

Intrasellar Rathke's Cleft Cyst and Acromegaly: an Unusual Coincidence

One Sentence Summary: Dual sellar lesions are relatively uncommon. Asymptomatic Rathke's cleft cyst, a relatively common entity, in concurrence with a pituitary adenoma, should be considered in the differential diagnosis of two distinct pituitary lesions.

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Key words

- ◉ somatotroph adenoma
- ◉ acromegaly
- ◉ Rathke's cleft cyst
- ◉ growth hormone
- ◉ pituitary adenoma

Abstract

▼
The concomitant presence of 2 histologically different pituitary lesions is relatively uncommon. Cases of coexistent growth hormone (GH) secreting pituitary adenomas and Rathke's cleft cysts are limited to 14. The preoperative clinical and

radiological features of dual sellar lesions are variable and diagnosis is usually confirmed only by histology. We describe a case of a GH-secreting pituitary adenoma complicated by the presence of an asymptomatic intrasellar Rathke's cleft cyst and review the already reported cases.

Introduction

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Dual sellar lesions, defined as 2 histologically different pituitary lesions in co-existence, are relatively uncommon. Most contributions of dual sellar pathology reported to date include the combination of a pituitary adenoma with a second sellar lesion that may be of neoplastic, vascular, congenital or inflammatory origin [1]. Though Rathke's cleft cysts (RCCs) are encountered in up to 33% of normal pituitary glands in unselected autopsy specimens [2,3], their co-existence with a pituitary adenoma is relatively rare. In surgical series of pituitary adenomas the rate of RCC coincidence ranges from 0.51% to 1.7% [1,4,5], whereas in studies based mainly in radiological findings it rises to 3.5% [6]. Dual sellar lesions can be either attached to each other or clearly separated [1]. In both cases the preoperative radiological diagnosis is challenging since the lesions might exhibit similar signal intensities on magnetic resonance imaging (MRI). We report a case of a GH-secreting pituitary adenoma co-existing with an asymptomatic intrasellar RCC and describe our diagnostic and therapeutic approach regarding this uncommon entity. In order to answer the question whether co-existence of a somatotroph pituitary tumor with a Rathke's cleft cyst has been previously described, a computerized literature search in MEDLINE was performed for the period between January 1995 and October 2014. The keywords "Rathke's cyst" and "pituitary adenoma" were

entered as free-text terms. Overall, 84 articles were retrieved and 25 were selected as relevant. Additionally, the citation lists of all relevant publications and review articles were hand-searched. No language limitations were applied. Finally, 8 articles were found to report the clinical entity in question, in a total of 14 cases.

Case Report

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A 53-year-old woman was referred to the outpatient clinic of the Department of Endocrinology due to acromegalic features and joint pain that initiated 3 and 1 year ago, respectively. Clinical evaluation of the patient revealed the presence of oily skin, coarsening of facial features with soft tissue as well as acral enlargement. Her blood pressure, pulse rate and BMI were as follows: 135/90 mm Hg, 94 bpm, 24.2 kg/m², respectively. She reported no visual impairment and upon examination, her visual fields were intact. No symptoms or signs of other pituitary hormone excess – apart from growth hormone – were recorded. The patient reported a history of multinodular non-toxic goiter, colon polyps, carpal tunnel syndrome, and degenerative arthritis. Basal and dynamic hormonal testing confirmed the diagnosis of active acromegaly showing increased levels of insulin-like growth factor 1 (IGF-1) and failure to suppress growth hormone (GH) on 75 gr oral glucose tolerance test (OGTT) [IGF-1 = 1774 IU/L (age and sex adjusted range = 370–1390);

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GH_{nadir}=3.1 ng/ml]. Serum prolactin (PRL), adrenocorticotropin hormone (ACTH) and cortisol levels were within normal limits [PRL=16.1 ng/ml (range=4.9–40); ACTH=21.2 pg/ml (range=10–60); cortisol=15.1 mg/dl (range=5–25)]. Thyroid function was normal, whereas gonadotrophins [(follicle-stimulating hormone (FSH) and luteinizing hormone (LH)] levels were increased, in accordance with the post-menopausal status of the patient. OGTT also confirmed the presence of glucose intolerance, whereas no other biochemical or hematological abnormalities were recorded.

MRI of the sella showed enlargement of the pituitary gland which was heterogeneously enhanced after gadolinium (Gd) administration (◉ Fig. 1a). In particular, 2 lesions with hypointense signal on T1-weighted sequences and differential post-contrast characteristics (◉ Fig. 1b) were described: 1) one at the right pituitary side, with a diameter of 1.6×0.7 cm, extending to the right cavernous sinus, which was mildly enhanced and 2) a second one, on the left pituitary side, with a diameter of 0.8×0.6 cm, which in contrast to the first lesion was not enhanced at all, apart from its periphery. The above findings were separated by a well enhanced normal pituitary.

The patient was initially treated with somatostatin analogues with inadequate clinical and biochemical control of the disease. A few months later a transsphenoidal surgical tumor debulking was decided and the left sided lesion was electively resected according to the neurosurgeon's best clinical judgment, due to easier and safer accessibility. Histological findings of the lesion resected were diagnostic of Rathke's cleft cyst.

Postoperative laboratory evaluation was confirmative of persistent active acromegaly [IGF-1=1786 IU/L (age and sex adjusted range=370–1390); GH_{nadir}=5.8 ng/ml]. ◉ Fig. 1c shows the post-operative MRI of the sella, with the left sided lesion having been excised, whereas the right-sided lesion remaining intact with the same characteristics as pre-neurosurgery.

Consequently, instead of a second surgery, which was persistently declined by the patient, CyberKnife radiosurgery was performed and complementary pegvisomant treatment was initiated until the effects of radiosurgery became apparent. The choice of medical treatment was based on the fact that she had been unresponsive to maximal doses of somatostatin analogue administration presurgery.

Discussion



The concomitant presence of a pituitary adenoma with RCC occurs infrequently. We report a case of a GH-secreting pituitary adenoma in co-existence with RCC; a combination that has only been described in 14 cases to date, upon literature review (◉ Table 1) [5–12]. The chance of surgical cure in our patient was remote due to the right cavernous sinus extension of the lesion. However, neurosurgical intervention was mandatory due to lack of complete response to medical treatment. Surprisingly, the resected lesion proved to be a RCC.

Although rare, the concurrence of pituitary adenomas and RCCs might not be merely coincidental [1]. RCCs are benign sellar lesions that are believed to originate from embryonic remnants

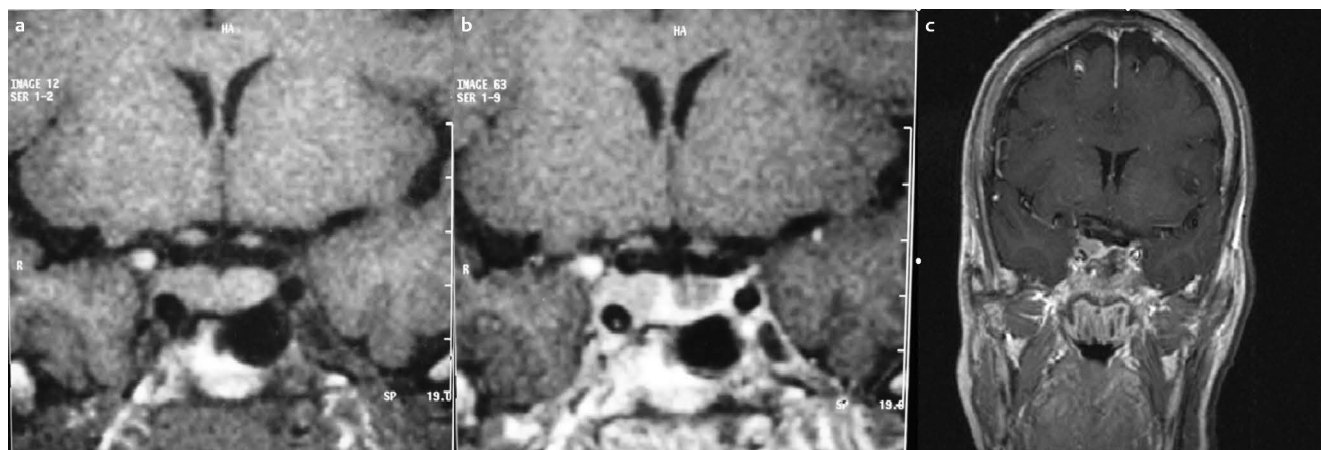


Fig. 1 MRI of the sella: **a** unenhanced and **b** after gadolinium administration. Coronal sections showing enlargement of the pituitary gland by 2 hypointense lesions, one at the right pituitary side and one at the left pituitary side clearly separated by a well enhanced pituitary. **c** Post-surgery MRI, depicting the right-sided lesion unchanged and the absence of the left-sided lesion.

Table 1 Reported cases of concomitant GH-secreting pituitary adenomas and RCCs.

Author	No of cases reported	Sex	Age (years)	Radiological diagnosis	Histological diagnosis of GH-secreting adenoma	Histological diagnosis of RCC
Nishio et al., 1995 [10]	2	1F/1M	35/44	No	Yes	Yes
Sumida et al., 2001 [6]	6	3F/3M	44–56–67/18–46–48	Yes	Yes	2 Yes/ 4 No
Bader et al., 2004 [8]	1	F	47	Yes	Yes	Yes
Noh et al., 2007 [5]	1	F	62	No	Yes	Yes
Gupta et al., 2011 [9]	1	M	20	No	Yes	Yes
You et al., 2012 [12]	1	F	46	No	Yes	Yes
Wang et al., 2012 [11]	1	F	22	No	NS	Yes
Azarpira et al., 2013 [7]	1	F	50	No	Yes	Yes

F female, M male, NS not stated

of Rathke's pouch [3, 13]. Pituitary adenomas, on the other hand, are epithelial tumors derived from adenohypophyseal cells via clonal alteration [14]. Since Rathke's pouch gives rise to adenohypophysis through proliferation of its anterior wall between the 3rd and 5th month of gestation [3], it has been suggested that pituitary adenomas and RCC have a shared ancestry [1]. Though intriguing, this hypothesis of common embryonic origin remains to be established.

It is reported that asymptomatic, small RCCs are found incidentally in 11–33% of random post-mortem examinations [2, 3]. It is only the larger RCCs causing compression symptoms that lead to diagnostic procedures, but these are far less common. In our patient, RCC would not have been diagnosed, if the symptomatology of acromegaly due to the coexistent somatotroph adenoma had not been present.

It could be argued that there exists no histological proof of a somatotroph adenoma in our patient. However, we have no reason to doubt that the right-sided pituitary lesion was actually the GH-secreting adenoma, since, in combination with the clinical and hormonal characteristics, it exhibited a typical radiological appearance.

The differential diagnosis of RCC from other pathologies is sometimes difficult and should be based on combinations of clinical, laboratory and imaging data, with the final diagnosis being absolutely dependent on histology.

RCCs show variable size, location and signal intensity on MRI T-weighted images. They are typically located intermediary, between the anterior and posterior pituitary lobes, with a variable size that has been reported to range from a few mm to 5 cm [3]. In the majority of cases they present as intra and/or suprasellar lesions and rarely occupy only the suprasellar region [3, 15]. They typically appear as homogenous, non-enhancing, non-calcified cystic lesions, although a peripheral cyst wall enhancement might be present in approximately half of the cases [15], as in our case. Their signal intensity on T-weighted images varies widely depending on cyst content [3]. Approximately 50% of RCCs display hypointense signal on T1-weighted images and 50% appear hyperintense. On T2-weighted images, up to 70% of RCCs display hyperintensity whereas 30% are iso- or hypointense [15].

Nuclear imaging might be a useful tool in the differentiation of pituitary adenomas from other sellar lesions [16, 17]. Positron emission tomography (PET), with the use of different biological molecules, such as ¹⁸F-fluorodeoxyglucose, has proved efficacious for in-vivo tumor characterization, localization, and differential diagnosis of pituitary lesions. The present case might serve as a vivid example of the necessity of further presurgical diagnostic work-up, possibly with molecular imaging techniques, when MRI is inconclusive for dual sellar findings.

Intra-operative measurement of GH has also been tested as an index of successful adenoma removal, however, this technique has proven to be neither sensitive, nor specific enough for this purpose [18].

In conclusion, dual sellar lesions, although rare, are being recognized more often owing to the evolution and routine use of imaging techniques. The variable imaging characteristics of RCCs render their preoperative radiological diagnosis difficult. However, the possibility of a co-existing RCC should always be considered in a patient with dual sellar lesions involving a non-enhancing cyst, like structure.

Discosure summary: All authors have nothing to disclose. We have no conflict of interest.

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