Case Report

SELLAR ATYPICAL TERATOID/RHABDOID TUMOR: ANY PREOPERATIVE DIAGNOSTIC CLUES?

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ABSTRACT

Objective: Our objectives were to describe a rare adult-onset sellar atypical teratoid/rhabdoid tumor (AT/RT) and to identify preoperative diagnostic clues for this aggressive tumor.

Methods: A case report and review of the relevant literature.

Results: A 36-year-old female presented with headache for 1 month and blurry vision for 6 days. Imaging identified a large sellar mass with suprasellar extension that was indistinguishable from a pituitary adenoma. Hormonal studies revealed hypopituitarism and hyperprolactinemia. A presumptive diagnosis of pituitary macroadenoma was made, but the histologic, immunohistochemical, electron microscopic, and cytogenetic studies of the tumor supported a diagnosis of AT/RT. Despite multiple surgical resections, radiation, and chemotherapy, the tumor recurred and regrew relentlessly. The patient died 2.5 years after presentation.

Conclusion: This case highlights the importance of suspecting aggressive sellar masses in management planning and prognosis counseling. Short duration of headache and visual changes associated with a large sellar mass are diagnostic clues for sellar AT/RT or other rapidly expanding sellar masses. Endocrinologists should pay attention to symptom duration in patients with large sellar masses. **(AACE Clinical Case Rep. 2015;1:e2-e7)**

Abbreviations:
AT/RT = atypical teratoid/rhabdoid tumor; **INI1** = integrase interactor 1; **MRI** = magnetic resonance imaging

INTRODUCTION

Pituitary adenomas account for the majority of sellar masses, but other rare lesions are possible and include many benign entities such as Rathke's cleft cyst, craniopharyngioma, meningioma, and hypophysitis (1). Very rarely, malignant tumors can present as a sellar mass (1,2). About a quarter of the sellar malignancies are metastatic, and three-quarters are primary. Differentiating between malignant and benign sellar masses is important because it helps determine the best treatment option and offers prognostic insight for the patients. A history of primary malignancies and imaging evidence of gross invasiveness suggest the malignant nature of a sellar mass (2); however, the preoperative diagnosis of primary malignant sellar mass without gross invasiveness poses a challenge. Here, we report the case of a patient with a very rare primary malignant sellar tumor, atypical teratoid/rhabdoid tumor (AT/RT), and discuss whether any preoperative clues suggest a malignancy diagnosis.

CASE REPORT

A 36-year-old African American female presented to the emergency department with nausea, vomiting, and blurry vision for 6 days. She had experienced a headache in the preceding month, which her primary care physician attributed to stress. The patient had reportedly been seen by an ophthalmologist for the blurry vision 5 days before but was told that no significant findings were noted. She denied galactorrhea, irregular menstrual periods,

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polyuria, or visual field changes. Her past medical history included obesity, hypertension, and a left ovarian dermoid cyst resected 2 years before. She had no family history of cancer. Physical examination by the emergency department physicians did not reveal gross neurological deficits, but an experienced neurosurgeon identified a bitemporal visual field deficit and partial left cranial nerve VI palsy. Her hemogram and electrolytes were normal, but a head computed tomography scan demonstrated a 3-cm mass in the sella. The patient was admitted for further evaluation. Her endocrine laboratory values were as follows: prolactin 50.2 ng/mL (normal 3.8-23.2), luteinizing hormone <0.5 mIU/mL (0.6-19), follicle-stimulating hormone 2.9 mIU/mL (3-20), estradiol <20 pg/mL (37-298), thyrotropin 0.60 μIU/mL (0.39-4.60), "low" free thyroxine, morning cortisol 5.4 mcg/dL (6-19), and insulin-like growth factor-1 107 ng/mL (114-492). Pituitary magnetic resonance imaging (MRI) confirmed a large sellar mass measuring 3.3 × 3.2 × 2.3 cm with compression of the optic chiasm and invasion into the left cavernous sinus (Fig. 1 *A-D*). The mass exhibited heterogeneous enhancement following gadolinium administration and might have contained a cystic component on the left. The brain parenchyma was normal without masses, but the ventricles were slightly enlarged. The patient was diagnosed with probable nonfunctioning pituitary macroadenoma that caused hypopituitarism and hyperprolactinemia. She was treated with hydrocortisone and thyroxine and underwent transsphenoidal resection of the sellar mass a few days later. Intraoperatively, the tumor appeared slightly more fibrous than most pituitary adenomas and had necrotic areas. A complete resection was thought to be achieved.

Histologically, the mass was not consistent with pituitary adenoma. The tumor tissue smear showed atypical epithelioid-like spindle cells with abundant pink cytoplasm, prominent nucleoli, and rhabdoid features (Fig. 2 *A*). Tissue sections revealed that the tumor was composed of atypical epithelioid-like spindle cells with pink cytoplasm and prominent nuclei arranged in a fascicular pattern; focally, some tumor cells exhibited rhabdoid features (Fig. 2 *B-D*). Extensive immunohistochemical studies were done to further characterize this tumor. The tumor was strongly positive for vimentin and focally positive for epithelial membrane antigen, smooth muscle actin, and desmin and negative for chromogranin A, synaptophysin, cytokeratin AE1/AE3, myoglobin, CD68 (KP-1), CD31, Factor VIII, S-100, human melanoma black 45(HMB-45), alpha-fetoprotein (AFP), placental alkaline phosphatase (PLAP), glial fibrillary acidic protein, Leu-7, CD117, CD34, and any pituitary hormones. Electron microscopy showed rhabdoid cells with cytoplasmic thin filaments and dense bodies (Fig. 3). Finally, fluorescence in situ hybridization demonstrated loss of heterozygosity for the integrase interactor 1 *(INI1)/hNSF5* gene (Fig. 3). The histological, immunohistochemical, electron microscopic, and cytogenetic features were all consistent with AT/RT (3-5).

Postoperative pituitary MRI demonstrated incomplete resection or recurrence. Two months after the first operation, the patient underwent another transsphenoidal resection that debulked the tumor but left a significant portion of the mass in the right suprasellar compartment. A few days later, she underwent a right craniotomy to further debulk the tumor. The patient had an unremarkable recovery after the second and third operations, but MRI still showed residual tumor. She received external beam radiation to the sellar area. At 8.5 months after the third operation, the patient continued to have poor vision in the right eye and a lateral visual field defect in the left. MRI showed either a small recurrent or stable residual sellar tumor (Fig. 1 *E*). The patient presented with almost complete right visual loss 3.5 months later, tumor recurrence was confirmed by MRI (Fig. 1 *F*), and the patient underwent stereotactic radiosurgery and chemotherapy with temozolomide. She was again treated with external beam radiation, and her vision slightly improved. Over the next year, she underwent another 3 operations to debulk the tumor and received chemotherapy regimens with cytoxan, adriamycin, and vincristine and with cisplatin and VP16 due to tumor recurrence and growth into the left temporal lobe with hydrocephalus. She became blind with palsy of cranial nerves III, V, and VI; developed diabetes insipidus that was treated with desmopressin; and continued to require cortisol and thyroxine replacement. She died of sepsis 2.5 years after her initial presentation.

DISCUSSION

We described an adult female patient with a primary sellar AT/RT. The diagnosis was based on the tumor's histologic, immunohistochemical, electron microscopic, and cytogenetic features. AT/RT is a poorly differentiated malignant tumor possibly derived from mesenchymal cells (3). The spindle-shaped tumor cells are epithelioid-like but have rhabdoid features. Rhabdoid cells are a distinct feature of AT/RTs that can be appreciated on tissue smears and sections and electron microscopy. As AT/RTs often display a wide spectrum of histologic features and multi-lineage immunophenotypic differentiations that overlap with other poorly differentiated and embryonal neoplasms including medulloblastoma, primitive neuroectodermal tumors, sarcomas, germ cell tumors, high-grade gliomas, and poorly differentiated carcinomas, a rather extensive panel of ancillary diagnostic studies is frequently required to reach the correct AT/RT diagnosis. For example, the absence of immunohistochemical markers S-100 and HMB-45 rules

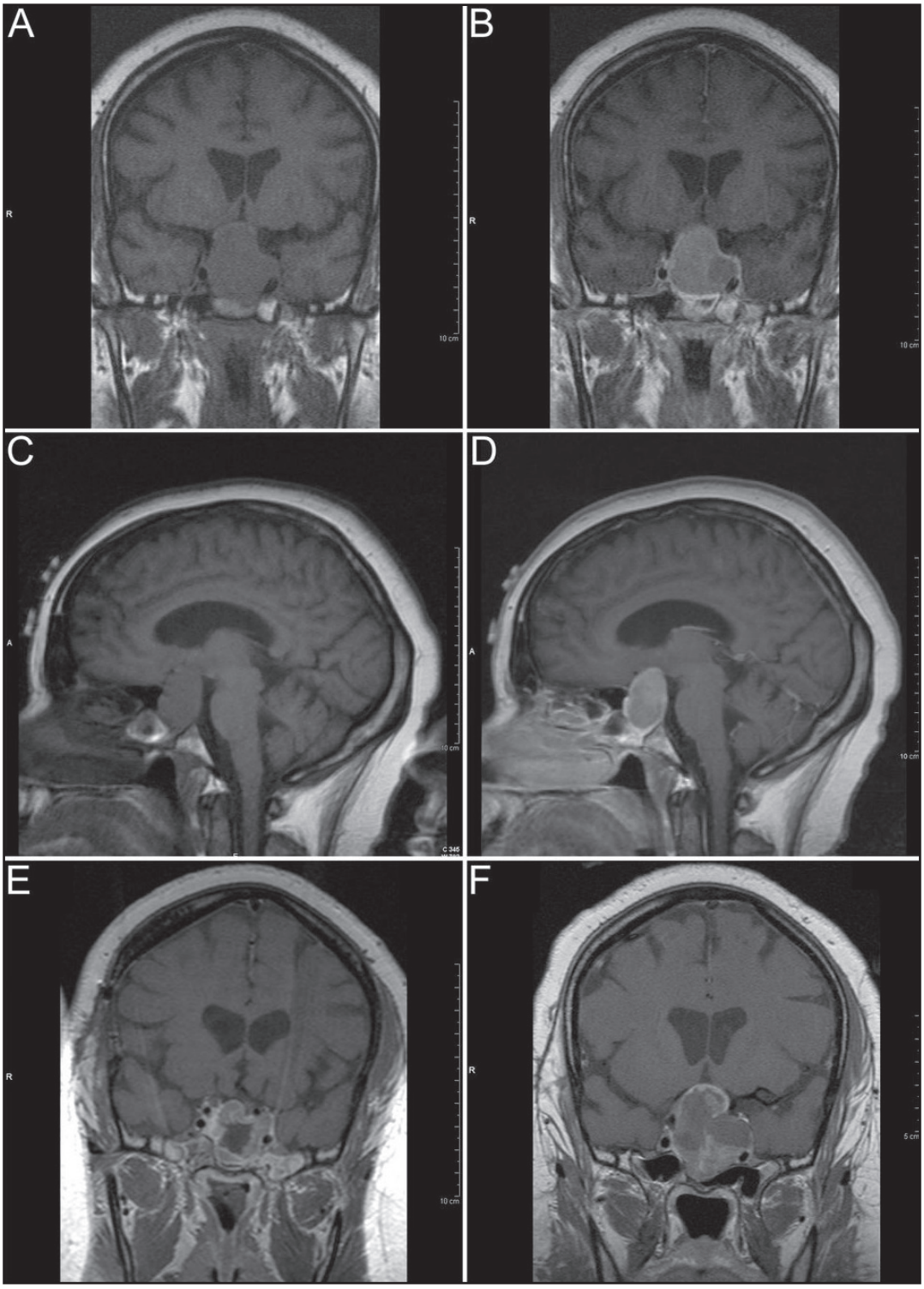

Fig. 1. T1-weighted magnetic resonance images of the sellar mass. *A-D*, Images at presentation. *A-B*, Coronal views. *C-D*, Sagittal views. *A*, *C*, T1-weighted images without gadolinium-enhancement. *B*, *D*, T1-weighted images with gadolinium-enhancement. Note the large sellar mass with suprasellar extension and heterogeneous enhancement. *E*, Image at 1 year after presentation, after 3 operations to remove the mass. *F*, Image at 3.5 months after *E* was taken. Note the rapid regrowth of the residual tumor.

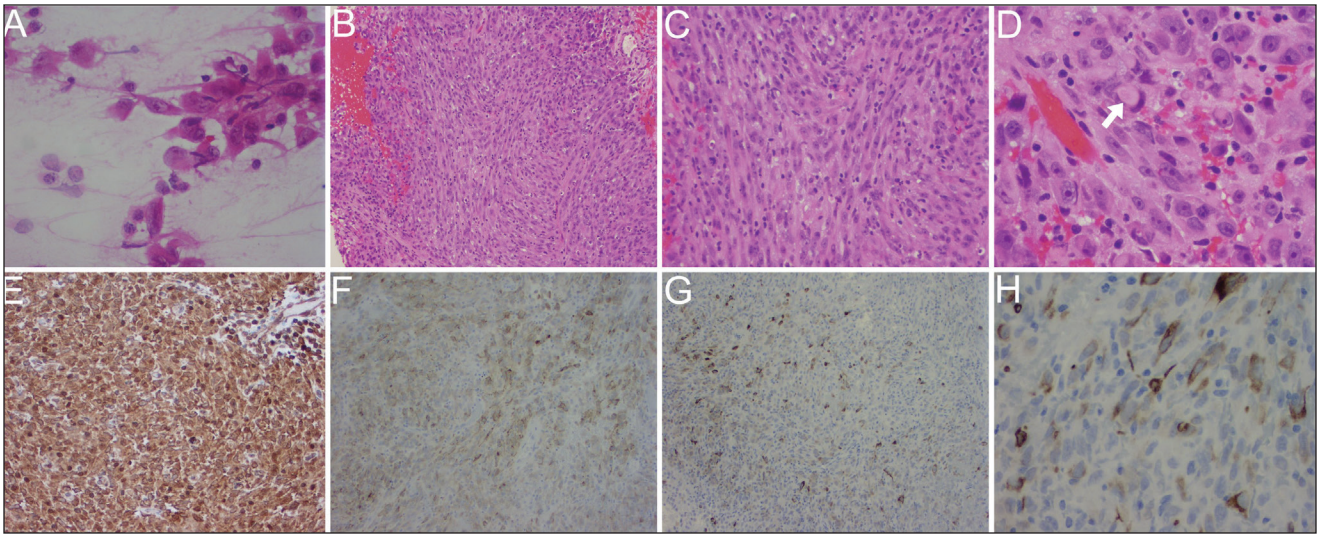

Fig. 2. Histology of the sellar mass. *A-D*, Hematoxylin and eosin stain. *E-H*, Immunostain. *A*, Tissue smear showing atypical epithelioid-like spindle cells with abundant pink cytoplasm, prominent nucleoli, and rhabdoid features, ×40. *B*, Atypical epithelioid-like spindle cells arranged in a fascicular pattern, ×10. *C*, Higher magnification showing epithelioid-like spindle cells with pink cytoplasm and prominent nuclei arranged in fascicular pattern, ×20. *D*, Focal tumor cells exhibiting rhabdoid features (arrow), ×40. *E*, Vimentin, ×20. *F*, Epithelial membrane antigen, ×10. *G*, Smooth muscle actin, ×10. *H*, Desmin, ×40.

out melanoma, and the absence of AFP and PLAP rules out a germ cell tumor. Most specifically, the loss of heterozygosity for the INI1/hSNF5 gene confirms the AT/RT diagnosis.

The pathogenesis of AT/RT is not entirely clear, but chromosomal 22 deletion is very common (4,5). The deleted chromosome 22 area contains the *INI1/hSNF5* tumor suppressor gene. *INI1/hSNF5* is a component of the chromatin remodeling SWI/SNF complex and is critical in suppressing rhabdoid tumor pathogenesis. AT/RT occurs mostly in the central nervous system of children (3). AT/RT can also occur in adults, and its most common primary site is supratentorial (6,7). There have been several reports of primary sellar AT/RT in adults, but they are mostly in the neurosurgical literature and not familiar to endocrinologists (Table 1) (8-14). There is no specific treatment for sellar AT/RT. Most patients undergo surgical resection followed by radiation therapy and/or chemotherapy, but there is no consensus on the best strategy (8-14). Stereotactic radiosurgery and external beam radiation are both used, but their efficacies are unclear without a control group (the present case and 9,13). Various chemotherapeutic regimens such

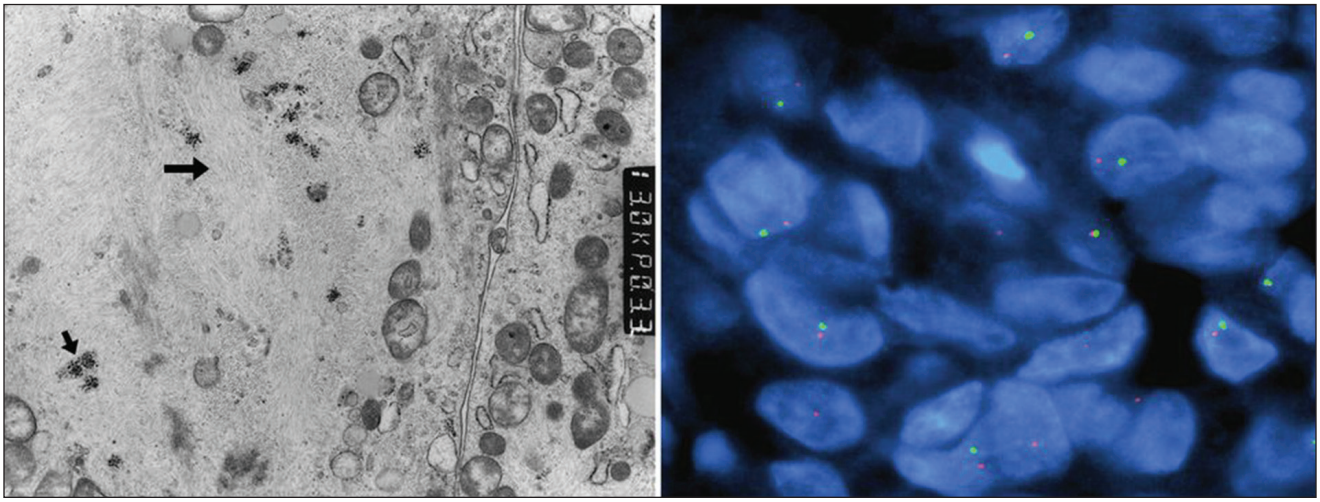

Fig. 3. Electron microscopy and fluorescent in-situ hybridization of chromosome 22. *Left*, Electron microscopy showing a rhabdoid cell with a cytoplasmic thin filament whorl (*long arrow*) and dense bodies (*short arrow*). *Right*, Fluorescence in situ hybridization for the *INI1/hNSF5* gene showing a test (green) to reference (red) probe ratio <0.8, which is consistent with loss of heterozygosity for the *INI1/hNSF5* gene. *Blue* = nuclei.

Table 1
Summary of Previously Described Cases of Sellar AT/RT and the Present Case

Case	Age	Sex	Symptoms	MRI	Pituitary function	Preoperative diagnosis	Treatments	Outcome
Raisanen et al, 2005 (8)	20	F	Vision loss of unknown duration	2.0-cm heterogeneously enhancing mass	ND	ND	Resection, radiation, chemotherapy	Alive at 28 months
Raisanen et al, 2005 (8)	31	F	ND	1.6-cm enhancing mass	ND	ND	Resection, radiation	Died at 9 months
Arita et al, 2008 (9)	56	F	Headache and double vision for 2 months	2.5-cm heterogeneously enhancing mass	ND	ND	Resection, radiation	Died at 23 months
Las Heras et al, 2010 (10)	46	F	Headache of unknown duration	ND	ND	ND	ND	ND
Schneiderhan et al, 2011 (11)	61	F	Sixth cranial nerve palsy of unknown duration	Heterogeneously enhancing mass (~2 cm)	ND	Pituitary macroadenoma	Resection	Died at 3 months
Schneiderhan et al, 2011 (11)	57	F	Headache, double vision, and oculomotor nerve palsy of unknown duration	Heterogeneously enhancing mass (~2 cm)	ND	Pituitary macroadenoma or metastasis	Resection, radiation, chemotherapy	Alive at 6 months
Chou et al, 2013 (12)	43	F	Headache and double vision for 10 days	Heterogeneously enhancing mass (~2 cm)	ND	Pituitary macroadenoma	Resection, radiation	Alive at 2 weeks
Moretti et al, 2013 (13)	60	F	Headache and double vision of unknown duration	Heterogeneously enhancing mass (>1 cm)	"Normal pituitary function"	Pituitary macroadenoma	Resection, radiation, chemotherapy	Died at 30 months
Shitara et al, 2014 (14)	44	F	Visual disturbance for 2 months	Heterogeneously enhancing mass (~2 cm)	ND	Lymphocytic hypophysitis	Resection, radiation, chemotherapy	Died at 17 months
Lev et al, 2014 (present case)	36	F	Headache for 1 month and blurry vision for 6 days	3.3-cm heterogeneously enhancing mass	Hypopituitarism	Pituitary macroadenoma	Resection, radiation, chemotherapy	Died at 29 months

Abbreviations: AT/RT = atypical teratoid/rhabdoid tumor; MRI = magnetic resonance imaging; ND = not described.

as doxorubicin and cisplatin; doxorubicin and vinorelbine; carboplatin and taxol; ifosfamide, cisplatin, and etoposide; temozolomide as a single agent; cytoxan, adriamycin, and vincristine; and cisplatin and VP16 have been used, but none seems to be particularly effective in controlling AT/RT progression (the present case and 11,13).

Sellar AR/RT carries a poor prognosis; most patients die within a few years of presentation (Table 1) (8-14). The grave prognosis of sellar AT/RT is in stark contrast to the benign clinical course of most pituitary adenomas. It is thus clinically relevant for endocrinologists, who are usually the primary physicians caring for patients with sellar masses, to identify preoperative diagnostic clues that may lead to the suspicion of sellar AT/RT. Imaging characteristics of AT/RTs and pituitary adenomas are remarkably similar; on MRI, both are isointense with brain parenchyma on T1-weighted imaging and enhance following gadolinium administration (8-14). Indeed, in all cases of sellar AT/RT, including the one reported here, the presenting sellar masses are large (~2-3 cm), but MRI usually did not reveal any suspicious features that would suggest tumors other than pituitary adenomas. Only 1 of the previously reported cases of sellar AT/RT provided pituitary functional studies (13). The pituitary hormone deficiency and hyperprolactinemia in our patient are also typically seen in patients with large nonfunctioning pituitary adenoma, so the endocrine findings, although important for guiding hormone replacement, do not differentiate AT/RTs from

large nonfunctioning pituitary adenomas. Our case and those described previously suggest that the only clue of sellar AT/RT is clinical: the duration of symptoms that led to the imaging study. All adult patients with primary sellar AT/RT, including the patient described here, were females between 20 and 61 years (8-14). All patients presented with headache and/or visual changes such as blurry vision and visual field defects; the durations of headache were 10 days and 1 month, and those of visual changes were 6 days, 10 days, 2 months, and 2 months (Table 1). Although similar symptoms are also common for pituitary adenomas that grow slowly, the duration of headache before presentation in patients with pituitary adenomas is usually longer than 1 year, and that of visual changes is 3.5 to 12 months (15,16), much longer than those reported in patients with AT/RT. Presumably, the rapid expansion of sellar AT/RT results in the new onset and rapid worsening of headache and visual changes that prompt the patients to seek medical attention rather urgently. It is important to note that the short duration of symptoms before imaging studies is not specific for AT/RT; rather, it should be a diagnostic clue to other rapidly expanding sellar masses such as metastases to the sella, other primary sellar malignancies, and aggressive pituitary adenomas (2,17,18).

CONCLUSION

In summary, we report here a rare case of adult-onset sellar AT/RT. This case demonstrates that sellar AT/RT may cause hypopituitarism and hyperprolactinemia and suggests that short duration of headache and visual changes associated with a large sellar mass are diagnostic clues for sellar AT/RT or other rapidly expanding sellar masses. Endocrinologists should pay attention to symptom duration in patients with a large sellar mass.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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