly positive
- CK20: Negative

- PAX8: Negative
- Thyroglobulin: Negative
- TTF-1: Negative
- Napsin A: Negative

Stage 2:

- CK18: Intensely positive (Figure 7)
- GATA 3: Positive (Figure 8)
- Ki67: 5–10%
- SOX 10: Negative
- DOG1: Negative
- Parotid Cystadenoma (2022):
- TTF-1: Negative
- PAX8: Negative
- S100: Negative
- SMA: Positive
- Ki67: 5%

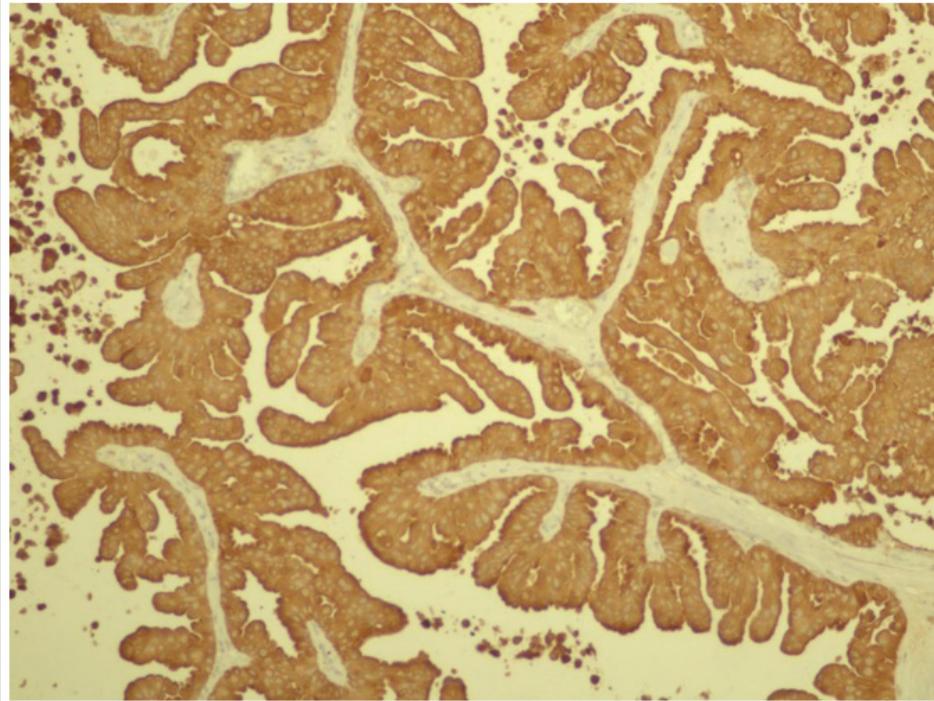


Figure 6: Photomicrograph stained with CK7 showing positive neoplastic cells (x100).

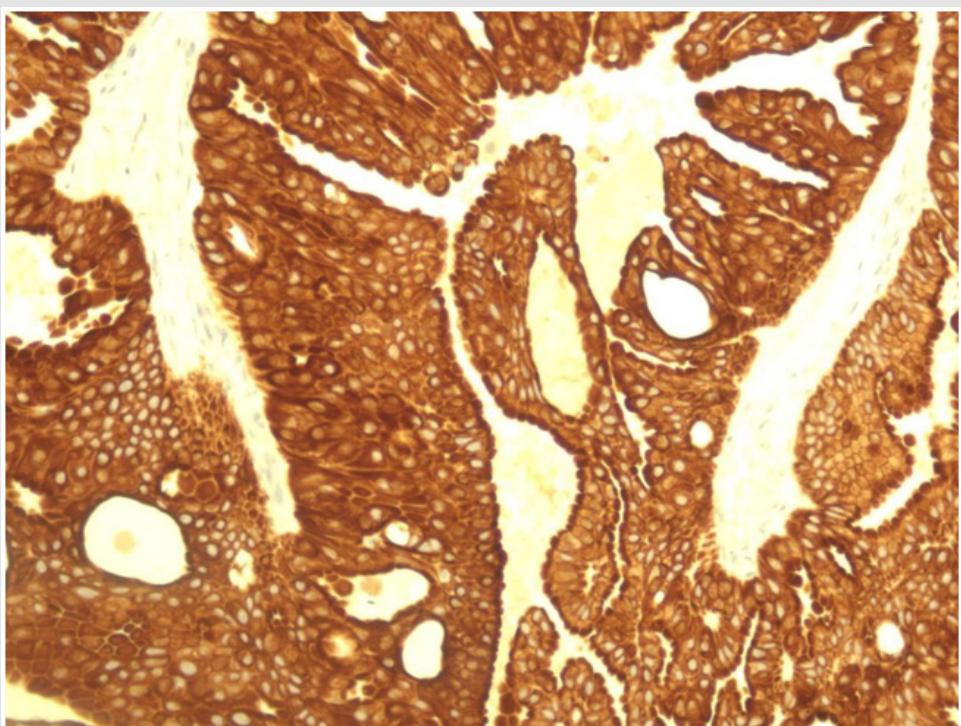


Figure 7: Photomicrograph stained with CK18 showing positive neoplastic cells (x200).

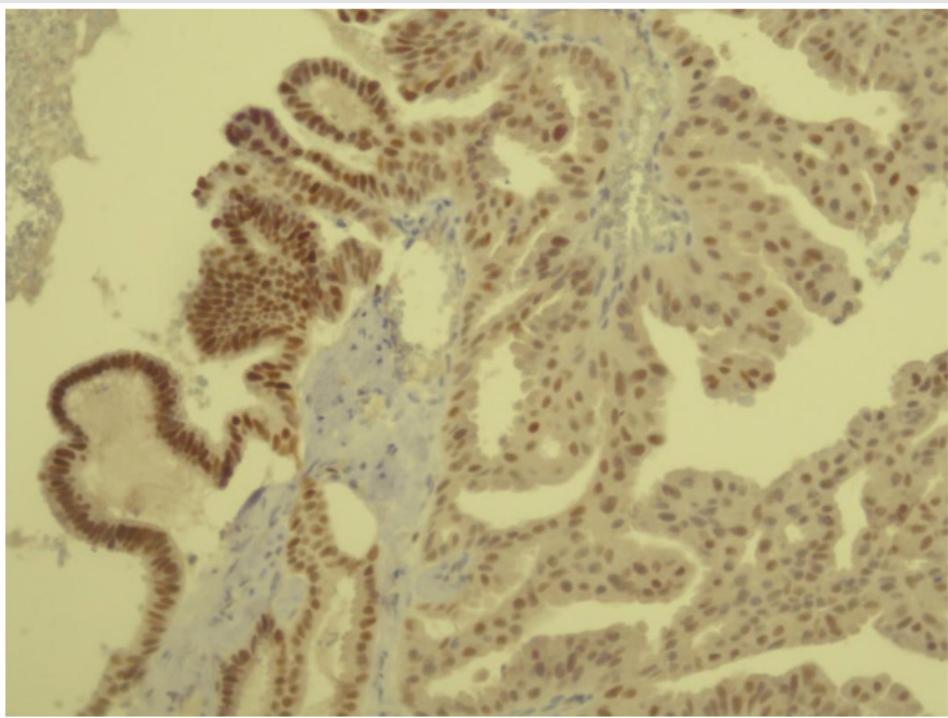


Figure 8: Photomicrograph stained with GATA 3 showing positive neoplastic cells (x200).

Discussion

A variety of non-salivary gland tumors—both benign and malignant—can present within the parotid region. Benign lesions commonly include lipomas, histiocytomas, schwannomas (neurilemmomas), hemangiomas, lymphangiomas, neurofibromas, and embryomas. Malignant tumors comprise approximately 29% of all parotid masses, with metastatic disease accounting for 21% to 42% of these cases [7]. Among non-salivary malignancies found in the parotid area, those originating from lymphatic tissue are the most frequently encountered. Other less common but notable malignant entities in this anatomical location include chondrosarcoma, neuroblastoma, fibrosarcoma, and malignant melanoma. While metastases from tumors located below the clavicle are rare, malignant melanoma and squamous cell carcinoma are the most likely to spread to the parotid gland from distant primary sites [8]. Clear cell renal cell carcinoma (ccRCC) represents the most common histological subtype of renal cancers, arising from the epithelial lining of the proximal renal tubules and is well known for its variable metastatic potential. Although classically associated with a triad of hematuria, flank pain, and a palpable mass, these symptoms are concurrently present in only 10% of patients at diagnosis [1].

The unique vascular characteristics of RCC contribute to its metastatic behavior. Owing to the kidney's significant blood supply—receiving nearly one-quarter of the cardiac output—and the tumor's production of angiogenic factors such as vascular endothelial growth factor (VEGF), RCC exhibits a marked tendency toward hypervascularity [4]. This vascular nature facilitates its spread via the bloodstream, often forming tumor thrombi that can extend into the inferior vena cava. Additionally, lymphatic dissemination is a recognized metastatic route [5]. The lungs, liver, brain, and skeletal system represent the most frequent sites of RCC metastasis [7]. Bone involvement tends to be osteolytic and predominantly affects the axial skeleton, especially the thoracolumbar vertebrae (T2-L5). The jaws are also susceptible to RCC metastasis, with the mandible involved in approximately 16% of skeletal cases originating from renal tumors [9-11]. While lungs, bones, liver, and brain are typical sites for ccRCC metastases, the involvement of head and neck structures—particularly the cervical lymph nodes and salivary glands—is rare and often unexpected [12]. Such metastatic patterns may present several years after initial treatment, as in the case of our patient, who developed metastases over a decade after a partial nephrectomy for T1 ccRCC.

Metastatic spread of renal cell carcinoma (RCC) to the head and neck region is uncommon. Among the documented cases, the thyroid gland is the most frequently affected site, followed by the parotid gland to a lesser extent. Metastases involving the sublingual and submandibular glands are exceedingly rare [5,13]. Additional reported sites of RCC metastasis include the skin, nasal cavity, lips, hard palate,

tongue, paranasal sinuses, and tonsils [14]. In a postmortem review of 1,451 RCC cases, Siatoh, et al. identified metastases to the ear, nose, and throat (ENT) region in 5% of cases, although none involved the parotid gland [11]. RCC is recognized for its atypical metastatic patterns. Literature reports indicate that parotid gland metastases can manifest either before or after treatment of the primary tumor [15]. Clinically, patients with parotid metastases from RCC typically present with a painless, palpable mass in the parotid region; however, symptoms such as pain, tenderness, pulsation, tinnitus, or ipsilateral facial nerve weakness may also occur [15]. In some instances, concurrent masses may be observed in the thyroid, submandibular, or sublingual glands. Additionally, approximately one-third of patients with advanced disease exhibit bone metastases, which contribute significantly to morbidity, including pain, pathological fractures, spinal cord compression, and hypercalcemia [4].

The diagnostic process is complicated by the long latency period and the unusual anatomical distribution. Head and neck metastases may mimic primary neoplasms of those regions, making accurate diagnosis heavily reliant on thorough patient history and advanced histopathological evaluation. In our case, initial imaging showed findings suspicious for a new primary parotid malignancy or lymphoma due to the appearance and location of nodules. However, detailed immunohistochemistry (IHC) revealed a staining pattern consistent with metastatic ccRCC. The IHC panel demonstrated intense positivity for CK7 and CK18, and moderate GATA3 expression [9]. While GATA3 is classically associated with urothelial and breast carcinomas, it can occasionally be expressed in ccRCC [10]. The absence of markers such as PAX8, TTF-1, CK20, and thyroglobulin helped rule out primary tumors of thyroid, lung, and gastrointestinal origins. Additionally, the patient's history of renal carcinoma and prior benign parotid cystadenoma made it imperative to carefully exclude a second primary tumor. It is also noteworthy that the patient underwent parotidectomy in 2022 for a benign cystadenoma with no evidence of malignancy at that time. Whether the current nodules represent new metastatic lesions or possible missed micrometastases cannot be definitively concluded, but the immunophenotype and clinical course strongly support a metastatic renal origin.

Management of such rare metastases is not standardized and should be individualized. Surgical excision, as performed here, can offer both diagnostic clarity and symptom relief. Systemic therapy options, including targeted therapies and immune checkpoint inhibitors, are evolving and were discussed in the multidisciplinary setting, given the patient's comorbidities and lifestyle factors. This case reinforces the importance of long-term follow-up in patients with a history of renal cancer, regardless of initial stage or apparent remission. Furthermore, clinicians should maintain a high index of suspicion for metastatic disease when evaluating new masses, particularly in patients with a known malignancy history.

Conclusion

This case underlines the capacity of ccRCC to remain dormant for prolonged periods before reactivating in unusual anatomical locations. It highlights the critical role of high-resolution imaging, targeted immunohistochemistry, and long-term follow-up in patients with a history of renal cancer. Clinicians should maintain a broad differential when assessing neck masses in patients with previous malignancy, and consider late metastasis—even in the context of prior benign findings such as parotid cystadenoma.

Patient Evolution and Current Status

Following surgery in early 2025, the patient underwent a PET-CT scan in March 2025 (Figures 9 & 10). The imaging showed no evidence of local recurrence or distant metastasis, apart from mildly FDG-active left latero-cervical lymph nodes. Given the short interval (<3 months) from surgery, the metabolic activity was interpreted with caution, and follow-up was recommended to assess SUV evolution. No other pathological FDG uptake was noted. In April 2025, the

patient was evaluated by the urology team, who ordered a PSA test and three-day consecutive urinary cytology. Results revealed a PSA level of 8.088 ng/mL and acellular smears on all cytological samples. Subsequently, in June 2025, a transrectal ultrasound-guided prostate biopsy was performed. The pathology report identified multifocal glandular hyperplasia, multifocal high-grade prostatic intraepithelial neoplasia (HGPIN) predominantly in the left lobe, and nonspecific chronic active prostatitis. No evidence of invasive carcinoma was found. Currently, the patient is undergoing systemic chemotherapy and remains under close multidisciplinary surveillance. Despite ongoing treatment, his general condition is stable, with preserved daily function. Follow-up evaluations are coordinated by oncology, urology, and head and neck surgery teams. Continued clinical and radiological monitoring is planned to assess for potential disease progression or secondary primary lesions. Additionally, three other nodular lesions with similar characteristics are identified: one located in the infraparotid region measuring 17 x 12 mm, and two intraparotid lesions, the largest measuring approximately 7 mm.

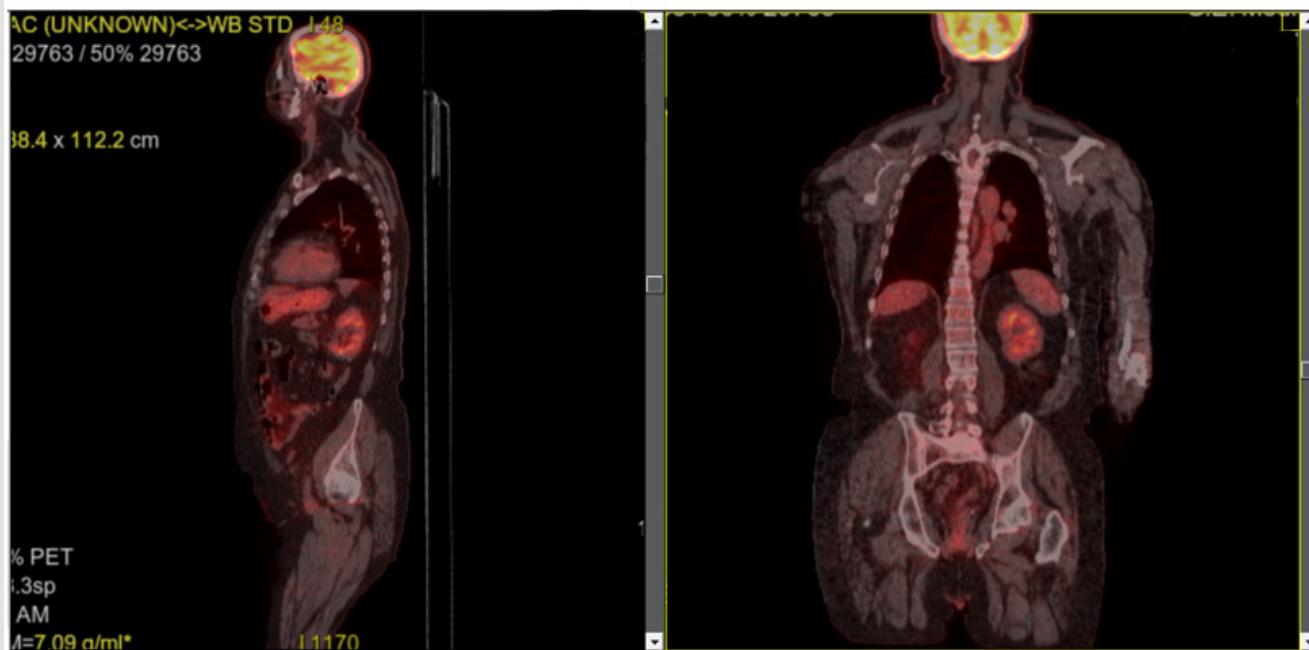


Figure 9: PET-CT scan performed in the context of post left partial nephrectomy. Beam-hardening artifacts are present at the surgical site, limiting evaluation to some extent. No focal FDG uptake is identified in the left renal region to suggest local recurrence.

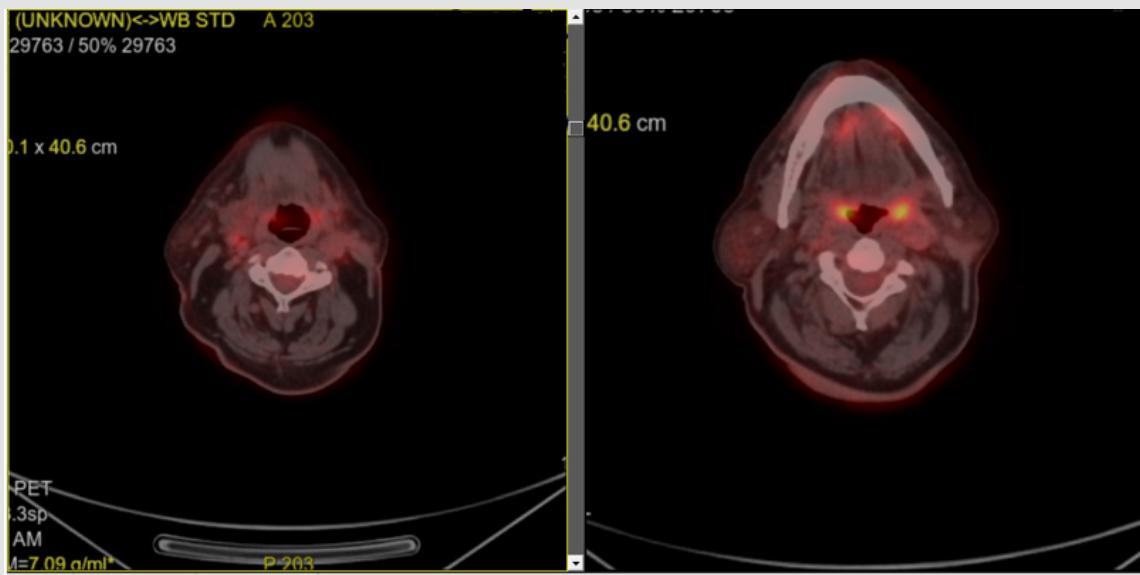


Figure 10: PET-CT head and neck (axial acquisition): Postoperative changes in the left parotid region and status post left selective laterocervical lymphadenectomy (15.01.2025), with no evidence of metabolically active local recurrence. Mild FDG uptake (SUV max 1.65) in left level II-III lymph nodes (up to 13 mm), likely reactive; follow-up recommended. Right laterocervical lymph nodes (up to 8 mm) show no significant metabolic activity (SUV max 0.65). Bilateral tonsillar inflammatory changes noted.

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