

# Recurrent pituitary abscess: case report and review of the literature

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## Summary

A 26-year-old woman presented with severe postpartum headaches. Magnetic resonance imaging (MRI) revealed a symmetric, heterogeneous enlargement of the pituitary gland. Three months later, she developed central diabetes insipidus. A diagnosis of postpartum hypophysitis was suspected and corticosteroids were prescribed. Six months later, the pituitary mass showed further enlargement and characteristics of a necrotic abscess with a peripheral shell and infiltration of the hypothalamus. Transsphenoidal surgery was performed, disclosing a pus-filled cavity which was drained. No bacterial growth was observed, except a single positive blood culture for *Staphylococcus aureus*, considered at that time as a potential contaminant. A short antibiotic course was, however, administered together with hormonal substitution for panhypopituitarism. Four months after her discharge, severe headaches recurred. Pituitary MRI was suggestive of a persistent inflammatory mass of the sellar region. She underwent a new transsphenoidal resection of a residual abscess. At that time, the sellar aspiration fluid was positive for *Staphylococcus aureus* and she was treated with antibiotics for 6 weeks, after which she had complete resolution of her infection. The possibility of a pituitary abscess, although rare, should be kept in mind during evaluation for a necrotic inflammatory pituitary mass with severe headaches and hormonal deficiencies.

## Learning points:

- The possibility of a pituitary abscess, although rare, should be kept in mind during evaluation for a necrotic inflammatory pituitary mass with severe headaches and hormonal deficiencies.
- In a significant proportion of cases no pathogenic organism can be isolated.
- A close follow-up is necessary given the risk of recurrence and the high rate of postoperative pituitary deficiencies.

## Background

Pituitary abscesses are very rare (0.2–1% of all pituitary diseases) (1) and are associated with a high mortality risk. Two-thirds are primary pituitary abscesses and occur in a previously healthy gland, while secondary abscesses arise from pre-existing lesions, such as an adenoma, a craniopharyngioma or a complicated Rathke's cleft cyst. Pituitary abscesses can be caused either by haematogenous seeding or by direct extension

from an adjacent infected tissue (sphenoid sinusitis, meningitis, contaminated cerebrospinal fluid fistula or cavernous sinus thrombophlebitis). The responsible pathogenic microorganism is not isolated in almost 50% of cases (2). The typical MRI findings are those of a sellar heterogeneous cystic mass with a thick peripheral ring enhancement. Mortality and morbidity are reduced by early transsphenoidal surgery, appropriate antibiotic



therapy and hormonal replacement treatment. A close follow-up is necessary, given the risk of recurrence and the high rate of postoperative pituitary deficiencies.

## Case presentation

We report the case of a 26-year-old Caucasian female patient with no significant medical history. In July 2014, after a first normal pregnancy, she gave uncomplicated birth to a healthy girl. The patient did not breastfeed although she had normal milk production, and she quickly resumed normal menstrual cycles. Two months after delivery, the patient complained of persistent headaches.

## Investigation

A cerebral MRI was performed, revealing a symmetric enlargement of the pituitary gland with a heterogeneous signal (data not shown). Shortly thereafter, the patient developed polyuria (6–7 L per day) and polydipsia. The laboratory analyses (morning urinary osmolality=92 mosmol/kg) and a short water deprivation test confirmed the diagnosis of central diabetes insipidus. The hormonal profile was otherwise normal (Table 1). A new pituitary MRI showed a stable symmetric but heterogeneous enlargement of the pituitary gland and a loss of the normal posterior lobe bright signal. Furthermore, post-contrast T1-weighted coronal sections disclosed a large necrotic center surrounded by an enhanced peripheral ring. The diagnosis of postpartum hypophysitis with necrotic transformation was suspected and corticotherapy (methylprednisolone, 32 mg/day) was prescribed, with initial clinical improvement.

Six months later (May 2015), the patient had her first appointment in our hospital for worsening headaches. She was still treated with methylprednisolone (8 mg/day) and desmopressin. Repeat MRI showed disease progression with significant enlargement of the necrotic pituitary gland contacting the optic chiasm, as well as an enlargement of the pituitary stalk and contrast retention within the hypothalamus, thus suggesting extension of the inflammatory process (Fig. 1A and B). Apart from a low-grade fever of 37.5°C she had no systemic features of infection. Blood chemistry showed a low C-reactive protein level and no increased leukocytosis. Neurological and ophthalmological examinations gave normal results. In particular, there was no sign of meningism. Endocrine tests showed a deficiency of the thyrotropic and gonadotropic axes, a partial deficiency of the corticotrope axis (after withdrawal of methylprednisolone) and a moderate increase in prolactin level (Table 1). Blood and urine cultures for bacteria were sterile, with the exception of a single positive blood culture for *Staphylococcus aureus*, considered at that time as a contaminant. Syphilitic serology was negative. Fused FDG PET/RMI did not show any peripheral lesion suggestive of a systemic disease. Instead, it revealed an enhanced fixation in the pituitary mass with restricted central diffusion.

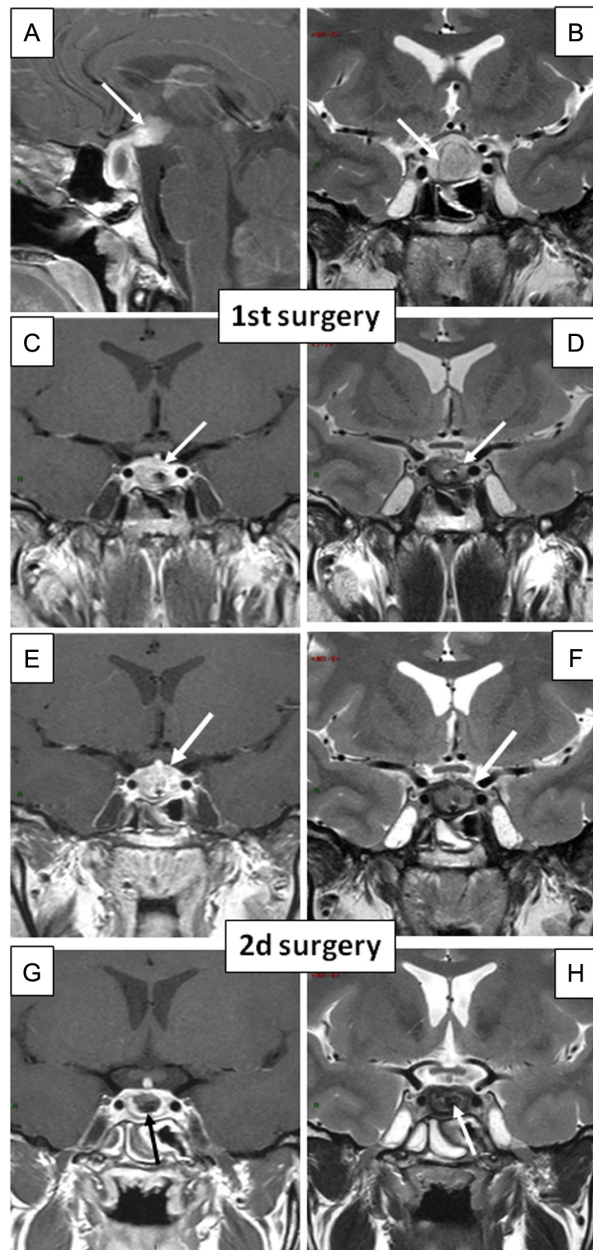
## Treatment

A diagnostic pituitary biopsy and surgical resection were proposed. Transsphenoidal surgery was performed, disclosing a pus-filled cavity, which was drained. Surgery was uncomplicated. Pathological examination of the operative specimen showed numerous polymorphonuclear leucocytes infiltrating pituitary cells, surrounded by peripheral areas of nonspecific necrosis with many

**Table 1** Evolution of the endocrine parameters.

Parameters	September 2014 – at first diagnosis	May 2015 – at 1st appointment in our hospital <sup>§</sup>	July 2015 – before first surgery	Normal values
CRP (mg/L)	ND	4	9	<5
Morning cortisol (nmol/L)	590	202	154	130–500
Morning ACTH (pg/mL)	ND	<2	8.6	5.0–49
TSH (U/L)	4.08	1.42	1.39	0.27–4.20
FT4 (pmol/L)	15.9	10.9	7.1	12–22
FT3 (pmol/L)	ND	3.6	3.1	3.1–6.8
Prolactin (µg/L)	20.0	25.0	69.9	5.0–23.0
IGF-I (ng/mL)	ND	190	168	131–320
LH (IU/L)	4.3	5.4	2.3	2.4–12
FSH (IU/L)	5.9	3.9	4.4	3.5–12.5

<sup>§</sup>Under treatment with glucocorticoids (methylprednisolone 8 mg/day).  
CRP, C-reactive protein; ND, not determined.



**Figure 1**

Serial magnetic resonance imaging (MRI) examinations performed in the patient. (A and B) Post-contrast T1-weighted view in mid-sagittal plane (A) and coronal T2-weighted view (B) of the initial MRI examination showing a pituitary abscess extending to the floor of 3rd ventricle (arrow in A) surrounded by a 'pyogenic membrane' disclosing T2-weighted hypointense intensity (arrow in B). (C and D) First follow-up MRI performed 2 months after first surgery showing a decrease in the size of pituitary abscess (arrows) together with a small susceptibility artifact due to micro-clipping (post-contrast T1-weighted (C) and T2-weighted views (D) in coronal plane). (E and F) Follow-up examination performed 4 months after the first surgery showing an increase in size of the pituitary abscess (thicker arrows to be compared to those in C and D) (post-contrast T1-weighted (E) and T2-weighted views (F) in coronal plane). (G and H) Control examination 2 months after second surgery showing a roll of Gelfoam within the remaining abscess cavity, which has been evacuated (post-contrast T1-weighted (G) and T2-weighted views (H) in coronal plane).

macrophages and a few T lymphocytes (Fig. 2A, B, C and D). There was no evidence of granuloma or caseation and the polymerase chain reaction (PCR) for detecting mycoplasma tuberculosis complex in formalin-fixed tissue specimens was negative. IgG4 immunoreactivity was negative. Moreover, the pathological studies dismissed the existence of any tumor but could not rule out pre-existing lymphocytic hypophysitis. No bacterial growth was observed in the culture of the drained material and the antibiotics (ceftriaxone) were stopped after 7 days.

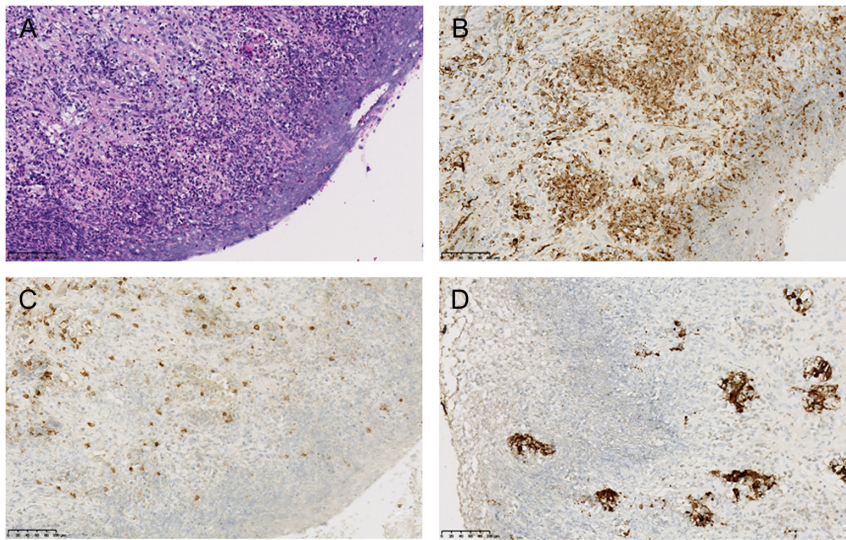
The patient was discharged from the hospital with complete remission of the headaches and on hormone replacement therapy with hydrocortisone twice daily (15/5 mg) and levothyroxine (75 µg/day).

### Outcome and follow-up

No residual active lesion was observed on the postoperative MRI performed two months later (Fig. 1C and D). Four months after surgery, severe headaches recurred. Pituitary MRI was suggestive of a recurrent inflammatory mass of the sellar region (Fig. 1E and F). The patient underwent a re-operation of the abscess. Pathological examination of the second specimen was similar to the first one, with more necrosis and fibrosis (data not shown). Aspiration fluid was however now positive for *Staphylococcus aureus*. The patient was treated with intravenous flucloxacillin for 2 weeks and oral rifampicin in association with moxifloxacin for another 4 weeks, in accordance with reported sensitivities from the laboratory. This led to a complete and sustained resolution of the infectious process (Fig. 1G and H).

### Discussion

Recurrent primary pituitary abscess is a very rare condition. To our knowledge, only 8 cases have been reported in the literature (excluding those secondary to previous pituitary surgery) (Table 2) (2, 3, 4, 5, 6, 7, 8). Our clinical case highlights the difficulty to make this diagnosis before surgery due to its rarity and the nonspecific presentation, usually without systemic signs of infection. The initial differential diagnosis included postpartum hypophysitis and pituitary apoplexy. Clinical postpartum history and the first radiological imaging were indeed consistent with postpartum hypophysitis. However, central pituitary necrosis or hemorrhage is rather rare in such cases. Pituitary apoplexy was another possibility as our patient had acute onset of headaches, but there were no signs of



**Figure 2**

Pathological examination of the operative specimen after the first surgery. (A) Hematoxylin-eosin (magnification,  $\times 200$ ) stained section showing destruction of pituitary gland architecture by a heterogeneous inflammatory process composed mainly of polymorphonuclear neutrophils with abscess areas. (B) Peripheral areas of nonspecific necrosis with an accumulation of macrophages, which are immunopositive for the CD68 antigen ( $\times 200$ ). (C) Presence of very few T lymphocytes revealed by CD3 immunoreactivity ( $\times 200$ ). (D) Immunohistochemical staining for chromogranin A showing spotty areas of residual pituitary tissue.

meningism, and MRI features were not typical of such a diagnosis. As postpartum hypophysitis was the initial working diagnosis, our patient was treated with high dose of methylprednisolone. The early and transient improvement of the headaches was probably related to the nonspecific anti-inflammatory effects of this drug. We also make the hypothesis that pituitary necrosis complicating hypophysitis and prolonged corticotherapy were predisposing factors leading to secondary abscess.

As in our case report, in the four largest case series of pituitary abscess (including 24, 29, 33 and 66 patients, respectively) (3, 9, 10, 11), headache is the most common symptom at presentation (70–92%). Anterior pituitary dysfunction due to the destruction and necrosis of the gland (54–85%) followed by visual disorders (27–50%) (3, 9, 10, 11) are other frequent symptoms (12). Central diabetes insipidus is seen in more than half of the patients (4, 11, 12, 13). Moderate fever (14–33%) and signs of meningeal irritation are less frequent (2). Interestingly, fever was present in only 1 of the 8 reported cases of recurrent primary pituitary abscesses. The diagnosis was delayed in our patient because of the lack of clinical signs of infection and the absence of meningeal signs. However, the MRI findings were suggestive of a pituitary abscess, even if no pathogenic microorganism was isolated during the anatomic-pathological examination of the first operative specimen. Typically, a pituitary abscess appears on MRI as an intrasellar heterogeneous cystic mass with iso or hypointense signal on T1 weighted images and iso or hyperintense signal on T2 weighted images. After gadolinium administration, the lesion usually presents a thick ring enhancement (3, 14, 15, 16, 17).

The pathogenesis of pituitary abscess includes direct involvement of the pituitary gland by haematogenous route or by direct extension from an adjacent infected tissue. In 50–70% of cases, no obvious source of infection can be determined (3, 17). In our case, there were no signs of local or systemic infection. The corticotherapy may have contributed to the latent development of infection within an already necrotic center of pituitary tissue. About one-third of the abscesses are secondary, occurring in a pre-existing lesion, such as an adenoma, a craniopharyngioma or a Rathke's cleft cyst (14). In the present case, however, the pathological examination dismissed the existence of any tumor.

Transsphenoidal surgery is considered as the treatment of choice if a pituitary abscess is suspected. Craniotomy is avoided because it is more invasive and has a greater rate of intracranial dissemination of the infection. However, although the management is mainly surgical, some cases have been managed conservatively (18, 19). Medical treatment includes antibiotic therapy, which should be given for about 4–6 weeks. In our patient, antibiotics were stopped after only 7 days following the first surgery while the recurrent lesion was treated for 6 weeks with complete resolution of the infection. Empirical treatment with ceftriaxone is indicated while awaiting microbiology and histological confirmation. The most commonly isolated pathogens are *Staphylococcus* spp. (as in the present case) and *Streptococcus* spp., followed by *Neisseria* spp., *Micrococcus*, *Citrobacter* spp., *Escherichia coli*, *Brucella*, *Salmonella*, *Corynebacterium* and *Mycobacterium* (20). However, in immunosuppressed patients, *Aspergillus*, *Candida* and *Histoplasma* are the most frequent pathogens.



**Table 2** Patients with recurrent primary pituitary abscess as reported in the literature.

Reference	Age/sex	Presenting complaints	Endocrine status	Treatment	Bacteriology	Time for recurrence (months)	Outcome
(2)	69/M	Headache, hemianopsia	Panhypopituitarism	TS drainage	Gram positive cocci	48	Fatal
(2)	69/M	Headache, hemianopsia	Panhypopituitarism	TS drainage	<i>S. aureus</i>	15	Recovered
(3)	24/M	Headache, visual deterioration	Not mentioned	TS drainage	<i>Aspergillus</i>	18	Recovered
(4)	12/F	Fever, headache, visual deterioration	No deficiency	TS drainage	<i>Acinetobacter</i>	12	Recovered
(5)	53/M	Headache, visual deterioration	Panhypopituitarism	TS drainage	Negative	132	Fatal
(6)	66/F	Headache	Panhypopituitarism	3 TS drainage	<i>S. aureus, H. influenzae</i>	3/32	Recovered
(7)	76/F	Diabetes insipidus	Anterior hypopituitarism	Antibiotics	Negative	48	Recovered
(8)	47/M	Headache	Panhypopituitarism	TS drainage, corticotherapy	Negative	ND	Recovered
Present case	26/F	Headache, diabetes insipidus	Panhypopituitarism	TS drainage	<i>S. aureus</i>	4	Recovered

ND, no data; TS, transsphenoidal surgery.

The responsible pathogenic microorganism remains unknown in 50% of cases (2).

Hormone replacement therapy is given based on hormone deficits of the pituitary gland. The most determining factor for the persistence of pituitary hormone deficiencies is the duration of symptoms before diagnosis. It is important to recognize this condition among patients presenting with sellar masses, as early diagnosis and treatment improve survival outcome.

The recurrent nature of the lesion was confirmed by the detection of pus during the first and second surgical procedures with evidence of acute or chronic inflammation on both histopathological examinations. Additionally, the culture of the second specimen was positive for *Staphylococcus aureus*. The shorter than optimal course of antibiotics after initial surgery likely contributed to the clinical recurrence of the abscess. In that case, although the post-surgery MRI was normal, the relapse should be considered as the resurgence of a persistent subclinical abscess rather than a true recurrence. In the so far nine reported cases of recurrent pituitary abscess including ours (Table 2), the recurrence occurred 3 months to 11 years after the initial infection. The sex ratio was of 1.7 (M/F) and the mean age at diagnosis was 52 years. The treatment was mainly surgical and only one patient was treated with antibiotics only. The pathogenic organism could not be isolated in 38% of cases.

In conclusion, the possibility of a pituitary abscess, although rare, should be kept in mind during evaluation for a necrotic inflammatory pituitary mass with severe headaches and hormonal deficiencies. In agreement with a few reported cases in the literature, this case highlights the difficulty to diagnose a pituitary abscess before surgery. Furthermore, in a significant proportion of cases no pathogenic organism can be isolated. We also advocate that patients be regularly followed after surgery in order to diagnose a potential late recurrence.

**Declaration of interest**

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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**Patient consent**

Written informed consent was obtained from the patient for publication of the submitted article and accompanying images.



#### Author contribution statement

R Furnica wrote the case report. D Maiter and O Alexopoulou reviewed and corrected the manuscript. T Duprez prepared and commented the radiological images. J Lelotte prepared and commented the pathological images of the operative specimen.

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