

# **Pituitary Abscess Manifesting as Meningitis and Photophobia Associated With Rathke's Cleft Cyst in a Child**

## **—Case Report—**

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### **Abstract**

**A 12-year-old girl presented with complaints of headache, lethargy, photophobia, and fever. Cerebrospinal fluid examination revealed bacterial meningitis. Magnetic resonance (MR) imaging showed a cystic lesion with peripheral enhancement in the pituitary fossa. The patient underwent transnasal-transsphenoidal surgery (TSS). The diagnosis was pituitary abscess associated with Rathke's cleft cyst. Postoperatively, the patient recovered rapidly. However, recurrence of the pituitary abscess causing meningitis occurred four times and required repeated TSS. She had diabetes insipidus and received hormone replacement. This case requiring repeated emergency surgeries shows that follow-up examinations including MR imaging and pituitary endocrine evaluation are necessary because the rate of recurrence is high in patients with pituitary abscess associated with Rathke's cleft cyst.**

Key words: pituitary abscess, Rathke's cleft cyst, meningitis, photophobia, treatment

### **Introduction**

Pituitary abscess is a rare entity which accounts for less than 1% of all cases of pituitary disease.<sup>9,26)</sup> Pituitary abscess may develop in a normal pituitary gland due to hematogenous seeding or by direct extension of adjacent infection. Other risk factors are underlying immunocompromised condition, previous pituitary surgery, and irradiation of the pituitary gland.<sup>5)</sup> Pituitary abscess occurred in association with preexisting growing lesions in 37% of all reported cases, including pituitary adenoma in 11.4%, Rathke's cleft cyst in 5.4%, and craniopharyngioma in 5%.<sup>4)</sup> Only 19 cases of pituitary abscess associated with Rathke's cleft cyst have been reported. The most common presenting clinical features of pituitary abscess are headache, visual disturbance, and pituitary insufficiency.<sup>26)</sup> Photophobia is a rare symptom of pituitary abscess.

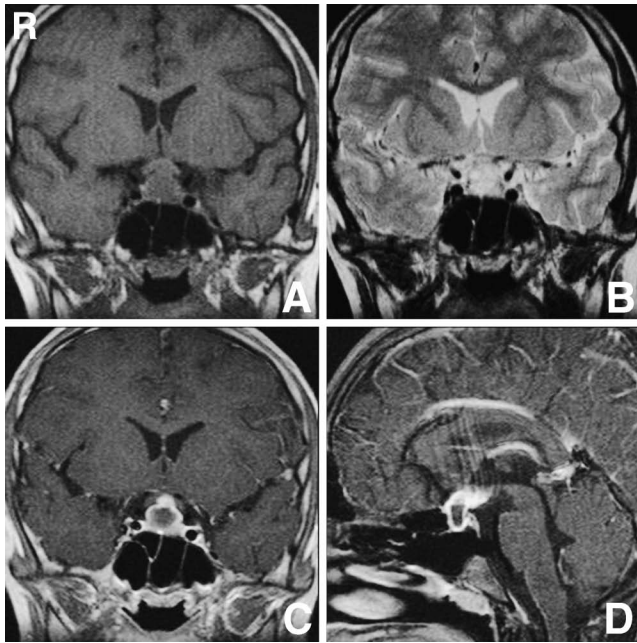
Here we report a case of repeated, recurrent pituitary abscess manifesting as meningitis and photophobia in a child.

### **Case Report**

A 12-year-old girl presented with repeated episodes of fever and headache occurring as frequently as once every month for 3 months. She had been treated with medication under a diagnosis of common cold. She was admitted to a local pediatric hospital complaining of high fever, severe

headache, and general fatigue 1 week prior to transferring to our hospital. Physical examination revealed stiff neck. White blood cell count was 8150 cells/mm<sup>3</sup> and C-reactive protein (CRP) level was 12.8 mg/dl. Cerebrospinal fluid (CSF) examination revealed cell count of 2661 with 63.3% neutrophils, total protein value of 78 mg/dl, and glucose level of 29 mg/dl. Bacterial culture of the CSF was negative. Magnetic resonance (MR) imaging demonstrated a cystic enhanced lesion in the pituitary fossa. She was treated under a diagnosis of bacterial meningitis caused by a pituitary abscess with administration of panipenem/betamipron and cefotaxime. Her symptoms improved but she suffered a relapse and was referred to our hospital for further examinations and treatment.

On admission, the patient had complaints of headache, nausea, lethargy, stiff neck, and photophobia. Her body temperature was 39°C. Neurological examination showed no visual disturbance, such as visual loss or visual defect. White blood cell count was 8340 cells/mm<sup>3</sup> and CRP level was 1.83 mg/dl. CSF examination revealed cell count of 3467 with 84.1% neutrophils, total protein value of 60 mg/dl, and glucose level of 27 mg/dl. Endocrine examinations were all within normal limits: thyroid-stimulating hormone (TSH) 0.58 mIU/ml (normal range 0.2–4.0), follicle-stimulating hormone 1.8 mIU/ml, luteinizing hormone <0.2 mIU/ml, adrenocorticotropic hormone (ACTH) 10.7 pg/ml (7.4–55.7), and arginine vasopressin 2.18 pg/ml (0.3–4.2). Computed tomography showed a low density cystic lesion without calcification in the intrasellar region. No bone erosion was seen at the sella floor. MR imaging revealed a mass lesion measuring 17 × 11 × 9



**Fig. 1** A: Preoperative coronal T<sub>1</sub>-weighted magnetic resonance (MR) image showing an isointense lesion in the pituitary fossa. B: Preoperative coronal T<sub>2</sub>-weighted MR image showing a high intensity lesion in the pituitary fossa. C, D: Preoperative coronal (C) and sagittal (D) T<sub>1</sub>-weighted MR images with contrast medium showing a cystic lesion with ring enhancement.

mm with suprasellar extension into the pituitary fossa (Fig. 1). The lesion was isointense with peripheral enhancement after administration of contrast material on T<sub>1</sub>-weighted images and was hyperintense on T<sub>2</sub>-weighted images. The pituitary stalk appeared to be thickened by enhancement after injection of contrast agent. No sphenoidal sinusitis was observed. The diagnosis was pituitary abscess associated with meningitis.

The patient underwent emergency transnasal-transsphenoidal surgery (TSS). The sella floor was not eroded and the dura was intact. A yellowish-white mucous content exuded after incising the pituitary gland (Fig. 2). The lesion shrank after draining the contents. The cavity was thoroughly irrigated with saline. No definitive capsule or tumor was identified. Postoperatively, her symptoms rapidly improved. Bacterial culture of the content was negative. Histological examination of the specimen showed infiltration by neutrophils and plasma cells. The patient was treated with meropenem and ceftriaxone antibiotics for one month. She received hydrocortisone and 1-desamino-8-arginine vasopressin (DDAVP) for diabetes insipidus (DI).

Twenty-eight days after the surgery, severe headache, high fever, and photophobia suddenly recurred (Fig. 3). MR imaging revealed enlargement of the cystic lesion, suggesting recurrence of the pituitary abscess. Emergency TSS was performed to open and irrigate the cyst. Histological examination of the granulation tissue in the cavity

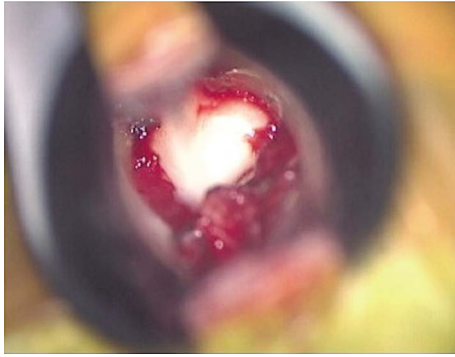
showed infiltration of chronic inflammatory cells, neutrophils, lymphocytes, or plasma cells, and revealed epithelial cells with immunocytochemistry for cytokeratin (Fig. 4). The histological diagnosis was pituitary abscess associated with Rathke's cleft cyst. Postoperatively, she recovered rapidly. Thirty-five days later, the patient suddenly presented with headache, nausea, and photophobia. Emergency TSS was carried out. The pituitary gland was re-explored and the cyst was decompressed. A drainage tube was placed in the cyst cavity for 3 days. Twenty-one days after the third surgery, the patient's symptoms recurred again. TSS was performed and alcohol fixation of the cavity was done. Twenty-eight days later, the symptoms repeated again. The patient underwent emergent TSS with wide opening and irrigation of the cavity.

Detailed evaluations were conducted for systemic disease that can cause pituitary cystic lesion, such as tuberculosis or Wegener's granulomatosis. Furthermore, the neutrophil and bone marrow functions were examined to determine whether the patient was in an immunocompromised condition. No conditions were detected that could have accounted for the high rate of symptom recurrence.

Ten months after the fifth surgery, the patient was symptom-free without recurrence except for pituitary dysfunction. Serial MR imaging showed gradual decrease in size and finally disappearance of the lesion. Hormonal examination also showed low ACTH and TSH levels. Hydrocortisone and L-thyroxine replacement were continued postoperatively and intranasal DDAVP was given for DI. Her hormone levels gradually improved and she did not develop panhypopituitarism during follow up.

## Discussion

Nineteen cases of pituitary abscess associated with Rathke's cleft cyst have been reported as summarized in Table 1.<sup>2,3,7-9,12-14,16,17,19,21-24,26</sup> Twelve patients were female, seven were male, and the mean age of these patients was 44.1 years (range 12-69 years). Three were pediatric cases. The most common presenting clinical feature was visual disturbance in 13 of the 19 cases including either visual defects or visual impairment. Meningitis was diagnosed in 4 cases. Only one patient had photophobia and visual disturbance. In the present case, the presenting symptoms at each episode included photophobia without visual disturbance. We observed that direct compression to the optic nerve was slight on MR imaging and visual function was intact. However, inflammation extending to the optic nerve may have caused photophobia. Endocrine dysfunction was observed in 9 of the 19 patients. Three had panhypopituitarism, 4 had DI, and 3 had hyperprolactinemia at the initial presentation. DI and hyperprolactinemia were caused by a stalk effect and not by direct destruction of pituitary tissue. Preoperative endocrine dysfunction might have recovered in the normal postoperative course. In particular, preoperative DI could improve. However, panhypopituitarism is less likely to recover and hormone replacement therapy would be needed. In our case, we performed minimally-invasive surgery to

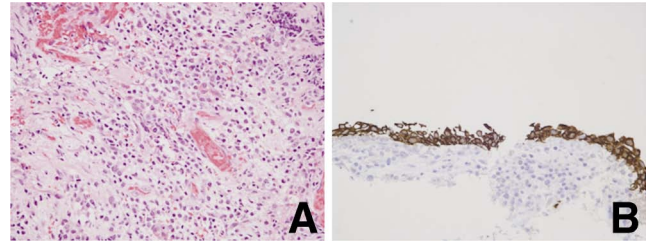


**Fig. 2** Intraoperative photograph showing yellowish-white mucous content exuding after incising the pituitary gland and the cavity.

preserve the pituitary function because the patient was in a growth phase. The patient was treated with administration of hydrocortisone and L-thyroxine for anterior hypopituitarism and intranasal DDAVP for DI. Pituitary function fully recovered after hormone replacement therapy for one year in a previous pediatric case.<sup>18)</sup>

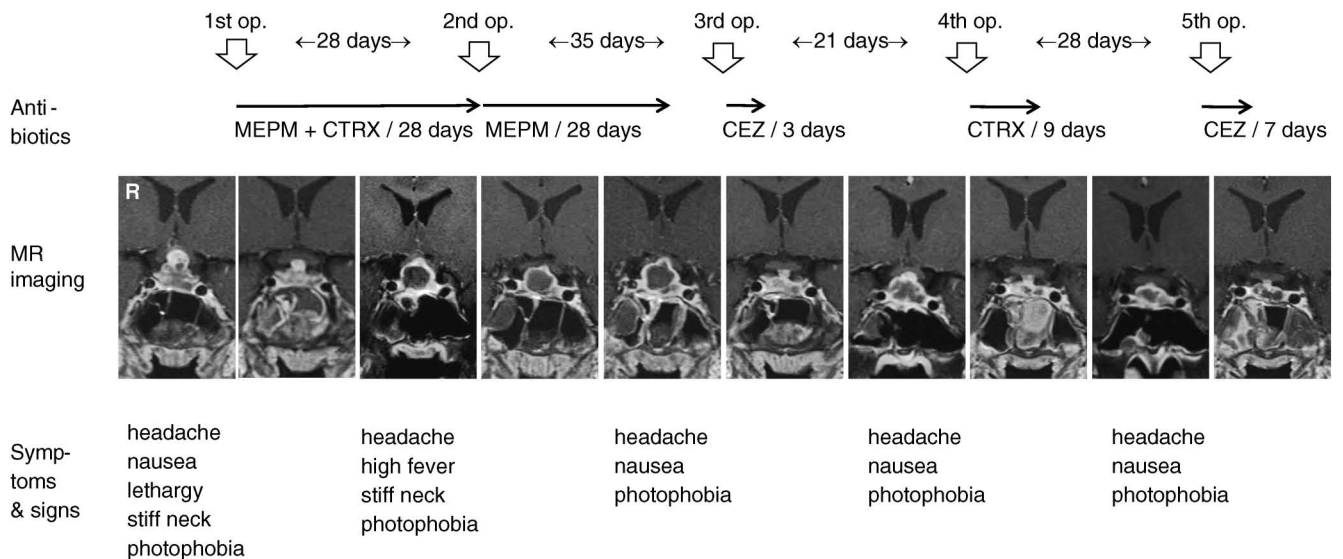
The neuroimaging differential diagnosis of intrasellar cystic lesions include adenoma, craniopharyngioma, Rathke's cleft cyst, pituitary abscess, and carcinoma.<sup>5)</sup> MR imaging shows pituitary abscess as a cystic lesion with central low intensity and rim enhancement after administration of contrast medium. However, the neuroimaging findings are not specific for the Rathke's cleft cyst abscess and therefore preoperative differential diagnosis remains difficult.

The most recommended management for pituitary



**Fig. 4** Photomicrographs of the granulation tissue in the cavity showing infiltration of chronic inflammatory cells, neutrophils, lymphocytes, or plasma cells (A: Hematoxylin and eosin stain,  $\times 100$ ), and immunocytochemistry positive for cytokeratin indicating epithelial cells (B:  $\times 100$ ).

abscess is transsphenoidal drainage and antibiotic therapy.<sup>26)</sup> The transcranial approach may involve the risk of intracranial dissemination of infection. Opening of the sphenoid sinus or insertion of a pituitary-nasal drain might be helpful for intractable cases.<sup>6,12,19,20)</sup> We attempted the insertion of a drainage tube and alcohol fixation. In addition, antibiotic administration was continued for 2 months. However, symptoms recurred four times despite postoperative antibiotic therapy. No organisms were isolated from the pus culture. Six previous cases were identified with bacterial organisms. The most common pathogens of pituitary abscess are considered to be aerobic bacteria such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Two reported cases were successfully treated using only antibiotic therapy without surgery.<sup>10,25)</sup> One case was successfully treated with hormone replacement therapy.<sup>15)</sup> The selection of the appropriate antibiotics was difficult because bacterial cultures were negative in most cases.



**Fig. 3** Clinical course showing the intervals between surgeries, antibiotics and duration of administration, magnetic resonance (MR) imaging findings before and after surgeries, and signs and symptoms at onset or recurrence. CEZ: cephazolin, CTRX: ceftriaxone, MEPM: meropenem, op.: operation.

**Table 1 Summary of 19 reported cases of pituitary abscess associated with Rathke's cleft cyst**

Case No.	Author (Year)	Age (yrs)/ Sex	Initial symptoms	Surgery	Gram stain/cultures	Hormone replacement therapy	Recurrence (interval)
1	Obenchain and Becker (1972) <sup>16)</sup>	50/F	HA, VD, fever	1st TC 2nd TC	<i>Staphylococcus epidermidis</i>	ACTH, TSH	yes (4 wks)
2	Steinberg et al. (1982) <sup>22)</sup>	47/M	HA, VD, meningitis	autopsy	—	no	no
3		41/M	HA, VD	TC			
4	Sonntag et al. (1983) <sup>21)</sup>	39/M	HA, VD, nausea, lethargy, photophobia	1st TS 2nd TC	negative	no	yes (4 wks)
5	Nakashima et al. (1983) <sup>14)</sup>	60/M	HA, fever, thirst, polyuria	TS	—	ACTH, TSH, DI	no
6	Bognàr et al. (1992) <sup>2)</sup>	33/F	VD, DI, amenorrhea	1st TS 2nd TC	<i>Staphylococcus aureus</i> <i>Streptococcus pyogenes</i>	—	yes (2 wks)
7		53/F	DI	TS	negative	no	no
8	Kimura et al. (1994) <sup>12)</sup>	66/F	HA, meningitis	TS	negative	no	no
9	Sato et al. (1995) <sup>19)</sup>	67/M	lethargy, DI, meningitis	TS	negative	ACTH, DI	no
10	Jain et al. (1997) <sup>9)</sup>	42/M	VD	1st TC 2nd TC	negative	no	yes (8 yrs)
11	Ono et al. (1997) <sup>17)</sup>	14/F	VD	TS	negative	panhypo.	no
12	Thomas et al. (1998) <sup>24)</sup>	29/F	VD, galactorrhea, amenorrhea	TS	anaerobic streptococci	—	no
13	Israel et al. (2000) <sup>8)</sup>	13/F	VD	1st TC	<i>Acinetobacter lwoffii</i>	DI	yes (5 mos)
14	Vates et al. (2001) <sup>26)</sup>	66/F	HA	TS	negative	no	no
15	Celikoglu et al. (2006) <sup>3)</sup>	48/F	VD	TS	negative	—	no
16		37/F	VD, galactorrhea, amenorrhea	1st TS 2nd TS	negative	no	yes (9 mos)
17	Dutta et al. (2006) <sup>7)</sup>	12/F	VD, HA, fever	1st TC 2nd TC	<i>Acinetobacter</i> <i>Staphylococcus</i> species	no	yes (1 yr)
18	Takayasu et al. (2006) <sup>23)</sup>	69/M	VD, fever	TS	<i>Pseudomonas aeruginosa</i>	—	no
19	Koutourousiou et al. (2009) <sup>13)</sup>	52/F	HA, meningitis	TS	<i>Enterococcus faecium</i>	no	no

ACTH: adrenocorticotropic hormone, DI: diabetes insipidus, F: female, HA: headache, M: male, panhypo.: panhypopituitarism, TC: craniotomy, TS: transsphenoidal surgery, TSH: thyroid-stimulating hormone, VD: visual disturbance.

Seven of the 19 patients suffered recurrence of symptoms, with two recurrences in all 7 patients. The period to recurrence was 2 weeks to 8 years. Squamous metaplasia in the cyst wall increases the risk of relapse in patients with Rathke's cleft cyst.<sup>11)</sup> Squamous metaplasia is caused by inflammation which may result in encapsulation of the cyst, facilitating the reaccumulation of cyst fluid within the sella.<sup>1)</sup> In cases of pituitary abscess associated with Rathke's cleft cyst, recurrence may occur by the same mechanism.

In our case, no definitive abscess within the cavity was confirmed after intraoperative irrigation. Our case recurred four times in a little more than one-month period despite standard treatment with TSS and antibiotic therapy. Aggressive treatment including removal of the normal pituitary gland or radiotherapy was not performed to avoid complications such as severe panhypopituitarism or delayed radiation-induced complications in such a young patient. The antibiotics were possibly not effective for the pituitary abscess because bacterial and fungal cultures were negative during the clinical course. Furthermore, although detailed evaluations were negative, repeated recurrence of the abscess might be related to hypopituitarism or immunocompromised condition. The symptoms suddenly relapsed and emergency operations

were needed every time. However, the patient has remained free of symptoms except for pituitary dysfunction, which gradually improved during the clinical course.

Appropriate antibiotic therapy and hormone replacement therapy are necessary as well as TSS for the treatment of pituitary abscess. Careful follow-up examinations including MR imaging and pituitary endocrine evaluation are necessary because the rate of recurrence is high in patients with pituitary abscess associated with Rathke's cleft cyst.

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