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Review

Rathke's cleft cyst recurrence after transsphenoidal surgery: A meta-analysis of 1151 cases

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ABSTRACT

Rathke's cleft cysts (RCC) arise from the development of the Rathke's cleft pouch. These commonly occurring cysts are typically asymptomatic, but sometimes present with headaches, endocrine dysfunction, and visual loss. Recurrence is common after either drainage or surgical removal. The purpose of this study was to review published outcomes for RCC management, and determine whether specific factors, including patient demographics, cyst pathology, radiologic parameters, or surgical techniques predispose to their recurrence. A systematic review of studies for RCC from 1990 to 2012 was conducted. Patients were identified using a Medline/PubMed search, and from the bibliographies of relevant articles obtained from the primary search. Relevant studies reporting recurrence rate were identified, and data were extracted regarding patient demographics, presenting symptoms, cyst characteristics, surgical treatment, and outcomes. A meta-analysis for recurrence rates was also performed. Twenty-eight journal articles comprising a total of 1151 RCC revealed an average follow-up of 38 months (range 16–79 months). In the studies reviewed, there was a relatively equal distribution of treatment approaches, with 35% subtotal resection, 33% gross total resection, and 32% complete drainage with wall biopsy. The microsurgical transsphenoidal approach was found to have a higher recurrence rate (14% *versus* 8%) and new endocrine dysfunction rate (25% *versus* 10%) compared to the endoscopic approach. The data demonstrates a notable overall recurrence rate for RCC (12.5%). However, there appears to be no conclusive evidence that more aggressive resection of the cyst wall results in lower rates of recurrence.

1. Introduction

Rathke's cleft cysts (RCC) are benign sellar and/or suprasellar lesions thought to arise from the remnants of the Rathke pouch [1]. Rathke's cleft describes the region that forms between the adenohypophysis and neurohypophysis during the third or fourth week of gestation. RCC arise when the Rathke's cleft does not regress fully and remains patent [2].

The cyst wall is formed by an epithelial membrane, while the inside is filled with a mucinous, gelatinous, or caseous cystic fluid [3]. Although RCC are typically asymptomatic, some lesions exhibit growth and symptomatically compress surrounding neurovascular structures, requiring subsequent surgical therapy [4]. Common symptoms are visual and/or endocrine disturbances, [2] the most common symptom being headache [5]. For symptomatic RCC, surgical decompression through a transsphenoidal approach (microscopic or endoscopic) is commonly performed [1,6,7]. Complex cases of RCC that are very large or purely suprasellar with significant lateral extension may necessitate an open transcranial approach [4,8].

Successful decompression of the cyst commonly results in improved visual and endocrine function, as well as alleviation of headaches [9]. On the other hand, aggressive resection of the cyst wall has a notable rate of postoperative endocrine dysfunction, especially diabetes insipidus (DI) at a rate of 19% [2]. One of the primary features of RCC is their tendency to recur, making their optimal treatment and management strategy one that not only involves cyst decompression from neural structures, but also removal of the cyst wall to minimize recurrence.

There is no consensus over the most effective method of resection that alleviates symptoms and prevents recurrence while minimizing postoperative complications. Some feel that a complete drainage of cyst contents and biopsy of the cyst wall has the same efficacy as a gross total resection; however, the complete drainage of the cyst has a lower rate of postoperative disturbances [2,10]. In addition, there are other factors that reportedly may predict recurrence, including the presence of inflammation and squamous metaplasia in the cyst wall, MRI rim enhancement, use of packing material, and cyst location. In this report, we perform a systematic

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review and meta-analysis of the current literature on surgical management of RCC in order to determine particular factors that influence recurrence.

2. Materials and methods

2.1. Literature search strategy

A systematic review of published literature on patients with RCC was performed. The PubMed database was searched from 1990 to 2012 for "Rathke AND cleft AND cyst AND treatment", and "features AND Rathke's". Titles were reviewed to identify studies that appeared to involve RCC. Abstracts were subsequently examined, followed by review of acquired full-text articles. Lastly, the references in the retrieved articles were examined for associated studies. Institutional Review Board approval was not required since this study qualified as "nonhuman subject research."

2.2. Selection criteria and data management

All English-language studies reporting RCC were included. Articles were only included if they reported diagnosis, treatment, follow-up, and recurrence. Nonhuman, radiologic, cadaveric, anatomic, histologic, and molecular studies were excluded, as were sources with insufficient or unextractable data. Articles with unobtainable full text were also excluded. Assessment of study quality was performed, however there were few quality scales that could account for case series and case reports as they were developed for cohort, case-control, and randomized controlled studies [11,12]. Using the Quality Assessment Tool for Quantitative Studies (Effective Public Health Project 2007), it was determined that all of the studies included in this review were given the global rating of "weak" [13–15].

2.3. Data extraction

Two independent observers extracted data, and any discrepancies were discussed with inclusion into the database only occurring after consensus. Outcome measures extracted included demographic data (age, sex), symptoms (headache, endocrine dysfunction, visual deficit), cyst location (suprasellar, intrasellar, both), radiographic imaging, surgical approach (microsurgical transsphenoidal, endoscopic transsphenoidal, craniotomy), surgical technique performed (subtotal resection [STR], gross total resection [GTR], drainage and biopsy), complications, recurrence, and follow-up. Surgical techniques were defined as follows: drainage referred to emptying the cyst contents into the sphenoid sinus (via marsupialization, fenestration, simple drainage) and included a biopsy of the cyst wall; STR was a resection of the cyst wall beyond what was needed for a biopsy, but without removal of the entire cyst wall, along with total drainage of the cyst contents; and GTR was the removal of the entire cyst capsule and contents.

2.4. Data analysis

This study used StatsDirect (StatsDirect Ltd, Altrincham, UK) for meta-analysis, sensitivity/subgroup analysis, forest plots, and funnel plots. DerSimonian and Laird's random-effects model was used to pool the recurrence rate from aggregated observational studies to form a weighted parameter estimate [16]. The random effects model was used because it assumes that the studies included are a sample of all potential studies, thus allowing between-study variability to be estimated [17]. Heterogeneity was determined using the I^2 statistic to assess for consistency. Visual inspection of the funnel plot along with Egger's test was used to determine the presence of publication bias. Sensitivity analysis was performed by excluding each individual study to determine if there were any deviations in the overall estimate and by performing the same analysis after excluding studies with small sample size ($n < 10$). MedCalc (MedCalc Software, Ostend, Belgium) was used to create 2×2 contingency tables to perform chi-squared tests to determine differences in recurrence rates based on surgical treatment.

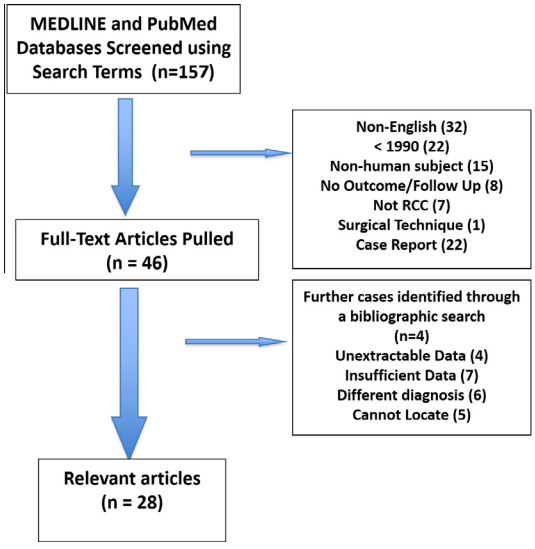

Fig. 1. Flow diagram of studies that were identified, excluded, and included in the current review. RCC = Rathke's cleft cysts.

Table 1
Articles retrieved from the studies included in the current review

Study	Year	Patients, n
Aho et al. [2]	2005	118
Benveniste et al. [30]	2004	62
Billeci et al. [18]	2004	14
El-Mahdy and Powell [29]	1997	14
Frank et al. [7]	2005	22
Higgins et al. [35]	2011	61
Iannelli et al. [1]	2012	4
Isono et al. [9]	2001	15
Jahangiri et al. [36] (pediatric)	2011	14
Jahangiri et al. [36] (adult)	2011	147
Jayarao et al. [37]	2011	2
Kasperbauer et al. [34]	2002	29
Kim et al. [24]	2004	53
Kleinschmidt-DeMasters et al. [28]	1995	16
Koutourousiou et al. [38]	2008	15
Lillehei [32]	2011	82
Madhok et al. [39]	2010	35
Mukherjee et al. [40]	1997	12
Potts et al. [6] (sellar)	2011	76
Potts et al. [6] (sellar with suprasellar extension)	2011	56
Potts et al. [6] (purely suprasellar)	2011	19
Raper and Besser [41]	2009	12
Ross et al. [22]	1991	43
Sade et al. [26]	2005	10
Shin et al. [42]	1999	26
Voelker et al. [27]	1991	8
Wait et al. [31]	2010	73
Wen et al. [43]	2010	22
Xie et al. [5]	2011	23
Zada et al. [10]	2008	10
Zhong et al. [25]	2012	45