Rare disease

A pituitary abscess masquerading as recurrent hyponatremia and aseptic meningitis

Michael Gonzales,¹ Paul Ellis Marik,² Romesh K Khardori,³ John T O'Brian³

¹Department of Medicine, Eastern Virginia Medical School, Norfolk, Virginia, USA

²Division of Pulmonary and Critical Care Medicine, Eastern Virginia Medical School, Norfolk, Virginia, USA

³Division of Endocrinology, Eastern Virginia Medical School, Norfolk, Virginia, USA

Correspondence to Dr Paul Ellis Marik, marikpe@evms.edu

Summary

Pituitary abscess is a rare condition. In the setting of multiple surgical interventions, the risk of its development increases. A 49-year-old man presented with episodes of altered mental status. He had two surgeries for a recurrent suprasellar arachnoid cyst. The second surgery was complicated by a persistent cerebrospinal fluid (CSF) leak that required two repairs following which he developed panhypopituitarism and central diabetes insipidus. Twelve months after his last surgery he was diagnosed with aseptic meningitis. This was followed by recurrent hospitalisations for severe hyponatremia blamed on poor medication compliance. He was subsequently hospitalised for the evaluation of a febrile illness. Brain MRI showed ventriculitis and enhancement of the sella. Exploratory surgery revealed a purulent collection in the sella and a mucosal graft which had been used to repair the CSF leak. After drainage of pus and replacement of the graft he recovered completely but requiring life-long hormonal replacement.

BACKGROUND

Despite the advent of meticulous radiological techniques the diagnosis of a pituitary abscess remains a challenge. Clinical suspicion is paramount in establishing the condition.

CASE PRESENTATION

A 49-year-old gentleman presented to the hospital in 2008 with complaints of headaches, dizziness and blurring of vision. He reported a history of craniotomy with removal of an arachnoid cyst in 1993. His surgery was uncomplicated and he had no reported hormonal deficits and was not on any medications. He had not had follow-up imaging after his surgery. He had no polyuria, nocturia, weight loss, decreased appetite or sexual dysfunction. He weighed 82 kg and was 1.70 m tall. He was afebrile; his blood pressure was 125/75 mm Hg with no postural drop. He was not cushingoid, acromegalic or eunuchoid and secondary sexual characteristics were preserved. He had no gynaecomastia and testicular volumes were >20 cm³ bilaterally. His cardiovascular, respiratory and abdominal examinations were normal. Formal visual assessment revealed right lateral hemianopsia. A brain MRI showed expansion of the sella by a cystic non-enhancing lesion that extended above the sella pressing upon the frontal lobes. He underwent endoscopic transseptal-transsphenoidal excision of the sellar/suprasellar mass which was identified to be a recurrent arachnoid cyst. At the time of surgery, a cerebrospinal fluid (CSF) leak was identified which was repaired with a mucosal flap. Unfortunately, he developed a persistent postoperative CSF leak as well as tension pneumocephalus. He was taken back to the operating room and underwent an endoscopic repair of CSF leak. At that time, an inferior turbinate mucosal graft was created, secured with fibrin glue and the sphenoid sinus was obliterated

with hydroxyapatite. After his surgery he developed polyuria with daily urine volumes exceeding 7 litres with low urine specific gravities (1.001–1.005) and urine osmolarities (88–148 mos/kg). Water balance normalised with vasopressin with a >50% increase in urine osmolarity suggesting central diabetes insipidus. Pituitary function evaluation showed a low-normal serum follicle-stimulating hormone of 1.4 IU/l (reference 1.4–18.1 IU/l) an undetectable serum luteinizing hormone (LH) <0.1 (reference 1.7–8.6 IU/l) and decreased total testosterone 130 ng/dl (reference 241–827 ng/dl) and free testosterone 3.67 ng/dl (reference 5–21.0 ng/dl) suggesting hypogonadotropic hypogonadism. A low serum thyrotrophin of 0.05 mU/l (reference 0.35–5.50 mU/l) and low serum-free thyroxine (FT4) of 0.5 ng/dl (reference: 0.9–1.8 ng/dl) and low total triiodothyronine (total T3) 53 ng/dl (reference: 60–181 ng/dl) suggested central thyrotrophin insufficiency. Morning (8:00) serum cortisol was 8 mcg/dl (reference: 7–9 am, 4.3–22.48 mcg/dl) and adrenocorticotrophic hormone (ACTH) <5 pg/ml (reference: 6–48 pg/ml) were both low. He was later started on hormonal replacement with hydrocortisone, levothyroxine, testosterone gel and oral desmopressin.

Twelve months after his surgery he was admitted for altered mental status with a clinical picture consistent with aseptic meningitis. He was afebrile, had normal electrolytes (serum sodium 137 reference: 135–147 mEq/l, potassium 3.6 reference: 3.5–5.5 mEq/l, chloride 99 reference; and had no elevation in his peripheral white blood cell (WBC) count. Lumbar puncture showed a lymphocytic pleocytosis (658 mm³ and 58%) with an elevated protein (87.6 mg/dl; reference: 12.0–60.0 mg/dl) and normal glucose (61 mg/dl; reference: 40–70 mg/dl). Bacterial latex antigen studies were negative and CSF cultures did not have any growth. Herpes PCR and India ink CSF studies were negative. His brain MRI did not show

any abnormal enhancement or mass lesions. He was treated with broad-spectrum antibiotics for presumptive meningitis; however, his mental status improved in <24 h which was deemed to be not consistent with acute meningitis. He was hospitalised on two further occasions for hypernatremia (serum sodium 160–162 reference: 135–147 mEq/l) with aseptic meningitis. MRI done on both occasions did not show any abnormalities and he was thought to be non-compliant with therapy. He was declared incompetent after a psychiatric evaluation and was discharged to a nursing home.

A month later, with fever, rigours and altered mental status, he represented to the hospital. He complained of nape pain and had nuchal rigidity on exam. His peripheral WBC count was normal.

INVESTIGATIONS

A cloudy fluid was obtained on lumbar puncture and analysis showed a lymphocytic pleocytosis with (2185 cu/mm and 62%) an elevated protein (233 mg/dl reference: 12.0–60.0 mg/dl) and low glucose (8 mg/dl reference: 40–70 mg/dl). Bacterial latex antigen and CSF cultures were negative. MRI of his brain showed layering of fluid (pus) in the posterior horns of the ventricles with ependymal enhancement and enhancement of the superior margin of the sella turcica (figure 1).

TREATMENT

Intraoperative examination revealed copious amounts of pus between the hydroxyapatite and non-intact dural repair. The previous graft was evacuated and replaced with a fascia lata graft. Cultures from the old graft grew coagulate negative *Staphylococcus* and *Proteus mirabilis*. He recovered uneventfully after the surgery and completed a 4 week course of intravenous antibiotics.

OUTCOME AND FOLLOW-UP

The patient has remained stable on hormonal replacement.

DISCUSSION

Pituitary abscesses are rare and can be estimated to represent <1% of all cases of pituitary disease presenting to a specialist.¹ A common risk factor is a history of pituitary surgery.² However, the majority of patients lack a specific causative history. The diagnosis is further made difficult by the paucity of typical infectious manifestations. Furthermore, patients frequently have hormonal deficiencies either secondary to surgery or the infectious process which complicates the clinical picture. Patients therefore usually have a chronic indolent course and a high index of suspicion is needed to establish the diagnosis.

The first description of a pituitary abscess was provided by Simmonds in 1914.³ The diagnosis of a pituitary abscess represents a unique challenge for many reasons. First, it is a rare disorder that is difficult to diagnose before surgery. Approximately 200 case studies of pituitary abscess have been reported in the literature, the majority of which were diagnosed postoperatively.⁴ Liu *et al*² reported a case series of 33 patients of 2984 pituitary surgeries. Vates *et al*⁵, reported 24 cases drawn from a series of more than 3500 patients who underwent pituitary

surgery. As such, they are estimated to constitute <1% of all pituitary disease seen by specialists. The majority of pituitary abscess are thought to arise primarily from normal pituitary tissue; however, approximately 30% are associated with a pituitary adenoma,^{6–8} craniopharyngioma^{4,9} or Rathke's cleft cyst.^{5,10,11} Infection of the pituitary can arise from local spread of a regional process (sinusitis, meningitis, cavernous sinus thrombophlebitis and dental caries),^{12–14} or from spread of a systemic microbial infection (sepsis).¹⁵ Infection can also arise secondarily from a neurosurgical intervention of the pituitary; either transsphenoidally or transcranially.^{2,5} Other risk factors include an underlying immunocompromised condition and previous pituitary radiation.⁵ It is important to note that majority of patients may not have clearly identifiable causal history.^{1,2} In our case, the multiple surgeries required to resolve the patient's CSF leak was a clear determinant in the development of the pituitary infection.

Pituitary abscess can have varied signs and symptoms similar to those seen in other space-occupying sellar lesions such as headache, vomiting, visual disturbances and hormonal deficiencies. In two case series of pituitary abscesses, headache was the most common presenting complaint.^{2,4} The headache is usually long standing, non-specific and with no characteristic pattern or location. The visual disturbances range from unilateral or bilateral ophthalmoplegia occurring in 27–68% of cases described.^{4,16} According to the literature, 30–50% of patients have anterior pituitary hormone deficiency or central diabetes insipidus at presentation.¹⁷ In Liu's series of 33 patients, 85% of patients were diagnosed with hypopituitarism whereas 70% had central diabetes insipidus.² In another review of 24 cases, 60% had complete anterior hypopituitarism and 28% of patients had central diabetes insipidus on presentation.⁴ Life-long substitutive hormonal therapy is usually needed. The classical infective signs and symptoms such as fever and an elevated peripheral WBC count are uncommon. In one review, a third of patients had fever or leucocytosis and 25% of cases had signs of meningeal irritation.⁴ In the largest series reported, only 18% of patients had fever and an elevated peripheral WBC count.² The non-specific symptoms can contribute to the chronic and indolent course of this disease and the delay in the diagnosis. The average time between the onset of symptoms and diagnosis of a pituitary abscess has been reported to be 8.3 months (ranging from 7 to 36 months).² In our case, our patient's admissions for hypernatremia also made the diagnosis more difficult as his altered mental status was attributed to this finding. In retrospect, the recurrent episodes of aseptic meningitis was a red flag to an underlying inflammatory process, which then led to the overt infectious symptoms seen late in his course. Our patient was not diagnosed until 12 months after the last surgery to correct the CSF leak. It is important to note that hypocortisolaemia can mask the symptoms of diabetes insipidus in the immediate postoperative period; in our case the patient had mild secondary adrenal insufficiency which could explain partly which his death instinct (DI) manifested overtly; in addition, he received hormonal replacement after this was uncovered that would have unmasked DI even further.

Figure 1 MRI T1-weighted images (T1WI) reveal enhancement of the sella and ependyma in the posterior horns (A, B). T2-weighted images reveal layering of debris in the posterior horn of the ventricle hypointense relative to the cerebrospinal fluid (C). Changes on diffusion-weighted imaging suggest that the collection is purulent in nature (D). Sagittal T1WI showing hypointensity in sella and sphenoid representing methacrylate, and absence of any distinct pituitary bright spot. (E) Coronal T1 postcontrast image showing enhancement of the sella (F).

The preoperative diagnosis of a pituitary abscess remains difficult as the radiological images for both the primary and secondary forms is only suggestive and confirmation is only obtained at surgery. However, recurrent aseptic meningitis should arouse suspicion to pituitary abscess.^{18 19} Pituitary abscess is usually recognised by CT as a low-density mass in the sella that is usually associated with a high-density rim that enhances with

contrast. On MRI, pituitary abscesses occur as cystic lesions appear hypointense on T1-weighted (T1WI) and hyperintense on T2-weighted (T2WI) imaging, with a peripheral ring enhancement after gadolinium injection.²⁰ However, this is not absolute, as the proteinaceous content of the abscess can also result in a hyperdense appearance on CT and a hyperintensity on T1WI, but central hypointensity with peripheral ring-form

hyperintensity on proton density-weighted and T2WI.²¹ Furthermore, there are other more common sellar lesions, both tumorous and non-tumorous, which may mimic the appearance of a pituitary abscess. Aside from an abscess, the differential diagnosis of cystic sellar lesions include pituitary adenomas, carcinomas, arachnoid cysts, Rathke's cleft cysts and metastatic lesions.²² In our case, the previous surgical repair of the sellar floor with hydroxyapatite grafts rendered visualisation of the sella and all other pathological changes more difficult. The classic 'cystic' enhancing lesion is not seen. Instead, we saw some enhancement of the sella and the layering of purulent substances in the ventricular system seen in ventriculitis. However, the surgical findings were consistent with a pituitary abscess.

Surgical decompression via a transsphenoidal approach provides the most optimum means of treating a pituitary abscess to prevent further spread of the infection and compromise of vision. In few cases, however, medical therapy has been successful.^{23–24} The most common intraoperative finding is collection of creamy to yellow pus with or without an identifiable thin cystic capsule.¹ Gram stain is usually negative and cultures are only positive 36–50% from specimens obtained intraoperatively.^{1–2} Organisms isolated include Gram-positive, Gram-negative bacteria, mycobacteria,^{25–26} *Candida* spp.,²⁷ *Aspergillus* spp.^{28–29} and *Toxoplasma gondii*.³⁰ Intravenous antibiotic therapy directed towards the causative organisms is required to prevent recurrence of infection; however, there is no consensus on the duration of therapy. Recurrence of the infection, although rare has been reported and requires repeat intervention.²⁴

Learning points

- ▶ Pituitary abscesses must be considered in any patient with a history of sellar surgery who presents with altered mental status.
- ▶ Imaging may not show the typical cystic enhancing lesion due to changes in the sella related from surgery.
- ▶ The diagnosis of a pituitary abscess is confirmed at surgery and imaging is only suggestive.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Dalan R**, Leow M. Pituitary abscess: our experience with a case and review of literature. *Pituitary* 2008;**11**:299–306.
2. **Liu F**, Li G, Yao Y, *et al*. Diagnosis and management of pituitary abscess: experiences from 33 cases. *Clin Endocrinol* 2011;**74**:79–88.
3. **Simmonds M**. Zur Pathologie der Ag hypophysis. *Verh Dtsch Pathol* 1914;**17**:208–12.
4. **Ciappetta P**, Calace A, D'Urso PI, *et al*. Endoscopic treatment of pituitary abscess: two case reports and literature review. *Neurosurg Rev* 2008;**31**:237–46.
5. **Vates GE**, Berger MS, Wilson CB. Diagnosis and management of pituitary abscess: a review of twenty-four cases. *J Neurosurg* 2001;**95**:233–41.
6. **Jain KC**, Varma A, Mahapatra AK. Pituitary abscess: a series of six cases. *Br J Neurosurg* 1997;**11**:139–43.
7. **Hatiboglu MA**, Iplikcioglu AC, Ozcan D. Abscess formation within invasive pituitary adenoma. *J Clin Neurosci* 2006;**13**:774–7.
8. **Jaiswal AK**, Mahapatra AK, Sharma MC. Pituitary abscess associated with prolactinoma. *J Clin Neurosci* 2004;**11**:533–4.
9. **Obrador S**, Blazquez MG. Pituitary abscess in a craniopharyngioma. Case report. *J Neurosurg* 1972;**36**:785–9.
10. **Celikoglu E**, Boran BO, Bozbuga M. Abscess formation in Rathke's cleft cyst. *Neural India* 2006;**54**:213–14.
11. **Thomas N**, Wittert GA, Scott G, *et al*. Infection of a Rathke's cleft cyst: a rare cause of pituitary abscess. Case illustration. *J Neurosurg* 1998;**89**:682.
12. **Verdalle P**, Roquet E, Hor F, *et al*. Pituitary abscess. A rare complication of sinusitis. *Rev Laryngol Otol Rhinol* 1997;**118**:327–9.
13. **Shono T**, Nishio S, Muratani H, *et al*. Pituitary abscess secondary to isolated sphenoid sinusitis. *Minim Invasive Neurosurg* 1999;**42**:204–6.
14. **Kroppenstedt SN**, Liebig T, Mueller W, *et al*. Secondary abscess formation in pituitary adenoma after tooth extraction. Case report. *J Neurosurg* 2001;**94**:335–8.
15. **Jung Y**, Kim JD, Chadaga R, *et al*. Pituitary abscess following general sepsis in a diabetic patient. *JAMA* 1976;**235**:1476.
16. **Dalan R**, Leow MK. Pituitary abscess: our experience with a case and review of the literature. *Pituitary* 2008;**3**:299–306.
17. **Dutta P**, Bhansali A, Singh P, *et al*. Pituitary abscess: report of four cases and review of literature. *Pituitary* 2006;**9**:267–73.
18. **Guillame D**, Stevenaert A, Grisar T, *et al*. Pituitary abscess with recurrent aseptic meningitis. *J Neurol Neurosurg Psychiatry* 1990;**53**:925–6.
19. **Ford J**, Torres LF, Cox T, *et al*. Recurrent sterile meningitis caused by a pituitary abscess. *Postgrad Med J* 1986;**62**:929–31.
20. **Kabuto M**, Kubota T, Kobayashi H, *et al*. MR imaging and Ct of pituitary abscess: case report and review. *Neurol Res* 1996;**18**:495–8.
21. **Hwang SL**, Howng SL. Pituitary abscess: CT and MRI findings. *J Formos Med Assoc* 1996;**95**:267–9.
22. **Sabbah P**, Bonardel G, Herve R, *et al*. CT and MRI findings in primary pituitary abscess: a case report and review of literature. *J Neuroradiol* 1999;**26**:196–9.
23. **Kaur A**, Agrawal A, Mittal M. Presumed pituitary abscess without infectious source treated successfully with antibiotics alone. *J Neuroophthalmol* 2005;**25**:185–8.
24. **Dechambenoit G**, Datie A, Grunitzky EK, *et al*. Pituitary abscess, treated by medication. *Rev Neurol* 1993;**149**:567–71.
25. **Chelara K**, Bouzaidi K, Azaiz O, *et al*. Tuberculous meningitis with pituitary abscess. *J Neuroradiol* 2003;**30**:188–91.
26. **Dutta P**, Bhansali A, Singh P, *et al*. Suprasellar tubercular abscess presenting as panhypopituitarism: a common lesion in an uncommon site with a brief review of literature. *Pituitary* 2006;**9**:73–7.
27. **Heary RF**, Maniker AH, Wolansky LJ. Cerebral pituitary abscess: a case report. *Neurosurgery* 1995;**36**:1009–12.
28. **Iplikcioglu AC**, Bek S, Bismaz K, *et al*. Aspergillus pituitary abscess. *Acta Neurochir* 2004;**146**:521–4.
29. **Ramos-Gabatin A**, Jordan RM. Primary pituitary aspergillosis responding to transsphenoidal surgery and combined therapy with amphotericin-B and 5-fluorocytosine: case report. *J Neurosurg* 1981;**54**:839–41.
30. **Zhang X**, Li Q, Hu P, *et al*. Two case reports of pituitary adenoma associated with *Toxoplasma gondii* infection. *J Clin Pathol* 2002;**55**:965–6.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Gonzales M, Marik PE, Khardori RK, O'Brian JT. A pituitary abscess masquerading as recurrent hyponatremia and aseptic meningitis . *BMJ Case Reports* 2012;10.1136/bcr-2012-006436, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow