Giant sellar metastasis from renal cell carcinoma
A case report and literature review
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Abstract
Rationale: Sellar metastasis is a rare and complex disease whose clinical features are strongly associated with the primary malignancy. Here, we present a rare case of giant sellar metastasis spread from renal cell carcinoma (RCC).
Patient concerns: A 30-year-old Chinese woman was admitted to our hospital, reporting headache, nasal congestion, nausea, vomiting, and a sharp decline in her right eye vision.
Diagnoses: Brain magnetic resonance imaging (MRI) revealed an invasive sellar mass with cavernous sinus and nasal cavity extension. Additionally, the patient had a medical history of right radical nephrectomy for clear-cell RCC.
Interventions: The patient underwent a successful subtotal resection of the tumor. Final pathological diagnosis confirmed sellar metastasis from RCC. After surgery, the patient was referred to our medical oncology department and received further systemic therapy.
Outcomes: No light perception remained in her right eye even after prompt surgical decompression. Follow-up MRI showed subtotal resection of the giant sellar metastasis.
Lesson: Sellar metastasis, although rare, should be particularly considered for elderly patients with deteriorating visual function and medical histories of cancer.
Abbreviations: ACTH = adrenocorticotropic hormone, ccRCC = clear cell renal cell carcinoma, MRI = magnetic resonance imaging, PRL = prolactin, RCC = renal cell carcinoma, SM = sellar metastasis.
Keywords: pan-hypopituitarism, renal cell carcinoma, sellar metastasis, visional function

1. Introduction
Sellar metastasis (SM) is a rare disease caused by the migration of distant malignant tumors to the sellar region. Breast and lung cancer are the 2 most common sources of metastases to the sellar region.[1] Renal cell carcinoma (RCC) is a relatively rare source of distant metastases to this region. Clinical manifestations of SM largely depend on tumor size and location; reported symptoms include visual field defects, headache, pituitary gland dysfunction, diabetes insipidus, and ophthalmoplegia.[2] Occasionally, these symptoms are the first manifestation of occult malignancy. Clinically, SM should be considered in differential diagnoses of patients with rapid tumor growth and histories of malignancy. Although histopathological confirmation is critical to a definitive diagnosis of SM, many published cases of SM were clinically presumed rather than histologically confirmed.[1] Here, we present a case of giant SM from RCC, which was successfully resected and confirmed by histopathology. In addition, we provide a literature review with basic statistics regarding this rare neurosurgical topic.

2. Case report
In June 2017, a 30-year-old Chinese woman presented to our clinic reporting headache, nasal congestion, nausea, vomiting, and a sharp decline in her right eye vision. The intermittent headache, located mainly in bilateral frontotemporal regions, first occurred 2 months earlier and decreased after taking pain relievers. One month earlier, the headache worsened and was associated with nasal congestion, hyposmia, nausea, and vomiting. She had also suffered a sharp decline in her right eye vision over 6 days. She denied polyuria, diplopia, dysphonia, and other symptoms. When admitted to our hospital for further evaluation, she had lost most of the sight in her right eye. Eye examination revealed her pupils were equally round with direct light re
diminished on the right eye

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As our patient had a history of ccRCC, and a rapid onset and progressive symptoms of headache and decreased visual function, a metastasis from RCC was presumably diagnosed. Endoscopic endonasal transsphenoidal surgery was immediately performed to restore the patient’s partial right vision. Follow-up MRI showed subtotal resection of the giant sellar metastasis (Fig. 1C, D). Unfortunately, no light perception remained in her right eye even after prompt surgical decompression. Immunohistochemistry revealed that tumor cells were positive for the markers PAX-8, CA9, RCC, and vimentin, and negative for CD10 and epithelial membrane antigen, consistent with the diagnosis of a ccRCC metastasis (Fig. 2). Also, the Ki-67 index was 15%, indicating highly active tumor cells. After surgery, the patient was referred to our medical oncology department and received further systemic therapy. Through follow-up via telephone in July 2018, the patient was still alive receiving chemotherapy and showed no relief of her visual disability.

3. Discussion

Metastases to the sellar area are rare, accounting for only 0.87% of all reported intracranial metastases.\(^\text{[3]}\) Reportedly, the most common sources are breast cancer in women (29%), and lung cancer in men (30%).\(^\text{[1]}\) Renal cell carcinoma is the ninth most common cancer worldwide,\(^\text{[4]}\) and is a relatively rarer source of distant metastases to sellar region. Table 1 summarizes 21 full-text, English-language case reports of SMs from RCC (including this case report) that could be searched from 1992 to 2018 in PubMed,\(^\text{[5–19]}\) whereas Table 2 shows basic statistical analyses of some characteristic parameters in these studies. We found the median patient age is 56.6 years old which is similar to the finding...
Figure 2. A, Tumor epithelial cells with clear cytoplasm and small granular nuclear chromatin were demonstrated by light microscopy (H&E, ×100). B, Tumor cells demonstrate diffuse reactivity for the tumor marker, PAX-8 (×100). C, Renal cell carcinoma (RCC, ×100). Additional immunohistochemical staining revealed a predominance of vimentin, and CA9 with no evidence of CD10 and epithelial membrane antigen, consistent with a diagnosis of clear-cell RCC.

Table 1
Literature review of 21 reported cases of sellar metastasis from renal cell carcinoma.

| Authors and year | Age and sex | Manifestations and pituitary function | MRI and size | Pathology | Medical history and other metastases | Management | Interval from RCC to SM | Survival status |
|------------------|-------------|----------------------------------------|-------------|-----------|-------------------------------------|------------|------------------------|----------------|
| Present study    | 30, F       | Headache, visual decline, normal       | 4.8 ± 3.6 cm,ellar mass with bone destruction | ccRCC      | ccRCC, lung                          | Transphenoidal resection + radiotherapy + chemotherapy | 3 m          | Still alive in July 2018 |
| Y. Zhao et al, 2018 | 40, M     | None, primary hypothyroidism           | unknown     | ccRCC      | ccRCC, unknown                       | Transphenoidal resection + radiotherapy               | Unknown      | Death                  |
| Di Nuzzo V et al, 2018 | 59, M     | Pituicyte node                         | Absence     | ccRCC, chest lymph, pancreas, cerebellum | Gamma knife surgery + sorafenib                      | 14 y         | Still alive before case report |
| Wendel C et al, 2017 | 61, M     | Normal                                | 1.8 ± 3.4 cm,ellar mass, brain, nasal septum | ccRCC      | ccRCC, lung                          | Surgical resection + radiotherapy + sorafenib          | 2 y          | Still alive before case report |
| Paydarsh M et al, 2016 | 50, M     | Pituicyte node                         | Absence     | ccRCC      | ccRCC, lung                          | Antihypertensive therapy                              | SM was first found | Still alive before case report |
| Ramek J et al, 2016 | 54, F      | Eyelid ptosis, worsening vision, headache, pan-hypothalamic area | 2.5 cm, bone destruction | ccRCC      | ccRCC, pancreas, lungs               | Surgical resection + radiotherapy + chemotherapy      | 6 y          | Death 8 m after surgery |
| Heung JM et al, 2013 | 40, F     | Headache, vision worsened, hyperprolactinemia, hypocortisolism | 2.5 cmellar mass, suprasellar extension | ccRCC      | RICC, chest lymph, lung, adrenal gland, pituitary gland | Chemotherapy + surgical decompression                  | 3 y          | Still alive before case report |
| Yang L et al, 2013 | 51, M      | Blurred vision, hemianopia, ptosis of eyelid, diplopia, hyperprolactinemia, ACTH deficiency | Diffuse enlargement of pituitary gland | ccRCC      | ccRCC, adrenal gland, bone, retroperitoneal lymph node, lung | Srsatib + surgery + radiot technology   | <7 m         | Death 9 m after surgery |
| Ginsberg R et al, 2013 | 45, M      | Visual deterioration, decreased libido, pan-hypothalamic area with increased prolactin level | 3.6 ± 2.4 cmellar mass, eroding the sellar floor | ccRCC      | No significant medical history       | Surgical resection + stereotactic radiography          | SM was first found | Not described |
| Kramer PK et al, 2010 | 74, M     | Visual deterioration, abducent nerve palsy, pan-hypothalamic area with increased prolactin level | 1.2 ± 0.9 cmellar mass | RICC      | RICC, lung                           | Chemotherapy + radiotherapy + tumor resection         | 5 y          | Still alive before case report |
| Gopin T et al, 2007 | 67, M     | Diencephalitis, diabetis, blurry vision, headache, impotence, diabetes insipidus, pituitary area with increased prolactin level | 2.0 cmellar mass with erosion of sellar floor | RICC      | RICC, panhypothalamic syndrome, lung | Surgical resection + radiation therapy                | 27 y         | Still alive before case report |
| Gopin T et al, 2007 | 51, M     | Headache, visual deficits, ACTH and gonadotropin deficiency | 2.3 cmellar mass with optic chiasm deficiency | ccRCC      | ccRCC, lung, scalp                   | Surgical resection + whole brain radiation treatment  | About 10 y    | Still alive before case report |
| Gopin T et al, 2007 | 53, M     | Headache, lethargy, decreased libido, increased thirst, diabetes insipidus, third nerve palsy, diabetes insipidus, pituitary area with increased prolactin level | Invasive sellar and parasellar mass | ccRCC      | No significant medical history       | Surgical resection + radiation therapy                | SM was first found | Death 12 m after surgery |
| Gopin T et al, 2007 | 67, F      | Fatigue, ACTH and gonadotropin deficiency | 2.5 cmellar mass with optic chiasm deficiency | None       | RICC, pancreas                       | Stereotactic radiotherapy + chemotherapy + sorafenib | 7 y          | Still alive before case report |
| Gopin T et al, 2007 | 61, F      | Arenal mental status, panhypothalamic area with increased prolactin level | 1.9 cmellar mass with optic chiasm deficiency | None       | ccRCC, lung                          | Declared treatment of stereotactic radiotherapy + tyrosine kinase inhibitor | 3 m          | Still alive before case report |
| Palkod J et al, 2005 | 70, M     | Headache, bilateral hemianopia, diabetes insipidus, pan-hypothalamic area with increased prolactin level | Sellar mass eroding the sellar base | RICC      | RICC                               | Surgical resection + stereotactic radiosurgery        | 6 y          | Still alive before case report |
| Basaria S et al, 2004 | 77, F     | Blurred vision, reduced appetite, fatigue, diplopia, ptosis, hemianopia, diabetes insipidus, pituitary area with increased prolactin level | 2.0 ± 0.2 cmellar mass compressing the optic chiasm | RICC      | RICC, lung, spleen                   | Surgical resection + stereotactic radiosurgery         | 2 m          | Death 12 m after surgery |
| Yokoyama T et al, 2004 | 63, M     | Visual field deficit, headache, hemianopia, diabetes insipidus, pan-hypothalamic area with increased prolactin level | Sellar mass with erosion of the bony floor and dorsum sella turica | None       | RICC, lung, bone                    | Stereotactic radiotherapy                             | 8 y          | Still alive before case report |
| Weber J et al, 2003 | 62, M     | Headache, visual loss, bilateral hemianopia, normal pituitary area, pineal tumor | Large sellar mass | ccRCC      | ccRCC, adenocortical adenoma        | Surgical resection                                   | 4 y          | Death from pneumonia  |
| Beckett DJ et al, 1998 | 56, M     | Lethargy, vomiting, loss of libido, pan-hypothalamic area | Large sellar mass | RICC      | RICC, no significant medical history | Surgical resection + radiotherapy                  | SM was first found | Still alive before case report |
| Kuruppu H et al, 1992 | 57, M     | Lethargy, vomiting, loss of libido, pan-hypothalamic area | Large sellar mass | Metastatic ccRCC | Metastatic ccRCC, no significant medical history | Surgical resection + radiotherapy                  | SM was first found | Still alive before case report |

ACTH=adrenocorticotropic hormone, ccRCC=clear cell renal cell carcinoma, F=female, M=male, m=month, PRL=prolactin, RCC=renal cell carcinoma, SM=sellar metastasis, y=year.
of Al-Aridi et al that median age of SM patients is 56 years.\cite{11} However, whereas the previous study found SM to be equally distributed by sex,\cite{11} we were surprised to find significantly higher incidence of SM from RCC in men (71.4%) than in women (28.6%; Table 2). We attribute this difference mainly to the higher incidence (62.2%) of RCC in men.\cite{11} Regarding pathological subtype, we found ccRCC makes up almost all the reported literatures of SM from RCC (Table 1), which may be because ccRCC is the most common histological subtype.\cite{20} In addition, we found about 60% of patients with SM from RCC develop metastasis simultaneously in the lung, followed by pancreas (20%), bone (20%), and adrenal gland (15%; Table 2).

SM is usually asymptomatic; only 20% of patients show symptoms.\cite{21} Although the median interval from RCC to SM is 6.2 years (Table 2), in some cases SM was detected earlier than the primary RCC (Table 1).\cite{12,14} Headache, pituitary dysfunction, visual deterioration, diabetes insipidus, and ophthalmoplegia are common presentations of metastases in the sellar region. Whereas hypopituitarism, visual defects, and headache are not helpful in differentiating SM from pituitary adenoma, diabetes insipidus, and cranial neuropathies are reported to be strong indicators of SM.\cite{22} Nevertheless, we found visual disturbance (66.7%) and pan-hypopituitarism (60%) were the 2 most common symptoms in patients with RCC metastasis to the sellar region (Table 2); indeed, our present case presented a giant sellar mass extending along the cavernous sinus and optic nerve, but without diabetes insipidus or cranial neuropathy. The patient’s MRI image showed an intact pituitary gland, located above the tumor. To our knowledge, this is the first report to describe a huge sellar metastasis (diameter > 4 cm) that did not invade the pituitary gland or cranial nerves related to eye movements.

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### Author contributions

ZS and CY wrote the first draft of the manuscript. XB revised the manuscript substantially and approved its final version. RW participated in patient care.

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