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Sellar collision tumor involving pituitary gonadotroph adenoma and chondroma: a potential clinical diagnosis

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Abstract We report on a 74-year-old male patient who presented with progressive neuroophthalmologic symptoms soon after the administration of a long-acting gonadotropin-releasing hormone agonist for treatment of a prostate cancer. Imaging revealed a destructively growing and extensively calcified sellar mass inconsistent with a pituitary adenoma. A transseptal transsphenoidal tumor mass reduction yielded a histological diagnosis of a collision tumor comprised of a gonadotroph adenoma intermingled with osteochondroma. We discuss a potential causal relationship between the administration of the long-acting gonadotropin-releasing hormone agonist and the sudden appearance of the previously unsuspected sellar lesion. Although the association of these two tumors is very likely coincidental, the possibility of causal relationship is addressed.

Keywords: Gonadotropin-releasing hormone agonist · Gonadotroph pituitary adenoma · Collision tumor · Osteochondroma

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Introduction

There is a broad differential diagnosis of clinically non-functioning sellar mass lesions, but the overwhelming majority of these histologically and immunophenotypically correspond to gonadotroph pituitary adenomas. Less frequent sellar tumors—among them collision tumors—may not be identified as such preoperatively, although some diagnostic clues (e.g., calcifications; cystic change) are likely to argue against conventional pituitary adenoma from the outset. We recently had the opportunity of studying a patient with a hitherto undocumented type of sellar collision tumor, the clinical and imaging aspects of which nevertheless allowed for its composite character to be postulated preoperatively.

Case report

A 74-year-old male patient received a first dose of a long acting gonadotropin-releasing hormone agonist (GnRH-agonist, Gosereline 3.6 mg) for treatment of a recently detected prostate cancer. Subsequently he developed severe headache accompanied by nausea and vomiting, followed by the occurrence of a right third cranial nerve palsy. Laboratory evaluation including endocrine testing was only notable for a considerably increased serum level of follicle-stimulating hormone (FSH; 21.3 IU/l; normal range 1–12 IU/l) (Table 1). Magnetic resonance imaging (MRI) and computed tomography (CT) disclosed a partially calcified destructively growing skull base tumor of 29 × 27 × 25 mm originating from the sella turcica with invasion of the cavernous, sphenoid, and ethmoid sinuses (Fig. 1).

In the face of massive tumor bulk and the compromise of perilesional anatomy, a limited exploration via

Table 1 Laboratory results at admission and after operation and radiotherapy

	Normal range	At admission	Postoperative and postradiotherapy
Cortisol	nmol/L	521	
TSH	0.2–0.4 mU/L	0.43	0.97
FT4	9–26 pmol/L	15	12.7
FSH	1–12 IU/L	21.3	17.3
LH	2–12 IU/L	7.0	<0.1
Total testosterone	6.3–26.3 nmol/L	20	0.43
Prolactin	4–19 μg/L	9.2	3.5
IGF-1	64–188 ng/ml	149	72

transseptal transsphenoidal route was opted for to provide histological diagnosis along with rapid chiasmal decompression. Ultimately, only the calcified part of the tumor (approximate volume 1 ml, 2.5 × 1.4 × 0.3 cm) was amenable to resection. Postoperative ophthalmological examination nevertheless indicated improvement of the visual field. The endocrine evaluation showed partial pituitary insufficiency and a persistently increased level of FSH. A subsequent conventional fractionated radiotherapy (54 Gy) was administered.

Histologically, the specimen consisted of a composite adenomatous–chondromatous lesion. The first component, a chromophobe pituitary adenoma was composed of sheets of epithelial cells with clear cytoplasm. Rather nondescript in itself, this tumor was remarkable for its being focally colonized by osteoclastic giant cells. Gonadotropic phenotype of tumor cells was evidenced by immunostaining for FSH and α-subunit. The second component, an organoid association of trabecular bone and hyaline cartilage was reminiscent of osteochondroma, as it occurs in less unconventional locations. Intimately associated with the chondromatous moiety throughout, adenoma cells were alternately seen either encircling islands of cartilage or expanding, plug-like, osseous trabeculae supporting chondroid matrix (Fig. 2).

Discussion

Sellar collision tumors—the simultaneous occurrence of two or more distinct primary tumors—are remarkably uncommon [1]. They consist mainly of a pituitary adenoma and a Rathke's cleft cyst [1–3], while double adenomas [1, 4, 5] occur less frequently. Further documented examples include pituitary adenoma coexisting with craniopharyngioma [6], arachnoid cyst [7], colloid cyst [8] or epidermoid cyst [9], Schwannoma [10], plasmocytoma [11], and meningioma [12]. Sellar collision without an adenomatous component is exceedingly uncommon [13].

To our knowledge, we present the first example of a sellar collision tumor involving gonadotrophic adenoma along with a benign cartilage-producing moiety with features of chondroma. Chondrogenic neoplasms of the sellar region, both benign and malignant, are very uncommon [14–18]. Chondromas tend to frequent the cartilagineous growth plate of long bones, a structure the sphenoid bone is devoid of [19]. Although chondromas have no pathognomonic radiologic features, CT shows irregular and mottled calcification in 60% and local bone destruction occurs in 50% of intracranial chondromas [14].

Whereas sellar collision tumors are mostly diagnosed histologically, the sequence of events in connection with the extensive calcification could have allowed for this presumptive preoperative diagnosis in the case presented herein.

First, if GnRH-agonists trigger symptoms of rapid sellar enlargement as acute headache, ophthalmoplegia and decreased visual acuity, the underlying pathology most likely is a gonadotroph pituitary adenoma. Possible mechanisms are the long-standing stimulatory effect on tumoral gonadotropin secretion (Table 1) and an increase in cellular volume, precipitating the compression of sellar

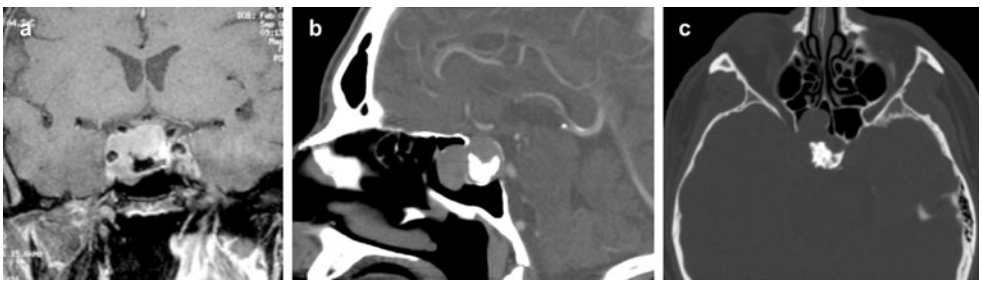

Fig. 1 MRI shows a destructively growing, gadolinium-enhancing skull base tumor in the sellar region, displacing the optic chiasm (**a**) with extensive calcification in CT scan (**b**) as well as bone erosion and infiltration of the adjacent sinuses (**c**)

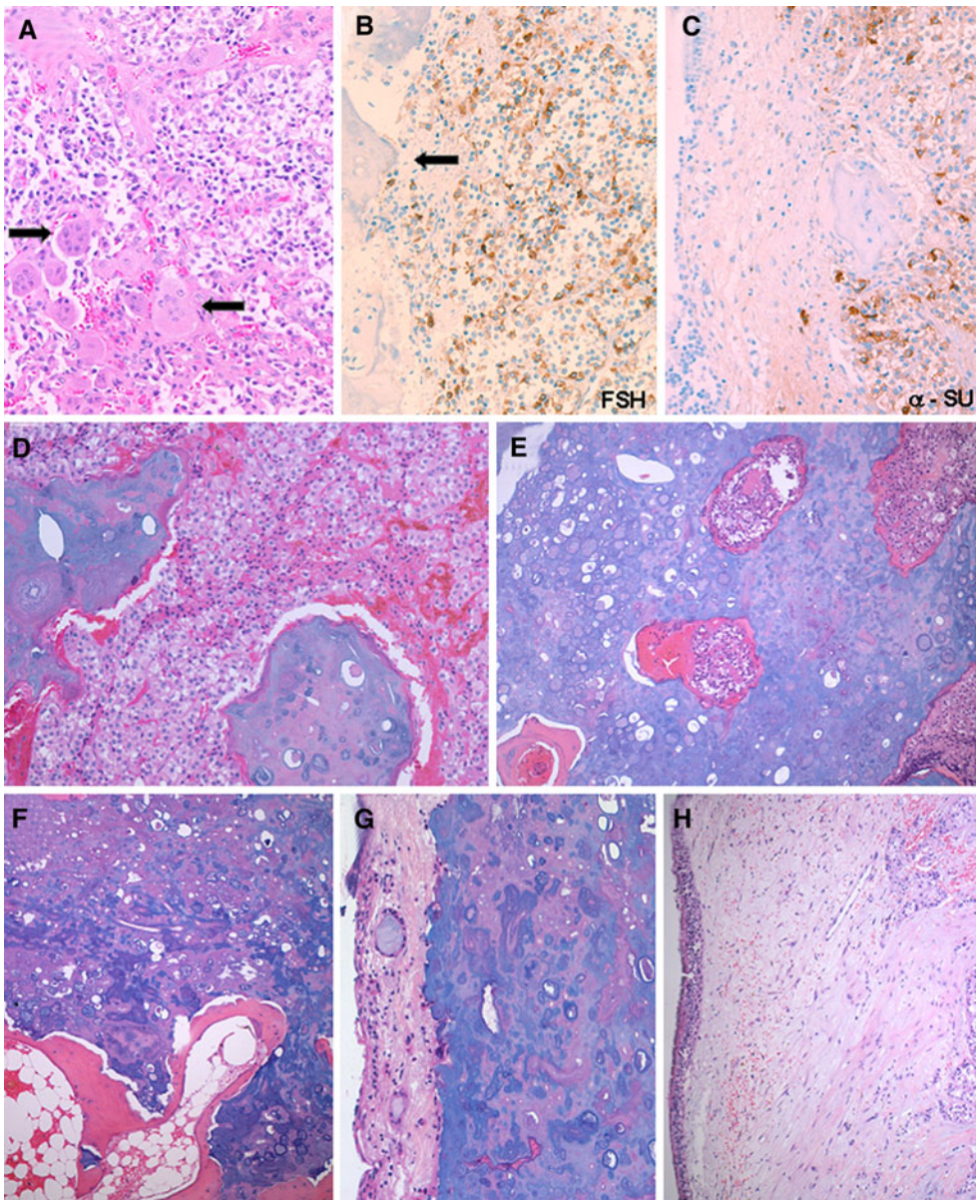

Fig. 2 Microscopic features of composite adenomatous-chondromatous lesion obtained at resection. (**a**) shows chromophobe pituitary adenoma composed of sheets of epithelial cells with clear cytoplasm. Rather nondescript in itself, this tumor was remarkable for its being focally colonized by osteoclastic giant cells (*arrows*). Gonadotropic phenotype of tumor cells is evidenced by immunostaining for FSH (**b**) and α-subunit (**c**). Invasion of bone (**b**–*arrow*) as well as respiratory mucosa of sphenoid sinus (**c**) is appreciated. Intimately associated with the chondromatous moiety throughout, adenoma cells were alternately seen either encircling islands of cartilage (**d**) or expanding, plug-like (**e**), osseous trabeculae supporting chondroid matrix. The organoid association of trabecular bone and hyaline cartilage (**f**) is reminiscent of osteochondroma, as it occurs in less unconventional locations. (**g**) shows cartilagineous mass to broadly encroach upon sphenoid sinus mucosa, while adenoma cells (**h**) tend to display infiltrative growth. Photomicrographs not labeled otherwise represent hematoxylin and eosin staining. Immunohistochemical reactions (**b** and **c**) were visualized with polymer-bound horseradish peroxidase (Envision + ; Dako, Glostrup, Denmark) and 3, 3′-diaminobenzidine. Original magnifications: **a**–**d** and **g** ×200; **e**, **f**, **h** ×100

structures. As in the presented case, this clinical syndrome occurs even in the absence of an actual hemorrhage or infarction [20].

Although potentially life-threatening, pituitary apoplexy is rare and pretreatment testing would not be cost effective. Nevertheless, attention to pituitary disease prior to injection and during follow up is required.

Second, excepting the proverbial "pituitary stone" in an occasional prolactinoma, more than minute calcifications are not expected to be seen on imaging of pituitary adenomas [21]. If present, it is legitimate to entertain the possibility of a nonadenomatous sellar tumor. Calcifications are a standard fixture of adamantinomatous craniopharyngiomas. Likewise, sellar meningiomas may harbor

psammoma bodies [22]. In this context, two exceptional case reports on metaplastic ossification in a somatotroph cell adenoma and a gonadotroph cell adenoma have to be mentioned [23, 24].

Considering the high frequency of gonadotroph adenomas and the "first ever" character of the constellation documented here, the coexistence of a gonadotroph adenoma and a chondroma is very likely coincidental.

Some circumstantial evidence of a possible relationship between these two entities might be inferred from the observation that human pituitary adenoma cells exert proliferative and growth-promoting activity on chondrocytes via secretion of fibroblast growth factor (b-FGF) [25]. It is tempting to speculate that b-FGF secretion, which in turn is stimulated by pituitary tumor transforming gene (PTTG), may have contributed to the progression of the chondroma by a paracrine effect in the present case [26].

In addition to b-FGF, locally produced bone morphogenetic proteins (BMPs) and Activins, both members of the transforming growth factor β superfamily, may also be involved in the development of gonadotroph pituitary adenomas [27] and osteochondromas [28] as well.

Recently, there has been growing awareness of both nonadenomatous and combined neoplasms of the pituitary [1]. As illustrated here, exact nosological diagnosis of such lesions ultimately requires microscopic study. We nevertheless conclude that, in some cases, the unexpected or contradictory character of clinical and imaging findings may be apt to suggest the possibility of a collision tumor prior to the biopsy procedure.

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