Rathke cleft cysts: a review of clinical and surgical management

GABRIEL ZADA, M.D.

Department of Neurosurgery, University of Southern California, Keck School of Medicine, Los Angeles, California

The aim of this paper is to provide a comprehensive review of clinical, imaging, and histopathological features, as well as operative and nonoperative management strategies in patients with Rathke cleft cysts (RCCs).

A literature review was performed to identify previous articles that reported surgical and nonsurgical management of RCCs. Rathke cleft cysts are often incidental lesions found in the sellar and suprasellar regions and do not require surgical intervention in the majority of cases. In symptomatic RCCs, the typical clinical presentation includes headache, visual loss, and/or endocrine dysfunction. Visual field testing and endocrine laboratory studies may reveal more subtle deficiencies associated with RCCs. When indicated, the transsphenoidal approach typically offers the least invasive and safest method for treating these lesions. Various surgical strategies including cyst wall resection, intracystical alcohol injection, and sellar floor reconstruction are discussed. Although headache and visual symptoms frequently improve after surgical drainage of RCCs, hypopituitarism and diabetes insipidus are less likely to do so. A subset of more aggressive, atypical RCCs associated with pronounced clinical symptoms and higher recurrence rates is discussed, as well as the possible relationship of these lesions to craniopharyngiomas.

Rathke cleft cysts are typically benign, asymptomatic lesions that can be monitored. In selected patients, transsphenoidal surgery provides excellent rates of improvement in clinical symptoms and long-term cyst resolution. Complete cyst wall resection, intraoperative alcohol cautery, and sellar floor reconstruction in the absence of a CSF leak are not routinely recommended. (DOI: 10.3171/2011.5.FOCUS1183)

KEY WORDS • Rathke cleft cyst • transsphenoidal approach • pituitary adenoma • endoscopy • craniopharyngioma

Rathke cleft cysts (RCCs) are benign, epithelial-lined cystic remnants of the craniopharyngeal duct that are often discovered incidentally in the sellar or suprasellar region. These lesions remain asymptomatic in the majority of people. According to the findings of one cadaveric study, small RCCs were the most frequently encountered lesions of the sellar area and were noted to be present in 22% of specimens. Despite their relatively high prevalence, however, RCCs are found in only 2%–9% of patients undergoing transsphenoidal operations for symptomatic sellar region lesions. Only a small proportion of RCCs exert sufficient mass effect on surrounding structures to result in symptoms and require surgical intervention. The current review focuses on the clinical and operative management of RCCs, including preoperative evaluation and patient selection, intraoperative management, and follow-up care.

Abbreviations used in this paper: DI = diabetes insipidus; RCC = Rathke cleft cyst.

Clinical Presentation and Epidemiology

Symptomatic RCCs typically present during the 4th or 5th decade of life, with a slightly higher female preponderance. The typical symptoms associated with RCCs include headache, endocrine dysfunction, and visual loss. Visual loss has been reported to develop in 35%–50% of patients undergoing surgical intervention and may include deficits in visual fields as well as in visual acuity. Hyperprolactinemia and growth hormone deficiency are relatively common endocrinological findings associated with RCCs, followed by hypocortisolemia and hypogonadism. Diabetes insipidus (DI) has been reported as a presenting feature in approximately 7%–20% of patients with RCCs. In rare cases, RCCs may present with chemical meningitis, sellar abscess, lymphocytic hypophysitis, or intracystic hemorrhage. The term “Rathke cleft cyst apoplexy” has recently been described for cases with sudden-onset symptoms and imaging evidence of intracystic hemorrhage.
Although infrequent, RCCs occasionally cause symptoms in children, potentially resulting in somatic or sexual retardation in addition to the more common symptoms related to mass effect described above.37

Preoperative Assessment

All patients with cystic sellar lesions should undergo a comprehensive preoperative evaluation consisting of the appropriate ophthalmological, endocrinological, and neuroimaging studies. A formal visual field examination should be performed in any patient with visual symptoms or evidence of suprasellar cyst extension, as more subtle visual deficits are often detected. A thorough endocrinological history includes screening for symptoms related to fatigue, sexual dysfunction, physical or sexual development, menstrual history, and various hypersecretory endocrinopathies including hyperprolactinemia, Cushing disease, and acromegaly. Laboratory studies should include levels of serum prolactin, free T4, thyroid-stimulating hormone (TSH), morning fasting cortisol, adrenocorticotropic hormone (ACTH), insulin-like growth factor–1 (IGF-1), follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in women, and free testosterone in men. Hypothyroidism should be treated prior to considering elective surgical options.

It may be difficult to differentiate other cystic sellar or suprasellar masses from RCCs based on a patient’s history, laboratory values, and neuroimaging studies.10,39 Additional lesions that may be confused with RCCs include cystic craniopharyngiomas, arachnoid cysts, cystic pituitary adenomas, epidermoid tumors, sellar abscesses, and even intrasellar aneurysms. A general guideline is that a serum prolactin level greater than 200 ng/ml is typically consistent with a prolactinoma rather than hyperprolactinemia due to pituitary stalk compression, although this rule may not be as useful for smaller lesions measuring less than 10 mm in diameter. Selection of the appropriate neuroimaging studies including CT scanning, MR imaging, and CT/MR angiography may help differentiate the various cystic sellar lesions.

Imaging Features of RCCs

Magnetic resonance imaging remains the preferred modality for preoperative assessment of RCCs and for differentiating RCCs from other cystic sellar lesions.39 On MR images, RCCs often appear as well-circumscribed, centrally located spherical or ovoid lesions of the sellar region (Fig. 1). The majority are intrasellar or intra- and suprasellar, although purely suprasellar lesions may occur in a minority of patients (Fig. 2). A majority of RCCs are unilobar with a diameter ranging between 5 and 40 mm (mean ~ 17 mm).23,29,33 They are often identified as having an epicenter located between the anterior and posterior pituitary gland in the region of the pars intermedia. The normal pituitary gland may be displaced in any direction by an RCC, including circumferential splaying if the cyst arises in and remains encased within the gland.6,30 In the majority of cases, administration of Gd contrast demonstrates little or no enhancement of the cyst wall or contents on MR imaging, although a thin enhancing rim has been attributed to inflammation or squamous metaplasia of the cyst wall, or to a circumferential rim of displaced pituitary gland.6,23 The signal intensity of cyst contents on MR images demonstrates high variability on T1 and T2 sequences and has been reported to correlate with the nature of the cystic contents.2,19,35 Although most RCCs display a homogeneous signal intensity, up to 40% contain a waxy intracystic nodule composed of protein and cellular debris that typically does not enhance following contrast administration.5,7

Histopathology

The gold standard for establishing a diagnosis of RCC is histopathological analysis. At times, especially following drainage of an RCC, it may be difficult to obtain a surgical specimen of the cyst wall, occasionally resulting in an inability to obtain a conclusive histological diagnosis. On routine H & E analysis, RCCs typically demonstrate simple columnar or cuboidal epithelium, often with ciliated or mucinous goblet cells (Fig. 3).11 Pseudostratified columnar cells are also commonly observed. Squamous metaplasia of RCCs has been noted to occur in 9%–39% of patients and is associated with higher rates of cyst recurrence.1,23,25 Similarly, stratified squamous epithelium occurs in a minority of RCCs and is thought to pose a higher risk for cyst recurrence.25

Clinical Management

A majority of patients with RCCs that are discovered incidentally will remain asymptomatic. These lesions do...
Rathke cleft cysts

not require surgical management and can be monitored using serial imaging studies. Asymptomatic patients with small RCCs (diameter < 10 mm), normal visual field examination findings, and no evidence of endocrinopathy can be monitored with yearly MR imaging studies or perhaps even clinically if the initial cyst is small and the patient remains asymptomatic. In appropriate patients in whom progressive symptoms that are directly referable to RCCs develop and in those with visual field deficits or underlying laboratory evidence of endocrinopathy, surgical drainage of RCCs remains the preferred treatment option. As an alternative, nonsurgical option for selected asymptomatic patients with larger RCCs (diameter ≥ 10 mm) or those with suprasellar extension, yearly follow-up with MR imaging studies and formal visual examinations may be used to rule out cyst growth or progressive optic apparatus compression and guide surgical decision-making.

Intraoperative Management of RCCs

The transnasal transphenoidal approach has become the most common surgical approach for treating RCCs. In the last 15 years, endoscopic endonasal approaches have become widely used in the surgical management of these lesions. Although quite rare, open craniotomy may be required in complex cases of giant or purely suprasellar RCCs or in patients in whom a transsphenoidal approach is contraindicated. For most patients, however, extended endonasal approaches have obviated the requirement for craniotomy in all but the most complex RCCs. The benefits of the transsphenoidal approach for treating sellar and suprasellar lesions have been described elsewhere in detail. Routine corticosteroid administration is not necessary for patients with no laboratory evidence of preoperative hypocortisolemia. Postoperative screening for hypocortisolemia, however, should be performed in these patients.

Once the sellar region has been approached, bony removal of the appropriate extent of the sellar floor and adjacent parasellar skull base proceeds as required. In RCCs isolated to the suprasellar region, a transsphenoidal extended approach may be ideal for approaching the cyst and preserving normal gland function. Less frequently, large retrosellar and retroclival RCCs may require a transclival approach. Although cyst drainage could theoretically be accomplished via a small bony and dural opening, a wide dural opening is preferable because it is thought to facilitate ongoing cyst drainage and potentially prevent RCC regrowth. Upon opening the cyst capsule, its mucinous contents will often extrude under low pressure, and subsequent drainage can be facilitated with the use of a small suction tip. Obtaining a small piece of the anterior cyst wall for pathological examination early on may be easier than attempting this after drainage, especially for smaller cysts. In RCCs consisting of more fibrous, proteinaceous,
or waxy components, a small round angled curette can be useful for delivering these portions of the cyst contents. For typical RCCs located in the region of the pars intermedia, the surgeon must keep in mind that the posterior pituitary gland lies immediately posterior to the cyst wall, and care must be taken to not damage this portion of the gland. Similarly, complete resection of the cyst wall is not typically recommended, as it has been associated with a higher incidence of postoperative DI. Resection of a small portion of the anterior cyst wall for use as a pathological specimen, followed by wide fenestration of the capsule, is an optimal surgical paradigm for treating RCCs and avoiding damage to the posterior pituitary gland and pituitary stalk. After complete drainage of the cyst, the surgeon should assess for evidence of an intraoperative CSF leak, which can be facilitated by performing a Valsalva maneuver. The use of alcohol cauterization has not been shown to reduce recurrence rates of RCCs and should never be used in the event of an intraoperative CSF leak. Sellar floor reconstruction is not recommended in cases in which a CSF leak is not identified to promote continuous drainage of the cyst. If evidence of intraoperative CSF leakage is identified, it can be repaired with the use of a dural substitute and fibrin glue (for smaller, “weeping” leaks), or with an autologous abdominal fat graft and sellar floor buttress (for larger leaks). The use of a pedicled nasoseptal flap or lumbar drain is not required for the overwhelming majority of these lesions. Similarly, routine nasal packing is not routinely performed.

Clinical Outcomes and Follow-Up Strategies

Previous studies have demonstrated high rates (> 90%) of complete resolution of RCCs following surgical drainage. Similarly, improved headache and visual function have typically been reported in more than 80% of patients after surgical drainage. In 2005, Aho et al. reported the largest surgical series to date of RCCs treated in adults (118 patients), with an initial gross-total resection rate of 97% and a recurrence rate of 18% at 5 years. Although headache, visual symptoms, and hyperprolactinemia frequently improve after surgical treatment of RCCs, panhypopituitarism and DI are less likely to improve, and close postoperative surveillance in conjunction with an endocrinologist is warranted. The incidence of permanent DI after transsphenoidal drainage of RCCs has been reported in 3%–19% of patients and has been associated with complete cyst wall resection.

A small subset of patients harbor RCCs with more aggressive behavior, and they often present with clinical evidence of panhypopituitarism, DI, progressive visual loss, or symptoms similar to meningitis or hypophysitis. These more aggressive RCCs often demonstrate imaging features including a thickened, enhancing cyst wall; surrounding edema or inflammation; ossification; or even hemorrhagic features (Fig. 4). It has been suggested that RCCs may occasionally leak their caustic contents, resulting in a progressive cycle of chronic inflammation and cyst wall reactivity, and more pronounced clinical symptoms. Rathke cleft cysts with squamous metaplasia and transitional features (such as squamous epithelial cells) may cause them to resemble cystic craniopharyngiomas on histopathological analysis and imaging studies. It has been suggested that the 2 lesions are varying manifestations of a common epithelial precursor. Patients with multiple, often progressive clinical recurrences are often noted to have this subset of atypical RCC. In these patients, an argument can be made for a more definitive, complete cyst wall resection rather than repeated fenestration, even at the risk of developing hypopituitarism and DI that can subsequently be treated medically.

Overall long-term recurrence rates after fenestration or resection of RCCs have varied from 3% to 33% and have been reported to correlate with several factors, including the enhancement pattern of the cyst wall on imaging studies, the presence of squamous metaplasia, chronic inflammation or stratified epithelium, the aggressiveness of cyst wall resection, and the insertion of an abdominal fat graft. After surgical treatment of an RCC, MR imaging is recommended at the 3-month follow-up point and then on a yearly basis for 5 years. After this,
Rathke cleft cysts

imaging follow-up may be performed every 2–3 years if patients are clinically and endocrinologically stable, with overall follow-up for at least a decade after the operation.

Conclusions

Rathke cleft cysts are benign, epithelial-lined cysts that cause symptoms in a minority of patients in whom they are found. Headache, visual loss, and endocrine dysfunction are the most common presenting features. Transsphenoidal surgery remains the preferred option for patients with symptomatic RCCs or those with subclinical visual loss or hypopituitarism and offers excellent outcomes with regard to symptomatic improvement, preservation of normal pituitary function, and minimization of complications. Recurrence may pose a treatment challenge, especially in a subset of atypical RCCs with chronic inflammation or transitional features such as squamous metaplasia. Close neuroimaging, ophthalmological, and endocrinological follow-up is therefore warranted for up to a decade after resection.

Disclosure

The author reports no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

31. Saeger W, Lüdecke DK, Buchfelder M, Fahlbusch R, Quabbe...


Manuscript submitted March 16, 2011.
Accepted May 5, 2011.

Address correspondence to: Gabriel Zada, M.D., Department of Neurosurgery, LAC-USC Medical Center, 1200 North State Street #3300, Los Angeles, California 90033. email: gzada@usc.edu.