



Apoplexy of Rathke Cleft Cyst – a Case Report

Apoplexie Rathkeho cysty – kazuistika

Abstract

Symptomatic Rathke cleft cysts (RCCs) are rare sellar and suprasellar lesions, and apoplexy is one of the most unusual presentations. Only a few cases of hemorrhagic apoplexy of an RCC have been reported and their pathogenesis is still poorly understood. In order to present a diagnostic thread to reduce misdiagnosis rate preoperatively, we report a case of RCC apoplexy and review associated published literature. We also summarize clinicopathological relationships between clinical symptoms, imaging features and intraoperative visualization of intracystic content.

Abstrakt

Symptomatické Rathkeho cysty (Rathke Cleft Cysts, RCC) jsou zřídka se vyskytující ložiska selární a supraselární oblasti, přičemž apoplexie je jednou z nejméně obvyklých prezentací těchto cyst. Dosud bylo publikováno pouze několik případů hemoragické apoplexie RCC, přičemž patogeneze stále není objasněna. Za účelem snížení výskytu mylných předoperačních diagnóz popisujeme diagnostický postup u jednoho případu RCC a předkládáme přehled dostupné literatury na toto téma. Rovněž shrnujeme klinickopatologické vztahy mezi klinickými příznaky, výsledky zobrazovacích vyšetření a operačními vizualizacemi obsahu cyst.

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Klíčová slova

Rathkeho cysta – apoplexie – hemoragie

Introduction

Rathke cleft cysts (RCCs), residue of Rathke's pouch during embryogenesis, are sellar or suprasellar congenital cysts. These benign lesions have been described in 22% of normal autopsies [1]. Most of them are asymptomatic. They can be-

come symptomatic when they enlarge enough to compress surrounding structures. RCCs were found in only 2%–9% of patients undergoing transsphenoidal surgery for symptomatic sellar region lesions [2,3]. Rarely, RCCs can present in a manner similar to pituitary apoplexy, with

acute-onset headaches, visual field and acuity loss and oculomotor palsies. We report a case of RCC with acute blurred vision and apoplexy confirmed by surgery and histology. We also reviewed the RCC apoplexy cases reported in the literature and summarize clinical presentation,



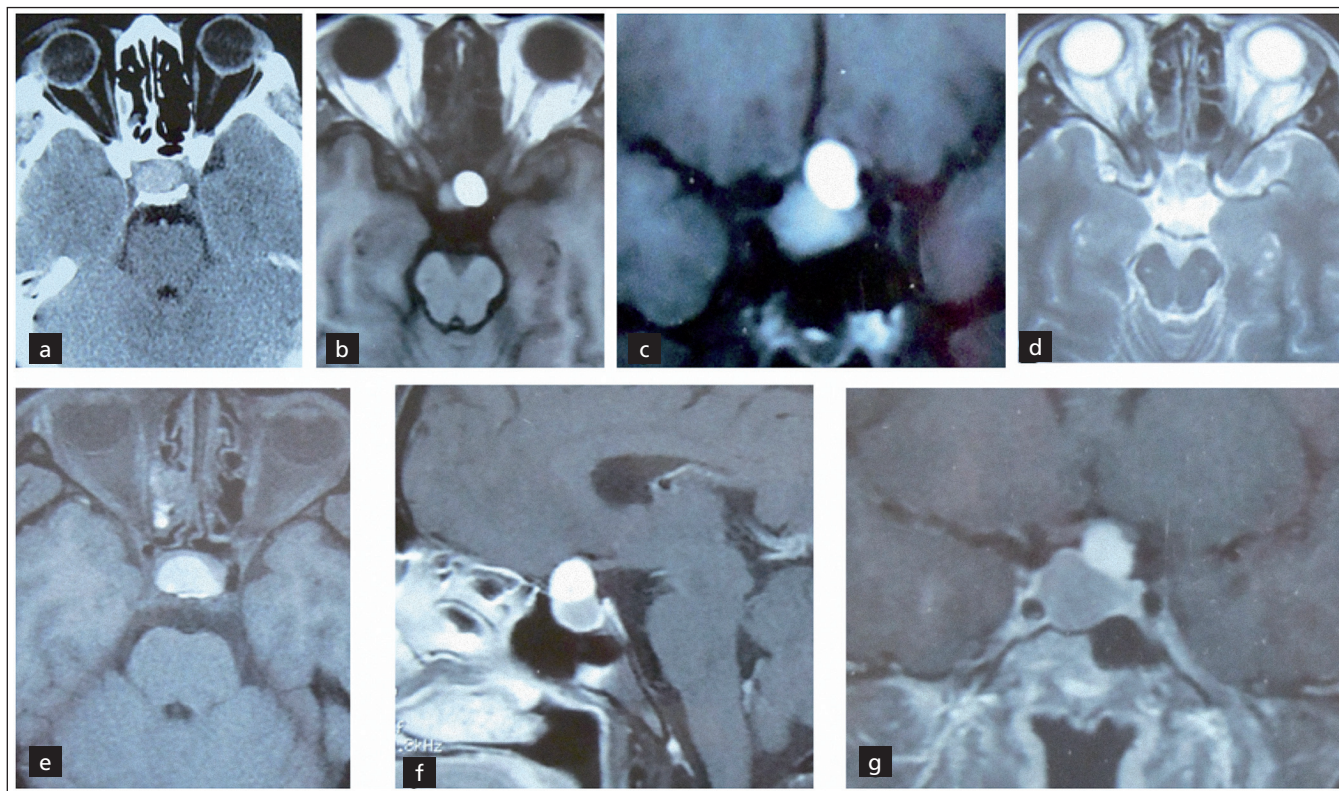


Fig. 1. Radiological work-up of the patient.

CT revealed a slight hyperdense intrasellar lesion (a). MRI T1-weighted axial (b) and coronal (c) images showed the lesion located intra- and suprasellarly with double-cystic shape. Suprasellar cyst was hyperintensity while intrasellar cyst was isointensity. The lesion was isointense on T2-weighted image (d). On FSE image (e), the intrasellar cyst had high signal which suggested lipid-rich content. The normal pituitary gland was compressed anteriorly and became crescent-shaped. After contrast agent injection, enhancement of the lesion was not seen on sagittal (f) and coronal (g) images. There was no nodule on cyst wall. The intrasellar lamina of enhancement was the compressed normal pituitary gland (f).

imaging characteristics and intraoperative findings.

Case report

A 47-year-old female presented with 3 years of mild headache that responded to an oral analgesic. She had irregular menstruation 2 years ago and menostasis without lactation a year ago. She suffered a sudden attack of blurred vision half year ago and aggravating headache a month ago. Her serum PRL was normal. Radiological finding is shown in Fig. 1.

The sudden aggravation of this patient's complaints was considered to be due to expansion of the contents of the pituitary fossa. Apoplexy of pituitary adenoma is the most common cause of sudden enlargement of an intrasellar lesion. However, on T1-weighted images, the signal of suprasellar cyst was too high to correspond to a signal of half-year-old blood. High signal on T1-weighted image could

be due to lipid-rich cystic content, as in Rathke cleft cyst. However, apoplexy of Rathke cleft cyst is extremely rare. Dermoid cysts principally originate at midline location, contain lipid-like fluid and tend to suddenly enlarge or even rupture. All these characteristics were consistent with the characteristics of this case. Therefore, differential diagnosis included, in the first place, dermoid cyst, and also pituitary apoplexy and Rathke cleft cyst.

Since the content of dermoid cysts could cause severe chemical meningitis, we utilized pterional approach that provided better exposure and control of the cyst content than transsphenoidal approach. Intraoperatively, a suprasellar cyst (Fig. 2b) was seen beneath the compressed optic nerve (Fig. 2c). The thin wall of the cyst was punctured and dark red necrotic-haemorrhagic fluid was extracted. After extraction, the cyst collapsed. The cyst wall was cut open and the cyst

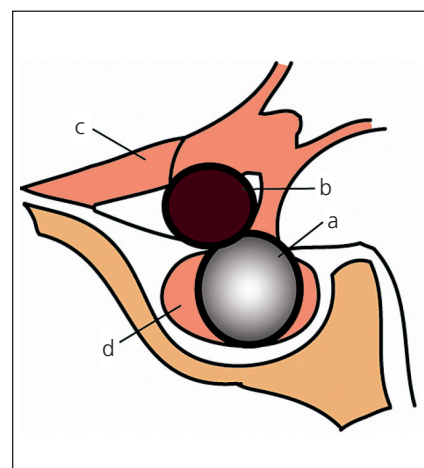


Fig. 2. Schematic diagram of intraoperative finding.

- a) Intrasellar part of the cyst with yellowish mucinous content.
- b) Suprasellar part of the cyst with hemorrhage-like fluid.
- c) Compressed optic nerve.
- d) Compressed anterior pituitary.

was entered (Fig. 2a). Yellowish mucinous content was seen. There was no septum between the “two” cysts. In fact, this was a single cyst with double-lobular shape. No intracystic nodule was found. Histology confirmed the diagnosis of Rathke cleft cyst (Fig. 3).

Review of the published literature

We reviewed the medical literature using PubMed to search for relevant publications on this entity. To review the literature, we used the following search terms: Rathke cyst apoplexy, Rathke cyst hemorrhage, and Rathke cyst. Case reports that documented the clinical presentation and confirmed the presence of bleeding into an RCC were selected (8 cases only) and were included in the analysis (Tab. 1).

Discussion

Clinical presentation

Symptoms of RCC apoplexy are similar with those of pituitary apoplexy but less severe [4]. Such symptoms include increasing headaches, visual changes, cranial nerve palsies, and variable degrees of hypopituitarism. They result from sudden increase in pressure on the pituitary and surrounding structures such as the sellar diaphragm, optic nerve and cavernous sinus. Most of RCC apoplexy patients have normal or slightly abnormal hormone level. Only 2 of 9 cases listed in Tab. 1 had mild endocrine abnormality. Chaiban et al [5] reported 4 cases of endocrine abnormality among 11 cases of RCC apoplexy, with 2 of them recovering immediately after the surgery and one recovering gradually. For the case in this article, we analyzed clinical pathological correlation (Tab. 2) after the diagnosis was confirmed. It would not have been possible to differentiate RCC apoplexy from pituitary apoplexy based on clinical presentation only.

MRI and cyst content

RCCs can be hypo- or hyperdense on CT scan. They are usually iso- or hyperintense on MRI T1-weighted image but a minority of cases may also be hypointense. The MRI signals of RCC on T1-weighted image depend on content components and concentration, especially the concentration of protein, cholesterol and triglycerides [6]. The cyst content appearance

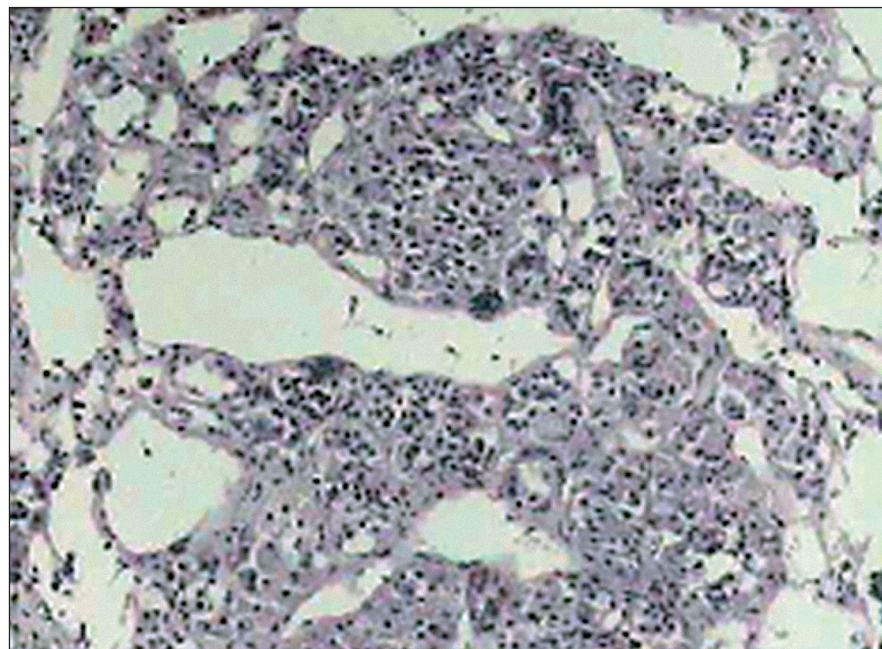


Fig. 3. Hematoxylin and eosin stain of cyst wall showed simple cuboidal cells and eudostratified ciliated columnar cells were orderly arranged.

is variable, including mucinous content, cholesterinic content, cytric oily liquid, similar purulent material, cerebrospinal fluid-like fluid and necrotic-haemorrhagic fluid etc. Among those, similar purulent material is known as concurrent infection, requires antibiotic therapy and predicts high recurrence rate [7]. Billeci et al [8] analyzed MRI signals and intraoperative appearance of RCC but no correlation was found. Similarly, we did not find any regularity on reviewed RCC apoplexy cases (Tab. 1). Therefore, intraoperative appearance of RCC content could not be estimated based on preoperative MRI signals.

MRI signals of RCCs are more complicated after intracystic hemorrhage. There are three types of the cyst according to whether or not the blood and the cyst content mix together within an RCC:

1. homogeneous mixing, cyst maintains homogeneous signal (case 1, 2, 3 and 4 in Tab. 1).
2. heterogeneous mixing, cyst presents mixed signal (case 5, 6 and 7 in Tab. 1).
3. not-mixing cyst has double-lobular shape, blood and content occupy separate lobes (case 9 in Tab. 1).

MRI signals of hemorrhage change regularly with time after hemorrhage [9]. None of the cases reviewed in Tab. 1 had

corresponding MRI signal and hemorrhage time to indicate that regularity of signal change was lost after the blood and the cyst content had mixed together. Interestingly, in the present case, the blood and the cyst content occupied one lobe each but the signal of hemorrhage did not coincide with hemorrhage time. Although MRI showed clear boundary between the two lobes, no septum was found intraoperatively between them. Therefore, we assume that the blood and the cyst content could still partially mix together. Consequently, hemorrhage time of apoplexy RCC could not be judged from MRI signal.

Shape of RCCs

Most of RCCs are elliptical single cysts and remain elliptical after apoplexy. The present case is the only one described as having double-lobular shape (Tab. 1). Russell reported 2 cases of dumbbell RCCs, with intrasellar part of the cyst being covered with simple ciliated columnar epithelium and suprasellar part being covered with squamous epithelium seen usually in craniopharyngioma. This means that these were concurrent RCCs and craniopharyngiomas. Some researchers assume that the RCC is a transitional lesion that precedes craniopharyngioma [10]. However, this theory remains controversial. Re-

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Tab. 1. Summary of clinical presentation, imaging characteristics, intraoperative findings, and outcomes in patients with RCC apoplexy in this article and case reports in the literature.

Case No. Author	Age (yrs) Sex	Sudden symptoms and time§	Shape of cyst	MRI signals			MRI signals fit hemorrhage time, or not✚	Pre-op endocrine finding	Pre-op diagnosis	Content of cyst	Surgical approach	Results
				T1	T2	nodule						
1. Onesti et al [25]	25 F	headache 4 days	single cyst	iso	—	no	—	normal	pituitary adenoma	central necrotic hemorrhage	trans- sphenoidal	normal
2. Kuris- aka et al [26]	8 F	headache several days	single cyst	hyper	hyper	no	—	normal	craniopharyngioma or RCC hemorrhage	hemorrhagic fluid, yellowish mucilage	trans- sphenoidal	normal
3. Nishioka et al [13]	46 F	headache visual field deficit 3 weeks	single cyst	hyper	— the intensity de- creased 3 weeks later	no	no	normal	RCC hemorrhage	blood, mucilage	trans- sphenoidal	normal
4. Pawar et al [27]	19 M	headache blurred vision 1 week	single cyst	hyper	hypo	no	no	normal	—	hemorrhagic fluid, clear mucilage	trans- sphenoidal	normal
5. Rosales et al [28]	34 M	headache diplopia several days	single cyst	mix	mix	no	—	high PRL, low T4, TSH normal	pituitary adenoma apoplexy	blood yellowish fabric content	trans- sphenoidal	normal
6. Binning et al [16]	24 F	headache unclear time	single cyst	mix	mix	yes	—	normal	pituitary adenoma	hemorrhagic fluid mucilage	trans- sphenoidal	normal
7. Binning et al [16]	54 F	headache visual field deficit time unclear	single cyst	mix	mix	yes	—	normal	pituitary adenoma	hemorrhagic fluid mucilage	trans- sphenoidal	normal
8. Raper et al [29]	72 F	headache visual field deficit 2 weeks	—	—	—	yes	—	abnormal ADH	—	thick brown fluid	trans- sphenoidal	diplopia
9. Case repor- ted in this article	47 F	blurred vision half a year, headache 1 month	double cysts'	hyper iso	iso iso	no (suprasellar) (intrasellar)	no	normal	dermoid cyst	suprasel- lar blood, intrasellar mucilage	pterional approach	normal

§ refers to time from appearance of symptoms to MRI examination, ✚ MRI signals variation with time since hemorrhage [9]: 24 hrs, T1 iso, T2 slightly high, 1–3 d, T1 slightly low, T2 very low, > 3 d, T1 very high, T2 very low, > 7 d, T1 very high, T2 very high, > 14 d, T1 iso, T2 slightly high, '—' refers to not mentioned in the literature or the information was not enough to draw a conclusion.

Kim et al [30] reported 4 cases of RCC hemorrhage of 53 cases of RCC. Chaiban et al [5] reviewed 11 cases of RCC apoplexy in their institution over the past 10 years. The above cases were not included in the analysis due to the detailed information was not available.

search into the reasons for intra-RCC hemorrhage is lacking. RCCs constitute of simple or columnar epithelium and this makes them fragile. Oka et al [11] considered small thin-walled vessels in the granulation tissue on the cyst wall to be the source of bleeding. The double-lobular

shape in our case was in accordance with this assumption; since the source of bleeding was located near the inner wall of the cyst, rather than at the center of the cyst, the blood did not mix with the cyst content completely and increased focal pressure on the cyst wall caused external

apophysis, resulting in the observed double-lobe shape.

Preoperative misdiagnosis

Misdiagnosis rate of RCC apoplexy is high. Of all the cases in Tab. 1, only one (case 3) was correctly diagnosed prior to

the surgery. RCC apoplexy is commonly misdiagnosed as pituitary apoplexy or craniopharyngioma. Pituitary adenoma accounted for 90% of patients who underwent sellar MRI and RCCs accounted for 19% of nonadenomatous sellar masses [12]. The great disparity in the incidence was an important reason for misdiagnosis. Moreover, RCCs lack characteristic MRI presentation. They can be iso- or hyper-intensive on T1-weighted image, and the signal on T2-weighted image is also variable due to variable concentration of mucitin and blood [13,14]. Byun et al [15] thought that short T1 and unenhanced nodule on the cyst wall suggested RCC diagnosis but specificity was low. Among the reviewed cases (Tab. 1), intracystic nodules were found in 3 cases only, of which case 6 and 7 were confirmed to have nodules intraoperatively and not preoperatively [16]. In some cases, the compressed normal pituitary gland presents intrasellar ring enhancement on MRI [8], likely to be mistaken for enhanced cyst wall (craniopharyngioma or cystic pituitary adenoma). RCC is preferred diagnosis if a sellar elliptical mass with smooth outline has homogeneous MRI signal without calcification or internal enhancement [17]. However, once there is an RCC apoplexy, the MRI signal is more complicated. Based on the cases reviewed in Tab. 1, when MRI is performed in a patient who has sudden symptoms of apoplexy, the main differential diagnosis includes RCC apoplexy and pituitary apoplexy. If the lesion has a mixed signal, one can hardly be differentiated from the other. If the lesion has homogeneous signal, the differential diagnosis includes RCC apoplexy and cystic pituitary apoplexy. Herein, the case with normal or slightly abnormal hormone levels suggests RCC apoplexy, while the case with hypopituitarism suggests cystic pituitary apoplexy [4]. Ring enhancement cannot be used as an evidence for the diagnosis, as this could be a compressed normal pituitary gland.

Treatment

An asymptomatic RCC should be monitored while a symptomatic RCC requires surgery [18]. RCC apoplexy requires surgery as soon as possible. It is known that transsphenoidal surgery is the best option. However, there is a controversy

Tab. 2. Clinical-pathological correlation of the case reported in this article.

Time	Symptoms	Clinical pathological correlation
3 years ago	slight headache	intrasellar cyst compress sellar diaphragm upward. And nerves on diaphragm were stimulated.
2 years ago	irregular menstruation	pituitary dysfunction
half year ago	sudden blurred vision	apoplexy cyst enlarged suprasellarly, compressed the optic nerve, and caused difficulty focusing.
1 month ago	aggravated headachenausea	long-term difficulty focusing caused aggravated headache and nausea [31]

over the extent of resection. The focus of the controversy is in whether a total resection of the cyst wall and the content should be performed or only a partial resection (or biopsy) of the cyst wall plus cyst content drainage. The former is more aggressive with higher risk and complications but provides lower recurrence rate. The latter is safer, can improve symptoms but recurrence rate is higher. Madhok et al [19] reported 35 cases of RCC with total resection of the cyst by endoscopic transsphenoidal surgery. No complications were seen, only 2 cases recurred and did not require reoperation. Nevertheless, the current mainstream view is that it is sufficient to drain the cyst content and partially resect (or biopsy) the cyst wall. Mayo medical center analyzed 74 RCC cases and concluded that gross total resection was associated with more complications but did not reduce the overall rate of recurrence [20]. Especially for children, cyst content drainage plus cyst wall biopsy is preferable because of safety [21,22]. Transsphenoidal surgery can improve most patients' symptoms and endocrine abnormality [23,24]. All the 8 reviewed cases of RCC apoplexy (Tab. 1) underwent transsphenoidal surgery and their symptoms were relieved, as did the 11 cases of RCC apoplexy reported by Chaiban et al [5].

Conclusion

RCCs apoplexy is a rare condition. Clinical presentation is similar to but milder than that of pituitary apoplexy. It is difficult to differentiate RCC apoplexy from pituitary apoplexy based on MRI image only. Hemorrhage time in RCC apoplexy cannot be judged from an MRI signal. Ring en-

hancement cannot be used as evidence either. RCC apoplexy should be considered if a patient has symptoms of apoplexy, mild endocrine abnormality and sellar mass shows homogeneous signal on MRI. Surgery and histology are required to confirm the diagnosis. Cyst content drainage plus cyst wall partial resection (or biopsy) through transsphenoidal approach is the best option to manage RCC apoplexy.

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