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Renal Cell Carcinoma With Papillary Morphology Presenting as a Frontal Calvarial Metastasis: A Case Report

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Abstract

Calvarial metastasis can be the first clinical sign of renal cell carcinoma (RCC). A 68-year-old woman presented with a 45-day history of an enlarging, firm, fixed, tender 3×3 cm midline frontal swelling, initially thought to be an epidermoid lesion or a metastasis. Positron emission tomography/computed tomography showed a metabolically active right renal mass and lytic skeletal lesions, including a midline frontal calvarial lesion with a soft-tissue component. She underwent right radical nephrectomy and excision of the frontal lesion. Histopathology showed RCC with papillary morphology, World Health Organization/International Society of Urological Pathology grade 4, pT3a, with focal rhabdoid differentiation and tumor necrosis; immunohistochemistry was not performed. The frontal bone lesion was consistent with metastasis. She received sunitinib. About three months after nephrectomy, she developed headache and seizures, and brain imaging showed brain metastases; she received whole-brain radiotherapy. Her relatives later reported that she had died at home. An enlarging, fixed calvarial mass should not be assumed to be a primary cranial lesion; systemic staging is needed, and RCC, including tumors with papillary morphology, should be considered when a renal mass is found.

Categories: Urology
Keywords: bone metastasis, calvarial metastasis, papillary renal cell carcinoma, rhabdoid differentiation, skull metastasis

Introduction

Papillary renal cell carcinoma accounts for 10%-20% of renal cell carcinomas (RCCs) [1]. The 2022 World Health Organization (WHO) classification recognizes that the former type 2 papillary category is heterogeneous and defines several tumors that can show papillary architecture by their molecular features, including fumarate hydratase (FH)-deficient RCC and transcription factor E3 (TFE3)-rearranged RCC; these are usually distinguished by immunohistochemistry or molecular testing [2]. The pattern of metastatic spread in RCC differs by histological subtype. In an international cohort of 10,105 patients with metastatic RCC, bone metastases were present in 32% of patients with clear-cell tumors and 29% of those with papillary tumors, whereas brain metastases were present in 8% and 3%, respectively [3].

Metastatic tumors of the skull are often asymptomatic, and when they are identified, they must be distinguished from primary tumors of the skull. In a surgical series of 38 patients operated on for skull lesions, 12 had metastases, and in five of these 12 patients, the skull metastasis was the first sign of disseminated disease. Compared with patients with primary skull tumors, those with metastases were older and had a shorter history of symptoms (median, two versus 24 months) [4]. In adults, the differential diagnosis of a calvarial mass includes benign lesions, such as epidermoid cysts, osteomas, hemangiomas, and fibrous dysplasia, as well as meningioma, plasmacytoma, and metastasis. A calvarial metastasis is clinically important because it may be the first sign of disseminated disease and may extend toward the dura and brain.

Skull involvement is uncommon in RCC, and the published evidence consists mainly of case reports and small series. A calvarial mass as the first clinical presentation of RCC has been described in several reports [5-7]. In these reports, the renal tumor was of clear-cell histology or its subtype was not reported. In a PubMed search on November 2, 2026, combining title and abstract terms for RCC, skull or calvarium, and metastasis, 158 records were retrieved; restricting the search to papillary tumors retrieved five records, of which only one described a papillary RCC that came to attention through a skull lesion [8]. Recognizing this presentation matters, because excision of an apparently isolated calvarial swelling without systemic staging may delay the diagnosis of the primary tumor and of other metastatic sites.

We report a 68-year-old woman whose enlarging frontal swelling, first thought to be an epidermoid lesion or

a calvarial metastasis, proved to be the presenting feature of metastatic RCC with papillary morphology and focal rhabdoid differentiation, and we compare her course with the published cases of RCC presenting with skull involvement.

Case Presentation

A 68-year-old woman with no documented significant comorbidities presented to neurosurgery with a swelling in the forehead that had enlarged steadily over about 45 days. The swelling was her only complaint; she had no headache, seizures, weight loss, or other symptoms at that stage, and she was ambulatory and independent in daily activities. A history of trauma about one year earlier was recorded. On examination, there was a firm, noncompressible, fixed, tender midline frontal swelling of about 3×3 cm, with no local rise in temperature. An epidermoid lesion and a calvarial metastasis were considered in the initial differential diagnosis.

Contrast-enhanced computed tomography (CT) of the abdomen showed a heterogeneous mass with internal calcific foci in the upper and mid poles of the right kidney (Figure *1*). ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) showed that the renal mass, measuring 4.8×5.0×7.8 cm, was metabolically active, with a maximum standardized uptake value (SUVmax) of 9.2. It had lost the fat planes with the inferior surface of the right lobe of the liver and with the right crus of the diaphragm, but it preserved the fat plane with the right adrenal gland and did not infiltrate the right renal artery or vein. Metabolically active lytic skeletal lesions (SUVmax up to 11.1) involved the frontal bones in the midline, with a soft-tissue component measuring 2.3×2.8×2.8 cm that did not extend into the brain parenchyma (Figure *2*), as well as the left temporal bone, the left second rib, the left pedicle of the 12th thoracic vertebra, the fifth lumbar vertebra, and the sacrum. Increased uptake in the ileocecal junction, cecum, and ascending colon without a corresponding CT abnormality was reported as inflammatory. The findings favored a renal primary with skeletal metastases. Dedicated brain imaging was not performed before surgery.



FIGURE 1: Contrast-enhanced computed tomography of the abdomen

(A) Coronal venous-phase and (B) coronal arterial-phase images showing a heterogeneous mass with internal calcific foci in the upper and mid poles of the right kidney; the left kidney appears normal. (C) Axial arterial-phase image of the right renal mass. Arrows indicate the right renal mass. R: right side of the patient; L: left side of the patient.

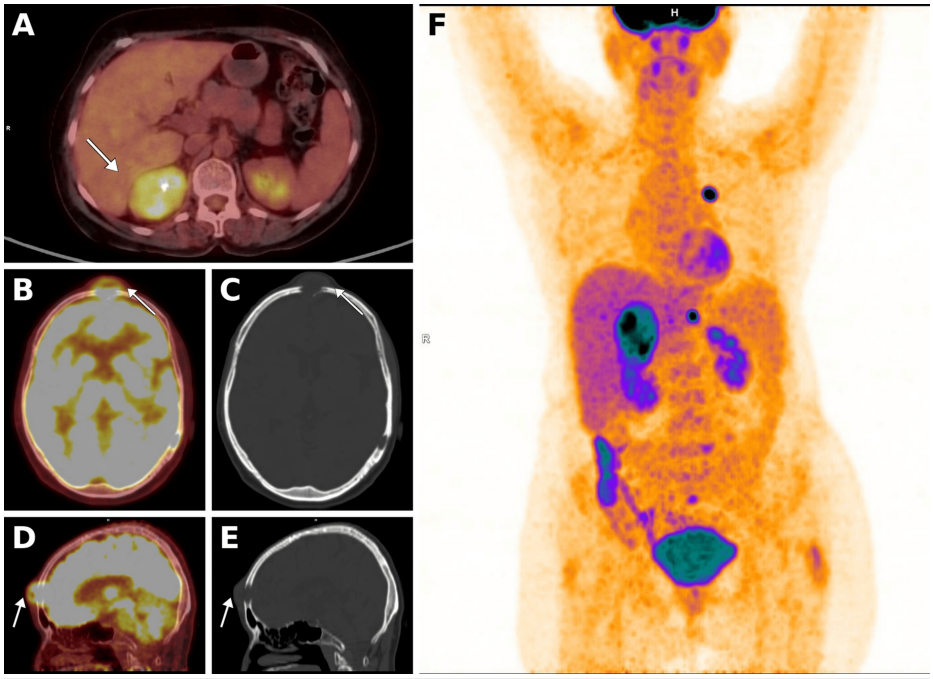


FIGURE 2: Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography

(A) Axial fused PET/CT image showing the metabolically active mass in the right kidney. (B) Axial fused PET/CT image and (C) the corresponding axial CT image showing the lytic midline frontal lesion in the axial plane; the CT image shows the defect in the frontal bone. (D) Sagittal fused PET/CT image and (E) the corresponding sagittal CT image showing the frontal lesion and its soft-tissue component. (F) Maximum intensity projection image; uptake in the right colon was reported as inflammatory. Arrows indicate the right renal mass (A) and the frontal lesion (B-E). PET/CT: positron emission tomography/computed tomography; CT: computed tomography; H: head; R: right side of the patient.

Formal risk stratification by International Metastatic RCC Database Consortium (IMDC) could not be established retrospectively, because the laboratory parameters required for its calculation were not completely available in the medical records. Nevertheless, she was ambulatory, functionally independent, and considered a suitable surgical candidate following multidisciplinary discussion with radiation and medical oncology. Given the resectability of the primary renal tumor and the accessible frontal calvarial lesion, surgery was undertaken to obtain histopathological confirmation from both sites and establish the diagnosis before planning subsequent systemic therapy and radiotherapy. Both procedures were performed in the same sitting under general anesthesia: the urology team performed right radical nephrectomy, and the neurosurgery team excised the frontal bone lesion. The kidney contained a unifocal tumor in the upper pole, extending into the middle pole, measuring 6.2×4.9×3 cm. It was predominantly papillary, tubular, and tubulocystic, and was composed of cuboidal to columnar cells with moderate nuclear pleomorphism, vesicular nuclei, conspicuous eosinophilic nucleoli, and moderate to abundant eosinophilic cytoplasm. Dystrophic calcification, psammoma bodies, and foamy macrophages were present. Some cells had abundant eosinophilic cytoplasm and nuclei with reverse polarity, and there was focal rhabdoid differentiation. Tumor necrosis was present. The tumor extended into the pelvicalyceal system but did not invade the renal sinus fat, renal vessels, adrenal gland, or perirenal fat; invasion of the pelvicalyceal system corresponds to pT3a in the eighth edition of the American Joint Committee on Cancer staging system. Lymphovascular emboli were identified; perineural invasion was not seen. The ureteric and renal vascular margins were clear. The pathological diagnosis, made on morphology because immunohistochemistry was not performed, was papillary RCC, World Health Organization/International Society of Urological Pathology (WHO/ISUP) grade 4, pT3a, with focal rhabdoid differentiation and tumor necrosis (Figure *3A*-C).

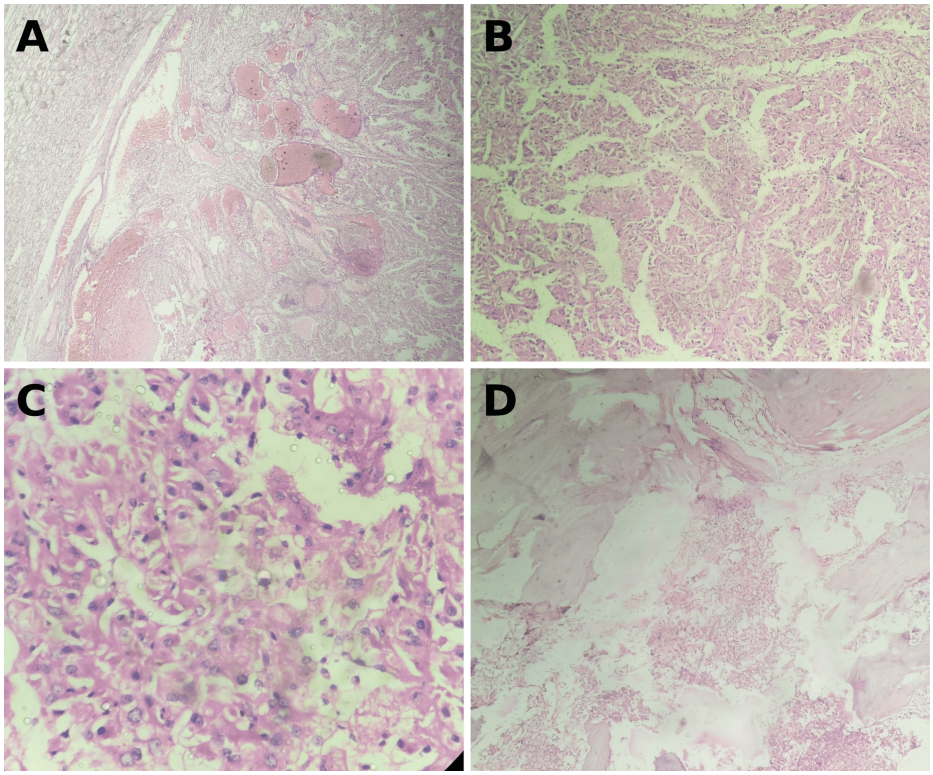


FIGURE 3: Histopathologic findings (hematoxylin and eosin stain)

(A) Low-power view of the renal tumor (4× objective). (B) Lesional cells arranged in papillae with fibrovascular cores (10× objective). (C) Papillae lined by cuboidal cells with apically placed nuclei, moderate nuclear pleomorphism, and abundant granular cytoplasm (40× objective). (D) Frontal bone specimen showing bony trabeculae with neoplastic cells infiltrating the intertrabecular spaces (40× objective). Scale bars are not available; magnifications refer to the objective lens.

The frontal bone specimen showed bony trabeculae infiltrated by neoplastic cells in alveolar, tubular, and focal solid patterns (Figure *3D*). The nuclei were moderately pleomorphic and vesicular with conspicuous nucleoli, and the cytoplasm was eosinophilic to vacuolated. The report concluded that the appearances were consistent with metastasis, which with the imaging and the renal tumor was taken to be metastatic RCC.

After assessment by medical oncology, she was started on sunitinib 25 mg daily; the treating oncologist chose this starting dose with a plan to increase it according to tolerance. About three months after nephrectomy, she developed headache and seizures, and brain imaging showed brain metastases. Because no dedicated brain imaging had been performed at presentation, it is not known whether these lesions were already present at diagnosis. She received palliative whole-brain radiotherapy (20 Gy in five fractions) and was discharged in a clinically stable condition. Her last documented hospital review was shortly after completion of radiotherapy, about three months after nephrectomy. She was subsequently lost to follow-up, and on telephone follow-up, her relatives reported that she had died at home; the date and cause of death are not known.

Discussion

Bone metastasis is well recognized in papillary RCC. In a multicenter series of 61 patients with metastatic papillary RCC, 24 (38%) had bone metastases [9], a proportion similar to the 29% reported for papillary tumors in the international cohort cited above [3]. Skeletal spread, taken alone, is therefore not unusual in advanced papillary disease.

What is less usual is a clinically apparent calvarial metastasis, and it has precedent in RCC. Gaetani et al. [5] described two patients in whom a calvarial mass led to the diagnosis. Jindal et al. [6] reported calvarial and cutaneous metastases as the first manifestation of a clinically silent RCC in a 35-year-old woman. Yeh et al. [7] described an 80-year-old man with a parietal skull nodule and a 7×7×8 cm renal tumor who, after nephrectomy and resection of the skull lesion, was disease-free at 22 months.

The closest published report is that of Mir et al. [8], which describes a 68-year-old woman with primary metastatic non-clear-cell RCC, multiple bone lesions, and a skull lesion. The skull lesion was resected and reported as poorly differentiated carcinoma of unknown origin, and cytoreductive nephrectomy then showed

oncocytic papillary RCC. Her skeletal disease progressed within three months, and she received sunitinib followed by cabozantinib, to which she responded (Table *1*). Our patient shares the age, sex, papillary morphology, and combination of skull and other skeletal lesions, but the sequence differed. The frontal swelling was her dominant complaint, imaging identified the renal mass before any operation, and the kidney and frontal lesion were dealt with in one operative course.

Study	Age (years)	Sex	Skull presentation	Renal histology	Other metastases	Treatment and outcome
Gaetani et al. [5] (two cases)	66 (case 1); NR (case 2)	Male (case 1); NR (case 2)	Calvarial mass as the first clinical presentation (case 1: painless, enlarging 5-cm occipital mass)	RCC diagnosed on histology of the excised calvarial mass	NR	Wide en bloc craniectomy in both cases; outcome NR
Jindal et al. [6]	35	Female	Bilateral frontal calvarial lesions, a left maxillary lesion, and an infraumbilical cutaneous nodule as the first presentation	RCC diagnosed by imaging with cytology of the metastases (metastatic adenocarcinoma); subtype not determined	Maxilla, skin	Planned for targeted therapy; declined cytoreductive surgery; died of massive hematuria about three weeks later
Yeh et al. [7]	80	Male	Left parietal skull nodule; clear cells on biopsy	7×7×8 cm right renal tumor; clear-cell RCC on skull biopsy	None found on staging	Nephrectomy and skull resection; disease-free at 22 months
Mir et al. [8]	68	Female	Skull lesion, resected; poorly differentiated carcinoma of unknown origin	Oncocytic papillary RCC	Multiple bone lesions	Skull resection and cytoreductive nephrectomy; skeletal progression within about three months; sunitinib, then cabozantinib after further bone progression, with response to second-line therapy
Present case	68	Female	Enlarging frontal swelling; lytic lesion with soft-tissue component	RCC with papillary morphology (no immunohistochemistry), WHO/ISUP grade 4, pT3a, focal rhabdoid differentiation, tumor necrosis	Multiple lytic skeletal lesions; later brain metastases	Nephrectomy with frontal excision, sunitinib, whole-brain radiotherapy; died at home (relatives' report); date and cause unknown

TABLE 1: Reported cases of renal cell carcinoma presenting with skull involvement, compared with the present case

NR: not reported in the accessible text (full text for Jindal et al.; abstract and article preview for Gaetani et al.; abstract for Yeh et al.); pT3a: pathological tumor stage T3a according to the tumor, node, metastasis (TNM) classification; RCC: renal cell carcinoma; WHO/ISUP: World Health Organization/International Society of Urological Pathology

The nephrectomy specimen showed focal rhabdoid differentiation. In a clinicopathological analysis of 76 RCCs, rhabdoid differentiation was associated with aggressive behavior [10], and under the International Society of Urological Pathology grading system, its presence assigns a tumor to grade 4 [11]. This may be relevant to our patient's course, with brain metastases diagnosed about three months after nephrectomy. However, because no dedicated brain imaging was performed at presentation, these lesions may already have been present, and the prognostic significance of rhabdoid differentiation cannot be established from a single case.

Brain metastasis from papillary RCC has been reported [12], though less often than from clear-cell disease (3% versus 8% in the international cohort) [3].

The renal tumor also showed nuclei with reverse polarity. Papillary renal neoplasm with reverse polarity, an emerging entity in the 2022 WHO classification associated with KRAS mutations [2], is unlikely here given the high grade, tumor necrosis, rhabdoid differentiation, and metastatic behavior, although GATA3 immunostaining was not performed. Without immunohistochemistry, FH-deficient RCC and TFE3-rearranged RCC, which can show papillary architecture with high-grade eosinophilic cells, also cannot be excluded [2].

Management of a calvarial metastasis depends on the extent of systemic disease, symptoms, site, and resectability. Excision can give a tissue diagnosis and local control in selected patients [7], whereas widespread disease needs systemic therapy and radiotherapy. The role of cytoreductive nephrectomy has narrowed: in the CARMENA (Cancer du Rein Métastatique Nephrectomie et Antiangiogéniques) trial of metastatic clear-cell RCC, sunitinib alone was noninferior to nephrectomy followed by sunitinib in patients with intermediate- or poor-risk disease [13], and evidence for non-clear-cell RCC is limited. In our patient, removal of the primary tumor and the calvarial lesion in the same sitting provided a histological diagnosis from both sites before palliative treatment.

This report has limitations. Immunohistochemistry was not performed on either specimen and could not be performed retrospectively, so the papillary subtype rests on morphology, FH-deficient or TFE3-rearranged RCC cannot be excluded, and the renal origin of the frontal metastasis was inferred from its histologic appearance together with the imaging findings and the renal tumor. Baseline brain imaging and a photomicrograph of the rhabdoid areas were not available, and the absence of a documented baseline IMDC risk assessment is also acknowledged as a limitation. In addition, the patient was eventually lost to follow-up, and the date and cause of death are not known, so we cannot comment on the response to treatment or on survival.

Conclusions

This case shows that an enlarging, fixed calvarial swelling in an older adult should not be presumed to be a benign or primary cranial lesion. A short history, tenderness, and fixity to bone should prompt imaging of the lesion and systemic staging before excision, because the calvarial lesion may be the first sign of an unsuspected visceral primary tumor. When staging reveals a renal mass, RCC should be considered, including tumors with papillary morphology, in which skeletal spread is not unusual; immunohistochemistry is needed to confirm the subtype. Whole-body staging, with CT or, where available, PET/CT, can identify other metastatic sites and help plan the treatment of the renal tumor and the calvarial lesion. Because a calvarial metastasis lies close to the brain, baseline brain imaging, preferably magnetic resonance imaging, may be considered at presentation rather than only when neurological symptoms appear. Adverse histological features, such as rhabdoid differentiation, should be recorded, although their prognostic significance in an individual patient is uncertain.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Acquisition, analysis, or interpretation of data: Naveen Kumar Yadlapalli, Sree Gouri Sivaram Rajappagari, Vineet Anand Kondaguli, Lakshmi Prasanna Karanam

Drafting of the manuscript: Naveen Kumar Yadlapalli, Anil Kumar Nallabothula, Sree Gouri Sivaram Rajappagari, Lakshmi Prasanna Karanam

Critical review of the manuscript for important intellectual content: Naveen Kumar Yadlapalli, Anil Kumar Nallabothula, Sree Gouri Sivaram Rajappagari, Vineet Anand Kondaguli, Lakshmi Prasanna Karanam

Supervision: Anil Kumar Nallabothula

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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references were verified by the authors against the original sources. The authors critically reviewed and revised the manuscript and accept full responsibility for its content.

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