Case Report

A 39-year-old male presented to his primary care physician with a severe headache, fever and chills. The patient subsequently presented to the Emergency Department of an outside hospital due to worsening symptoms and the onset of substernal chest pain. His electrocardiogram was normal although the cardiac biomarkers were significantly elevated. In addition to working up the patient's cardiac compliant, computed tomography of the head was obtained due to the patient's persistent headache and the presence of horizontal nystagmus on exam. This scan revealed a large sellar mass. To further characterize this mass, a brain magnetic resonance imaging (MRI) was obtained. This revealed a 3.3 cm × 2.9 cm × 3.1 cm cystic mass in the sellar region [Figure 1]. He was then transferred to our institution for further management of his non-ST elevation myocardial infarction and sellar mass. Endocrine labs were obtained and were found to be significant for hypogonadotropichypogondism, with a total serum testosterone level of 23 ng/dL (normal range, 175-780 ng/dL), with all other pituitary labs within normal limits.

The patient subsequently underwent minimally invasive endoscopic transnasaltransphenoidal pituitary resection. Once the pituitary was exposed, an incision was made into the gland, releasing a large amount of fluid from the cyst. After removal of the lining of the cyst cavity, the wound was closed with a septal flap. The patient had an uneventful post-operative course and was discharged in a stable condition.

Histological examination of the mass showed adenohypophysial tissue with focal monomorphic proliferation consistent with an adenoma [Figure 2a]. Also seen was...
cytokeratin-immunopositive cuboidal epithelium consistent with an RCC [Figure 2b]. Immunohistochemical studies demonstrated tumor cells immunopositive for chromogranin, synaptophysin and human chorionic gonadotropin. However prolactin, adrenocorticotropic hormone (ACTH) and growth hormone were seen to be negative.

Discussion

Origin and histology
RCCs were first described by Luschka in 1860, and are thought to arise from the remnants of Rathke’s pouch. During the third or fourth week of development, this structure is formed by the infolding of the roof of the stomodeum. Between the anterior and the posterior walls that form the lobes of the pituitary gland is a central lumen known as Rathke’s cleft. During normal development, this structure is obliterated. However, this cleft may persist, resulting in the formation of a cyst due to the secretion of products from the epithelial cells lining the intermediate lobe. As the Rathke’s pouch forms the craniopharyngeal duct, it has been proposed that RCCs and craniopharyngiomas represent a continuum of ectodermally derived epithelial lesions. This is supported by papillary craniopharyngiomas having foci of ciliated and mucin-producing epithelia similar to that found in Rathke’s cleft. However, despite pituitary adenomas and RCCs having a common embryologic ancestry, their co-existence may be coincidental.

Clinical presentation
RCCs have been found incidentally in 11-33% of post-mortem examinations, and were associated with 1.7% of the pituitary adenoma cases in a study involving 464 patients. However, symptomatic RCCs associated with pituitary adenomas occur more rarely, having only been described in less than 40 cases. These cysts are typically less than 3 mm in diameter and remain intrasellar. However, one-third of the RCCs may have suprasellar extension leading to compression of the adjacent structures and increased intracranial pressure. Vision loss may occur due to impingement of the optic chiasm and optic nerve, while pressure on the cavernous sinus may result in extraocular muscle palsy or ptosis due to cranial nerve dysfunction. Headaches, such as those that occurred in our patient, may occur due to leakage of the contents of the cyst and resulting irritation.

Figure 1: Magnetic resonance imaging (MRI) images of a cystic sellar lesion found to be a combined Rathke’s cleft cyst with pituitary adenoma. (a) Axial T1-weighted MRI, (b) axial T2-weighted MRI, (c) sagittal T1-weighted MRI and (d) sagittal T1-weighted post-contrast MRI showing peripheral enhancement

Figure 2: (a) Pituitary adenoma is present among hemorrhage, (b) Cuboidal epithelial lining was immunopositive for cytokeratin and is consistent with a Rathke cleft cyst component (a and b hematoxylin and eosin, ×20)
Table 1: Characteristics and clinical presentation of patients with a pituitary adenoma and Rathke’s cleft cyst

| Patient | Author, year | Sex | Age | Hormone Produced | Symptoms | Headaches | Visual | Hormonal |
|---------|--------------|-----|-----|------------------|----------|-----------|--------|----------|
| 1       | Bader, 2004 (2) | F   | 47  | GH               | Y        | Binasal field defect | Acromegaly, carpal tunnel |
| 2       | Hiyama, 1986 (7) | F   | 35  | Prolactin        | N        | Bitemporal hemianopsia | Acromegaly, galactorrhea |
| 3       | Ikeda, 1987 (10) | F   | 31  | Prolactin        | Y        | Yes | Amenorrhea, galactorrhea |
| 4       | Ikeda, 1992 (9)  | M   | 50  | GH               | N        | LU temporal quadrantanopsia | Acromegaly, libido loss |
| 5       | Kaku, 2005 (12) | M   | 42  | None             | Y        | Bitemporal hemianopsia | None |
| 6       | Kepes, 1978 (16)| F   | 79  | NS               | NS       | NS | NS |
| 7       | Matsumori, 1984 (18)| F   | 28  | Prolactin        | N        | Bitemporal hemianopsia | Amenorrhea, galactorrhea |
| 8       | Miyagi, 1993 (21)| M   | 44  | None             | N        | None | None |
| 9       | Nakasu, 1989 (23)| F   | 21  | Prolactin        | N        | None | Amenorrhea |
| 10      | Nishio, 1995 (25)| M   | 44  | GH               | N        | None | Acromegaly, libido loss |
| 11      | Sumida, 2001 (32)| F   | 67  | GH               | NS       | None | Acromegaly |
| 12      | Trokoudes, 1978 (34)| F   | 38  | Prolactin        | N        | None | Amenorrhea |
| 13      | Vancura, 2006 (35)| M   | 70  | None             | N        | Diplopia | None |
| 14      | Noh, 2007 (27)  | F   | 62  | GH               | N        | None | Acromegaly |
| 15      | Noh, 2007 (27)  | F   | 30  | Prolactin        | N        | None | Amenorrhea, galactorrhea |
| 16      | Noh, 2007 (27)  | F   | 31  | Prolactin        | Y        | None | Amenorrhea, galactorrhea |
| 17      | Noh, 2007 (27)  | M   | 32  | Prolactin        | N        | None | Amenorrhea, galactorrhea, decreased libido |
| 18      | Noh, 2007 (27)  | F   | 34  | Prolactin        | N        | None | Amenorrhea, galactorrhea, lethargy |
| 19      | Swanson, 1985 (33)| F   | 34  | None             | Y        | Yes | Amenorrhea |
| 20      | Trokoudes, 1978 (34)| F   | 38  | Prolactin        | N        | None | Amenorrhea |
| 21      | Noh, 2007 (27)  | F   | 62  | GH               | N        | None | Acromegaly |
| 22      | Radhakrishnan, 2011 (29)| F   | 16  | None             | N        | None | Amenorrhea |
| 23      | Koutourousiou, 2010 (37)| F   | 42  | ACTH             | NS       | NS | Cushing’s disease |
| 24      | Koutourousiou, 2010 (37)| M   | 76  | None             | NS       | NS | None |
| 25      | Noh, 2007 (27)  | M   | 54  | ACTH             | N        | None | Cushing’s disease |
| 26      | Present report   | M   | 39  | None             | Y        | Horizontal nystagmus | None |

*NS – not specified

This may cause aseptic meningitis or hypophysitis.

Compression of the pituitary stalk by RCCs may impair dopamine transport to the anterior pituitary, resulting in hormonal abnormalities such as hyperprolactinemia. This presents with galactorrhea, amenorrhea and hypogonadism. However, the cause of this hyperprolactinemia may be unclear when a pituitary mass is present as it may also be due to a prolactin-secreting adenoma. Generally, prolactin-secreting adenomas result in a
serum prolactin concentration >200 ng/mL, whereas values below this indicate pituitary stalk compression as the more likely cause.\textsuperscript{14} RCCs have also been reported to occur with adenomas secreting ACTH and growth hormone.\textsuperscript{2,13,15,31,35,36} As untreated subclinical hypopituitarism may result in adverse effects on sexual function, skeletal integrity and cardiovascular function, the hypothalamic–pituitary axis should always be evaluated when a pituitary mass is present.\textsuperscript{37}

**Imaging**

MRI is the recommended modality for visualization of the pituitary gland and parasellar regions. Because of the diverse composition of RCCs, MRI features are variable.\textsuperscript{31} These cysts may contain mucinous fluid, mucopolysaccharides and hemosiderin deposits, affecting their appearance on MRI. The presence of hemorrhage or mucopolysaccharides within the cyst causes high T1-weighted image intensity, whereas the presence of cerebrospinal fluid-like fluid causes a low intensity on T1-weighted images.\textsuperscript{38} Also, mucinous fluid may have a high- or iso-intense appearance on T1-weighted images depending on the viscosity of the fluid. Despite the inconsistent features of RCCs, it has been suggested that a hallmark of these cysts is a lack of post-enhancement on MRI.\textsuperscript{14} As a result, pre-operatively diagnosing a pituitary adenoma and concomitant RCC is rare as differentiation from a cystic pituitary, craniopharyngioma, arachnoid cyst or pars intermedia cyst is difficult. Although imaging studies with clinical and laboratory data may narrow the differential diagnosis, a histological analysis of the mass is the only way to reach a definitive diagnosis.

**Management**

Treatment for pituitary masses typically includes normalization of the hormonal abnormalities and alleviation of mass effect. Surgical therapy is recommended for hormone-secreting tumors resistant to medical therapy, acute hemorrhage and masses impinging on the surrounding structures. Operative management of pituitary adenomas and suspected RCCs involves transsphenoidal resection. This approach is minimally invasive and has been proven to safely excise these masses completely, allowing for the restoration of pituitary function. However, the recurrence rates for pituitary tumors such as GH-secreting adenomas are significant, ranging from 5.4% to 10%.\textsuperscript{51} Therefore, adjuvant therapy such as radiosurgery may be indicated. On the other hand, the risk of recurrence of RCCs is low, with further treatment rarely necessary although suprasellar extension, large cyst size and packing of the sella are risk factors for recurrent cyst formation.\textsuperscript{29} Post-operative care includes monitoring of hormone levels, surveillance MRI scans and neuroophthalmologic testing.

**Conclusion**

We present a report of a patient with a pituitary adenoma in combination with a symptomatic RCC. This rare combination is thought to occur due to the common embryological ancestry of these lesions. These combined tumors are difficult to diagnose pre-operatively due to the variable signal intensity and position of the RCCs. However, the presence of a non-enhancing cyst with a pituitary adenoma suggests the possibility of an accompanying RCC. Treatment of these lesions involves surgical resection to decrease mass effect and medical management to normalize hormonal imbalances.

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