Collision tumors composed of meningioma and growth hormone-secreting pituitary adenoma in the sellar region
Case reports and a literature review
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Abstract
Rationale: Collision tumor is a rare disease that represents the coexistence of two histologically distinct neoplasms in the same area without histological admixture or an intermediate cell population zone. To our best knowledge, 13 cases besides our 2 cases have been reported till now, and our report represents the first publication regarding a collision tumor composed of growth hormone (GH)-secreting pituitary adenoma and sellar meningioma.
Patient concerns: We collected two cases of collision tumors composed of meningioma and GH-secreting adenoma in the sellar region from 2014 to 2015 at Peking Union Medical College Hospital (PUMCH).
Diagnosis: Two cases were diagnosed with solid sellar tumors, and two tumor types were suspected with magnetic resonance imaging (MRI). Blood hormone tests revealed increased insulin-like growth factor 1 (IGF-1) and GH levels.
Interventions: Both cases underwent transsphenoidal microsurgical resection of pituitary adenoma.
Outcomes: The tumor was completely resected, and the pathological examination after the operation revealed meningioma and GH-secreting pituitary adenoma.
Lessons: Collision tumors consisting of pituitary adenomas with other sellar neoplasms are rare. Histological examination is necessary because preoperative studies cannot guarantee an accurate diagnosis. If a collision tumor is suspected prior to operation, a craniotomy may need to be considered before other operation methods to avoid reoperation.

Keywords: characteristics, collision tumor, therapy, transsphenoidal microsurgical resection

1. Introduction
Collision tumor is a rare disease that represents the coexistence of 2 histologically distinct neoplasms in the same area without histological admixture or an intermediate cell population zone.[1] Different histogenesis and tumorigenic pathways represent the mosaic of 2 concurrent tumors. Notably, the term “collision tumor” should be distinguished from another similar term, mixed tumor, which is 2 different neoplasms with histologically admixed cell types. Here, we report 2 cases of cerebral collision tumors composed of 2 benign components in the sellar region. To the best of our knowledge, this study represents the first report of a collision tumors consisting of meningioma and growth hormone (GH)-secreting pituitary adenoma. A detailed medical history is important for choosing the best treatment for collision tumors.

2. Case reports
2.1. Case 1
A 58-year-old female developed an acromegalic appearance and snoring over 15 years. Nine years ago, the patient complained of a headache with no dizziness or vision loss. Her past medical history included thyroid adenoma, hypertension, and a varicose vein in a lower limb. After admission, physical examination revealed enlargement of her fingers and toes, mandibular protrusion, and a broadened nose and lips. Blood hormone tests revealed increased insulin-like growth factor 1 (IGF-1) (991 ng/mL) and GH (15.9 ng/mL) levels, but a glucose suppression GH test could not be obtained. Other anterior pituitary hormones were within the normal range. Enhanced magnetic...
resonance imaging (MRI) of the sellar region showed a slightly hyperintense mass (3.3 x 1.9 x 2.0 cm in size) on T1-weighted images and an iso-hyperintense mass on T2-weighted imaging, with heterogeneous contrast enhancement near the sellar floor (Fig. 1). The left cavernous sinus was completely surrounded by the mass (Knosp 4), while the right side was not invaded, and the optic chiasm was not compressed. The patient was diagnosed with GH-producing pituitary adenoma and underwent transsphenoidal pituitary resection surgery. The tumor was gray and heterogeneous, mostly soft and fragile, and partly tough with a rich blood supply. After successful resection of the tumor, the saddle decreased to a normal size. The sellar floor was reconstructed with artificial dura mater, and no cerebrospinal fluid leakage was observed. A postoperative histopathologic examination confirmed the diagnosis of GH-secreting pituitary adenoma, and immunohistochemical results showed adrenocorticotropic hormone (ACTH) (+), follicle-stimulating hormone (FSH) (+), luteinizing hormone (LH) (+), prolactin (PRL) (+), thyroid-stimulating hormone (TSH) (+), P53 (+), and Ki-67 (index approximately 1%) (Fig. 2). GH and IGF-1 levels decreased to normal immediately after surgery. However, postoperative MRI revealed a remnant of the tumor that could not be removed transsphenoidally, and the remainder of the tumor was diagnosed as meningioma according to MRI. Based on the postoperative imaging result, the patient was treated with a craniotomy within 3 months after the transsphenoidal pituitary resection operation because the headache symptom returned. During the operation, the tumor exhibited a dark red color and was rubbery with an abundance of blood vessels. The tumor was completely resected, and the pathological examination after the operation revealed meningioma. The postoperative imaging is shown in Figure 1. The pathology result is shown in Figure 3.

2.2. Case 2

One year ago, a 58-year-old female detected enlargement of her superciliary ridge, fingers, and toes, as well as broadening of her nose and lips. Meanwhile, she suffered from severe snoring. No special medical history was reported except for cured tuberculosis and hepatitis. Blood hormone tests revealed increased IGF-1
(1291 ng/mL) and GH (21.2 ng/mL) levels, but a glucose suppression GH test could not be obtained. Enhanced sellar MRI showed a mass (1.12 × 0.54 × 1.07 cm in size) with a short signal on T1-weighted imaging and a short signal on T2-weighted imaging, with a low signal surrounding the high signal on T2-weighted imaging. The right cavernous sinus was completely surrounded (Knosp 4) by the mass, while the left side was not invaded (Fig. 4), and the optic chiasm was not compressed. The patient was diagnosed with GH-producing pituitary adenoma and underwent transsphenoidal pituitary resection surgery. The tumor was gray and heterogeneous, mostly soft and fragile, and partly tough with a rich blood supply. After successful resection of the tumor, the sellar floor was reconstructed with artificial dura mater, and no cerebrospinal fluid leakage was observed. A postoperative histopathologic examination confirmed the diagnosis of GH-secreting pituitary adenoma (Fig. 5). GH and IGF-1 levels decreased to normal immediately after the surgery. However, postoperative MRI revealed a remnant of the tumor that could not be removed transsphenoidally, and the rest of the tumor was suspected to be a meningioma based on imaging. Four months after the first operation, the patient experienced frequent headaches. Based on the postoperative imaging result, the patient was treated with a craniotomy. During the operation, the tumor exhibited a dark red color and was rubbery with a rich blood supply. In addition, the postoperative pathological examination revealed meningioma. The postoperative imaging result is shown in Figure 4, and the pathology result is shown in Figure 6.

3. Discussion

The coexistence of pituitary adenoma and intracranial tumor outside the sella is not uncommon, especially in patients who have received radiotherapy for a pituitary mass.[2] However, only a few publications have described collision tumors consisting of pituitary adenoma and a different sellar neoplasm. Neither of the patients described in this article received any radiotherapy before their intrasellar tumors were detected, which made their cases rarer. We carefully reviewed cases in which pituitary adenoma coexisted with another type of neoplasm, and we found only reports of craniopharyngiomas,[3,4] gangliocytomas,[5–8] schwannomas,[7] and meningiomas. The patient who underwent the second operation in this article was treated for a meningioma that was confirmed histologically (Fig. 6).
| Authors                  | Year | Age, y | Sex | Clinical presentation                  | Collision type 1          | Collision type 2      | Surgical approach(s)                                    | Follow-up                                      |
|-------------------------|------|--------|-----|---------------------------------------|---------------------------|-----------------------|--------------------------------------------------------|-----------------------------------------------|
| Case 1 in this article  | 2014 | 58     | F   | Acromegaly                            | GH-secreting PA           | Meningioma            | First transsphenoidal approach for resection, second craniotomy | N/A                                           |
| Case 2 in this article  | 2015 | 58     | F   | Acromegaly                            | GH-secreting PA           | Meningioma            | First transsphenoidal approach for resection, second craniotomy | N/A                                           |
| Karsy et al[9]          | 2015 | 70     | F   | Altered mental status, mutism, and incontinence | Non-secreting PA | Meningioma            | Transnasal, transsphenoidal approach for resection | N/A                                           |
| Koutourousiou et al[11] | 2009 | 38     | N/A | Acromegaly                            | GH-secreting PA           | Schwannoma            | Sub-labial transsphenoidal approach for resection | No evidence of recurrence of the adenoma 2 y after surgery |
| Tanfover et al[8]       | 2014 | 39     | F   | Acromegaly                            | GH-secreting PA           | Gangliocytoma         | Transsphenoidal approach for resection                 | No recurrence, and the patient is clinically and biochemically in remission |
| Prabhakar et al[2-3]    | 1971 | 29     | M   | Bifrontal headache, vision loss, acromegaly | PA                        | Craniopharyngioma    | Right frontal craniotomy                                | Died 4 d after surgery with uncontrolled diabetes insipidus; necropsy not performed |
| Wheatley et al[3]       | 1986 | 61     | M   | Deteriorating vision                  | Prolactin-secreting PA    | Craniopharyngioma    | Subfrontal approach                                    | Fatal postoperative cardiac arrest; PA confirmed by autopsy |
| Yoshida et al[1-4]      | 2008 | 29     | M   | Atrial fibrillation                   | PA                        | Adenomatous craniopharyngioma | Transsphenoidal                  | N/A                                           |
| Golden et al[7]         | 2009 | 47     | M   | Headache, vision loss                 | PA                        | Adenomatous craniopharyngioma | Transsphenoidal                  | Uneventful and no recurrence in 1 y             |
| Moshkin et al[1]        | 2009 | 12     | M   | Partial hypopituitarism               | PA                        | Adenomatous craniopharyngioma | Right frontal craniotomy         | Uneventful and no recurrence in 10 mo          |
| Sargis et al[17]        | 2009 | 59     | M   | Progressive vision loss               | Gonadotropin-secreting PA | Adenomatous craniopharyngioma | Subtotal transcranial resection | N/A                                           |
| Jin et al[3]            | 2013 | 47     | F   | Deteriorating vision                  | Non-secreting PA          | Adenomatous craniopharyngioma | First transsphenoidal resection of the tumor, second right frontal craniotomy using an interhemispheric transtemporal approach | 3-mo follow-up MRI confirmed complete resection of the tumor |
| Finzi et al[3]          | 2013 | 75     | F   | Diplopia and slight increase in serum prolactin | Typical pituitary silent subtype 2 | Adenomatous craniopharyngioma | Endoscopic endonasal transsphenoidal tumor resection | Complete recovery, no recurrence in 10 mo |

F=female, M=Male, N/A=not available, PA=pituitary adenoma.
and meningioma. Finzi et al propose that the term “mixed tumor” should be limited because of neoplasms in which endocrine and non-endocrine components are strictly admixed; this admixture distinguishes “mixed pituitary adenoma/craniopharyngioma” from collision tumors. We summarize all reported cases of collision tumors with pituitary adenoma in Table 1 (only cases that could be strictly defined as “collision” were included). Although Amirjamshidi et al reported 2 cases of coexisting PA and suprasellar meningioma, these cases were not included in the table since histological evidence was not provided to confirm the diagnosis of collision tumor. Moreover, the authors claimed that the coexisting tumors in their cases were not collision tumors and were likely coincidental. Although articles have provided many explanations for the pathogenetic relationship between concomitant tumors, none have provided clear evidence. In both of our cases, GH-secreting pituitary adenoma combined with meningioma was diagnosed after pathological examinations. To the best of our knowledge, this report represents the first publication regarding a collision tumor composed of GH-secreting pituitary adenoma and sellar meningioma.

3.1. Pituitary adenoma and sellar meningioma

The association between pituitary adenomas and meningiomas has been widely explored. Pituitary adenoma is the first diagnosis considered for sellar lesions, and 10% to 15% of central nervous system tumors identified as pituitary adenoma are found through autopsy and 23% through thin-section MRI. Meningioma is one of the most common benign cranial neoplasms. Thus, the coexistence of pituitary adenoma and intracranial meningioma is not rare. Meanwhile, giant intrasellar meningiomas mimicking pituitary adenomas have been well described in previous studies. However, few articles regarding collision tumors composed of pituitary adenoma and meningioma have been published. To date, Karsy et al reported the only case study of coincident pituitary adenoma and sellar meningioma in which mental changes were the chief complaint and a non-secreting pituitary adenoma was identified by pituitary laboratory tests and postoperative pathology. In addition, a pathological examination revealed a coexisting, microscopic fibroepithelial meningioma.

MRI is commonly used to diagnose sellar masses. However, due to their similar imaging characteristics, preoperative differential diagnosis of pituitary adenoma and intrasellar meningioma or a collision tumor composed of both is not possible with MRI. Our patients had a slightly hyperintense or low signal on T1-weighted imaging and an iso-hyperintense or high signal on T2-weighted imaging. Due to the same signals obtained during imaging, these 2 tumors appear to be a single tumor. Thus, postoperative pathological examination is necessary for a final diagnosis.

The formation of a collision tumor composed of pituitary adenoma and meningioma is difficult to explain. In terms of the tumorigenesis of these neoplasms, one possible explanation is that GH secretion in GH-secreting pituitary adenoma induces meningioma growth 

3.2. Craniopharyngioma with pituitary adenoma

Although both are common pathologies in the sellar or suprasellar areas, collision tumors composed of craniopharyngioma and pituitary adenoma components are rare. To date, 14 cases of collision tumors composed of pituitary adenoma and craniopharyngioma have been reported. Prolactin type were the most frequently reported, with 8 cases, and 2 cases of ACTH and a case of TSH were also reported; the remaining 3 cases were silent. Adamantinomatous-type craniopharyngioma is the most well documented, and the main clinical manifestations include deteriorating vision and abnormal secreting hormone symptoms, which is similar to the diagnosis of pituitary adenoma or craniopharyngioma alone. However, CT and MRI cannot identify the coexistence of pituitary adenoma and craniopharyngioma. Due to the non-distinguishing clinical and imaging features of craniopharyngioma, a collision tumor composed of craniopharyngioma and pituitary adenoma is difficult to differentiate from pituitary adenoma alone before operation; histological studies are required for diagnosis.

3.3. Gangliocytomas of the sellar region

Gangliocytomas account for 0.5% of all brain tumors and rarely occur in the sellar region, with an incidence of 0.52% to 1.26% within clinical sellar tumor series. Reports of collision tumors composed of gangliocytomas and pituitary adenomas are rare. Koutrourouisi et al reported 3 cases of gangliocytoma associated with GH-secreting pituitary adenoma. However, the association was actually an admixture of 2 cell types, which does not fit the definition of collision tumor that we mentioned earlier in this article. MRI and other radiological examinations cannot provide an accurate diagnosis of this tumor type, and the diagnosis should ultimately be based on histopathologic examinations. However, the use of pathological examinations in differential diagnosis is still controversial.

Some therapies have been identified during the study of the underlying mechanism of collision tumors composed of gangliocytomas and pituitary adenoma. During early embryogenesis, hypothalamic neurons are thought to migrate abnormally in the anterior hypophyseal parenchyma and result in pituitary adenoma. Another theory suggests that ganglion cells can release pituitary hormones, thus promoting adenoma formation. A third theory suggests neuronal transformation of pituitary adenoma cells. Nevertheless, this theory is still a topic of debate; Koutrourouisi et al stated that this theory challenges the understanding of embryology. In a recent study, Kontogeorgos et al argued that neuronal and adenomatous parts of these tumors may share a common progenitor cell that may differentiate into distinct cell types.

3.4. Intrasellar schwannomas

Only 1 case of GH-secreting pituitary adenoma coexisting with an intrasellar schwannoma has been published. The authors did not find an interaction between GH-secreting pituitary adenomas and intrasellar schwannomas and considered the finding incidental. Intrasellar schwannomas are rare. To date, no more than 18 cases have been reported. Preoperative diagnosis through MRI or clinical presentation was not possible in all these cases. Regarding the origin of intrasellar schwannomas, several theories have been put forward. If cranial nerve symptoms are observed, a schwannoma may have extended into...
the sella from a cranial nerve within the cavernous sinus.[28,30] Other possible origins include the perivascular nerve plexus, multipotential mesenchymal cells, displaced neural crest cells, ectopic Schwann cells, and lateral sellar nerve plexus.[34,40]

4. Conclusion

Collision tumors composed of pituitary adenomas and other sellar neoplasms are rare. Our report is the first regarding collision tumors composed of GH-secreting pituitary adenoma and sellar meningioma. Histological examination is necessary because preoperative studies cannot ensure an accurate diagnosis. Furthermore, the etiology of a collision tumor composed of meningioma and pituitary adenoma is unknown. If a collision tumor is suspected before operation, a craniotomy may need to be considered before other operation methods to avoid reoperation.

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