Clinical Case Report

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Secondary pituitary abscess following transsphenoidal surgery with recurrent meningitis

A case report

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Abstract

Rationale: The transsphenoidal surgical (TS) approach to sellar masses is the preferred surgical route in most cases. Secondary pituitary abscess (PA) following TS is an extremely rare but serious postoperative complication with potentially high disability and mortality.

Patient concerns: We describe an uncommon case of secondary PA in a 42-year-old woman, who underwent uncomplicated transsphenoidal procedures without cerebrospinal fluid leak, to treat primary Rathke cleft cyst. Without obvious cause, the patient suffered recurrent meningitis with complaints of headache, hyperpyrexia, and chills from 1 month after the operation.

Diagnosis: There were no significant imaging findings until a new rim-enhancement lesion was seen in the sellar region on magnetic resonance imaging during the 6th episode of meningitis 11 months after the initial surgery. A diagnosis of secondary PA was considered;

Interventions: Therefore, she underwent a 2nd TS with pus evacuation and antibiotic treatment.

Outcomes: She improved remarkably and had no recurrence of symptoms during the 9-month follow-up.

Lessons: Our aim was to present this rare case and discuss the most likely etiologies and preventive measures for this condition. In patients with recurrent meningitis but dormant imaging manifestations after TS, the possibility of secondary PA should considered. Adequate surgical drainage with microbiology-guided antibiotic therapy is the 1st choice for treatment.

Abbreviations: ACTH = adrenocorticotropic hormone, CSF = cerebrospinal fluid, E2 = estradiol, F = serum cortisol, FSH = follicle-stimulating hormone, FT3 = free triiodothyronine, FT4 = free thyroxine, LH = luteinizing hormone, MRI = magnetic resonance imaging, PA = pituitary abscess, T1WI = T1 weighted imaging, T2WI = T2 weighted imaging, TS = transsphenoidal surgery, TSH = thyroid-stimulating hormone.

Keywords: dormant imaging manifestation, Rathke cleft cyst, recurrent meningitis, secondary pituitary abscess, transsphenoidal surgery

1. Introduction

Transsphenoidal surgery (TS) to treat sellar and suprasellar lesions has evolved over the last 100 years. With developments and advancements in surgical techniques, it is widely recognized that TS is an effective and safe therapeutic option in patients with pituitary tumors.[1] Although TS is recommended as the primary therapy for these tumors because of the lower blood loss, minimal operative trauma, and shorter postoperative recovery time,[2] TS may lead to several surgical complications including intracranial hemorrhages, cerebrospinal fluid (CSF) rhinorrhea, cranial nerve palsy, and anterior pituitary deficiency.[3–5]

Secondary pituitary abscess (PA) following TS is a rare but potentially life-threatening complication, and sellar anatomical disruption by previous pituitary surgery is the most common risk factor for its development.[6,7] However, literature on secondary PA following TS is largely limited to case reports or small case series because of the rarity and a lack of knowledge of the disease.[8–11] The rarity of secondary PA following TS, lack of radiographic features, and ambiguous clinical signs often lead to misdiagnosis, preoperatively.

We present a 42-year-old woman who suffered secondary PA following TS. Uniquely, the patient presented with recurrent typical symptoms of meningitis 1 month after the initial TS for Rathke cleft cyst but without imaging evidence. To the best of our knowledge, this is the 1st reported case of secondary PA presenting with unusual clinical and imaging features. To clarify the most likely etiologies, clinical signs, radiologic features, and treatment of this rare disease, we also reviewed the related literature.

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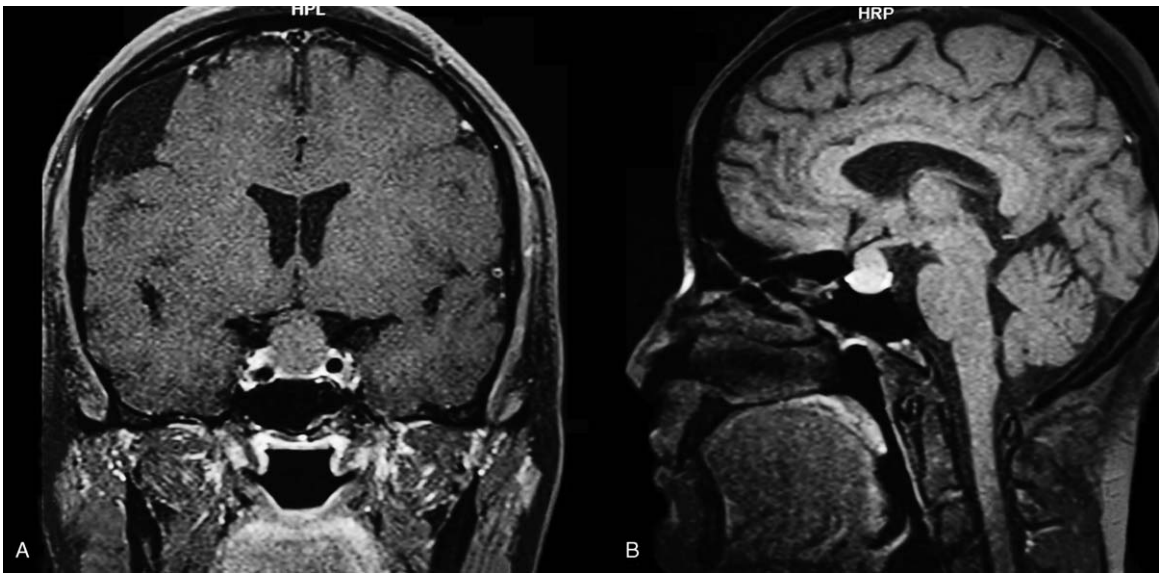

Figure 1. Preoperative magnetic resonance imaging features of primary Rathke's cleft cyst before initial transsphenoidal surgery on March 2016. An oval cystic mass was seen in the sellar region (size: 11.1 mm × 17.8 mm × 15.8 mm), which displayed inhomogeneous enhancement on coronal (A) and sagittal (B) T1-weighted post-gadolinium images.

2. Case report

2.1. History and initial operation

A 42-year-old woman presented to PUMCH with complaints of headache and dizziness for more than 1 year. Endocrine function and visual field examinations were normal. Magnetic resonance imaging (MRI) revealed an 11.1 mm × 17.8 mm × 15.8 mm cystic mass within the sella (Fig. 1). She underwent endoscopic TS excision of the sellar mass in March 2016 without operation-related complications and with no intraoperative CSF leak, in particular. The patient's initial recovery was uneventful, and her symptoms improved. The postoperative histopathologic examination diagnosis was Rathke cleft cyst.

2.2. Recurrent meningitis

One month after surgery, the patient was admitted to a local hospital complaining of throbbing headache, dizziness, high fever with chills, and nonprojectile vomiting. On physical examination, she had neck rigidity. CSF examination revealed an increased protein level of 3.7 g/L, low glucose level of 1.5 mmol/L, and high white blood cell count of $12{,}000 \times 10^6$/L with neutrophilic pleocytosis (>90%). The possibility of acute bacterial meningitis was considered, and she was treated with intravenous antibiotics (3rd-generation cephalosporin). During follow-up, the patient presented with recurrent meningitis 5 times from April 2016 to December 2016 with no radiologic evidence (Fig. 2), and no pituitary endocrinal dysfunction. Her symptoms resolved after 7 to 14 days of empirical intravenous antibiotic

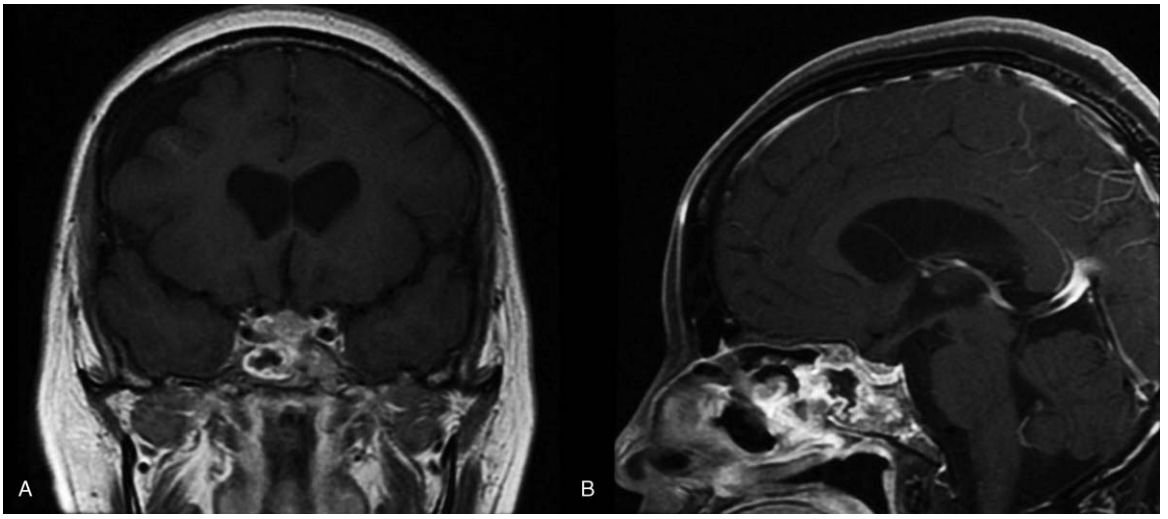

Figure 2. Magnetic resonance imaging (MRI) features of the pituitary 9 months after the initial transsphenoidal surgery. MRI was performed when the patient presented with typical signs and symptoms of recurrent meningitis on December 2016. Postgadolinium coronal (A) and sagittal (B) MRI showed regular changes in the sellar region postoperatively without clinically significant radiographic findings.

each episode, but Gram stain and CSF culture were non-confirmatory.

2.3. Clinical presentation and examination

At the beginning of February 2017, 11 months after initial TS, she was again admitted to PUMCH with complaints of severe headache, hyperpyrexia, and a maximum body temperature >40°C. She was hospitalized for progression of symptoms including left eye blurred vision and generalized body fatigue. Visual field assessment revealed a left temporal hemianopic field defect. Elevated infection indicators on blood biochemical examinations and CSF testing confirmed the diagnosis of bacterial meningitis. A diagnosis of hypopituitarism, including hypogonadotropism, hypothyroidism, and hypocortisolism, was made based on clinical presentation and endocrine laboratory values. MRI of the pituitary gland demonstrated a new emerging sellar mass measuring 15.9 mm × 14.2 mm × 18.0 mm. The lesion compressed the optic chiasm with isointense signals on T1-weighted imaging and was slightly hyperintense on T2-weighted imaging. Following intravenous administration of gadolinium contrast material, the sellar mass demonstrated obvious rim enhancement (Fig. 3).

2.4. Interventions

Based on the patient's complaints, clinical signs, and radiologic characteristics, a diagnosis of secondary PA with recurrent meningitis was considered, and she was treated with empirical intravenous antibiotics preoperatively (ceftazidime, 2 g, q12 hours). Hormone replacement with hydrocortisone (20 mg, bid) and levothyroxine (100 μg, qd) were also required. After 10 days of antibiotic therapy, the infection was controlled, and her symptoms had improved. She then underwent a 2nd TS. Intraoperatively, we resected scar and necrotic tissue in the sphenoid sinus. Creamy, yellowish, purulent fluid flowed from the pituitary fossa when the sellar floor dura were opened. Specimens of the necrotic tissue, pus, and the wall of the abscess were obtained for culture and pathologic examination. No CSF leakage was seen during surgery.

2.5. Postoperative course

Postoperatively, the patient received ceftazidime (2 g, q12 hours) for 2 weeks intravenously followed by oral antibiotics (3rd-generation cephalosporin) for an additional 2 weeks. She was afebrile and her visual field defect resolved fully, furthermore, hormone replacement therapy was adjusted based on the results of endocrine evaluation. Histopathologic examination confirmed an abscess capsule, necrosis, and granulation tissue with acute or chronic inflammation containing numerous polymorphonuclear leukocytes and macrophages, which was compatible with a diagnosis of PA. However, bacterial, anaerobic, and mycobacterial cultures were negative.

The patient's postoperative course was unremarkable and close follow-up was performed at 3 and 6 months after the 2nd TS. Her improved symptoms included a healthy mental state, and good appetite and physical strength. Follow-up MRI showed complete resection of the secondary PA without recurrence (Fig. 4). Pituitary function also recovered except for the need for a low dose of levothyroxine (50 μg, qd) and prednisone (2.5 mg, qd) as replacement therapy. Changes in the patient's pituitary function over the course of the disease are shown in Table 1.

Informed consent has been obtained from the patient for the purpose of publication.

3. Discussion

The PA is a rare but serious intrasellar infection associated with high disability and mortality.[12] The overall incidence of PA is 0.4% to 1.1% in operative pituitary lesions.[6,13] PAs are described as either a primary or secondary abscess according to their etiology.[14] Most PAs are idiopathic and occur in a previously healthy gland, whereas PAs in approximately one-third of patients are associated with preexisting pathologic lesions, such as craniopharyngioma, Rathke cleft cyst, or

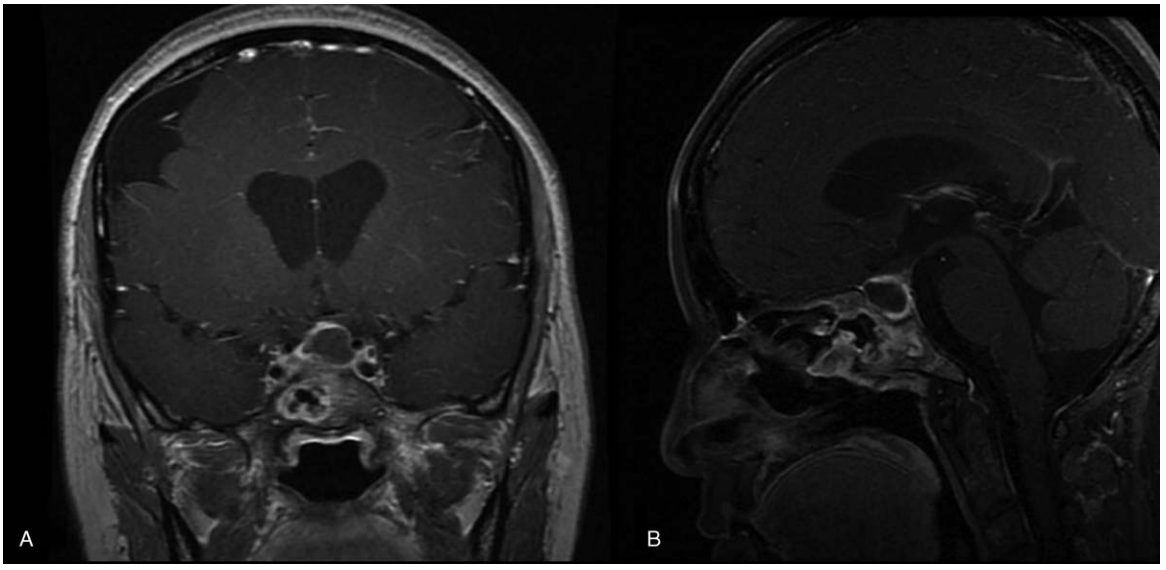

Figure 3. Typical magnetic resonance imaging (MRI) features of secondary pituitary abscess 11 months after the initial transsphenoidal surgery (February 2017). A new emerging mass (size: 15.9 mm × 14.2 mm × 18.0 mm) filled the sella turcica with typical rim enhancement after gadolinium injection in coronal (A) and sagittal (B) views on enhanced MRI.

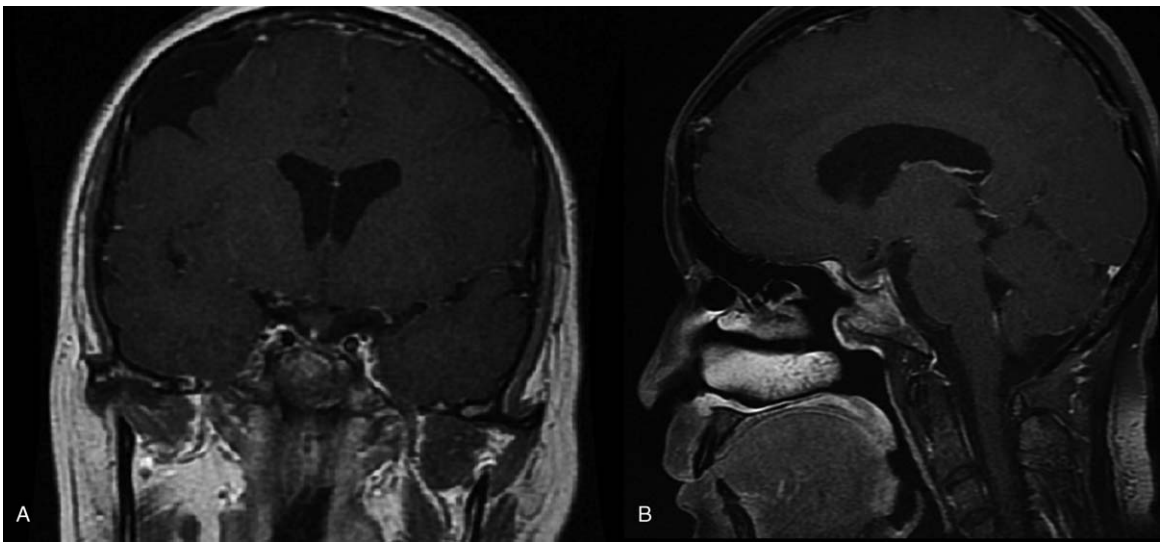

Figure 4. Postoperative magnetic resonance imaging (MRI) at the 7 months' follow-up on September 2017 following transsphenoidal debridement surgery. Postoperative coronal (A) and sagittal (B) views of the dense-enhancement image showed resolution of the abscess and no recurrence or residual pituitary abscess.

pituitary adenoma.[15,16] Reports of secondary PA following TS are even rarer because of challenges in accurate preoperative diagnosis.[17] However, with TS as the mainstay of surgical treatment for pituitary tumors, secondary PA is a rare but severe complication. Therefore, in this study, we clarified the typical clinical signs, most likely etiologies, possible preventive measures, and recommended therapies for secondary PA following TS by presenting a rare case report and summarizing a comprehensive literature review.

The clinical signs of secondary PA are nonspecific. Retrospective case series report that the most common presenting complaints were headache (69.7–91.7%), anterior pituitary hypofunction (54.2–81.8%), diabetes insipidus (41.4–69.7%), and visual disturbance (25–50.0%).[7–9] Although secondary PAs are described as a type of infectious disease, inflammatory manifestations such as fever or leukocytosis occur in less than one-third of patients, and the incidence of meningitis is <25%.[6,18] Earlier studies suggested that leakage of irritant contents from the abscess into the CSF space led to recurrent episodes of meningitis.[19,20] However, our patient suffered recurrent meningitis with dormant imaging manifestations early after the 1st TS. Therefore, based on our patient's characteristics, we attribute the pathogenesis of secondary PA to three factors: bacterial colonization of the sphenoid sinus, reduced local immunity in the sellar region, and reduced systemic immunity. In most cases, secondary PA shows no signs of infection because bacterial virulence is insufficient or bacterial spread is inhibited by local and systemic immunity. Also, secondary PA can develop rapidly with strong bacterial virulence and severe immunosuppression. In our patient, there was a balance between bacterial invasion and immunoresistance early after the initial TS, which resulted in the recurrent bacterial meningitis but not abscess development in the sellar area. With weakened immunity from the repeated meningitis, secondary PA occurred when the balance shifted.

Although no definitive etiology has been described from present literatures, proposed mechanisms for secondary PA after TS include either hematogenous seeding or direct extension from an adjacent infected tissue, such as from sphenoid sinusitis.[21–23] Our patient demonstrated serious inflammation in granulation and necrotic tissue of the sphenoid sinus during the 2nd endoscopic TS and subsequent histopathologic examination. Sphenoid sinusitis was probably related to the sphenoidotomy size, postoperative nasal care, and reaction to foreign bodies.[22,24] Given this, we speculate that disruption of the normal structures including the sphenoidal sinus and the sellar floor

Table 1

Pituitary endocrine function testing before surgery and during follow-up.

Endocrine test	Reference range	Before initial TS (2016/03)	Recurrent meningitis (2016/12)	Secondary PA after TS (2017/02)	Follow-up after second TS (2017/09)
TSH, μIU/mL	0.38–4.34	1.757	2.435	0.093	0.042
FT3, pg/mL	1.80–4.10	2.37	2.69	2.05	3.19
FT4, ng/dL	0.81–1.89	1.114	1.000	0.476	0.740
F, μg/dL	4.0–22.3	15.57	9.79	<0.50	<0.50
ACTH, pg/mL	0–46	34.9	25.3	<5.00	<5.00
FSH, IU/L	–	7.48	10.01	5.25	4.48
LH, IU/L	–	6.24	12.02	0.99	1.78
E2, pg/mL	–	83.00	87.00	<5.00	<5.00

ACTH = adrenocorticotropic hormone, E2 = estradiol, F = serum cortisol, FSH = follicle-stimulating hormone, FT3 = free triiodothyronine, FT4 = free thyroxine, LH = luteinizing hormone, MRI = magnetic resonance imaging, PA = pituitary abscess, TS = transsphenoidal surgery, TSH = thyroid-stimulating hormone.

combined with foreign bodies, such as wadding materials from the initial TS for Rathke cleft cyst may have facilitated the development of local necrosis and the spread of microbial infection in our patient.[25] Sphenoid sinusitis results in rare but serious complications such as secondary PA via retrograde infection.[26,27]

Immunocompromise is a reported major cause of secondary PA.[6,8] In our patient, 2 major factors may explain decreased immune function in the sellar region. First, the size of the Rathke cleft cyst was large (11.1 mm × 17.8 mm × 15.8 mm) at the initial diagnosis, and resulted in compression of normal pituitary tissue and inhibition of pituitary immune function.[14,28] Second, Rathke cleft cysts originate from epithelial cells of the developing Rathke pouch. After the 1st TS, the residual cyst wall and mucous material encapsulated in Rathke pouch contributed significantly to the nidus for infection, which is a possible cause of recurrent meningitis.[29,30] Also, surgical intervention may have increased our patient's vulnerability to infection because of impaired vascularization and attenuation of resistance.

Considering our proposed etiology, the following procedures may help prevent secondary PA following TS: First, it is critical to thoroughly disinfect the nasal cavity and sphenoid sinus using iodophors and hydrogen peroxide during the initial TS. Second, minimizing unnecessary artificial wadding materials implanted in the sphenoid sinus and protecting the sphenoid sinus mucosa as much as possible during the 1st TS may prevent a nidus of infection and improve local immunity by protecting the mucosa. Finally, it is essential to enhance systemic immunity with good nutrition and therapy for chronic diseases. Bacterial culture of the nasal cavity is also recommended to guide prophylactic antibiotic administration, because empirical antibiotics may not be sensitive to colonized bacteria.

These recommendations will help minimize the incidence of secondary PA after TS. However, once secondary PA develops, surgical drainage via a transsphenoidal approach is the optimal treatment to prevent further spread of the infection and vision compromise.[15] Any foreign body or devascularized tissue should be removed during surgical exploration.[11] In our patient, once the imaging findings of secondary PA appeared, the 2nd TS was performed quickly to achieve satisfactory prognosis including full recovery of her visual field and improved pituitary function. Antibiotic therapy should be started as soon as PA is suspected, and broad-spectrum antibiotic therapy can be used until specific organisms are identified in cultures.

4. Conclusion

Secondary PA following TS is a rare disease of unknown etiology and a serious threat for complications following TS. Because of its rarity, similar clinical presentations, and imaging features, secondary PA is difficult to diagnose preoperatively and is often misdiagnosed as recurrence or residual primary pituitary lesions. Therefore, based on the findings in our patient, prior pituitary surgery, signs of meningeal inflammation, and increased infectious indicators are significant clues for a diagnosis of secondary PA even with negative early radiographic findings. Heightened suspicion should also arise with new radiographic changes compared with previous postoperative MRIs, especially with rim enhancement of the lesion. Timely and efficient surgical drainage, especially by the transsphenoidal approach, combined with prolonged microbiology-guided antibiotic management results in lower mortality and a higher recovery of pituitary hormone function and the visual field.

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Writing – review & editing: Xinjie Bao, Ming Feng, Renzhi Wang.

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