Spontaneous involution of Rathke cleft cysts: is it rare or just underreported?

Report of 9 cases

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Rathke cleft cysts (RCCs) are benign cystic lesions of the sella that arise from the remnants of Rathke pouch. Although most are asymptomatic, symptoms can result from mass effect and commonly include headache, endocrinopathy, or visual field disturbance. Although asymptomatic patients undergo conservative treatment, patients with symptoms are typically treated surgically. The authors report 9 patients with symptomatic cystic sellar lesions and imaging characteristics consistent with an RCC; in all cases there was spontaneous involution of the lesions, and in 5 of 7 patients presenting with headache the symptom resolved. Spontaneous involution of an RCC may be more common than the paucity of prior reports would suggest, especially because the natural history of both symptomatic and asymptomatic RCCs is poorly understood. The potential for spontaneous involution, together with the clinical course of the patients reported here, supports a conservative approach for patients with symptomatic RCCs presenting solely with headache. (DOI: 10.3171/2009.10.JNS091070)

KEY WORDS • Rathke cleft cyst • spontaneous involution • natural history

Rathke cleft cysts are benign cystic lesions of the sella that constitute approximately 1% of intracranial lesions.2,20 They arise from the remnants of Rathke pouch, which is the anlage of the anterior pituitary gland during embryogenesis. Rathke cleft cysts are usually found incidentally on imaging and most remain asymptomatic.20 Symptoms resulting from progressive enlargement include headaches, endocrinopathies, and visual disturbances secondary to suprasellar extension.2,7,8,11,15,17,21,23

Asymptomatic patients with imaging suggestive of RCC are usually managed conservatively while symptomatic patients are typically treated surgically. Although visual disturbances and endocrinological dysfunction represent a clear indication for surgery, headaches cannot be definitively linked to these sellar cysts. Rathke cleft cysts in patients with headache may still be coincidental rather than causative. Nevertheless, headache is often an accepted indication for surgery, with a reported improvement in up to 85–95% of patients postoperatively.5,8,10

The natural history of RCCs and other sellar cystic lesions has not been well described in the literature. Series are lacking that document radiological follow-up in asymptomatic patients or in patients presenting with headache but treated conservatively.7 The clinical outcome of symptomatic patients who did not undergo surgery is also unknown. Herein, we report 9 cases of symptomatic RCC in which 7 patients presented with headache and all lesions underwent spontaneous involution. This phenomenon has rarely been reported in the literature, with a total of 12 other cases previously described.3,10,12,14,18,22

Case Reports

Between 1999 and 2008, 51 patients with RCCs diagnosed according to radiological criteria were seen at The
Of this cohort, 22 underwent surgery, and the remainder have been followed without operative intervention. In 9 (31%) of the 29 patients treated conservatively, we have seen spontaneous decrease in the cyst size over time, and we report their cases here. We illustrate the cases of 4 of these patients in the current report.

Case 1

This 57-year-old man with mycosis fungoides presented with an 8-month history of headache relieved by fluticasone nasal spray. He had been treated with bexarotene until the onset of the headache, with good control of cutaneous disease. Computed tomography scanning showed no abnormalities in the sella or sinuses, and MR imaging revealed a cystic pituitary lesion that extended into the suprasellar cistern and to the optic chiasm. Neurological examination showed normal findings without visual field deficit or oculomotor abnormality. Pituitary hormone studies revealed mild central hypogonadism (testosterone 220 ng/dl [reference range 241–827]). Because this lesion had initially been diagnosed elsewhere as a pituitary adenoma, transphenoidal resection was planned, but surgery was postponed due to the patient’s work schedule. Repeated MR imaging 5 months later, in preparation for surgery, showed spontaneous decrease in cyst volume of 90% (Fig. 1). As a result, surgery was cancelled and interval scanning was recommended. He remains asymptomatic off fluticasone 7 months after detection of the cyst involution, and mild hypogonadism persists.

Case 2

This 32-year-old woman presented with a 2-year history of headache and spots in her visual fields. Her headaches improved after she discontinued oral contraceptives and reduced caffeine intake. She sought further evaluation as she wished to become pregnant. Neurological status and pituitary function were normal. Magnetic resonance imaging revealed a midline cystic sellar (8 × 8 × 11–mm) lesion that was hyperintense on T2-weighted images. Interval MR imaging was recommended and surgical intervention was deferred. Two years after discovery of the RCC and after a recent pregnancy and vaginal delivery (which included a prolonged labor of 24 hours), MR imaging revealed a decrease in cyst size to 4 × 3 × 8 mm (Fig. 2). The patient remained asymptomatic. Further conservative management was undertaken, with no regrowth of the cyst over the ensuing 2 years.

Case 3

This 29-year-old woman was incidentally found to have a cystic sellar lesion on a CT scanning performed as part of an evaluation for deviated nasal septum. An RCC measuring 11 × 9 × 7 mm, without suprasellar extension, was confirmed on MR imaging (Fig. 3). We also observed an asymptomatic arachnoid cyst in the right middle cranial fossa. Due to the absence of symptoms and any hormonal deficit, no intervention was undertaken and the patient was followed for 30 months, at which time a slight decrease in cyst size (10 × 8 × 5 mm) was noted. A year later the mass decreased further to 8 × 6 × 5 mm, and conservative management continues.
Case 4

This 18-year-old woman presented with an 8-day history of severe and unrelenting headache with episodic blurry vision. She also complained of fatigue, depression, and a weight gain of 45 pounds over the past 2 years. Neurological examination showed normal findings without any visual field deficits or oculomotor abnormalities. Pituitary hormone studies revealed an elevated adrenocorticotropic hormone level (67 pg/ml [reference < 46]) with normal 24-hour urine free cortisol and decreased free T4 (0.7 mg/dl [reference range 0.9–1.8]). Magnetic resonance imaging demonstrated a 10 × 7 × 6-mm cystic sellar lesion without suprasellar extension. The patient chose conservative management and returned for repeated imaging 6 months later, at which time the lesion had decreased in size (to 9 × 4 × 4 mm). Six months later, it had decreased further (to 8 × 3 × 3 mm) (Fig. 4). The patient remains asymptomatic 20 months after detection of the cyst involution. No surgery is currently planned.

The clinical presentation, laboratory evaluation, and radiographic characteristics of all 9 patients in our series are summarized in Table 1.

Discussion

General Description

Rathke cleft cysts are rare lesions with a female/male predominance of 2:1 and an age of presentation ranging from 4 to 73 years (mean 38 years), with the highest frequency occurring in the 5th to 6th decades. Although their origin is debated, RCCs are believed to derive from a dorsal diverticulum of the stomatodeum, which begins to form around the 24th day of life. The anterior wall of the developing Rathke pouch forms the pars tuberalis and pars distalis, while the posterior wall forms the poorly differentiated pars intermedia. The residual lumen of this pouch reduces to form a narrow cleft. Failure to regress can result in an expanding and symptomatic RCC. Pouch remnants extending superiority toward the pars tuberalis accounts for the suprasellar extension seen in some RCCs. In addition to RCCs, other known cystic lesions of the sella include cystic pituitary adenomas, craniopharyngiomas, arachnoid cysts, and pars intermedia cysts as well as dermoid/epidermoid cysts.

The majority of RCCs are asymptomatic. In cases of symptomatic lesions resulting from progressive enlargement, the patients most commonly present with headaches, endocrinopathies, and visual disturbances secondary to suprasellar extension. Rarely, patients may present with atypical symptoms including hypothalamic dysfunction, intracystic abscess, hypophysitis, aseptic meningitis, and sphenoid sinusitis. Acute onset of severe headaches may be associated with intracystic hemorrhage; aseptic meningitis, local inflammation, increased intrasellar pressure, and hypocortisolism can be possible causes of cyst-related headaches as well.

Rathke cleft cysts are characteristically lined with goblet and simple ciliated cuboidal or columnar epithelial cells. Intracystic contents vary from clear, low-viscosity fluid to yellow, highly viscous, mucinous fluid with calcifications and cholesterol crystals. Leakage of mucinous contents or hemorrhage resulting from an expanding cyst may result in an inflammatory-induced spectrum of metaplastic changes, progressing from simple columnar/cuboidal epithelium to a stratified squamous epithelium with keratinization and papillary projections, which is histologically similar to that found in craniopharyngiomas. These changes are thought to be responsible for peripheral cystic enhancement on imaging studies.
et al. have demonstrated a 5-fold increase in cyst enhancement in the presence of squamous metaplasia.

**Radiological Evaluation**

Numerous studies have been conducted to identify MR imaging characteristics of RCCs. Generally, RCCs appear hypo- or hyperintense on CT scans whereas on T1-weighted MR images they are iso- to hyperintense but can be hypointense. Rathke cleft cysts that are hypointense on T1-weighted MR images may be either hypo, iso-, or hyperintense on T2-weighted sequences while hyperintense lesions tend to be either hyper- or hypointense. The intensity varies along a spectrum dependent on the protein, cholesterol, and mucopolysaccharide concentrations in the cyst fluid. This variability makes a definitive diagnosis difficult to establish based on MR imaging signal intensity alone. Although the presence of an intracystic nodule is highly suggestive of an RCC (as seen in Case 2), similar neuroimaging characteristics are sometimes seen in acute hemorrhage accompanying pituitary apoplexy. Hemorrhage into an RCC can also occur, in which case they too can present similar to pituitary apoplexy. The severity of clinical symptoms correlates with increasing MR imaging signal intensity when adjusted for cyst size. Although the lack of postcontrast enhancement on MR imaging has been suggested as another hallmark of RCCs, peripheral ring enhancement has been seen in up to 50% of patients with RCC and was present in 2 of our patients.

In cases in which the diagnosis of RCC was suspected on imaging but never confirmed histopathologically, other cystic lesions that are known to spontaneously regress, such as arachnoid cysts, must also be considered. In other cases, the RCC has been confirmed histologically because surgery was ultimately performed either for recurrence of symptoms or due to concern about chronic treatment with steroids. Although our cases lacked histological confirmation of RCC, the lesions’ radiological features were entirely consistent with this diagnosis and exclude with reasonable surety the other cystic lesions of the sella mentioned above.

**Spontaneous Involution of Sellar Cysts**

Spontaneous decrease in size of RCCs has rarely been reported, with only 12 cases extant in the literature (Table 2). In some of these reports, headache was the only symptom, and patients were found to have spontaneous cyst regression after a period of conservative management. In our series, 5 (71%) of 7 patients who presented with headache experienced resolution of the headache as the cyst regressed. Nishio et al. reported 2 such cases—one involving a 14-year-old boy and the other a 31-year-old woman—in both of which the patient presented with headache and no visual or endocrinological dysfunction.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs),†</th>
<th>Sex</th>
<th>Suprasellar Extension</th>
<th>Symptoms</th>
<th>MRI Characteristics</th>
<th>Interval (mos)‡</th>
<th>Pituitary Function†</th>
<th>Resolution of Headache§</th>
<th>Follow-Up After Regression (mos)</th>
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<tbody>
<tr>
<td>1</td>
<td>57, M</td>
<td>yes</td>
<td>headache</td>
<td>T1: hypointense, T2: hyperintense</td>
<td>5</td>
<td>low testosterone</td>
<td>no</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>32, F</td>
<td>no</td>
<td>headache &amp; spots in vision</td>
<td>T1: hypointense, T2: hypointense</td>
<td>44</td>
<td>normal</td>
<td>yes</td>
<td>17</td>
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<tr>
<td>3</td>
<td>29, F</td>
<td>no</td>
<td>none, incidentally found</td>
<td>T1: hypointense, T2: hypointense</td>
<td>31</td>
<td>normal</td>
<td>18</td>
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<td></td>
</tr>
<tr>
<td>4</td>
<td>18, F</td>
<td>no</td>
<td>headache w/ episodic blurry vision</td>
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<td>7</td>
<td>elevated ACTH</td>
<td>yes</td>
<td>14</td>
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<tr>
<td>5</td>
<td>17, F</td>
<td>no</td>
<td>headache</td>
<td>T1: hypointense, T2: hypointense</td>
<td>21</td>
<td>normal</td>
<td>yes</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>14, M</td>
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<td>headache, low-percentile growth</td>
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<td>11</td>
<td>GH slightly low</td>
<td>yes</td>
<td>46</td>
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</tr>
<tr>
<td>7</td>
<td>6, M</td>
<td>yes</td>
<td>headache, aggressive behavior</td>
<td>T1: hypointense, T2: hypointense</td>
<td>41</td>
<td>normal</td>
<td>yes</td>
<td>10</td>
<td></td>
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<tr>
<td>8</td>
<td>5, M</td>
<td>no</td>
<td>low-percentile growth</td>
<td>T1: hypointense, T2: hyperintense</td>
<td>100</td>
<td>Low testosterone &amp; TSH (GH normal)</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>29, F</td>
<td>yes</td>
<td>headache</td>
<td>T1: hypointense, T2: hyperintense</td>
<td>18</td>
<td>normal</td>
<td>no</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

* ACTH = adrenocorticotropic hormone; GH = growth hormone; TSH = thyroid-stimulating hormone.
† At discovery of cyst.
‡ Interval between discovery of cyst and regression.
§ At discovery of cyst regression.
Spontaneous involution of Rathke cleft cysts

The imaging findings were consistent with an RCC, and both lesions exhibited spontaneous regression during follow-up. In other cases of cyst regression, surgery was initially recommended because of visual or hormonal disturbances. However, patients were found to have spontaneous clinical and radiological regression prior to their scheduled surgeries. Simmons and Simmons reported a presumed RCC in a 15-year-old girl who presented with a 1-year history of amenorrhea and decreased LH and FSH. The patient returned a few days prior to surgery and repeated MR imaging revealed spontaneous reduction of the cyst to a thin slit with peripheral enhancement within a normal pituitary gland. Repeated evaluation showed restoration of LH and FSH to normal levels. Regular menstrual cycles resumed several months later.

The likelihood of spontaneous regression of an RCC over time has not been well quantified. During a mean follow-up period of 5 years, Igarashi et al. reported decrease in cyst size in 4 of 10 patients with cystic, thin-walled sellar lesions; in 3 of these patients the lesion later increased again, became symptomatic, and required surgery, which provided histological confirmation that they were RCCs. The overall incidence of cyst regression in our conservatively managed patients was 31%, but follow-up was not uniform in length and referral bias may prevent extrapolation of this incidence to RCCs in the general population.

Half of our patients fell within the pediatric age range (< 18 years), with involution occurring between 1 and 8 years after the cyst was discovered. Only 2 cases have been previously reported within the pediatric age range, and the only paper reporting long-term follow-up results of conservatively managed RCCs confined itself to adult patients. We could not distinguish any age-dependent factors influencing RCC involution. It is possible that embryological mechanisms controlling the normally observed involution of the Rathke pouch in early life may extend into childhood and make the regression of RCCs in the pediatric population more common than in adults. However, proving that hypothesis will require longitudinal examination of large numbers of patients stratified by age.

We cannot state with certainty that the cyst regressions in our cases are permanent. Extended follow-up has not yet been obtained, and it is possible that cyst regrowth may occur, as in the series of Igarashi et al. and Saeki et al., just as it is possible that the cyst may stay dormant over time. Knowledge of the mechanism of regression in any given case might allow prediction of the risk of cyst recurrence.

The incidence of new anterior hypopituitarism after transsphenoidal fenestration and drainage of the RCC is relatively low, but postoperative diabetes insipidus is more common and sometimes persists. The relatively common spontaneous regression of RCCs in our conservatively managed patients supports avoidance of these risks in asymptomatic patients.

Regression Mechanism

The mechanism of regression is largely unknown. Some authors have hypothesized that the changes in cyst size are due to imbalances between secretion and absorption of cystic fluid. Others have suggested that repeated cyst ruptures may be the main factor. In our Case 2, for example, the patient’s prolonged labor and sustained elevated intracranial or intrasellar pressures could have potentially caused cyst leakage or rupture. Rupture of a sellar cyst, as likely occurred in Case 2, has not previously been reported in association with parturition. The role of steroid therapy in this phenomenon is also uncertain.
Maruyama et al. have reported on a patient in whom steroid treatment was associated with a decrease in cyst size and improvement in symptoms, whereas a decrease in steroid dose led to reversal of the effects. The patient in our Case 1 was being treated with the steroid fluticasone, which could in theory account for regression of the cyst (although this seems unlikely). However, neither Cases 3 nor 4 had any obvious factors that could explain cyst regression. Importantly, spontaneous regression in both cases was seen in the absence of steroid therapy. It is also possible for a decrease in RCC to occur in those occasional patients in whom blood flowing into the cyst causes its expansion and in whom the cyst size decreases as the blood reabsorbs. In the 2 patients reported by Nishio et al., and the 2 reported by Saeki et al., cyst regression was the result of this mechanism. However, none of the patients in this report had radiological features consistent with an intracystic hemorrhage.

Conclusions

We believe that spontaneous RCC regression may be an underreported phenomenon within the poorly understood natural history of these lesions. Although headache is often an accepted indication for surgery, we advocate a more conservative approach in patients presenting solely with headache since spontaneous regression is possible. Because headache may be unrelated to the observed cyst, careful clinical and radiological follow-up evaluation seems reasonable in these patients, particularly given the small but real risk of diabetes insipidus after resection of an RCC. In patients presenting with visual or endocrine dysfunction due to persistent mass effect from RCC, surgery is still recommended because of the unpredictable clinical course and the potential risk of irreversible damage from mass effect.

Disclaimer

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

References


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