Surgical management of Rathke's cleft cysts

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Purpose of review

Rathke's cleft cysts arise from embryonic remnants of Rathke's cleft. The purpose of this paper is to review the current knowledge pertaining to Rathke's cleft cysts. Recent studies regarding the management of Rathke's cleft cysts are also discussed.

Recent findings

Rathke's cleft cysts generally exhibit a benign clinical course. Magnetic resonance imaging is the diagnostic imaging study of choice. Although the most consistent sign to differentiate Rathke's cleft cysts is the lack of enhancement of the cyst wall on contrast-enhanced magnetic resonance images, the presence of an intracystic nodule of low signal intensity on T2-weighted images and possibly high signal intensity on T1-weighted images is highly characteristic of Rathke's cleft cysts. Surgical management is the treatment for symptomatic Rathke's cleft cysts, although asymptomatic lesions may be followed conservatively. Drainage of the cyst contents is the primary goal of surgery; aggressive total resection of the cyst wall, however, may be associated with greater endocrine morbidity. Recurrence may be more common than previously noted when a longer follow-up period is observed.

Summary

Incidental Rathke's cleft cysts may be followed with serial imaging. Symptomatic Rathke's cleft cysts are best removed via the transsphenoidal route. Extended postoperative follow-up is indicated in all patients.

Keywords

Rathke's cleft cyst, symptomatic, transnasal–transsphenoidal approach

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Abbreviations

MRI magnetic resonance imaging
RCC Rathke's cleft cyst

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Introduction

Rathke's cleft cysts (RCCs) are non-neoplastic cysts that arise from glandular rests of Rathke's cleft in the area of the intermediate lobe of the pituitary gland. Commonly found at autopsy on a microscopic scale, 80% of RCCs occur at the interface between the anterior and posterior lobes of the pituitary [1]. RCCs can cause visual or endocrine disorders when their mass compresses the visual apparatus, pituitary gland, or hypothalamus.

Embryology

The most common theory about the origin of RCCs is that they develop from embryonic remnants of Rathke's pouch. It is thought that during the third or fourth week of gestation a rostral outpouching of the ectodermal primitive oral cavity meets a downward projection from the neuroectodermal diencephalon. Together, these structures give rise to the anterior lobe, pars tuberalis, and pars intermedia of the pituitary gland [2,3]. Rathke's pouch is created by the development of the adenohypophysis and neurohypophysis in the region of the pars intermedia. If this pouch fails to regress and enlarges with fluid, it becomes a symptomatic RCC. Other theories have been proposed to explain the development of these lesions, including an endodermal rather than an ectodermal origin [4–6] or reverse metaplasia of pituitary cells [7,8].

Pathology

RCCs consist of a single or pseudostratified epithelium with an underlying layer of connective tissue. The cell composition of the epithelium may include ciliated, goblet, squamous, and basal cells [6]. RCCs are classified pathologically as a distinct category among other cystic epithelial lesions, including dermoid cysts, epidermoid cysts, and craniopharyngiomas.

Relationship between symptomatic Rathke's cleft cyst and craniopharyngioma

RCCs often cannot be distinguished radiographically from craniopharyngioma and other intrasellar cysts, and microscopic diagnosis can be difficult. As a result, Harrison *et al.* [2] suggested that these cysts are best viewed as a continuum of epithelial-lined cystic lesions. Harrison *et al.* [2] detailed the histology of each of these intrasellar cysts separately, and also found substantial overlap of characteristics in their cases and in the literature; however, their descriptions of the surgical outcomes were limited. We recently published [9••] a large series of patients with 5-year follow-up in which we suggested that

the closer relationship between craniopharyngioma and RCC proposed by Harrison and colleagues [2] was supported by our recurrence results. Of the 38 patients in our study with a diagnosis of squamous metaplasia, 12 (32%) experienced a recurrence, supporting the theory that RCCs with squamous metaplasia represent a more aggressive pathological entity that may approach the natural history of craniopharyngioma.

Radiographic evaluation

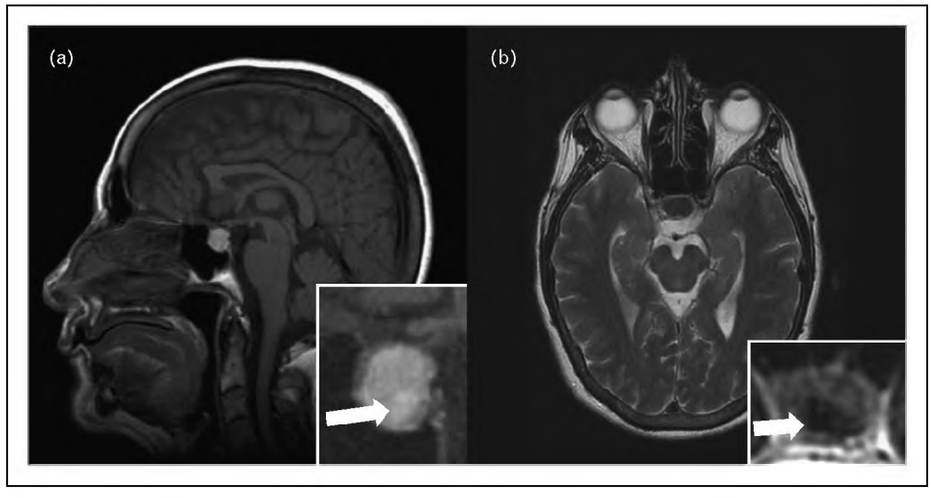
Intrasellar cyst differential diagnosis includes epithelial cyst, epidermoid cyst, dermoid cyst, RCC, and craniopharyngioma. Magnetic resonance imaging (MRI) is the diagnostic study of choice in diagnosing RCCs; however, the signal intensity is often extremely variable on T1 and T2-weighted imaging, the location of the cyst may not be consistent, and overall no single, unique, or consistent pathognomonic sign can be identified [10–12]. Furthermore, as indicated above, RCCs may appear similar to other cystic sellar and suprasellar lesions such as craniopharyngiomas and pituitary adenomas. Various signs that may differentiate RCCs from other lesions include smooth contours, the lack of a cyst wall or extracystic solid component, the absence of calcification, homogeneous attenuation, and the absence of enhancement [1,10–19].

The most consistent sign to differentiate RCCs from cystic pituitary adenomas and craniopharyngiomas that lack an associated solid lesion is the enhancement characteristics of the cyst wall on contrast-enhanced MRI. RCCs do not generally enhance, whereas the other lesions invariably have enhancement of their walls. Although RCCs can appear to have enhancement, this is actually caused by enhancement of the adjacent normal pituitary gland. Dynamic pituitary studies, however, will clearly differentiate enhancement of the normal pituitary that occurs early after contrast administration from cyst wall enhancement that occurs after enhancement of the pituitary.

Another sign that can be used to confirm the diagnosis of RCC is the presence of an intracystic nodule, which may be visible in some cases of RCCs (Fig. 1) [20••]. This nodule is consistently low signal intensity on T2-weighted images, and may have high signal intensity on T1-weighted images. A nodule has been associated with a pathologically confirmed RCC in 17, 43, and 77% of cases described in three series in the literature [13,21,22]. In a recent publication, Binning *et al.* [20••] found that an intracystic nodule was demonstrated in 40% of patients with a tissue-confirmed diagnosis of RCC and in 47% of patients diagnosed radiographically. At surgery, the waxy, solid nodules were floating freely without a connection by any membrane. A pathological evaluation demonstrated a mucinous epithelial-lined cyst containing acellular proteinaceous material with a white nodule of adherent soft tissue that represents cellular debris. Biochemical studies demonstrated that the nodules consisted of cholesterol and protein.

Although the intracystic nodule with its characteristic imaging qualities is unique to RCCs, nodules may also occur with craniopharyngiomas. In contrast to RCCs, craniopharyngiomas typically have a well-defined cystic mass with a mural nodule, which is characteristically hypointense on T1-weighted images and hyperintense on T2-weighted images, and strongly enhances heterogeneously with contrast [23].

Figure 1 MRI appearance of intracystic nodule in Rathke's cleft cyst



Magnetic resonance imaging of a tissue-confirmed Rathke's cleft cyst with a nodule in the posterior aspect of the cyst (arrow in inset) that displays high signal intensity on T1-weighted imaging (a) and low signal intensity on T2-weighted imaging (b). From Binning *et al.* [20••] with permission.

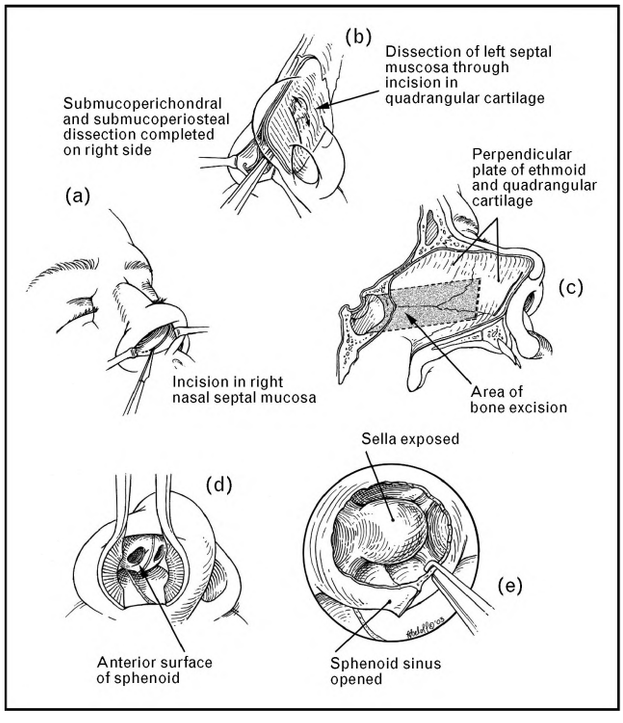
Surgical management: incidental Rathke's cleft cysts

RCCs are becoming a more common incidental finding as neuroimaging is used more often for the evaluation of other conditions; however, these lesions are usually benign and require only conservative management. In their recent survey, Sanno *et al.* [24] found that only 5.4% of RCCs increased in size during follow-up. Our experience supports the assertion that growth of these small, incidental RCCs may occur, but a course of conservative observation is warranted. We found that 69% of patients with an incidental finding of cyst demonstrated no growth for up to 9 years [9••]. It is our practice to follow all incidental presumptive RCCs with serial MRI studies over a 5-year period to determine the growth behavior of the cyst. Small lesions that do not change over this interval are then discontinued from follow-up. MRI-detected recurrence can also be followed with serial imaging alone if no growth progression is observed.

Surgical management: symptomatic Rathke's cleft cysts

Surgical resection of RCCs generally improves endocrine and visual function [25], but aggressive resection can result in postoperative endocrine dysfunction. The preferred method for draining an RCC is via the transnasal–transsphenoidal route (Fig. 2) [26–28], with the use of an operative microscope or endoscope.

Figure 2 Endonasal transsphenoidal approach



This approach is the standard for the drainage of Rathke's cleft cyst, and is usually performed through one nostril and with the aid of a microscope or endoscope. From Liu *et al.* [28] with permission.

There exists some difference in opinion as to what the goals of surgery should be with respect to the aggressiveness of the attempted removal of the cyst wall. In 1966, Fager and Carter [29] advised full evacuation of the contents of the cyst and substantial resection of the cyst wall, and this has become the most common treatment [30,31]. Ross *et al.* [3] later advocated the use of cauterization of the cyst wall and application of absolute alcohol if the subarachnoid space was not violated, in an attempt to kill the cellular wall of the cyst and thus potentially decrease recurrence. No complications were reported in two series with a total of 115 patients who underwent this technique [3,9••]; however, blindness, anosmia, and partial third nerve damage were reported in a patient who underwent four surgeries for recurrent RCCs when the subarachnoid membrane was violated and the alcohol mixed with the cerebrospinal fluid [32].

Aggressive surgical resection of the RCC wall can result in postoperative endocrine dysfunction, most commonly diabetes insipidus. In our study [9••], 22 cases of diabetes insipidus developed in patients in whom it was not present preoperatively. In our experience, radical resection of the cyst wall was associated with higher endocrine morbidity: nearly half of the patients undergoing radical resection in our series (14/33) developed diabetes insipidus postoperatively, whereas only 9% of those patients who underwent non-radical resection developed diabetes insipidus. Similarly, postoperative hypogonadism was more common after radical resection than after less radical resection (6 versus 2.5%).

Outcome

Although incidental asymptomatic lesions with imaging consistent with RCC can be followed conservatively, symptomatic RCCs are most successfully managed surgically. Improvements in headache, visual field defect, visual acuity, hyperprolactinemia, and amenorrhea–galactorrhea syndrome have been reported. Our data also show that preoperative hypopituitarism also improved after the removal of RCCs [9••]. This improvement was most impressive in growth hormone-deficient and hypogonadal patients, but was also observed in hypocortisolemic patients, whereas no improvement was seen in the eight patients with preoperative hypothyroidism. Diabetes insipidus has also generally failed to improve.

After surgical drainage, MRI scans with 2–3-mm spacing should be obtained in all patients at 3 months. Repeat MRI scans should be performed annually for 5 years, and approximately every 2 years thereafter.

Recurrence

Recurrence of symptomatic RCC has been variously estimated at between 0 and 33% [3,31,33–37]. In a study of 53 patients at three different institutions treated with various approaches [36], the authors reported an 11% recurrence rate. One study retrospectively reviewed 16 cases of RCC without recurrence, but did not include follow-up time [33]. Our series [9••] revealed an 18% recurrence rate in patients having at least a 5-year follow-up. Longer follow-up does seem to be associated with a greater reported recurrence rate, suggesting that recurrence may not be quite as rare as has previously been assumed.

We found that less radical resection was not associated with a greater rate of recurrence, but rather that squamous metaplasia of the cyst wall and the use of a fat and fascial graft during surgery were more highly associated with recurrences [9••]. As a result of the high complication rates associated with radical resection, the improved endocrinological complication rates for less radical resection, and the lack of correlation between radical resection and a decreased recurrence rate, it appears that total resection of the wall may not be the optimal treatment for symptomatic RCCs.

Conclusion

RCCs are cystic lesions that originate embryologically as a remnant of the cleft in the region of the pars intermedia. Differentiation of RCCs from other intra and suprasellar cystic lesions is based on MRI characteristics, a lack of enhancement of the cyst wall, and the presence of intracystic nodules. These nodules have consistent and characteristic signal intensities on MRI, and are thought to be diagnostic of RCC when present. RCCs generally exhibit a benign clinical course, and incidental lesions may be followed conservatively. Larger symptomatic lesions producing endocrinopathy from pituitary compromise and visual loss are handled with transsphenoidal drainage of the cyst, usually with histological confirmation of the cyst wall. In most cases, endocrinopathy and visual symptoms improve, but depending on the severity may not normalize. Postoperatively, all patients are monitored carefully for potential recurrence of the cyst over an extended (greater than 10-year) period.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 401).

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