Pediatric symptomatic Rathke cleft cyst compared with cystic craniopharyngioma

著者	Hayashi Yasuhiko, Kita Daisuke, Fukui Issei, Sasagawa Yasuo, Oishi Masahiro, Okajima Michiko, Tachibana Osamu, Nakada Mitsutoshi
journal or publication title	Child's Nervous System
volume	32
number	9
page range	1625-1632
year	2016-09-01
URL	http://hdl.handle.net/2297/45946

doi: 10.1007/s00381-016-3160-9

Clinical article

Pediatric symptomatic Rathke cleft cyst compared to cystic craniopharyngioma

Yasuhiko Hayashi[1], M.D.,Ph.D., Daisuke Kita[1], M.D.,Ph.D., Issei Fukui[1], M.D., Yasuo Sasagawa[1], M.D. Ph.D., Masahiro Oishi[1], M.D., Michiko Okajima[2], M.D.,Ph.D., Osamu Tachibana[3], M.D.,Ph.D., Mitsutoshi Nakada[1], M.D.,Ph.D.

Department of 1:Neurosurgery and 2:Pediatrics, Graduate School of Medical Science, Kanazawa University, Kanazawa, Japan

3:Department of Neurosurgery, Kanazawa Medical University, Kanazawa, Japan

A running head; Symptomatic Rathke cleft cyst in children

Key words; Rathke cleft cyst, symptom, craniopharyngioma, children

Corresponding author; Yasuhiko Hayashi, M.D., Ph.D

13-1 Takara-machi, Kanazawa, Ishikawa, 920-8641, Japan

TEL; +81-076-265-2384, FAX; +81-076-234-4262

e-mail; yahayashi@med.kanazawa-u.ac.jp

Abstract

Introduction

Symptomatic Rathke cleft cysts (RCCs) are rarely detected in neuroradiological screening and are less commonly found in children than in adults. However, when RCCs are observed in children, it is important to carefully distinguish a RCC from a cystic craniopharyngioma (CP) even if surgically treated or conservatively followed-up.

Methods

We conducted a retrospective review of clinical data from 11 patients with symptomatic RCCs whose ages were under 18 years and compared the data to data from 15 age- and sex-matched patients with cystic CP who were treated at our institute.

Results

The mean age of the patients with RCCs was 12.2 years (range, 6-18). There were 6 males and 5 females. As initial symptoms, nine patients presented with headache, while 2 each had impaired visual function, diabetes insipidus, and activity loss. The 14 patients with CP suffered from impaired visual function. Magnetic resonance imaging (MRI) mainly showed hyperintensity on T1-weighted images (WIs) and hypointensity on

T2-WI in patients with RCC. However, patients with CP had characteristic hyperintensity on T2-WI. The average maximum diameter of the RCCs was 19.0 mm on average (range, 8-33 mm). The RCCs were thus significantly smaller than CPs (34.9mm, range 21-54 mm). The RCCs were usually oval or dumbbell-shaped and regular in appearance, while the larger CPs were lobular and irregular. A preoperative endocrinological evaluation revealed insufficiencies in 4 axes in 5 patients with RCC. Postoperative endocrinological status improved in 3 patients, remained unchanged in 3, and worsened in 1. The gonadotropin axis was damaged in a majority (9) of the patients with CP preoperatively. Postoperative evaluation revealed deficits in 5 axes in 14 patients with CP, which is a significantly different trend than observed in patients with RCC. Eight patients underwent surgical procedures (transsphenoidal surgery (TSS) in 4, craniotomy in 4). Two of these patients experienced a recurrence of the cysts. One of these patients subsequently underwent two craniotomies followed by radiation and other underwent TSS. Among the 3 conservatively-treated patients, two experienced a transient worsening of their symptoms along with cyst enlargement. However, none of the 3 conservatively-treated patients required an operation.

Conclusions

When RCCs become symptomatic in children, the most common symptom they lead to is headache. The cysts are commonly small, regular, and oval in shape. Hypointensity of cyst contents on MRI is a characteristic of RCCs, which distinguishes them from CPs. Surgical intervention can be effective and lead to the relief of symptoms without a high rate of complications. However, there seems to be a relatively high recurrence rate following surgery. Thus, if the patient's symptoms remain minor, the surgical treatment option should be used only when prudent, as the patient's symptoms may improve over time.

Introduction

Rathke cleft cysts (RCCs) are the most common non-neoplastic cystic lesions in the sellar and the suprasellar regions. Their cyst walls are composed of epithelial cells and there is fluid with high protein concentration inside the cyst [1,2]. RCCs are found to arise from embryonic remnants of Rathke's pouch and are typically located at the pars intermedia between the adenohypophysis and the neurohypophysis [3,4]. Although they are reported in as many as 3-22% of all autopsy studies, they are seldom symptomatic during life [5,6]. The most common clinical symptoms associated with RCCs are headache, impaired visual function, and endocrinological insufficiency [7,8]. RCCs can also cause delayed or precocious puberty, amenorrhea/galactorrhea, growth retardation, weight gain, and hypogonadism [9-11]. As the peak age of patients presenting with RCCs symptoms is typically between 30 and 50 years, it is unusual to detect RCCs by magnetic resonance imaging (MRI) in asymptomatic children [7,12,13]. In addition, even among symptomatic patients, the rate of RCC prevalence is much lower in children compared to adults [14,15].

The radiological findings of RCCs are sometimes reported to be similar to those of cystic craniopharyngioma (CP). One should thus be careful to distinguish RCCs from

cystic CPs, as the two are quite different with regards to surgical procedures available for treatment, complications, and prognosis. It is well known that patients with CP require total removal of the tumor including the cyst wall. The rate of postoperative complications, such as hypopituitarism, diabetes insipidus, and recognition insufficiency is remarkably high [7,16]. Therefore, indications for the surgical treatment of symptomatic pituitary cysts should include histological confirmation of the surgical specimen, as well as confidence the surgery will lead to the relief of the symptoms. When an asymptomatic RCC is discovered in children, it is also important to follow up with radiological imaging and to carefully monitor the patient's clinical symptoms and signs [17].

The aim of this study is to review the clinical statuses of children with symptomatic RCCs treated either surgically or conservatively and to compare them with characteristics of children with cystic CPs. In order to do so, we will review the patients' symptoms, radiological and endocrinological findings, operative reports, recurrence rates, and outcomes.

Methods

This study was approved by the Kanazawa University Institutional Review Board. In this retrospective clinical study, 11 patients with RCC and 15 patients with cystic CP who consulted to Kanazawa University Hospital between 1997 and 2015 were enrolled. The patients were younger than 18 years of age at the onset of their symptoms. Both RCCs and cystic CPs were clinically diagnosed based on MRI findings. We considered the following items obtained from the patients' clinical charts: sex, age, symptoms including headache, impaired visual function, and radiological evaluation, endocrinological insufficiencies, operative reports, recurrence, outcomes, and follow-up periods. Postoperative outcomes were classified as: improved with relief of preoperative symptoms, unchanged with the continuation of symptoms, or worsening with deterioration of symptoms and/or occurrence of new postoperative symptoms.

Neuroradiological evaluation

A 3.0-Tesla MRI (GE Health care Japan Corp., Tokyo) was used to obtain horizontal, coronal, and sagittal images before and after gadolinium administration. The characteristics of the cysts (maximum diameter, shape, signal intensity of the cyst content, location, enlargement upon follow-up, and enhancement after administration of

contrast medium) were evaluated by MRI on both T1- and T2-weighted images (WIs). RCCs diagnosed neuroradiologically had to meet all of the following conditions to qualify for a conservative treatment course; 1) the cystic lesion is oval or dumbbell-shaped and is located in the sellar or suprasellar region, 2) the cystic lesion is circumferentially surrounded by the normal pituitary gland, and 3) the cyst wall has little or no enhancement, has no signs of invasion, and has no calcification [18]. Cystic CPs are considered those in which the cystic portion predominantly accounted for at least 60% of the tumors. This diagnosis was made using MRI [19].

Endocrinological evaluation

An endocrinological examination was performed preoperatively, and included measurements of plasma growth hormone (GH), insulin-like growth factor-I, prolactin, adrenocorticotrophic hormone (ACTH), cortisol, thyroid-stimulating hormone (TSH), triiodothyronine, thyroxin, luteinizing hormone, follicle stimulating hormone, and anti-diuretic hormone (ADH) levels. Insulin, corticotropin-releasing hormone, thyrotropin-releasing hormone, and luteinizing hormone-releasing hormone loading tests were carried out postoperatively to evaluate the reserve capacity of each hormone

tested preoperatively. Diabetes insipidus (DI) was considered to be present in patients with polydipsia and polyuria (total amount of urine volume per day greater than 3000ml with urine specific gravity of less than 1.005), and in those who used 1-desamino-8-D-arginine vasopressin (DDAVP). A water-deprivation test and/or hypertonic saline infusion test were performed to diagnose of postoperative permanent DI in patients [20]. A pediatric endocrinologist evaluated the results of the pituitary functional examinations.

Surgical procedures

The patients treated using surgical operations underwent transsphenoidal surgery (TSS), craniotomy, or both. TSS was performed using a microscope (1997-2004) or an endoscope (2005-2015). On the other hand, craniotomy was performed using a pterional or interhemispheric approach and a microscope. Patients with RCCs were treated with a partial cyst wall removal and complete aspiration of the cyst contents. Total removal of the cyst wall was attempted in all patients with CPs. When craniotomy was used in these patients a pterional or interhemispheric approach was selected based on tumor size and the direction of its extension. In contrast, when the patients

were treated by TSS, the procedure was performed using a microscope (1997-2004) or an endoscope (2005-2015), as described above for patients with RCC. Recurrence was defined as a re-accumulation of the fluid inside the cyst by MRI evaluation during the postoperative follow-up period. Pathological analysis of the resected cyst wall was performed to confirm the final diagnosis by a pathologist.

Statistical analysis

Chi-squared tests were used to compare the two patient groups. Mann-Whitney U-tests were used to make comparisons between the patients' ages and the maximum diameters of their cysts. These statistical analyses were performed using Microsoft Statview (ver. 5, SAS Institute Inc.). A p-value of < 0.05 was considered as statistically significant.

Results

A summary of the characteristics of the patients in our study with pediatric RCCs is shown in Table 1, while Table 2 summarized the results of comparisons between patients with RCCs and those with cystic CPs.

Patient characteristics and clinical symptoms

Of the 11 patients with RCC that were reviewed, 6 were male and 5 were female. The mean age of these patients was 12.2 years (range, 5-18). Of the 15 patients with CP that were reviewed, 8 were male and 7 were female. The mean age of these patients was 9.3 years (range, 4-18). Both groups had similar sex distributions ($p = 0.951$). In addition, the mean ages of the two groups were not significantly different ($p = 0.071$). Nine (82%) of the patients with RCCs presented with headache as their initial symptom ($p < 0.001$), while 2 (18%) each first complained of impaired visual function, diabetes insipidus, and activity loss (Tables 1 and 2). All the patients who suffered from headaches were relieved of their symptoms postoperatively without the use of medication. Visual impairment was completely diminished in the two patients initially complaining of the symptom. Postoperative endocrinological symptoms improved in 2 patients (partial DI in patient 4, and fatigue and anorexia in patient 6), were unchanged

in 1 patient (growth retardation and loss of activity in patient 5), and worsened in 1 patient (permanent DI in patient 1) (Table 1). Meanwhile, 14 out of 15 (93%) of the patients with cystic CPs had the initial symptom of impaired visual function ($p < 0.001$). In addition, endocrinological insufficiencies, such as growth retardation, and headache were initial symptoms in 2 patients (13%) each (Table 2). Impaired visual function was remarkably improved after surgical decompression of the optic nerves. Although headaches were relieved without medication, the endocrinological statuses of 14 out of 15 (93%) of the patients deteriorated remarkably. These patients were required to undergo hormonal replacement therapy following their surgeries.

Neuroradiological findings

Patients with RCCs had an averaged maximum cyst diameter of 19.0 mm (range, 8-33 mm). The cysts were characterized by hyper-intense signals on T1-WI in 7 patients ($p = 0.058$). Of these patients, 1 had a hyper-intense cyst and 6 had hypo-intense cysts on T2-WI. In addition, 4 patients had cysts that were hypo-intense on T1-WI and hyper-intense on T2-WI ($p = 0.391$). Although 6 of the patients had cysts that grew in size during the observation period, these enlargements were insignificant. The cysts

were largely oval or dumbbell-shaped in all of the patients with RCCs ($p < 0.001$). Seven patients had cysts that were located in the sellar region and had suprasellar extensions and 4 had cysts whose locations were restricted to the suprasellar region. Neither calcification nor hydrocephalus was found in any of the patients (Table 2). Representative MRIs of RCCs are shown in Figure 1.

The cystic CPs observed had an average maximum diameter of 34.9 mm (range, 21-54 mm) and were significantly larger than RCCs ($p < 0.001$). Four patients had cysts that were hyper-intense on T1-WI, 3 patients had iso-intense cysts, and 8 had hypo-intense cysts. All of the patients had cysts that were hyper-intense on T2-WI ($p < 0.001$). Five patients had cysts that were regular and oval, and 10 had irregular lobular cysts (Table 2). The diameters of the irregularly-shaped cysts were significantly larger than those of regularly-shaped ones (39.7 vs. 25.4 mm, $p < 0.001$). All of the cysts had calcification on their walls ($p < 0.001$). Six patients had cysts in the sellar region that extended into suprasellar regions and 9 had suprasellar cysts. The distribution of the cysts in these patients was thus not significantly different from that observed in patients with RCCs ($p = 0.234$) (Table 2). In 5 patients, hydrocephalus was detected, which is

significantly different when compared to patients with RCCs ($p = 0.033$). All of these patients had obstructive hydrocephalus at the foramen of Monro, which was relieved after tumor removal. However, the maximum diameters of the cystic CPs were significantly larger in patients with hydrocephalus (43.5 mm) compared to those in patients without hydrocephalus (29.3 mm) ($p = 0.001$). Representative MRI results for these CPs are shown in Figure 2.

Endocrinological findings

Preoperative endocrinological evaluation in patients with RCCs revealed insufficiencies in 4 axes and in 5 patients. Two patients had decreases in both cortisol and ACTH at baseline and a hypo-response to CRH loading postoperatively (patients 1 and 4). In one patient with ACTH solo-decline (patient 6) who had fatigue and anorexia as a symptom, the ACTH insufficiency recovered and his symptoms were relieved after surgical intervention. However, in another patient with declines in both ACTH and ADH (patient 4), the ACTH insufficiency did not improve after surgery. Two patients (patient 1 and 5) had impairments in TSH secretion before surgery, which were not improved preoperatively. Although GH levels were low in 2 patients preoperatively, one patient

with GH solo-decline (patient 3) had no symptoms related to GH insufficiency, which was diagnosed with hormones loading test including insulin and normalized after surgery. In the patient with declines in both GH and TSH secretion (patient 5) before surgery, neither hormonal insufficiency was improved following surgery. While ADH was lower in 2 patients who had manifestations of DI preoperatively, only one of the patients with ADH decline (patient 4) had symptoms of polydipsia and polyuria. A hypertonic saline infusion test revealed increased urine osmolality in this patient. This patient was diagnosed as having partial central DI, which recovered postoperatively with diminishment of symptoms. The patient with deficits in ADH secretion as well as in another axis before surgery (patient 1) revealed no improvement in the hormonal insufficiencies after surgery. He was diagnosed as central diabetes after a water deprivation test with the presence of polydipsia and hypotonic polyuria. Transient DI occurred in 2 patients (patients 3 and 7) postoperatively (Table 1).

In endocrinological evaluation of CPs, preoperative abnormalities were observed in 11 patients (73%). This frequency was not significantly different in patients with CP compared to those with RCCs ($p = 0.149$). Three patients had impairments in ACTH

(20%), 8 had deficits in GH (53%), and 9 had deficient gonadotropin secretion (60%). The number of patients with preoperative impairment of gonadotropin was significantly different in patients with CP compared to those with RCC ($p = 0.002$). Fourteen patients had hormonal abnormalities postoperatively ($p < 0.001$). The impaired secretions of pituitary hormones were as follows: gonadotropin in 10 patients (67%), GH in 13 (87%), TSH in 11 (67%), ACTH in 12 (80%), and prolactin in 5 (33%). The rates of all these impairments in hormonal function were significantly higher in patients with CPs compared to those with RCCs (Table 2). Permanent DI occurred in 9 (60%) of these patients. These patients were treated with routine administration of proper amounts of DDAVP. The number of patients with permanent DI was remarkably higher in the CP group than in patients with RCCs ($p = 0.006$) (Table 2). Decreased GH, TSH, and ACTH were replaced by a pediatric endocrinologist.

Operations

Eight patients with RCCs underwent surgeries. Four of these patients had TSS and 4 had craniotomies. The 3 patients who did not undergo surgery were treated conservatively. TSSs were routinely performed with partial cyst wall resection and

complete aspiration of cyst contents under a microscope (patients 1-5) or an endoscope (patiens 6,7,11). The patients who underwent TSS were 10 to 15 years of age. Therefore, their nasal cavities were not significantly smaller than those of adults. As a result, the TSSs were performed without any complications in patients with RCCs (Table 1).

All 15 patients with CP underwent surgeries. Eight of these patients had craniotomies (interhemispheric approach in 6, pterional approach in 2) and 7 had TSS. Differences in the use of surgical approaches were not significant between RCCs and cystic CPs (Table 2). Sellar tumors with suprasellar extensions were treated using TSS and tumors that were located in the suprasellar and did not extend into the intrasellar region were removed using craniotomies. Cyst contents were completely evacuated and the cyst walls were removed as much as possible unless the cyst wall adhered to adjacent vascular or neural structures.

Pathological findings

Pathological examination of the cyst wall was performed in all 8 patients. Five cysts were diagnosed as RCCs, as indicated by the presence of columnar or cuboidal cells

with microvilli lining the epithelium. Three patients had surgical specimens with microscopic bleeding from granulations on the cyst wall, five had an invasion of inflammatory cells, such as lymphocytes, and three had collagen fibers infiltration. These pathological features revealed the presence of acute- or chronic- phase inflammation, which had spread around the cyst wall. Patient 1 in the present study encountered re-accumulation of the cyst contents twice (Fig. 3A-C). All procedures for this patient, including the first transcranial surgery were performed without neurological complications. A surgical specimen of the cyst wall revealed typical squamous metaplasia, which was reported to mimic to papillary type of CP (Fig. 3D).

Pathological examinations of the cystic CPs in our study revealed typical adamantinomatous type of CP in all of the cases.

Recurrence on follow-up

In this study, patients with RCCs were followed up for 12-152 months. Two patients had a recurrence of RCCs (25.0%). One patient (patient 1) was treated with craniotomies after both recurrences and was subsequently treated with radiation (Fig. 3). The other patient (patient 6) had TSS upon cyst recurrence. During the follow-up of the

three conservatively-treated patients, two patients manifested a transient worsening of their symptoms with mild cyst enlargement. However, as the cyst enlargement did not progress in these patients; all 3 conservatively-treated patients continued to be treated the same way without undergoing an operation.

Six of the 15 patients with CPs had recurrences (40%). This difference of recurrence rates between the RCC group and the CP group was not a significant ($p = 0.184$), although the numbers of patients of both groups were limited (Table 2). All 6 patients underwent a second operation and 5 were treated with radiation. Three patients underwent surgery followed by radiation for the removal of their tumors and any remaining residues (20%). None of the patients were conservatively treated when follow-up MRI detected a recurrence of their tumors.

Discussion

Although RCC is rarely symptomatic in children, it is important to distinguish RCCs from cystic CP, as their treatment and prognosis are quite different from each other [7,16]. Even with pathological examination of the surgical specimen, it is difficult to distinguish RCCs from cystic CPs in some cases. This is because squamous metaplasia of the epithelial cells is considered to be a transitional form of progression from RCC to CP [21,22]. Therefore, the clinical characteristics of RCCs should be carefully considered in children. The symptoms, radiological and endocrinological evaluation, surgical considerations, and outcomes of these patients should then be compared to those of patients with CP. Although many authors reported a clinical comparison of RCCs with cystic CPs in all age group [23,24], this study is the first to offer the clinical comparison peculiar to children to elucidate the differences in the diagnosis and management.

The characteristic neuroradiological findings in patients with RCCs are summarized below and compared to those of patients with cystic CPs; 1) The maximum diameters of the cysts were relatively smaller in RCCs. 2) Although the RCCs were regularly oval or

dumbbell-shaped, the cystic CPs were superiorly lobulated, irregular, and extended. 3) 60% of the patients with RCCs had hypo-intense signals on T2-WI MRI, while all patients with cystic CP had hyper-intense signals. 4) The RCCs are mainly intrasellar, but 36% of the cases and cysts that were located in the suprasellar region. This was a remarkably higher rate compared to that observed in RCCs in adults. These RCCs could not be definitively differentiated from CPs by preoperative imaging [15]. 5) No RCCs had calcification, while calcification was observed in all cystic CPs [16,25]. 6) No hydrocephalus was found in patients with RCCs, while 5 patients with cystic CPs had obstructive hydrocephalus. Our results also suggested that cystic CPs with hydrocephalus were significantly larger than those without hydrocephalus and were enough to occlude the foramen of Monro.

The regularly oval shape of the RCCs, their hypo-intense signal on T2-WI MRI, and the lack of calcification on their cyst walls are important to note during preoperative diagnosis, as it would be of great benefit to neurosurgeons to distinguish RCCs from CP and avoid unnecessary cyst wall removal [7]. Although cystic CPs are typically of the adamantinomatous subtype as shown in our study, it is reported that some CPs in

children do not have calcification [26]. The signal intensities of RCCs on T1-WI and T2-WI MRI for RCC are highly variable and are reported to correlate with the nature of the cyst contents [27,28]. In addition, although the content of most RCCs display a homogenous signal up to 40% of cases contain waxy intracystic nodules, which lead to very hypointense signals on T2-WI. These nodules are important key findings in the diagnosis of RCC [7,29]. In contrast, T2-WI hyperintensities were found in all of the patients with CP in our study, despite the existence of a variety of signal distributions on T1-WI. Therefore, the findings of hypointensity and heterogeneity on T2-WI are considered to be important in distinguishing RCCs from CPs [15,30].

Preoperative endocrinological impairment of RCCs in children occurred in one axis in 2 patients and in two axes in 3 patients with RCCs. Postoperative evaluation showed improvements in 2 patients with one axis impairment and no change in 3 patients with two-axis impairment. It was noteworthy that no patient demonstrated postoperative endocrinological deterioration, except for transient delayed DI, which was observed in patients 3 and 7. Meanwhile, preoperative endocrinological impairment occurred in 10 (67%) out of 15 patients with cystic CP. Subsequently, postoperative endocrinological

evaluation demonstrated remarkable deterioration in 14 patients (93%). These results were quite different from those observed in patients with RCCs. No newly developed postoperative permanent DI was found in RCCs, but 9 patients (60%) had permanent DI in cystic CPs. This significant difference in postoperative endocrinological status is probably due to the procedure to remove as much of the cyst as possible in patients with CPs. However, recent advances in the administration of hormonal replacement can make such removal procedures possible.

The standard partial excision of the cyst wall and complete aspiration of cyst contents are considered to result in total resolution of RCCs, while minimizing complications [12,13,31]. Aho reported on the surgical treatment of a series of RCCs in adults. The initial gross total resection rate was 97% and the recurrence rate was 18% at 5 years [12]. Zada reported on a series of RCCs in children, which were treated surgically and had a recurrence rate of 11% at 3 years [15]. Jahangiri presented their RCC series and reported that the recurrence rates for the adult patients and the pediatric patients were similar, at 12% and 14%, respectively [14]. Some authors believe that there is a positive association between squamous metaplasia of the cyst

wall and recurrence of RCC [13,21,25]. In our series, one patient (case 1) with squamous metaplasia on the surgical specimen had two recurrences of RCC. He was treated using craniotomies three times, including the first operation, and was treated with radiation after surgery. The three patients treated conservatively did not require surgery during their follow-up periods. The decision to observe an incidentally-found RCCs in pediatric patients with normal hormonal values and no chiasmal compression seems to be a reasonable one [14]. Further accumulation of RCCs in children is required to clarify their natural history with the findings of neuroimaging.

Finally, in the aspects of the comparison to the RCCs between children and adults, the differences in clinical characteristics can be found in our study as follows; 1) In RCCs in children, the sizes of the cysts can increase during the observation period as Jahangiri et al. described [14], although the increases are insignificant and their symptoms are not progressive. Therefore, the surgical indication should be prudent if their symptoms are minor. 2) The suprasellar locations of the cysts might be more frequent in children, which require discrimination to the CP. However, other MRI evaluation, including the shape, size, and intensity of the cyst, enable us to diagnose as

RCCs. Therefore, it can be allowed to conclude that the clinical characteristics of RCCs in children are not basically different from those in adults.

Conclusion

In our series, we observed that RCCs are relatively small, have a regular oval shape, are hypointense on T2-WI MRI in 55% of cases, and have no calcification. The postoperative endocrinological status of patients with RCCs is stable and some cases with mild preoperative abnormalities can show improvements after treatment. Although surgical intervention can be performed to relieve the symptoms of these patients without a high rate of complications, the recurrence rate of RCCs seems to be relatively high. Thus, if symptoms are minor, a surgical indication needs to be considered prudently, as the symptoms of these patients may be alleviated without progression.

Conflict of Interest

All authors have no conflict of interests.

List of abbreviation

ACTH; adrenocorticotropic hormone

ADH; anti-diuretic hormone

CP; craniopharyngioma

DDAVP; 1-desamino-8-D-arginine vasopressin

DI; diabetes insipidus

GH; growth hormone

MRI; magnetic resonance imaging

RCC; Rathke cleft cyst

TSH; thyroid stimulating hormone

TSS; transsphenoidal surgery

WI; weighted image

References

1. Cohan P, Foulad A, Esposito F, et al. (2004) Symptomatic Rathke’s cleft cyt: a report of 24 cases. J Endocrinol Invest 27:943-948

2. Voelker JL, Campbell RL, Muller J (1991) Clinical, radiographic, and pathological features of symptomatic Rathke’s cleft cysts. J Neurosurg 74:535-544

3. Fager CA, Carter H (1966) Intrasellar epithelial cysts. J Neurosurg 24:77-81

4. Yoshida J, Kobayashi T, Kageyama N, et al. (1977) Symptomatic Rathke's cleft cyst. Morphological study with light and electron microscopy and tissue culture. J Neurosurg 47:451-458

5. Baskin DS, Wilson CB (1984) Transsphenoidal treatment of non-neoplastic intrasellar cysts. A report of 38 cases. J Neurosurg 60:8-13

6. Steinberg GK, Koenig GH, Golden JB (1982) Symptomatic Rathke’s cleft cyst. Report of two cases. J Neurosurg 56:290-295

7. Zada G (2011) Rathke cleft cysts: a review of clinical and surgical management. Neurosurg Focus 31:E1.

8. Wait SD, Garrett MP, Little AS, et al. (2010) Endocrinopathy, vision, headache, and recurrence after transsphenoidal surgery for Rathke cleft cysts. Neurosurgery 67:837-843

9. Jagannathan J, Dumont AS, Jane JA Jr, et al. (2005) Pediatric sellar tumors: diagnostic procedures and management. Neurosurg Focus 18:E6

10. Monzavi R, Kelly DF, Geffner ME (2004) Rathke's cleft cyst in two girls with precocious puberty. J Pediatr Endocrinol Metab 17:781-785

11. Setian N, Aguiar CH, Galvão JA, et al. (1999) Rathke's cleft cyst as a cause of growth hormone deficiency and micropenis. Childs Nerv Syst 15:271-273

12. Aho CJ, Liu C, Zelman V, et al. (2005) Surgical outcomes in 118 patients with Rathke cleft cysts. J Neurosurg102:189-193

13. Benveniste RJ, King WA, Walsh J, Lee JS, et al. (2004) Surgery for Rathke cleft cysts: technical considerations and outcomes. J Neurosurg 101: 577-584

14. Jahangiri A, Molinaro AM, Tarapore PE, et al. (2011) Rathke cleft cysts in pediatric patients: presentation, surgical management, and postoperative outcomes. Neurosurg Focus 31:E3.

15. Zada G, Ditty B, McNatt SA, et al. (2009) Surgical treatment of Rathke cleft cysts in children. Neurosurgery 64:1132-1137

16. Choi SH, Kwon BJ, Na DG, et al. (2007) Pituitary adenoma, craniopharyngioma, and Rathke cleft cyst involving both intrasellar and suprasellar regions: differentiation using MRI. Clin Radiol 62:453-462

17. Takanashi J, Tada H, Barkovich AJ, et al. (2005) Pituitary cysts in childhood evaluated by MR imaging. AJNR Am J Neuroradiol 26:2144-2147

18. Fan J, Qi S, Peng Y, Zet al. (2014) An isolated primary Rathke's cleft cyst in the cerebellopontine angle. J Neurosurg 121: 846-850

19. Dastoli PA, Nicácio JM, Silva NS, et al. (2011) Cystic craniopharyngioma: intratumoral chemotherapy with alpha interferon. Arq Neuropsiquiatr 69:50-55

20. Saeki N, Hoshi S, Sunada S, et al. (2002) Correlation of high signal intensity of the pituitary stalk in macroadenoma and postoperative diabetes insipidus. Am J Neuroradiol 23:822-827

21. Sato K, Oka H, Utsuki S, et al. (2006) Ciliated craniopharyngioma may arise from Rathke cleft cyst. Clin Neuropathol 25:25-28

22. Ogawa Y, Watanabe M, Tominaga T (2013) Rathke's cleft cysts with significant squamous metaplasia--high risk of postoperative deterioration and close origins to craniopharyngioma. Acta Neurochir (Wien) 155:1069-1075

23. Shin JL, Asa SL, Woodhouse LJ, et al. (1999) Cystic lesions of the pituitary: clinicopathological features distinguishing craniopharyngioma, Rathke's cleft cyst, and arachnoid cyst. J Clin Endocrinol Metab 84:3972-3982

24. Zada G, Lin N, Ojerholm E, Ramkissoon S, et al. (2010) Craniopharyngioma and other cystic epithelial lesions of the sellar region: a review of clinical, imaging, and histopathological relationships. Neurosurg Focus 28:E4

25. Kim JE, Kim JH, Kim OL, et al. (2004) Surgical treatment of symptomatic Rathke cleft cysts: clinical features and results with special attention to recurrence. J Neurosurg 100:33-40

26. Sartoretti-Schefer S, Wichmann W, Aguzzi A, et al. (1997) MR differentiation of adamantinous and squamous-papillary craniopharyngiomas. Am J Neuroradiol 18:77-87

27. Hayashi Y, Tachibana O, Muramatsu N, et al. (1999) Rathke cleft cyst: MR and biomedical analysis of cyst content. J Comput Assist Tomogr 23:34-38

28. Tominaga JY, Higano S, Takahashi S (2003) Characteristics of Rathke's cleft cyst in MR imaging. Magn Reson Med Sci 2:1-8

29. Binning MJ, Liu JK, Gannon J, et al. (2008) Hemorrhagic and nonhemorrhagic Rathke cleft cysts mimicking pituitary apoplexy. J Neurosurg 108:3-8

30. Naylor MF, Scheithauer BW, Forbes GS, et al. (1995) Rathke cleft cyst: CT, MR, and pathology of 23 cases. J Comput Assist Tomogr 19:853-859

31. Ross DA, Norman D, Wilson CB (1992) Radiological characteristics and results of surgical management of Rathke’s cysts in 43 patients. Neurosurgery 30:173-179

Figure Legends

Figure 1.

Representative case of Rathke cleft cyst. A 10-year-old girl suffered from visual field defect. (A) Coronal section of magnetic resonance imaging (MRI) on a T1-weighted image (WI) with contrast enhancement showed a regular oval cystic mass located in the sella region remarkably compressing the optic chiasm. (B) Sagittal section of MRI with T2-WI revealed a hetergenous hypointense signal for the cyst contents.

Figure 2.

Representative case of cystic craniopharyngioma. A 4-year-old boy presented with consciousness disturbance and impaired visual function. (A) Coronal section of MRI on T1-WI with contrast enhancement revealed a huge cystic mass extending from the suprasellar region toward the intra-third ventricle. (B) Sagittal section of MRI with T2-WI revealed a homogenous hyperintense signal for the cyst contents.

Figure 3.

A 12-year-old boy suffered from headaches. (A) Coronal section of MRI on T1-WI with contrast enhancement shows a hyperintense cystic lesion located in the sella region before the first operation (A), after the first recurrence (B), and after the second recurrence (C). (D) The pathological examination of the cyst wall revealed the presence of a Rathke cleft cyst with squamous metaplasia (hematoxylin-eosin staining, x200).

Tables Legends

Table 1.

Summary of the characteristics of the pediatric patients with Rathke cleft cysts

Table 2.

Comparison of the patients with Rathke cleft cysts with patients with cystic craniopharyngiomas

Table 1.

	Sex/Age	Symptom	Size (mm)	MRI	Location	Pre-OP	Post-OP	Surgery	Recurrence	Outcome	follow-up (M)
1.	M/12	HA	20	hyper / hyper	supra	ADH, TSH	ACTH, ADH, TSH	C / C / C	+	Improved	84
2.	F/12	HA	20	hyper / hypo	supra	-	-	C	-	Improved	152
3.	M/12	HA	20	hypo / hyper	supra	GH	(ADH)	C	-	Improved	138
4.	M/10	DI	22	hyper / hypo	sellar-supra	ACTH, ADH	ACTH	T	-	Unchanged	89
5.	M/16	VD	33	hypo / hyper	sellar-supra	GH, TSH	GH, TSH	C	-	Improved	115
6.	M/13	HA	15	hyper / hypo	sellar-supra	ACTH	-	T / T	+	Improved	66
7.	F/10	VD	20	hyper / hypo	sellar-supra	-	(ADH)	T	-	Improved	84
8.	F/12	HA	15	hyper / hypo	sellar-supra	-	*	-	*	Unchanged	60
9.	F/18	HA	13	hypo / hyper	sellar-supra	-	*	-	*	Unchanged	50
10.	M/ 5	HA	12	hyper / hypo	sellar-supra	-	*	-	*	Improved	87
11.	F/14	HA	8	hypo / hyper	supra	-	-	T	-	improved	12

ACTH; adrenocorticotropic hormone, ADH; anti-diuretic hormone, C; craniotomy, DI; diabetes insipidus, EI; endocrinological insufficiencies, GH; growth hormone, HA; headache, hyper; hyperintensity, hypo: hypointensity, M; month, MRI; magnetic resonance imaging, OP; operation, supra; suprasellar region, T; transsphenoidal surgery, TSH; thyroid stimulating hormone, VD; visual function deficiency, *; conservative treatment was done, (ADH); postoperative transient DI due to ADH deficit

Table 2.

Variables			Rathke Cleft Cyst	Craniopharyngioma	p value	
sex	**Male : Female**		6 : 5	8 : 7	0.951	
Age			12.2 ± 3.4	9.3 ± 4.2	0.071	
Symptoms	**HA**		9	2	< 0.001	*
	VD		2	14	< 0.001	*
	EI		4	2	0.168	
MRI findings						
Size		(mm)	19.0 (8-33)	34.9 (21-54)	< 0.001	*
Intensity	**T1**	hyper	7	4	0.058	
		iso	0	3	0.115	
		hypo	4	8	0.391	
	T2	hyper	4	15	0.001	*
		iso	0	0		
		hypo	6	0	0.001	*
Shape		regular	11	5	< 0.001	*
		irregular	0	10		
Locations	**Sellar**		7	6	0.234	
	Suprasellar		4	9		
Calcification			0	15	< 0.001	*
Hydrocephalus			0	5	0.033	*
Hormonal Deficits	**Pre-OP**	number	5	11	0.149	
		ACTH	2	3	0.908	
		GH	2	8	0.069	
		Gonadotropin	0	9	0.002	*
		TSH	2	0	0.086	
		PRL	0	0		
		ADH	2	0	0.086	
	Post-OP	number	3	14	< 0.001	*
		ACTH	2	12	0.020	*
		GH	1	13	< 0.001	*
		Gonadotropin	0	10	< 0.001	*
		TSH	2	11	0.006	*
		PRL	0	5	0.033	*
		ADH	1	9	0.008	*
Surgery	**craniotomy**		4	8	0.391	
	transsphenoidal		4	7	0.599	
Radiation			1	8	0.013	*
Recurrence			2	8	0.184	

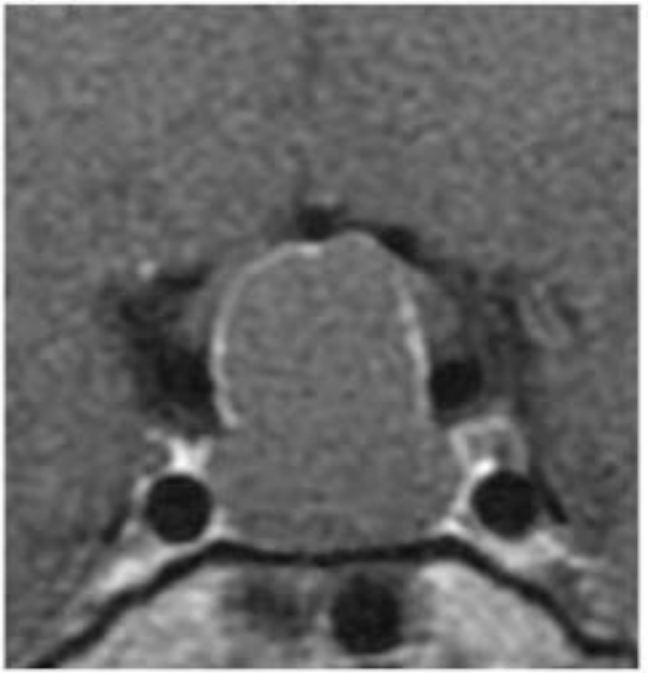
* : P<0.05

ACTH; adrenocorticotropic hormone, ADH; anti-diuretic hormone, DI; diabetes insipidus, EI; endocrinological insufficiencies, GH; growth hormone, HA; headache, hyper; hyperintensity, hypo: hypointensity, MRI; magnetic resonance imaging, OP; operation, supra; suprasellar region, TSH; thyroid stimulating hormone, VD; visual function deficiency

Figure 1

Yasuhiko Hayashi

(A)



(B)

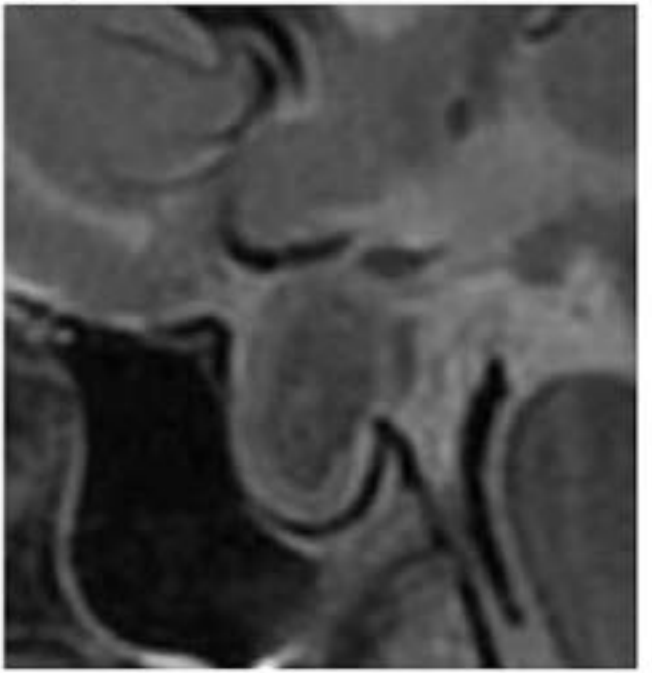


Figure 2

Yasuhiko Hayashi

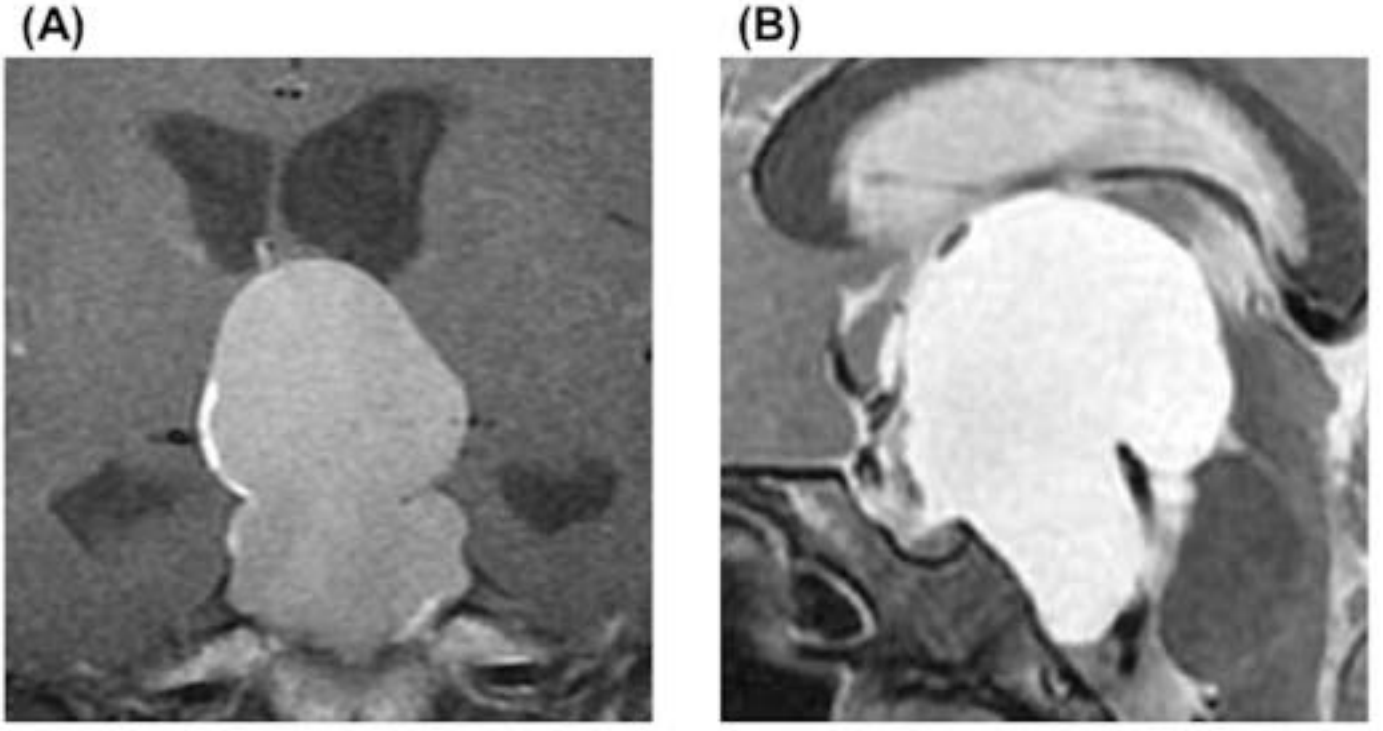


Figure 3

Yasuhiko Hayashi