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Case Report

Concurrent Papillary Craniopharyngioma and Growth Hormone-Secreting Pituitary Adenoma: A Rare and Aggressive Collision Tumor

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ABSTRACT

Background/Objective: Collision tumors composed of craniopharyngiomas and pituitary adenomas are extremely rare. We report a collision tumor formed by a papillary craniopharyngioma and a growth hormone-secreting pituitary adenoma, which is the first report of such a tumor, to the best of our knowledge.
Case Report: A 49-year-old man presented with 2 months of headaches and blurry vision. An exam demonstrated frontal bossing, enlarged jaw and hands, macroglossia, and bitemporal hemianopsia, and magnetic resonance imaging (MRI) showed a 4.1 cm sellar/suprasellar mass with mass effect on the optic chiasm. The tumor was resected twice via a craniotomy, the second time due to interval growth, with the pathology after both surgeries showing a papillary craniopharyngioma. IGF-1 was 517 ng/mL (68-225) and growth hormone suppression test was positive. Repeat MRI showed residual tumor with ongoing mass effect on the optic chiasm and radiation therapy was initiated. MRI showed interval growth of the mass and IGF-1 rose to 700 ng/mL after which the patient underwent a transsphenoidal resection of the tumor; the pathology showed a residual papillary craniopharyngioma and a PIT1 lineage adenoma with most cells expressing growth hormone. After developing numerous complications, the patient passed away.
Discussion: Collision tumors of the sella are often associated with an aggressive clinical course, as they often go undiagnosed preoperatively, thus reducing the likelihood of total resection and leading to higher rates of craniopharyngioma recurrence.
Conclusion: A pituitary mass with an aggressive clinical course should prompt a high index of suspicion for a sellar collision tumor, though prognosis remains poor.

Introduction

Craniopharyngiomas are sellar/parasellar tumors accounting for 2% to 5% of primary intracranial neoplasms.[1] Pituitary adenomas comprise 10% to 15% of intracranial tumors.[2] A collision tumor is coexistence of 2 or more histologically distinct tumors in the same anatomic location; rarely, a collision tumor includes a craniopharyngioma and pituitary adenoma.[3] When compared with a single craniopharyngioma or pituitary adenoma, collision tumors often result in a higher tumor burden and more aggressive clinical course.[4] A collision tumor formed by a craniopharyngioma and growth hormone (GH)-secreting adenoma is rare; the annual incidence of acromegaly is 0.2 to 1.1 cases per 100 000.[5] We describe a patient with a sellar/suprasellar collision tumor comprised of papillary craniopharyngioma and GH-secreting pituitary adenoma.

Case Report

A 49-year-old man with a history of hypertension, COPD, and polysubstance use presented to the hospital with 2 months of worsening blurry vision, headaches, and unsteady gait. The patient

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also experienced fatigue, decreased libido, and cold intolerance. The physical exam demonstrated frontal bossing, enlarged jaw and hands, macroglossia, and a 3/6 systolic heart murmur at the apex. A visual field exam revealed bitemporal hemianopsia. The laboratory workup showed prolactin (PRL) 105.2 ng/mL (4.0-15.2), thyroid-stimulating hormone (TSH) 0.399 uIU/mL (0.270-4.200), free thyroxine (FT4) 0.95 ng/dL (0.93-1.70), follicle-stimulating hormone (FSH) 0.8 mIU/mL (1.5-12.4), luteinizing hormone (LH) 0.3 mIU/mL (1.7-8.6), total testosterone 10 ng/dL (300-890) drawn at 6:00 AM, cortisol 8.5 ug/dL (6.0-18.4) and adrenocorticotropic hormone (ACTH) 32.1 pg/mL (7.2-63.3) drawn at 10:30 AM (Table). Insulin-like growth factor 1 (IGF-1) was not initially obtained, as IGF-1 binding protein 1 was drawn instead. Urine toxicology screen was positive for cocaine and amphetamines. An MRI of the pituitary showed a 4.1 cm mixed solid and cystic sellar/suprasellar mass extending into the sphenoid sinus with mass effect on the optic chiasm and hypothalamus (Fig. 1).

On hospital day (HD) 5, the patient received high-dose corticosteroids and underwent a right frontotemporal craniotomy with resection of the sellar/suprasellar tumor. The pathology showed a papillary craniopharyngioma (Fig. 2). He subsequently developed diabetes insipidus with urine output >200 mL/h and urine osmolality 79 mOsm/kg (50-1400), and started oral desmopressin 0.2 mg twice daily. A repeat FT4 of 0.76 ng/dL with TSH 0.496 mIU/mL prompted initiation of oral levothyroxine 25 mcg daily. The following week, an IGF-1 level was 517 ng/mL (68-225). A GH suppression test (GHST) was performed: after a 75 g oral glucose load, the GH levels measured 19.30 ng/mL (1 h) and 17.80 ng/mL (2 h) (Table). These findings confirmed a diagnosis of acromegaly.

A magnetic resonance imaging (MRI) of the sella on HD 20 showed the cystic component of the suprasellar mass grew to 2.5 cm, with an increased mass effect on the optic chiasm. On HD 23, he underwent a left frontal craniotomy with endoscopic resection of the suprasellar mass. The pathology, again, demonstrated a papillary craniopharyngioma. Postoperatively, MRI of the sella showed a residual 1.9 cm suprasellar mass with mild mass effect on the optic chiasm. Radiation therapy was initiated on HD 35, with a plan for 54 Gy in 30 fractions. On HD 44-45, the GH level was 10.90 ng/mL, IGF-1 level was 700 ng/mL, and IGF-1-binding protein-3 (IGFBP-3) was 7730 ng/mL (2314-5700). A subsequent GHST showed a baseline GH level of 8.57 ng/mL and a GH level of 9.09 ng/mL 2 hours after a 75 g oral glucose load (Table).

Highlights

- Collision tumors of the sella are an uncommon phenomenon.
- Concurrent craniopharyngioma and growth hormone-secreting pituitary adenoma are rare.
- Sellar collision tumors cause higher morbidity than single pituitary adenomas.

Clinical Relevance

This may be the first documented case of a collision tumor consisting of a papillary craniopharyngioma and a growth hormone-secreting pituitary adenoma. The patient's hospital course highlights the potential distinct complications that can result from such a tumor.

Despite the 2 resections and radiation therapy, an interval MRI of the sella showed growth of the sellar/suprasellar mass to 2.6 cm. This prompted a transsphenoidal resection of the sellar/suprasellar tumor on HD 54. The pathology showed residual papillary craniopharyngioma, a small component of a PIT1 lineage adenoma, and a tiny region of non-neoplastic anterior pituitary gland (Fig. 3). Most of the neuroendocrine cells in the sample were PIT1 lineage cells, the majority of which expressed GH, though some expressed TSH and PRL. A postoperative MRI of the sella showed significant debulking of the sellar/suprasellar mass with a residual 1.1 cm right sellar and a 1.5 cm suprasellar component. The subsequent IGF-1 level was 450 ng/mL (Table).

During the patient's extensive hospital stay he developed multiple complications including deep vein thromboses of the lower extremities, pulmonary emboli, severe mitral regurgitation due to a torn mitral valve leaflet chordae; meningitis and nonsustained ventricular tachycardia. He suffered a cardiac arrest on HD 64 and expired.

Discussion

Pituitary adenomas are the most common tumors in the sellar/parasellar region, comprising 10% to 15% of all intracranial tumors, whereas craniopharyngiomas are uncommon, accounting for 3% of all intracranial tumors.[4] Of the pituitary adenomas, prolactinomas are the most common; GH-secreting adenomas follow,

Table
Laboratory Measurements Throughout Hospitalization

Test	Reference range	HD 2-3	HD 6-22 (after craniotomy #1)	HD 44-46 (after craniotomy #2)	HD 57 (after TSS)
Prolactin	4.0-15.2 ng/mL	105.2			
TSH	0.270-4.200 uIU/mL	0.399	0.496		
FT4	0.93-1.70 ng/dL	0.95	0.76		
FSH	1.5-12.4 mIU/mL	0.8			
LH	1.7-8.6 mIU/mL	0.3			
Total testosterone	300-890 ng/dL	10 (6:00 AM)			
Cortisol	6.0-18.4 ug/dL	8.5 (10:30 AM)			
ACTH	7.2-63.3 pg/mL	32.1 (10:30 AM)			
IGF-1	68-225 ng/mL		517	700	450
GH	0.05-3.00 ng/mL		GHST: 19.30 (~1 h), 17.80 (~2 h)	10.90 GHST: 8.57 (before), 9.09 (~2 h)	
IGFBP-3	2314-5700 ng/mL			7730	

Abbreviations: ACTH = adrenocorticotropic hormone; FSH = follicle-stimulating hormone; FT4 = free thyroxine; GH = growth hormone; GHST = growth hormone suppression test; HD = hospital day; IGF-1 = insulin-like growth factor 1; IGFBP-3 = IGF-1-binding protein-3; LH = luteinizing hormone; TSH = thyroid-stimulating hormone; TSS = transsphenoidal surgery.

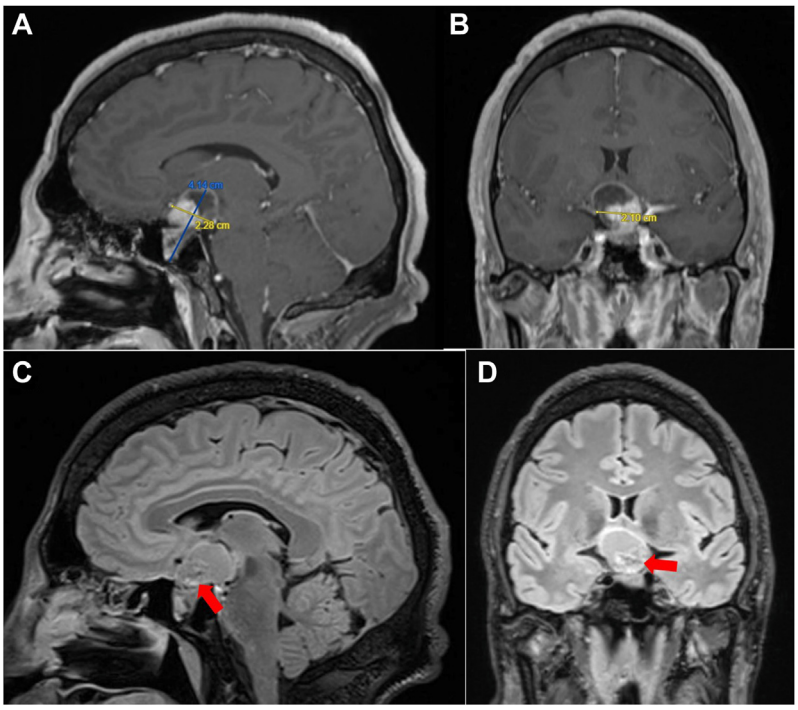

Fig. 1. MRI brain with and without intravenous contrast, dedicated pituitary protocol. There is a mixed solid and cystic sellar/suprasellar mass which measures 4.1 × 2.3 × 2.1 cm on postcontrast T1-weighted fat-suppressed images as seen in (*A*) sagittal and (*B*) coronal view. There is a solid avidly enhancing component that measures 1.6 × 1.6 × 1.6 cm at the anterior inferior aspect of the lesion (*red arrow*) as seen on T2/FLAIR images in (*C*) sagittal and (*D*) coronal view.

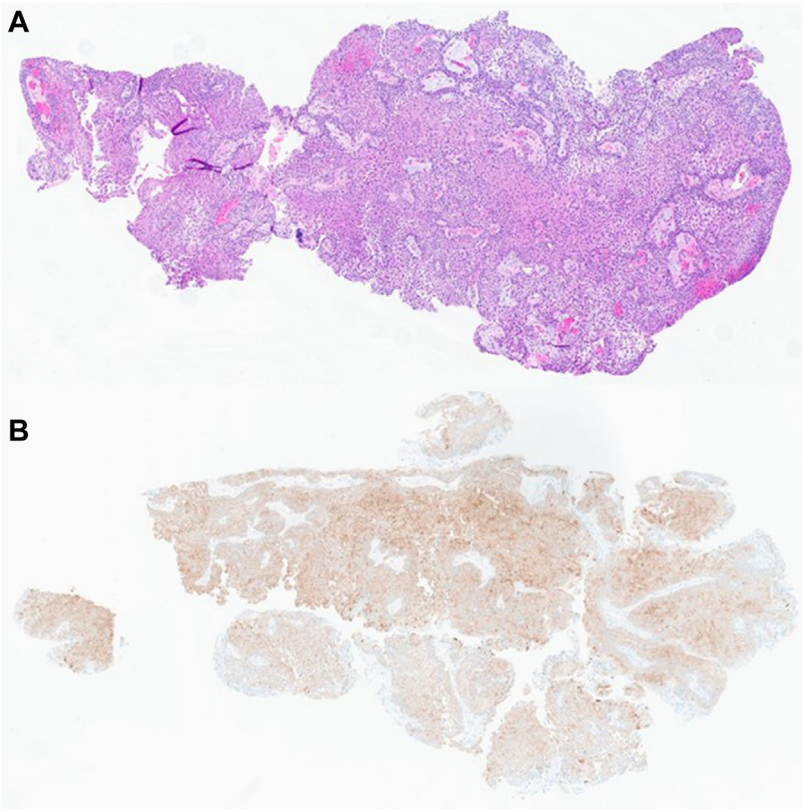

Fig. 2. Histopathology from first frontotemporal craniotomy and resection of tumor. Hematoxylin-eosin stain of the specimen from the first surgery demonstrating nonkeratinizing squamous epithelium with minimal basal palisading surrounding fibrovascular cores, consistent with papillary craniopharyngioma (*A*, original magnification ×40). The tumor cells are positive for BRAF V600E immunohistochemical staining (*B*, original magnification ×40).

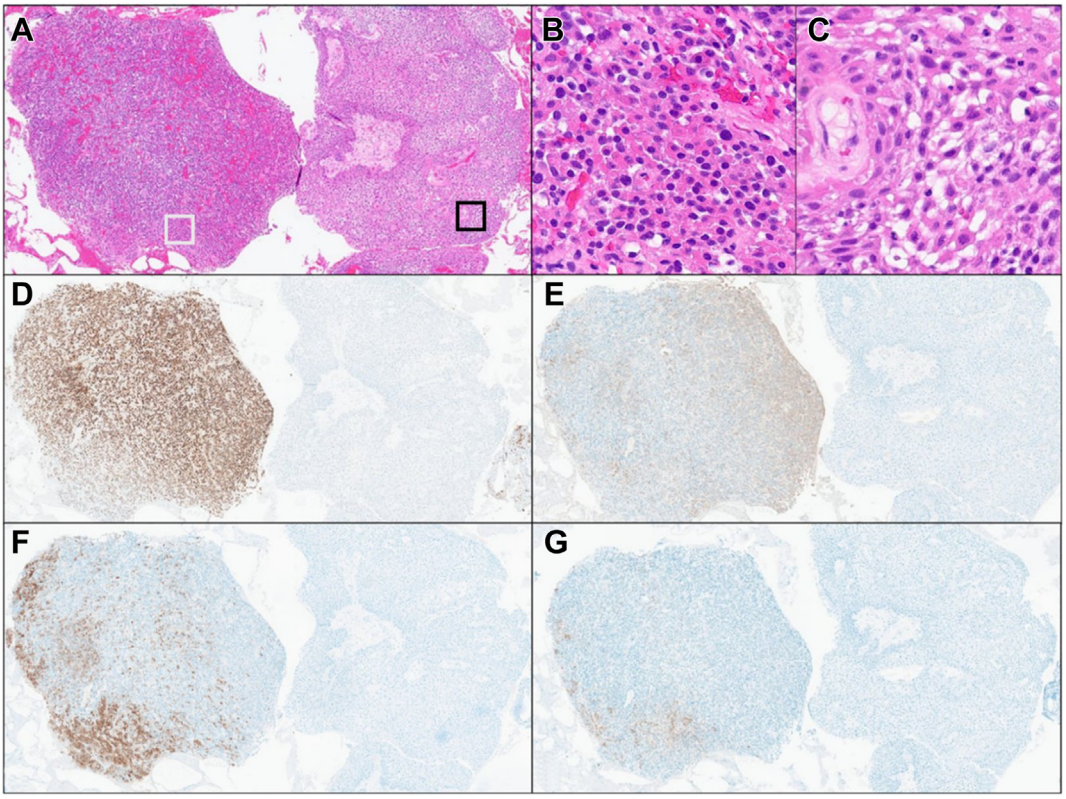

Fig. 3. Histopathology from transsphenoidal resection of tumor. Hematoxylin-eosin stains of the specimen from the third surgery demonstrate 2 tissue fragments with recognizably different morphology and architecture (*A*, original magnification ×40). Higher power magnification of the *Left* fragment in panel *A* (*white box*) shows a diffuse, sheet-like proliferation of monomorphic cells without acinar structures, consistent with pituitary adenoma (*B*, original magnification ×400). Higher power magnification of the fragment on the *Right* in panel *A* (*black box*) demonstrates nonkeratinizing squamous epithelium with a fibrovascular core, consistent with growing residual papillary craniopharyngioma (*C*, original magnification ×400). Immunohistochemical stains show that most cells of the largest adenoma fragment express PIT1 (*D*, original magnification ×40) and GH (*E*, original magnification ×40). Immunohistochemical stains for PRL (*F*, original magnification ×40) and TSH (*G*, original magnification ×40) highlight expression in some of the cells, which appear distinct from cells that express GH.

with an incidence of 3 to 4 cases per million per year.[1] Craniopharyngiomas include 2 histological variants – the more common adamantinomatous type, and the papillary type.[3] Collision tumors, defined as 2 or more histologically distinct tumors in the same anatomic location, are rare; when occurring in the sella, they typically include a pituitary adenoma and Rathke cleft cyst.[2,6] The collision of a pituitary adenoma and craniopharyngioma is very rare, with only 22 cases reported in the literature as of 2021.[4] We present a patient with a sellar/suprasellar collision tumor formed by a papillary craniopharyngioma and GH-secreting adenoma.

Our patient underwent a total of 3 surgeries to resect his sellar/suprasellar mass. The first and second surgeries, both resections via craniotomy, revealed a papillary craniopharyngioma. The third surgery, a transsphenoidal resection of the sellar/suprasellar tumor, showed a residual papillary craniopharyngioma with a small component of a PIT1 lineage adenoma. PIT1 lineage tumors contain either somatotrophs, lactotrophs, thyrotrophs, or a combination thereof.[7] In this case, most cells expressed GH. Some of the PIT1 lineage cells also expressed TSH and PRL. This finding raised the possibility of a plurihormonal PIT1 lineage tumor. While the patient's clinical presentation was consistent with acromegaly, there was no clinical evidence of a TSH-secreting adenoma. Furthermore, the mild hyperprolactinemia (PRL 105.2 ng/mL) suggested a pituitary stalk effect. The 2 distinct histologic findings identified upon surgical resection of the sellar/suprasellar tumor, along with clinical and biochemical evidence of acromegaly, suggest the presence of a collision tumor of a GH-secreting pituitary adenoma and papillary craniopharyngioma. As of 2021, there were 22 reported cases of collision tumors of pituitary adenomas and craniopharyngiomas, only 5 of which were GH-secreting adenomas and craniopharyngiomas.[1,4,5,8-10] Four of these cases described collision tumors with an adamantinomatous craniopharyngioma; the other did not indicate the type of craniopharyngioma. Therefore, to the best of our knowledge, this case represents the first reported collision tumor of a GH-secreting pituitary adenoma and papillary craniopharyngioma, and only the third documented case of a collision tumor of a pituitary adenoma and papillary craniopharyngioma.[4]

This case highlights the importance of maintaining a clinical suspicion for acromegaly and sellar collision tumors. The patient presented with classic acromegalic features, and the MRI showed a sellar/suprasellar mass. However, prior to his first surgery, IGFBP-1 was mistakenly obtained instead of an IGF-1 level.[11,12] As noted above, the first pathology indicated only a papillary craniopharyngioma. Later into his hospital course, an elevated IGF-1 level (517 ng/mL) and 2 subsequent GHSTs confirmed the diagnosis of acromegaly. After 2 surgeries and initiation of radiation therapy, his disease remained poorly controlled, as evidenced by the rising IGF-1 level, and another abnormal GHST. These findings prompted a transsphenoidal resection of the sellar/suprasellar tumor, the initial therapy of choice for most patients with acromegaly.[11,12] The patient succumbed to the disease 10 days later.

Sellar/suprasellar collision tumors often go undiagnosed preoperatively, leading to incomplete surgical resection and

recurrence, with overall worse prognosis compared with solitary craniopharyngiomas.[4] Collision tumor was suspected initially with surgical pathology showing papillary craniopharyngioma, coinciding with clinical and biochemical evidence of acromegaly. GH-secreting adenoma was confirmed at third surgical pathology. Literature on this topic is particularly rare. Some literature suggest that radiographic patterns of a solid mass with cystic components and coexistence of 2 distinct solid components may predict presence of a collision tumor. Total resection of sellar/suprasellar collision tumors with a single surgery is often not achieved, with reports of nearly 74% requiring a secondary intervention due to residual tumor or tumor progression; in these cases, adjuvant radiotherapy may improve local control.[4] Our patient underwent 3 surgical resections followed by radiation treatment as suggested, and the outcome was still poor. It has been reported that the 10-year overall survival in patients with collision tumors of pituitary adenomas and craniopharyngiomas is around 73%, while the 5-year overall survival in patients with solitary craniopharyngiomas is about 80% to 96%.[4] It is important to note that this patient developed severe complications during his hospitalization, which ultimately led to his demise. It is unclear how many of these were directly related to his sellar pathology; it is worth noting his history of polysubstance abuse may have contributed to underlying impaired cardiac function.

Conclusion

Vision changes and persistent headaches often prompt a workup for pituitary pathology. Compared with a single pituitary mass, a collision tumor of the sella leads to a larger tumor burden and a more complicated clinical course. Although rare, this case demonstrates the importance of maintaining a clinical suspicion for a sellar/suprasellar collision tumor.

Disclosure

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