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Case report

Spontaneous pituitary adenoma occurring after resection of a Rathke's cleft cyst

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ABSTRACT

Rathke's cleft cysts (RCC) are benign cystic lesions that originate from remnants of the epithelial lining of Rathke's pouch. RCC are known rarely to occur together with a concomitant pituitary adenoma. Here, we report a patient with a pituitary adenoma arising in the same location as a previously-resected RCC, 3 years post-operatively, and review the literature of "collision" sellar lesions. Consecutive transsphenoidal operations from a single-center between 2008 and 2016 were reviewed to identify patients with pituitary adenoma arising after surgical resection of RCC, and a systematic search of the literature was also performed to identify such patient reports, as well as reports of concomitant pituitary adenoma and RCC. Of 837 transsphenoidal operations from our own experience, one patient with pituitary adenoma occurring after RCC resection was identified and is reported here. A systematic review of the literature resulted in identification of 34 patients with concomitant RCC and pituitary adenoma and no incidents of pituitary adenoma occurring after resection of RCC. Concomitant occurrence of RCC and pituitary adenoma was more commonly diagnosed in women (61%), at a median age of diagnosis of 44 years. The RCC histological analysis in these patients consistently described ciliated columnar or cuboidal epithelium. Although rare, the presence of a new, pathologically-distinct lesions in the sella after prior surgical treatment, is possible. During post-operative monitoring, physicians should consider that what appears as a "recurrent" lesion may actually be growth of a new and entirely different lesion.

1. Introduction

Sellar lesions are among the most commonly diagnosed intracranial pathologies, and include a wide range of disease processes. Most frequent are pituitary adenomas, which comprise 10–15% of all intracranial tumors [1–3]. Embryological lesions of the sellar region, including Rathke's cleft cyst (RCC), an abnormal growth arising from within the anterior pituitary gland, are less common [4].

Although neither pituitary adenomas nor RCCs are particularly rare lesions, it is uncommon to find both disease processes in the same patient [5]. The incidence of concomitant occurrence of RCC and pituitary adenoma is unclear, but estimates range from 0.51% to 3.5% of intrasellar lesions [5–21]. Other studies have reported concomitance of other lesions in the sella, including schwannoma and GH-secreting adenoma, gangliocytoma and GH-secreting adenoma, and double pituitary adenoma [7,22–24]. Several of these studies have noted the likelihood of a possible common origin or other association between these various sellar lesions, due to the relatively high number of patients reported [7].

Despite this significant interest in so-called "collision lesions" of the sella, there have been no reports of a pituitary adenoma developing years after resection of an RCC. Here, we present a patient with spontaneous growth of a histologically-confirmed pituitary macroadenoma 3 years after primary RCC resection. We also review the literature of concomitant RCC and pituitary adenomas, in an effort to help guide clinical management of sellar lesions.

2. Methods

2.1. Retrospective review

The medical records of 837 consecutive patients who underwent transsphenoidal resection of a sellar lesion at our institution by the senior author (E.R.L.) between April 2008 and April 2016 were reviewed. Data collected included patient demographics, pre-operative imaging, operative course, pathological analysis, and post-operative clinical follow up.

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2.2. Review of literature

A PubMed search for reports including both RCC and pituitary adenoma, limited to human studies and the English language, was performed from the founding of the database through October 2015. 476 articles were identified. These were screened to identify reports of i) concomitant RCC and pituitary adenoma or ii) RCC resection followed by spontaneous growth of pituitary adenoma. The reference lists of identified articles were reviewed for other relevant reports that may have been missed by the initial search.

3. Results

3.1. Case report

Of 837 transsphenoidal operations for pituitary lesions, one case of pituitary adenoma occurring after prior resection of RCC was identified. This 43-year-old woman with an unremarkable medical history presented with headache, amenorrhea, and hyperprolactinemia in December of 2000. Her physical examination was normal, including intact visual fields, absence of focal neurological deficits, and no physical changes suggesting endocrine disease. Imaging revealed a cystic intrasellar lesion. She underwent transsphenoidal resection of the mass with gross findings typical for RCC (Fig. 1A, B). The sellar floor was opened and the fluid filled cyst was drained and cleanly dissected from the sellar walls. Histopathology revealed both keratin-positive epithelial lining cells and positive immunoperoxidase stain for Pan-k in the cyst lining cells. These features were diagnostic of RCC (Fig. 2A, B). The tissue stained negatively for follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), and human growth hormone (HGH). There were no post-operative complications and her symptoms gradually resolved over a 1-year period.

At a follow-up appointment in 2003, the patient underwent an MRI and was found to have a 13 mm lesion of the pituitary in the same region as her previously resected RCC. Differential diagnoses included recurrent RCC, pituitary adenoma, craniopharyngioma, arachnoid cyst, granular cell tumor, pituicytoma, meningioma, and pituitary oncocytoma. Based on the location and size of the lesion, it was felt that this was most likely a recurrence of the previously resected RCC.

The patient was asymptomatic, with an unremarkable physical examination and normal endocrine studies. Given the serum PRL of 18.6 ng/mL and a stable lesion size for several months, a period of watchful waiting was initiated. The lesion eventually increased in size, and the patient was treated with cabergoline from 2007 to 2010. In 2010, she began to develop headaches and further expansion of the mass was noted on MRI. During this time, she did not receive hormone replacement therapy, remained otherwise symptom free, and had a stable physical exam. By October 2012, the lesion had grown to $23 \times 13 \times 15$ mm, and exerted mass effect on both the left optic nerve and the pituitary infundibulum. Because the patient was asymptomatic beyond mild hyperprolactinemia without galactorrhea (24.4 ng/mL) she elected not to undergo an operation at that time.

In September 2013, the now 56-year-old patient presented again with a complaint of severe headache. Her MRI scan was unchanged. Neuroendocrine testing revealed stable mild hyperprolactinemia (25.4 ng/mL). Given the symptoms and the size of the lesion, endoscopic, endonasal, transsphenoidal resection of this presumed recurrent RCC was recommended (Fig. 1C). Incision of the dura surprisingly did not reveal a cyst, but instead a gray, loosely-organized pituitary tumor. The tumor was removed in its entirety. The patient experienced no post-operative complications and reported improvement in her headaches.

Histological examination of the tumor revealed a reticulin stain that demonstrated effacement of acinar architecture as well as immunochemistry positive for chromogranin, synaptophysin, cam5.2 and p53 consistent with a pituitary macroadenoma without any signs of RCC (Fig. 2C, D). Pituitary hormone markers (LH, FSH, TSH, PRL, ACTH, HGH, alpha-subunit) were negative. The prior histopathology slides from 2000 were reviewed at this time and confirmed the findings of focal keratin positive cyst lining consistent with RCC. There was no feature of adenoma present in the previous sample.

Follow up MRI scans in January and December of 2014 and in February of 2016 showed no evidence of interval recurrence of tumor (Fig. 1D). The patient's prolactin level had decreased to 6.1 ng/mL and she has been free of headache or visual symptoms since her second operation. She did not require pituitary hormone replacement therapy.

3.2. Review of the literature

A systematic search of the English scientific literature using the PubMed database resulted in identification of 34 reports of concomitant occurrences of RCC and pituitary adenomas, and no reports of pituitary adenoma occurrence after prior resection of RCC. The review of the literature is summarized in Table 1.

Among the 34 patients reviewed, the median age at diagnosis was 44 years. Women were more commonly affected (61%), with the most prevalent presenting symptoms being headache and amenorrhea. Galactorrhea was present in several patients who had hyperprolactinemia. MRI studies of these patients generally demonstrated varying signal intensities of the lesion. Nearly all patients underwent surgical resection. Non-functioning pituitary adenomas were present in 53% of patients, followed by GH-staining adenomas in 26%, ACTH-staining adenomas in 17% and GnRH-staining adenomas in 3%. The RCC histological analysis consistently described ciliated columnar or cuboidal epithelium.

4. Discussion

Although several articles have reported the concomitant presence of RCC and pituitary adenoma, there are currently no reports of a pituitary adenoma in the location of a previously resected RCC. Here, we present the first report, to our knowledge, of a patient who initially underwent surgical resection of a pathologically-confirmed RCC, followed by occurrence of a pituitary adenoma in the same area 3 years after initial surgery. The pathological process that may have resulted in two pathologically distinct lesions in the same location in this patient is unclear, and may be coincidental.

Similarly, the mechanism for concomitant sellar lesions is also uncertain [7]. In 1978, Kepes attributed the growth process of concomitant RCC and pituitary adenomas to "transitional cells" between the lining of the Rathke's cleft and the glandular cells of anterior pituitary, coining this entity "transitional cell tumors" [10]. It was not until 14 years later that Ikeda et al. rejected this theory, showing instead that embryologic cystic lesions (e.g., RCC) and cystic portions of adenomatous lesions were pathologically distinct [12].

In a more recent report published in 2010, Koutourousiou et al. speculated that there may be a common pathological process when two lesions arise in the sella, suggested by the relatively high number of patients reported in the literature [7]. Possible links that have been hypothesized include a common embryological origin, as in the case of RCC and craniopharyngioma, which are frequently considered to be two pathologically similar diseases of a common

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