

Renal Clear Cell Carcinoma Masquerading As Brain Arteriovenous Malformation: A Case Report and Review of the Literature

Review began 11/29/2024

Review ended 12/07/2024

Published 12/10/2024

© Copyright 2024

Fong et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.75447

Yew Weng Fong^{1, 2}, Sean Himel^{3, 2}, Cristina Cernei², Kathreena Kurian⁴, Kanjilal Banhisikha⁴, James Wareham⁵, Mario Teo²

1. Division of Neurological Surgery, Department of Surgery, Cathay General Hospital, Taipei City, TWN 2. Neurosurgery, Southmead Hospital, North Bristol NHS, Bristol, GBR 3. Neurosurgery, Department of Neurosurgery, University of Tennessee Health Science Center, Memphis, USA 4. Neuropathology, Southmead Hospital, North Bristol NHS, Bristol, GBR 5. Neuroradiology, Southmead Hospital, North Bristol NHS, Bristol, GBR

Corresponding author: Mario Teo, mario.teo@nbt.nhs.uk

Abstract

Cerebral arteriovenous malformations (AVMs) are tangles of abnormal vessels with early arteriovenous (AV) shunting that can lead to intracerebral hemorrhage, seizures, neurologic deficit, or headache. To date, only a few cases of carcinomas metastasizing to pre-existing cerebral AVMs have been reported in the literature. However, renal clear cell carcinoma (RCC) brain metastases that exhibit early AV shunting, where AVM pathology is not present, are extremely rare. We report a very rare case of early AV shunting phenomenon in RCC brain metastasis. This is a case of a 57-year-old man with no prior medical history who presented to the emergency department with an acute onset headache and speech difficulties. Contrast-enhanced computed tomography of the head revealed a left temporal intracerebral hemorrhage with a vascular nidus adjacent to the hematoma. A diagnostic cerebral angiogram (DSA) showed a Spetzler-Martin grade II AVM in the left para-Sylvian region, supplied by middle cerebral arteries with a superficial draining vein. Gadolinium-enhanced brain MRI revealed evolving methemoglobin and a small compact nidus adjacent to the hematoma in the distal left Sylvian fissure. The patient was stable until day 17 after hospital admission, when he deteriorated due to an interval repeat hemorrhage, requiring surgical excision of the AVM and the hematoma. Postoperative DSA revealed no residual shunting and complete resection of the AVM. However, there was a further re-bleed postoperatively, necessitating a second surgery. Pathology revealed an RCC without any specific pathological features indicative of an AVM. The patient recovered to his baseline but died in less than a year due to the progression of metastatic disease. In conclusion, RCC can exhibit an early AV shunting phenomenon, with the presence of enlarged, tortuous, pathologic nidus-like tumor-feeding vessels, which can mimic an AVM, which is extremely rare. This phenomenon poses significant treatment challenges, as the treatment goals are completely different for AVMs and metastatic disease.

Categories: Neurosurgery, Nephrology, Oncology

Keywords: brain arteriovenous malformation, brain metastasis, early arteriovenous shunting, intracerebral hemorrhage, renal clear cell carcinoma

Introduction

Intracerebral hemorrhage (ICH) is a devastating type of stroke accounting for 6.5% to 19.6% of strokes worldwide with high mortality [1]. Underlying etiologies include chronic hypertension, cerebral amyloid angiopathy, vascular malformations, neoplastic lesions, hemorrhagic transformation of an ischemia stroke, and venous thrombosis [2]. Certain distinctive hemorrhage patterns lead physicians to obtain advanced imaging studies to achieve a more complete diagnosis and therefore to formulate the most effective treatment strategies. In younger patients and when ICHs are in atypical locations of the brain, further vascular imaging studies such as computed tomography angiography (CTA) and magnetic resonance angiography (MRA) are warranted to assess for causative underlying pathologies.

Arteriovenous malformations (AVMs) contain vascular niduses with early arteriovenous (AV) shunting without intervening capillary beds. AVMs have the propensity to rupture as the walls of these arterial feeders, niduses, arterialized veins, and flow-related aneurysms weaken [3]. With an incidence of 0.94 per 100,000 people, AVMs have an approximate 2.3% risk of annual rupture. The mortality rate after AVM rupture is approximately 10%, with a 30-50% rate of morbidity [4].

The goal of treatment is to eliminate the risk of future hemorrhage, which can only be achieved with complete resection of the nidus. Microsurgical resection offers the highest obliteration rate with relatively low complication rates when performed by experienced neurosurgeons signifying it as the gold standard treatment for low-grade AVMs [5]. We present the case of a clinical and radiological AVM mimic that turned out to be a renal clear cell carcinoma (RCC) brain metastasis.

How to cite this article

Fong Y, Himel S, Cernei C, et al. (December 10, 2024) Renal Clear Cell Carcinoma Masquerading As Brain Arteriovenous Malformation: A Case Report and Review of the Literature. Cureus 16(12): e75447. DOI 10.7759/cureus.75447

Case Presentation

A 57-year-old man with no significant past medical history presented to the emergency department with an acute onset headache localized to the tempo-parietal region and speech difficulties. On examination, he was aphasic but was fully conscious, oriented to person, time, and place, and obeying verbal commands. He was otherwise neurologically intact. Laboratory studies revealed no significant abnormalities. Non-contrast CT and CTA of the head showed a left posterior temporal ICH near Wernicke's area and enlarged, tortuous blood vessels over the left cerebral hemisphere anterior to the hematoma (Figures 1A-1C). A contrast-enhanced MRI revealed evolving methemoglobin with mild perifocal edema in the distal left Sylvian fissure (Figure 1D). A diagnostic cerebral angiogram (DSA) showed a Spetzler-Martin grade II AVM nidus measuring 10 mm, supplied by middle cerebral artery (MCA) feeders centered at the M2/3 junction, with superficial drainage to the vein of Labbe (Figures 2A-2B).

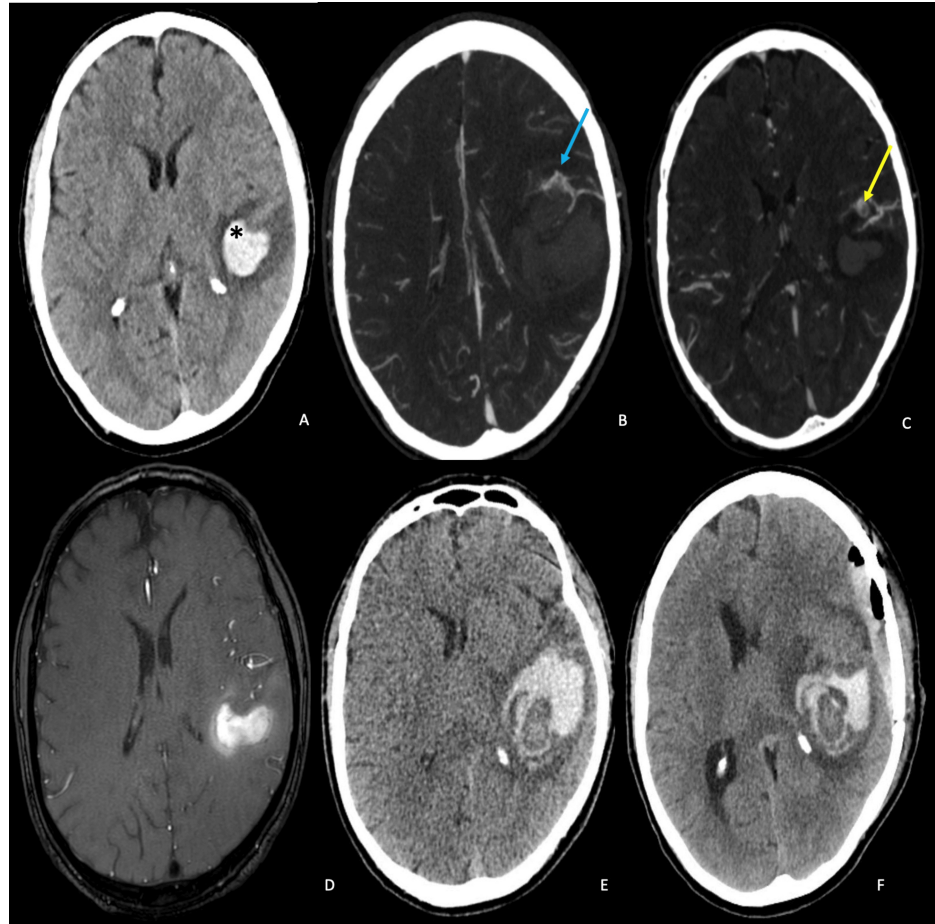


FIGURE 1: Serial imaging studies showing the disease progression.

(A) CT brain (axial view) showed a hematoma (*) in the left parietal region near the Sylvian fissure. (B, C) Brain CTA revealed a nidus-like lesion (Blue arrow), a rounded structure (Yellow arrow) with prominent cortical vessels in this region, suggestive of an arteriovenous malformation (AVM). (D) Gadolinium-enhanced brain MRI (axial view) showed evolving methemoglobin with mild perifocal edematous changes, consistent with evolving methemoglobin. (E) Brain CT was repeated on day 17 after the initial bleed showing a recurrent bleed. (F) Further rebleeding in the surgical cavity was noted, along with postoperative changes, including a mild subdural residual hematoma and pneumocephalus.

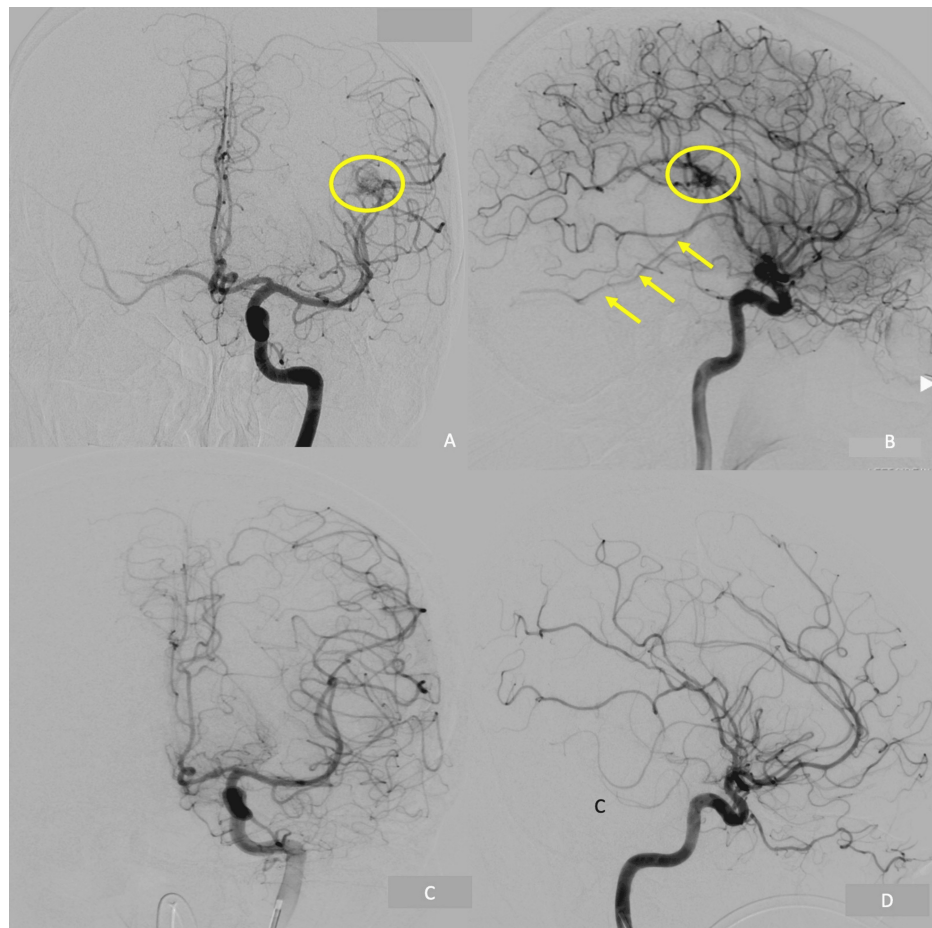


FIGURE 2: The diagnostic angiography of the right internal carotid pre- and post-surgical resection.

Anteroposterior view (A) and lateral view (B) of the pre-operative DSA of the right internal carotid artery showed the AVM nidus (Yellow circle) supplied by middle cerebral arteries with an early draining into the vein of Labbe (Yellow arrows); while (C, D) demonstrated the AVM nidus and early AV shunt were no longer visible.

AVM: arteriovenous malformation; DSA: diagnostic cerebral angiogram

Due to the eloquent location of the ICH and suspected AVM, clinical discussions centered around allowing the patient to recover from the hemorrhage followed by treatment (radiosurgery versus microsurgical resection) in a delayed fashion. Unfortunately, the patient experienced a second ICH on hospital day 17 (Figure 1E). After a neurovascular multidisciplinary team discussion, a neuro-navigation-guided craniotomy for hematoma evacuation and microsurgical resection of the lesion was offered to the patient and his family after a detailed explanation of the risks, benefits, indications, and alternatives. The patient and his family consented to the procedure. The operation was uneventful, however, on the postoperative CT scan the following day, it was noted that there was further ICH in the surgical cavity, necessitating an emergent repeat surgery for hematoma evacuation (Figure 1F). A DSA was repeated; however, no residual AVM was revealed (Figures 2C-2D). Histopathological examination of the pathology specimen obtained during the original operation revealed neoplastic cells stained positively for GFAP, CAM5.2, and PAX8 indicating metastatic renal cell carcinoma (Figure 3). The Verhoeff-von Gieson (EVG) stain showed accompanying abnormal distended blood vessels over the tumor which contain elastic laminae (Figure 3F). These findings were consistent with hemorrhagic metastatic clear cell carcinoma. Whole body CT scans later confirmed a renal cell carcinoma, measuring 7 cm, at the right upper pole, with lung metastasis (Figure 4).

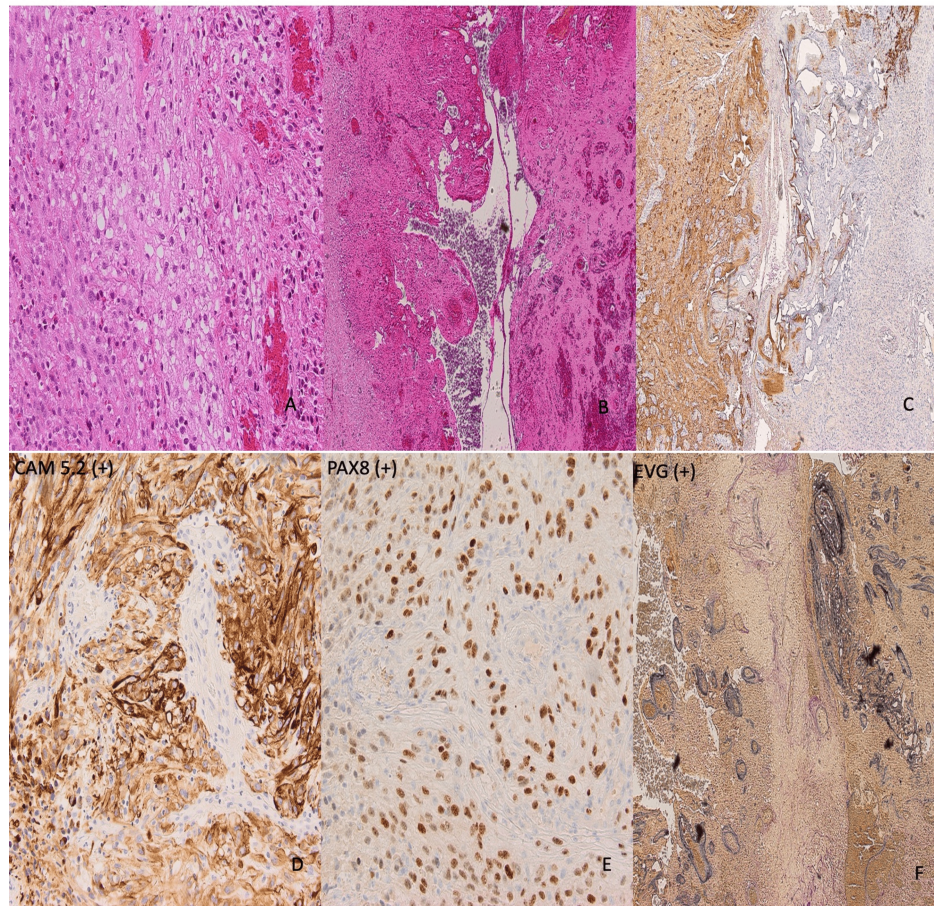


FIGURE 3: The photomicrographs of the surgical pathology specimens.

A) The photomicrograph of the specimen showed pleomorphic metastatic cancer cells with clear cytoplasm. (B) The left side displays metastatic tumor, while the right side shows reactive glial tissue. (C) GFAP is positive in the left-sided gliotic parenchyma and negative in the right-sided neoplastic cells. (D) CAM 5.2 is positive in neoplastic cells, (E) PAX8 (a renal cell carcinoma marker) is positive in the neoplastic cells. (F) EVG is stained positively in abnormal vessels.

EVG: Verhoeff-von Gieson

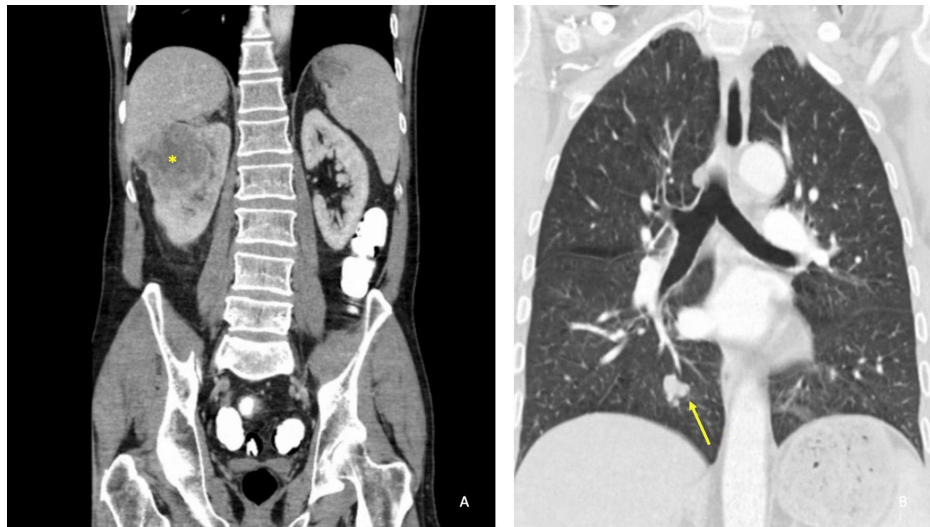


FIGURE 4: Computed tomography scan of the abdominopelvic (A) and chest (B) region.

(A) Coronal CT image of the abdomen showing a renal tumor (*) located at the right upper pole, measuring 7 cm.
(B) Coronal CT image of the chest showing lung metastasis (Yellow arrow).

Postoperatively, the patient improved to his presenting baseline. He was referred to the renal oncology team to commence systemic treatment. Due to ongoing metastatic disease progression, he died less than a year after the initial ICH presentation.

Discussion

RCC accounts for less than 5% of all malignant tumors, which commonly metastasize to the bones, lungs, lymph nodes, and liver. Metastasis in the brain constitutes around 10–16%, while the 5-year cumulative incidence of approximately 9.8% [6]. These metastatic brain tumors carry a higher risk of spontaneous hemorrhage when patients have received tyrosine kinase inhibitors (TKI) medications, or radiation therapy [7]. In our case, the tumor hypervascularity and the highly vulnerable feeding vessels likely contributed to the intracranial hemorrhage [8]. Although RCC brain metastases hemorrhage easily, they do not often masquerade as an AVM.

ICH is a critical medical condition with a broad spectrum of etiologies that include hypertension, vascular malformations, or neoplastic lesions. It is crucial to recognize the underlying etiology that contributes to each ICH to tailor effective treatment strategies. Identifying the hemorrhagic intracranial neoplastic lesion is not always possible with non-contrast CT or CTA alone. They may bleed in atypical locations, have irregular shapes, present with multiple hemorrhagic foci, have a heterogeneous hematoma appearance, have marginal enhancement, and have disproportionate perifocal edema [9]. MRI can be helpful in diagnosing underlying lesions; however, intra-axial hematomas often have heterogeneous features, and these vary over time. The transformation of these hematomas in the subacute to chronic phase may closely mimic tumor characteristics, and may also enhance over the periphery of the lesion with surrounding edema. AVMs generally present as hypointense on T1-weighted images (WI) and hyperintense with prominent flow voids on T2-WI [9]. Despite advanced imaging techniques, underlying tumors are often obscured by the surrounding hemorrhage [10]. Consequently, it can be difficult to discern whether the imaging findings represent a tumor, a tumor mimic, or simply a pure hematoma in one of its different phases of reabsorption.

Given our patient had no known risk factors and the hematoma was in an atypical location, the etiology of the spontaneous intraparenchymal hemorrhage was investigated. The CTA of the head revealed irregular vasculature with a nidus-like lesion that spatially coincided with the hematoma. Diagnostic cerebral angiography demonstrated an early AV shunt along with a tightly packed group of vessels that appeared to be a nidus, which led to the diagnosis of an AVM. We initially planned to closely observe the patient due to the lesion being a low-grade AVM (Spetzler-Martin-II: S1V0E1) located in an eloquent area with a likely long-term plan for radiosurgery. Before this plan could be enacted, the patient deteriorated with an interval bleed requiring the hematoma to be evacuated and the lesion removed. Subsequent pathological analysis revealed an unexpected diagnosis of metastatic RCC, with no evidence supporting the presence of an AVM.

Carcinomas with intracranial metastases to pre-existing true AVMs have been reported in the literature but are incredibly rare occurrences. To date, only eight cases have been reported as previously described. Kazama et al. summarized six reported cases of carcinomas that metastasized to the brain in the literature,

of which three cases were carcinomas originating from lung tissue, two from testicular tissue, and one from breast origin [11]. Two additional cases were found to have metastasized to the cerebral AVM with carcinomas of renal [12] and lung tissue [13] origin. The ages of these cases range from 19 to 73 years old. Three of the eight cases were female. Presenting symptoms varied, which included intracranial hemorrhage, seizures, and headaches. Six of the AVMs were found located in the supratentorial region, one in the infratentorial region, and one in the pons.

It has been proposed that the hypervascularity of the AVM may have entrapped tumor emboli, therefore leading to a higher chance of hematogenous metastasis [11,14]. To our knowledge, it is exceptionally rare for an intracranial metastatic RCC to manifest with an AVM-like shunt. The absence of an abnormal vascular structure resembling an AVM on pathological examination, further accentuates the presence of an AVM-like phenomenon in RCC brain metastasis in our case, rather than the presence of two separate disease entities—a true AVM and a metastatic tumor lesion, as reported by previous literature. The tangled vessels identified in the imaging studies were likely tumor-supplying vessels. The imbalance of the proangiogenic vascular endothelial growth factor (VEGF), erythropoietin (EPO), platelet-derived growth factor (PDGF), and insulin-like growth factor 2 (IGF2) could contribute to the structural and functional abnormalities in blood vessels, which may lead to early AV shunting in cerebral neoplasms [15]. The phenomenon of AV shunting in metastatic brain tumors from RCC could have significant implications for both diagnostic processes and therapeutic approaches.

The treatment goals are significantly different for these two different diseases. The surgical management of metastatic brain tumors aims for a gross total resection (GTR) whenever feasible to improve patient outcome; while the management of a ruptured AVM is to eliminate future recurrent bleeding through surgical resection, stereotactic radiosurgery, endovascular treatment, conservative management, or a combination of these treatment options. For low-grade ruptured AVMs, active intervention including surgical resection of the nidus is often the treatment of choice to eliminate the future risk of recurrent bleeding but should be a tailored approach for each patient based on multidisciplinary input. In this case, we treated the patient with surgical resection of the suspected AVM lesion to remove all AV shunting to prevent future rebleeding. The pathology revealed a metastatic tumor with AVM-like shunting complicating the clinical landscape. If the lesion was known to be a hemorrhagic brain metastasis, then the timing of the surgery and overall surgical plan would likely have been different. Therefore, it is significant to understand the possibility of the presence of AV shunting in metastatic renal cell carcinoma which can lead to different treatment paradigms.

Conclusions

To our knowledge, it is extremely rare for RCC with brain metastasis to display an early AV shunting phenomenon, accompanied by nidus-like tumor-feeding vessels mimicking an AVM, therefore leading to a completely different diagnosis. In this case, the initial imaging suggested an AVM when, in fact, it was a brain metastasis arising from RCC. Consequently, it is crucial to distinguish these two different disease entities, as their treatment goals vary significantly. We would be able to tailor a better treatment plan if this early shunting phenomenon in brain metastasis of RCC was recognized in advance, ultimately leading to better patient outcomes.

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.

Concept and design: Yew Weng Fong, Mario Teo

Acquisition, analysis, or interpretation of data: Yew Weng Fong, Mario Teo, Sean Himel, Cristina Cernei, Kathreena Kurian, Kanjilal Banhisikha, James Wareham

Drafting of the manuscript: Yew Weng Fong, Mario Teo, Sean Himel

Critical review of the manuscript for important intellectual content: Yew Weng Fong, Mario Teo, Cristina Cernei, Kathreena Kurian, Kanjilal Banhisikha, James Wareham

Disclosures

Human subjects: Consent for treatment and open access publication was obtained or waived by all participants in this study. issued approval NA. **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.

Acknowledgements

The co-authors contributed equally to this manuscript.

References

1. Feigin VL, Lawes CM, Bennett DA, Anderson CS: Stroke epidemiology: A review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. *Lancet Neurol*. 2003, 2:43-53. [10.1016/S1474-4422\(03\)00266-7](#)
2. Magid-Bernstein J, Girard R, Polster S, Srinath A, Romanos S, Awad IA, Sansing LH: Cerebral hemorrhage: Pathophysiology, treatment, and future directions. *Circ Res*. 2022, 130:1204-29. [10.1161/CIRCRESAHA.121.319949](#)
3. Laakso A, Dashti R, Juvela S, Niemelä M, Hernesniemi J: Natural history of arteriovenous malformations: Presentation, risk of hemorrhage and mortality. *Acta Neurochir Suppl*. 2010, 107:65-9. [10.1007/978-3-211-99373-6_10](#)
4. Grüter BE, Sun W, Fierstra J, Regli L, Germans MR: Systematic review of brain arteriovenous malformation grading systems evaluating microsurgical treatment recommendation. *Neurosurg Rev*. 2021, 44:2571-82. [10.1007/s10143-020-01464-3](#)
5. Alfter M, Albiña-Palmarola P, Cimpoca A, et al.: Multi-stage treatment for Spetzler-Martin grades III, IV, and V arteriovenous malformations: Preoperative embolization and microsurgical resection in a consecutive series of 250 patients. *J Clin Med*. 2023, 12:5990. [10.3390/jcm12185990](#)
6. Schouten LJ, Rutten J, Huveneers HA, Twijnstra A: Incidence of brain metastases in a cohort of patients with carcinoma of the breast, colon, kidney, and lung and melanoma. *Cancer*. 2002, 94:2698-705. [10.1002/cncr.10541](#)
7. Wronski M, Arbit E, Russo P, et al.: Surgical resection of brain metastases from renal cell carcinoma in 50 patients. *Urology*. 1996, 47:187-93. [10.1016/S0090-4295\(99\)80413-0](#)
8. Iwasa K, Nakazawa S, Kato T, Hatano K, Kawashima A, Fukuhara S, Nonomura N: Fatal tumoral hemorrhage from brain metastases of renal cell carcinoma after stereotactic radiotherapy and immune checkpoint inhibitor and vascular endothelial growth factor-targeted therapy combinations. *IJU Case Rep*. 2024, 7:225-9. [10.1002/iju5.12708](#)
9. Khanna A, Venteicher AS, Walcott BP, et al.: Glioblastoma mimicking an arteriovenous malformation. *Front Neurol*. 2013, 4:144. [10.3389/fneur.2013.00144](#)
10. Huisman TA: Tumor-like lesions of the brain. *Cancer Imaging*. 2009, 9:S10-3. [10.1102/1470-7330.2009.9003](#)
11. Kazama H, Yoshioka H, Kanemaru K, Murayama H, Hashimoto K, Yagi T, Kinouchi H: Metastasis of carcinoma to a cerebral arteriovenous malformation. *World Neurosurg*. 2021, 145:278-81. [10.1016/j.wneu.2020.09.138](#)
12. Albandar HJ, Roberto ES, See JR, Sabiers JH: Arteriovenous malformation and thyroid metastasis from underlying renal cell carcinoma, an unusual presentation of malignancy: A case report. *Oncol Lett*. 2017, 13:3323-7. [10.3892/ol.2017.5822](#)
13. Caranfa JT, Baldwin MT, Rutter CE, Bulsara KR: Synchronous cerebral arteriovenous malformation and lung adenocarcinoma carcinoma brain metastases: A case study and literature review. *Neurochirurgie*. 2019, 65:36-9. [10.1016/j.neuchi.2018.07.003](#)
14. Sundarakumar DK, Marshall DA, Keene CD, Rockhill JK, Margolin KA, Kim LJ: Hemorrhagic collision metastasis in a cerebral arteriovenous malformation. *J Neurointerv Surg*. 2015, 7:e34. [10.1136/neurintsurg-2014-011362.rep](#)
15. Mennitto A, Huber V, Ratta R, et al.: Angiogenesis and immunity in renal carcinoma: Can we turn an unhappy relationship into a happy marriage?. *J Clin Med*. 2020, 9:930. [10.3390/jcm9040930](#)