Differential Diagnosis and Management of a Pituitary Mass with Renal Cell Carcinoma

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The small pituitary mass was incidentally found in 40-years-old women with renal cell carcinoma. The endocrinological and ophthalmological evaluation revealed no deficit and the short-term follow-up was recommended. In 6 months later, the visual disturbance was reported and the size of mass was increased. The tumor was removed totally via the trans-sphenoid approach. The post-operative endocrinological insufficiency was not noticed. During one year of follow-up period, there was no evidence of recurrence without adjuvant radiotherapy. The clinical features of pituitary metastasis from renal cell carcinoma were similar to those of pituitary adenoma. The possibility of pituitary metastasis should be kept in mind in patients with sellar mass and renal cell carcinoma.

Key Words: Pituitary · Metastasis · Renal cell carcinoma.
out management 9 years ago prior to her current presentation. With these clinical backgrounds, a presumptive diagnosis of pituitary adenoma was made and regular follow-up was recommended because of the relatively rare incidence of pituitary metastasis.

Six months after the first visit, her vision worsened. Snellen visual acuity without correction at a 5 m distance in 200 lux of light showed a marked decrease in visual acuity from 1.0/1.0 to 1.0/0.4. Goldmann perimetry revealed superior temporal quadrantopia of the left eye. The follow-up MR imaging showed that the mass from 13 mm to 23 mm, and compression of the optic apparatus was observed (Fig. 2). The cocktail test showed hyperprolactinemia (prolactin, 74.4 ng/mL) and hypocortisolism (peak cortisol, 11.9 ug/dL). The other pituitary axes were intact, and there were no symptoms suggesting diabetes insipidus.

The patient underwent trans-sphenoid surgery to obtain a pathologic diagnosis and decompress the optic apparatus. The sellar floor was very thin and showed a mottled appearance. The tumor was gray and hypervascular (Fig. 3). Its hard consistency and the distinct demarcation helped to easily dissect it from the pituitary gland and cavernous sinus. However, we removed parts of the diaphragma sellae with the superior surface of the tumor because the tumor was strongly adhered to it. The tumor was completely removed in a piecemeal fashion, and the pathology was compatible with renal cell carcinoma (Fig. 4). The post-operative course was uneventful and her vision recovered to its previous original state within one month after surgery. The clinical and radiological follow-up has been continued without adjuvant therapy and hormone replacement.

**DISCUSSION**

The pituitary gland is an uncommon site for the metastasis of systemic malignancies. Metastatic pituitary tumors constitute less than 1% of all surgical specimens from transsphenoidal surgery for sellar or parasellar tumors. Breast and lung cancer account for two thirds of pituitary metastases, although metastases from almost all cancers have been reported. Additionally, renal cell carcinoma is a primary malignancy in only 2.6% of pituitary metastases.

The differential diagnosis of pituitary metastases from other pathologies is challenging. Most metastatic pituitary tumors involve the posterior lobe. A series of 190 symptomatic pituitary metastases identified the diabetes insipidus in 45.2% of patients. The putative causes for frequent involvement of the posterior lobe were the relatively wide contact with the adjacent dura and...
the direct arterial supply from the hypophyseal arteries, contrasting with the anterior lobe from the hypophyseal portal system. Therefore, the presence of diabetes insipidus or cavernous cranial neuropathy in patients with primary malignancy suggests to pituitary metastasis over relatively common pathologies such as adenoma and Rathke’s cleft cyst. However, pituitary metastasis from renal cell carcinoma shows similar symptoms and signs to pituitary adenoma. A recent study has revealed that the anterior pituitary dysfunction is more prevalent (90%) and diabetes insipidus is less prevalent (24%) in patients with pituitary metastases from renal cell carcinoma compared to those with other metastatic tumors. These clinical features make it difficult to differentiate the pituitary metastasis from renal cell carcinoma from common pituitary pathologies with clinical features except the rapid growth rate as the presented case. Additionally, visual field defects are more commonly found in patients with renal cell metastases (82%) than those with other primary malignancies. Therefore, the trans-sphenoid surgery was recommended as the first-line treatment in all cases in literatures and stereotactic radiotherapy was performed in patients refused the surgery. A half of patients underwent the radiotherapy as the adjuvant treatment (Table 1).

In the reported case, we attempted to characterize a pituitary lesion with $^{18}$F-FDG PET at the time of presentation. However, the lesion did not show uptake in $^{18}$F-FDG PET, contrasting with the metastatic tumors in other sites, such as the adrenal gland and abdominal lymph nodes. The follow-up $^{18}$F-FDG PET, the direct arterial supply from the hypophyseal arteries, contrasting with the anterior lobe from the hypophyseal portal system. Therefore, the presence of diabetes insipidus or cavernous cranial neuropathy in patients with primary malignancy suggests to pituitary metastasis over relatively common pathologies such as adenoma and Rathke’s cleft cyst. However, pituitary metastasis from renal cell carcinoma shows similar symptoms and signs to pituitary adenoma. A recent study has revealed that the anterior pituitary dysfunction is more prevalent (90%) and diabetes insipidus is less prevalent (24%) in patients with pituitary metastases from renal cell carcinoma compared to those with other metastatic tumors. These clinical features make it difficult to differentiate the pituitary metastasis from renal cell carcinoma from common pituitary pathologies with clinical features except the rapid growth rate as the presented case. Additionally, visual field defects are more commonly found in patients with renal cell metastases (82%) than those with other primary malignancies. Therefore, the trans-sphenoid surgery was recommended as the first-line treatment in all cases in literatures and stereotactic radiotherapy was performed in patients refused the surgery. A half of patients underwent the radiotherapy as the adjuvant treatment (Table 1).

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**Fig. 4.** The pathologic examination shows a nest of epithelial cells with clear cytoplasms and distinct cell membranes. The nests are separated by the highly vascularized stroma. Hematoxylin and eosin staining ($\times$200).

**Table 1.** Clinical features of the reported cases of pituitary metastasis from renal cell carcinoma

| Sex     | Age (years) | Interval from primary Dx. (years) | Status at diagnosis | Treatment |
|---------|-------------|----------------------------------|--------------------|----------|
|         |             |                                  | Hypopituitarism    | Diabetes insipidus | Visual symptom | Primary | Adjuvant |
| Male    | 59          | 9                                | (+)                | (-)         | (+)           | TSS     | (-)      |
| Male    | 53          | 0                                | (+)                | (+)         | (-)           | TSS     | RT       |
| Male    | 75          | 9                                | (-)                | (-)         | (-)           | TSS     | (-)      |
| Male    | 66          | 0                                | (+)                | (-)         | (-)           | TSS     | RT       |
| Male    | 51          | 0                                | (+)                | (-)         | (-)           | TSS     | RT       |
| Female  | 35          | 0                                | (+)                | (-)         | (+)           | TSS     | RT       |
| Male    | 63          | 4                                | (+)                | (-)         | (+)           | TSS     | RT       |
| Male    | 57          | 0                                | (+)                | (+)         | (-)           | TSS     | RT       |
| Male    | 59          | 0                                | (+)                | (+)         | (+)           | TSS     | RT       |
| Female  | 63          | 4                                | NA                 | NA          | NA            | TSS     | (-)      |
| Male    | 56          | 0                                | (+)                | (-)         | (-)           | TSS     | RT       |
| Male    | 54          | 3                                | (+)                | (-)         | (+)           | TSS     | (-)      |
| Male    | 73          | 8                                | (+)                | (-)         | (-)           | TSS     | (-)      |
| Male    | 62          | 4                                | (+)                | (+)         | (+)           | TSS     | (-)      |
| Female  | 77          | 0.25                             | (+)                | (-)         | (+)           | TSS     | SRT      |
| Male    | 63          | 8                                | (+)                | (+)         | (+)           | TSS     | SRT      |
| Male    | 70          | 6                                | NA                 | (-)         | (+)           | TSS     | RT       |
| Male    | 54          | NA                               | (+)                | (-)         | (+)           | TSS     | RT       |
| Male    | 67          | 27                               | (+)                | (+)         | (+)           | TSS     | RT       |
| Male    | 51          | 12                               | (+)                | (-)         | (+)           | TSS     | RT       |
| Male    | 53          | 0                                | (+)                | (+)         | (+)           | TSS     | RT       |
| Female  | 67          | 11                               | (+)                | (-)         | (-)           | SRT     | Chemotherapy |
| Female  | 61          | 1                                | (+)                | (-)         | (-)           | SRT     | Chemotherapy |
| Male    | 74          | 5                                | (+)                | (-)         | (+)           | TSS     | (-)      |
| Male    | 45          | 0                                | (+)                | (-)         | (+)           | TSS     | SRT      |
| Female  | 40          | 3                                | (+)                | (-)         | (+)           | TSS     | (-)      |

TSS : trans-sphenoid surgery, RT : radiotherapy, SRT : stereotactic radiotherapy, NA : not available
which was performed 2 months before the vision disturbance, also did not show increased uptake in the pituitary gland. Retrospectively, $^{18}$F-FDG PET was not helpful for differentiating the pituitary metastasis from other pathologies in the reported case. Recently, a report revealed that various pathological abnormalities were identified using MR imaging in 52.7% of patients who showed focal $^{18}$F-FDG accumulation. Additionally, the most common entity was pituitary adenoma, followed in incidence by metastasis and lymphoma. However, there was no significant difference in standardized uptake values between malignant and benign lesions. Therefore, the specific diagnosis of a pituitary lesion with $^{18}$F-FDG is not yet possible.

There were some characteristic of pituitary metastasis on the MR imaging, such as high signal intensity on T2-weighted images with iso- or hypointense signals, loss of high signal intensity in the posterior lobe on T1-weighted images, and a rapidly growing sellar mass with infiltrating features. However, these findings cannot be the pathognomic criteria for the diagnosis of pituitary metastasis, with the exception of growth rate. The rapid development of the visual field defect and growth on the follow-up MR images provided the clues for diagnosis. Therefore, the follow-up interval should be shorter in patients with asymptomatic pituitary lesions and systemic malignancies.

**CONCLUSION**

The differential diagnosis of pituitary metastasis from a renal cell carcinoma from pituitary adenoma is challenging. Short-term regular follow-up is mandatory in cases of pituitary lesions with underlying renal cell carcinoma.

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