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Case Report

Solitary metastasis from renal cell carcinoma to the choroid plexus: A case illustration and review of the literature

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ABSTRACT

Background: Metastatic renal cell carcinoma (RCC) of the choroid plexus is an exceedingly rare condition, with only 35 reported cases to date. Surgical resection of these tumors poses a unique challenge to neurosurgeons since evidence-based treatment guidelines are yet to be designed.

Case Description: The authors describe the case of a 58-year-old woman presenting with progressive neurological deterioration 5 years after a right nephrectomy for a WHO 2016 Stage I RCC. A head, contrast-enhanced, and magnetic resonance revealed signs of obstructive hydrocephalus and a homogeneously contrast-enhancing 5 cm mass located in the trigone of the right lateral ventricle. Furthermore, a search of the literature was performed in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. After screening for duplicates, 35 publications met the eligibility criteria. Finally, 17 manuscripts were included for analysis. Moreover, a detailed description of an illustrative case is provided. The median age at diagnosis for intraventricular metastasis from RCC was 62.9 years, showing a slight female prevalence. The lateral ventricles were reported as the most frequent location with only one patient presenting with obstructive hydrocephalus caused by the obliteration of Monro foramen. Management options included either open craniotomy or radiosurgery.

Conclusion: The management of choroid plexus metastasis from RCC is still controversial with various authors proposing different treatment strategies. In this article, in addition to an in-depth case description, a qualitative review of the literature on metastatic RCCs of the choroid plexus using the PRISMA is provided.

Keywords: Brain metastasis, Cerebrospinal fluid, Choroid plexus, Hydrocephalus, Renal cell carcinoma, Stereotactic radiosurgery

INTRODUCTION

Solitary metastases to the choroid plexus are very rare. Three large postmortem series have reported the frequency as being 0.9%, 2.6%, and 4.6% in patients with systemic cancer.[10,18] To date, 35 cases of choroid plexus metastasis from renal cell carcinoma (RCC) have been reported with only a few papers describing the neurosurgical approach operated for its resection.[5,8,10,15] Radiological features

of intraventricular solitary metastasis are not specific; therefore, pathological analysis is crucial for the differential diagnosis with the more frequent intraventricular meningioma.[17]

In the present report, the authors describe the case of a metastatic RCC to the choroid plexus of the right lateral ventricle in a 58-year-old patient treated with total nephrectomy 5 years before presentation. In addition, the first systematic review of the available literature on RCC causing metastasis to the choroid plexus is provided.

METHODS

Patient's medical history including comorbidities, concomitant medications, diagnosis, and treatment was taken from clinical records. Written informed consent for the case publication was obtained from the patient. A review of the literature was performed in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Screening was performed by reviewing article titles or full text up to October 2021 using the electronic databases PubMed and the Cochrane Library. The primary search included "RCC" and "Choroid plexus" in the article titles. Only publications in the English language were included and the extracted citations were then screened for duplicates. Later operator "and" was applied on the extracted records by the use of the above-mentioned terms to narrow the scope of the review. Thirty-five articles met eligibility criteria for our qualitative systematic review and 18 were excluded because not relevant. Finally, 17 papers were included in the qualitative analysis [Figure 1].[16]

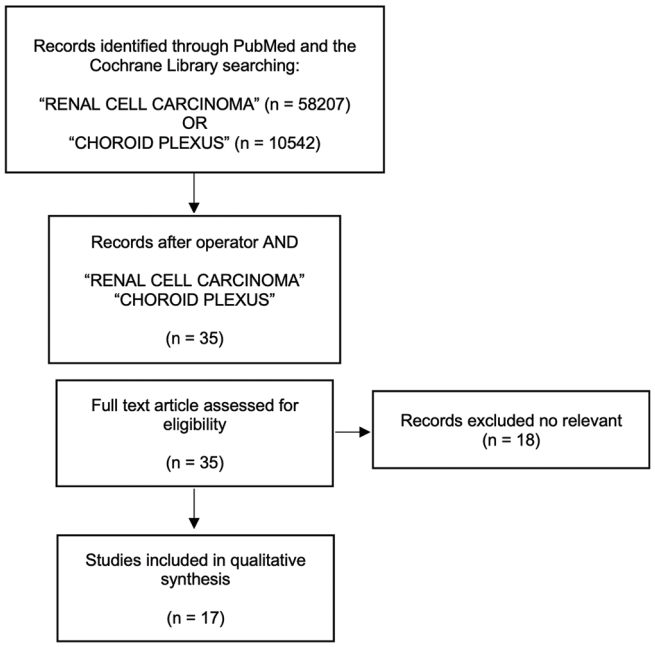

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol used for the systematic review.

ILLUSTRATIVE CASE

A 58-year-old right-handed woman presented to our attention with worsening headaches limiting her ability to perform daily tasks, gradual memory deficits, and progressive gait instability. The medical history was significant for a diagnosis of Stage I American Joint Committee on Cancer tumor-node-metastasis RCC that was treated with a right nephrectomy alone 5 years before presentation. At admission, her neurological examination was intact with no focal deficits and normal anal and urinary sphincter continence. A head, contrast-enhanced, and magnetic resonance imaging (MRI) investigation demonstrated a homogeneously contrast enhancing, 5 cm oval mass presumably originated from the choroid plexus in the trigone of the right lateral ventricle with signs of obstruction and dilation of the temporal horn and atrium of the contralateral ventricle [Figure 2]. Therefore, in the suspect of intraventricular meningioma or choroid plexus papilloma, the patient was taken into the operating room where she underwent a posterior parietal craniotomy with a transcortical approach for complete neuronavigated, microsurgical tumor resection. Intraoperatively, the body of the lateral ventricle was entered with release of cerebrospinal fluid and the tumor was observed to be attached to the choroid plexus within the posterior body of the lateral ventricle. The lesion appeared characterized by a hard elastic consistency and presented as extremely vascular with a marked bleeding tendency. The choroid plexus was extensively coagulated as was the anterior choroidal artery in this region and the tumor was resected in its entirety. Complete hemostasis was achieved, and an external ventricular catheter was placed into the atrium.

The postoperative period was unremarkable except for a transient left arm paresis that quickly subsided. The patient's amnesia gradually improved, and the headaches disappeared, and she was discharged after a control computed tomography (CT) [Figure 3] confirmed gross-total resection of the tumor with no signs of intraventricular hemorrhage.

The final pathological examination revealed the peculiar pattern of gland tissue with nests of clear cells set within a

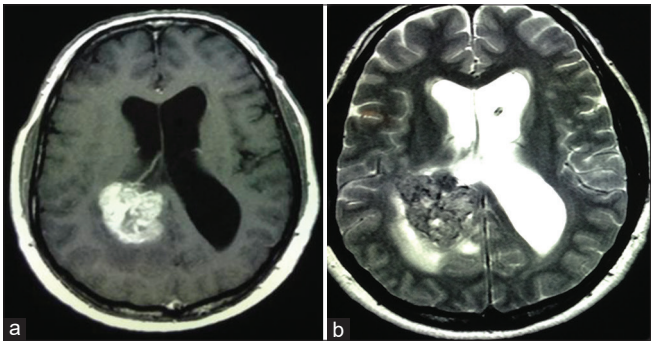

Figure 2: Axial (a) T1- and (b) T2-weighted MRI scans demonstrating a contrast-enhancing oval tumor located in the right lateral ventricle trigone causing obstructive hydrocephalus.

sinusoidal vascular network [Figure 4], consistent with the diagnosis of clear cell renal carcinoma metastasis. Six- and 12-month follow-up MRI investigations did not demonstrate any evidence of intracranial recurrence.

DISCUSSION

Analysis of previously reported cases

To date, 35 cases of solitary metastasis from RCC to the choroid plexus have been reported as summarized in [Table 1].[6,7,11,12,14,21,23,25] The average age at diagnosis for intraventricular tumor was 62.9 years (range 43–78), with a male-to-female ratio of 1:1.7 and an average time between the diagnosis of the primary tumor and the identification of the choroid plexus metastasis of 5.8 years (range 0–16). The prevalent localization is reported to be the choroid plexus of the lateral ventricles (30 cases) followed by the third ventricle (four patients). Only one patient was found with a lesion in right Monro foramen.

The mean follow-up time of this population was 25.8 months (range: 2 weeks–30 months), with one postoperative death and one vegetative state. Survival times were not reported in 7 cases (23%), whereas in the cohort described by Crisman *et al.*,[3] a median overall survival of 2.8 years was described, with 1- and 5-year overall survival rates of 76.7% and 28.3%. The therapeutic options deployed were various: 10 patients underwent neurosurgical procedure (eight resections, one stereotactic biopsy, and one ventricular drainage), 22 patients received radiosurgery (of which three patients had subsequently a WBRT). In three cases, the management was not documented.

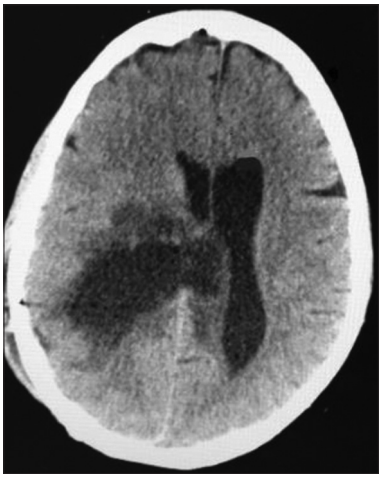

Figure 3: Postoperative CT scan showing no signs of residual tumor and intraventricular hemorrhage.

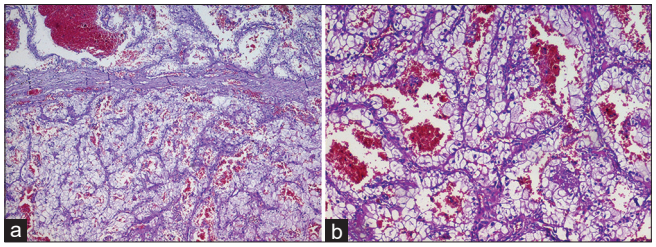

Figure 4: Metastatic clear cell renal carcinoma. Proliferation of anaplastic epithelial cells with clear cytoplasm and hyperchromatic, irregular nuclei, displayed in sheets detached by fine conjunctive septa including capillaries. a: 100x magnification, b: 400x magnification

Epidemiology of RCC metastases to the ventricular system

Approximately 10–40% of patients diagnosed with cancer will eventually develop brain metastases over the course of their disease with 0.9–4.5% of malignancies found in the ventricular system.[3,9] Several solid tumors have been reported to metastasize to the central nervous system (CNS)[1,4,24] with RCC representing the most frequent malignancy to disseminate within the ventricular system, where it causes 36–64% of all metastatic lesions.[3,20] In general, primary RCCs could be differentiated into two categories based on their growth rate and clinical features.[13] Slow-growing tumors do not exhibit any specific biochemical or clinical abnormality and have been associated with longer progression-free survival. Nonetheless, this peculiar behavior appears to be related to their ability to frequently invade the ventricular system and cause solitary metastasis particularly to the choroid plexus, which can occur 10 years after the initial diagnosis.[13] On the other hand, the rapidly progressive type tends to be associated with fever, increased erythrocyte sedimentation rate (ESR) and C-reactive protein, as well as the surge of alpha-2 globulin levels and other systemic abnormalities. It is probably due to its more aggressive behavior and, therefore, shorter overall survival that it has not been reported as a common cause of intraventricular metastases.

Metastasis to the choroid plexus

In line with the present review, Toms *et al.*[26] showed a median overall survival of 7 months from the onset of neurological symptoms and, further, demonstrated how survival could be negatively influenced by various factors, including weight loss, fever, elevated ESR, and location of the metastasis in the left temporal area. Significant differences exist between metastatic RCC and other malignancies that spread to the choroid plexus. For instance, in a cohort of 614 patients with brain metastasis, 24 (3.9%) were diagnosed with RCC-related lesions, 9 of whom (37.5%) presented an intraventricular mass, whereas only 5 patients (0.8%) with nonrelated RCC pathologies revealed an intraventricular metastasis of the choroid plexus ($P < 0.0001$).[20] Several hypotheses have been proposed to explain the tendency of RCC to frequently cause

Table 1: Patient demographics, tumor characteristics, and treatment.

Case	Year	Sex	Age	Region	Years after RCC diagnosis	Outcome	Surgical technique	Surgical approach
Shigemori *et al.*[21]	1987	M	58	Right lateral ventricle	2.5 years	Died 2nd day postoperative	Surgical resection	Transventricular
Mizuno *et al.*[14]	1992	M	59	Left lateral ventricle	4	Survived 29 months	Surgical resection	Posterior interhemispheric transcallosal
Suetake *et al.*[23]	1994	M	78	Right lateral ventricle	4 months	Vegetative state	Stereotactic biopsy	Nr
Kohno *et al.*	1996	M	66	Right lateral ventricle	7	Postoperative radiation therapy	Surgical resection	Interhemispheric transcallosal
Matsumura *et al.*	1997	M	68	Right lateral ventricle	7	Survived 30 months	Surgical resection	Transventricular via small corticotomy
Raila *et al.*	1998	F	47	Right lateral ventricle	0	Died after 3 weeks from secondary complications	Nr	Nr
Iwatsuki *et al.*[6]	1999	F	75	Left lateral ventricle	0	Nr	Nr	Nr
Hillard *et al.*	2003	F	54	Left lateral ventricle	4	Survived 60 months postoperative	Stereotactic radiosurgery	Posterior temporal
Quinones *et al.*	2004	F	61	Left lateral ventricle	10	Discharged	Surgical resection	Posterior contralateral transcallosal
Leach *et al.*[12]	2004	M	43	Third ventricle	1	Nr	Insertion of ventricular drain	Interhemispheric
Kadrian *et al.*	2004	F	54	Left lateral ventricle	16	Discharged	Stereotactic radiosurgery	Left middle temporal gyrus
Lauretti *et al.*[11]	2005	F	65	Right Monroe foramen	10	Died from pulmonary embolism	Surgical resection	Left transfrontal route
Tomiyama *et al.*[25]	2008	M	72	Third ventricle	5	Died 6 months after emergency VP shunt operation	No surgery	Nr
Karatay *et al.*	2015	M	53	Third ventricle	12	Died 13th day	Surgical resection	Interhemispheric transcallosal
Otani *et al.*	2015	M	68	Third ventricle	5	Disease-free after 2 years	Surgical resection	Interhemispheric transcallosal transchoroidal
Roh *et al.*	2019	M	65	Right lateral ventricle	15	Disease-free after 6 months	Fractionated stereotactic radiosurgery	Nr
Crisman *et al.*	2003–2019	13M 6 F	64	Lateral ventricles	5.7	2.8 years median overall survival	16 stereotactic radiosurgery 3 stereotactic radiosurgery + WBRT	Nr

solitary metastasis located to the choroid plexus, including hyperproduction of chemokines involved in tumor biology and cell migration,[20] loss of the tumor-suppressor gene VHL,[2] familiarity with Li-Fraumeni syndrome, and the inactivation of p53 and pRb through epigenetic disruption.[5]

Radiological and pathological diagnosis

For intraventricular metastases, the CT and MRI findings are nondefining, despite being crucial when planning for excision surgery or stereotactic radiosurgery (SRS), allowing

the identification of the location, and the number of lesions. In general, solitary metastases from RCC to the choroid plexus appear hyperdense on CT scans and homogeneously contrast enhanced, surrounded by excessive vasogenic edema and intraventricular hemorrhage.[3,17,27] On the other hand, intraventricular meningioma, the most frequently reported primary tumor in this location, is characterized by minimal brain edema and calcifications in 15–20% of the cases.[2] Therefore, given the low specificity of radiologic imaging tests, histologic analysis remains the gold standard for the diagnosis of intraventricular tumors.

Microscopic examination of choroid plexus metastases from RCC demonstrates nests of clear cells with the usual acinar pattern, along with hyperchromatic and pleomorphic nuclei contained in a clear cytoplasm and a stroma rich in small blood vessels.[8,18] Further analysis reveals positivity for keratin and epithelial membrane antigen, confirming the epithelial origin of the tumor, and negativity for chromogranin and transthyretin, ruling out benign tumors such as paraganglioma and choroid plexus adenoma.[17]

Current treatment and future perspectives

At present, there is no consensus over the treatment of intraventricular metastases and the preferred surgical approach is decided on several empirical factors including the location of the lesion, the size and number of tumors, and the patient's performance status.[8] Although microsurgical resection has been successfully adopted for most solitary metastasis in patients with a good clinical course, growing evidence suggests that SRS is associated with a median overall survival of 2 years (4–12 months with open surgical resection), an approximate 96% tumor control rate (compared with 79% for surgical resection), and a faster postoperative recovery.[3,8,22,24] Although open craniotomy with gross-total resection presents higher morbidity and mortality rates compared with SRS,[3] the latter should only be considered in case of intraventricular metastasis not exceeding 4 cm in diameter.[8] As for the present case, SRS did not represent the treatment of choice since the diameter of the lesion and the overall general status of the patient allowed for a gross-total microsurgical resection. For instance, recent evidence shows how fractionated SRS could be used for large intraventricular metastases if the patient has a poor Karnofsky score.[19] Nonetheless, when multiple lesions are identified with at least one measuring >4 cm, craniotomy followed by whole-brain radiotherapy treatment yields the best results in terms of overall survival.[22] Furthermore, preoperative embolization of the choroid plexus may help limit the blood loss and allow total resection.[20]

CONCLUSION

Metastatic RCC of the choroid plexus represents an extremely rare entity. For instance, due to the lack of evidence-based guidelines, treatment options remain solely grounded on empirical data. This systematic review of the literature shows that, although not always feasible, SRS is generally more effective in terms of overall survival, tumor control rate, and postoperative recovery when compared with open surgical techniques.

Authors' contributions'

AC, MS, ML, SI, and MB collected the case. NPF, FC, AL, and GG performed the literature research, wrote the paper, and assessed figures and tables. EDS reviewed and confirmed the histological diagnosis. GG, EDS, FC, AL, and NPF made the revision and supervised the project.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author on reasonable request.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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