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Intrasellar abscess following pituitary surgery

Kevin T. Huang[1] · Wenya Linda Bi[1] · Timothy R. Smith[1] · Amir A. Zamani[2] · Ian F. Dunn[1] · Edward R. Laws Jr.[1]

Abstract
Purpose Intrasellar abscess is an uncommon cause of mass lesions in the sella turcica. Few cases have been reported in the literature, and much remains unknown about the etiology and diagnosis of these lesions. We sought to review a series of patients with intrasellar abscess encountered at our institution and identify defining characteristics of their presentation and management.
Methods We conducted a retrospective chart review for intrasellar infection cases associated with a mass lesion. Included cases had clear demonstration of a mass lesion on imaging with subsequent positive microbiological cultures. Clinical presentation, management, post-operative course, neuroimaging, microbiology, and any perturbations in serum pituitary biochemical markers were examined.
Results All examined patients had a history of antecedent transsphenoidal pituitary surgery within the preceding 10 months. All presented with headaches, three with progressive visual loss, one with meningismus, one with fever in the setting of an active cerebrospinal fluid leak, and one with fever, meningismus, hypotension, and progressive somnolence. No patient presented with acute endocrine abnormalities. A majority did not initially have any diffusion restriction present on MRI, but in one case we were able to track the evolution of diffusion restriction over sequential MRI scans. Two patients had complete resolution of presenting symptoms, while three experienced improvement or stabilization of their neurologic deficit. There were no mortalities.
Conclusions Pituitary abscess remains a rare diagnosis that can be difficult to make and to confirm. In our series we found a strong association between culture-positive abscess and recent pituitary surgery. When present, prompt treatment with surgical drainage and aggressive post-operative antibiotics can lead to a favorable outcome.

Keywords Intrasellar abscess · Infection · Post-surgical complication · Literature review · Case series

Introduction

Abscesses within the sella turcica are rare lesions that represent less than 1 % of referred cases to large pituitary centers [1]. Prior literature on these lesions is largely limited to individual case reports or small case series because of their scarcity and challenges in accurate diagnosis [2–7]. On imaging, intrasellar abscesses can mimic cystic adenomas and Rathke's cleft cysts, the latter of which can cause localized inflammation through leakage of cyst contents [8]. Thus, some debate exists on whether the entirety of previously published cases of pituitary abscesses qualify as true abscesses related to active infectious processes [9]. Given the continued need for more data, we present five patients who were evaluated and treated at our institution with culture-positive pituitary abscesses.

Methods

We retrospectively reviewed pituitary surgery cases operated upon between 1995 and 2014 at our institution, and identified five cases of intrasellar abscess. Clinical

✉ Edward R. Laws Jr.
elaws@partners.org

[1] Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School, 15 Francis Street, PBB-3, Boston, MA 02115, USA

[2] Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA

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presentation, prior medical and surgical history, neuroimaging characteristics, treatment details, microbiology, pathology, post-operative course, and perioperative hormone function were reviewed. Cases of pituitary abscess were defined by the presence of known cystic mass lesion and positive cultures grown from intra-operative specimens. Cases that were not culture-proven were explicitly excluded. Cases were not excluded on the basis of any other criteria, including demographic variables and past medical and surgical history.

Results

Clinical presentation

We identified five patients with intrasellar abscess (4F/1 M, mean age 45 years, range 32–63 years), all of whom underwent sellar surgery within the prior year, ranging from three weeks to 10 months before presentation and diagnosis (median 74 days, range 26–311 days, Table 1). Primary pathologies leading to prior surgery included pituitary adenoma (n = 3), Rathke's cleft cyst (n = 1), and arachnoid cyst (n = 1). Notably, four of these patients experienced a complicated post-operative course following their primary surgery: two with cerebrospinal fluid leaks, one with epistaxis requiring embolization, and one with frank bacterial meningitis.

On presentation, all patients had complaints of headaches, two manifested constitutional signs of infection (with one presenting in sepsis), and three presented with progressive visual complaints (Table 1). Pre-operative inflammatory markers were varied, with only one patient having an abnormally prolonged pre-operative erythrocyte sedimentation rate (ESR) (Table 2). Two patients had elevated C-reactive protein (CRP) levels and only one had an elevated white blood cell count. Pre-operative MR imaging was notable for rim-enhancement in all five patients, but diffusion restriction was an inconsistent finding, as three patients did not show any clear signs of diffusion restriction (Fig. 1). No patient presented with complaints of progressive endocrinopathy, and none had any change from his or her baseline endocrine status (Table 3).

Treatment and post-operative course

Clinical suspicion of intrasellar abscess prompted transsphenoidal drainage of the sellar lesion in all five cases. Intra-operative findings were notable for frank purulent material in four cases. In the remaining case, the cystic fluid was noted to be more consistent with cerebrospinal fluid. In one case, an intrasellar abdominal fat graft was suspected to have contributed to the infection and was consequently removed. A general principle of surgical management was the removal of any and all foreign material. All patients were managed with at least 6 weeks of culture-guided intravenous antibiotic therapy, and all but one continued a subsequent multi-week regimen of oral antibiotics (Table 4).

Of our five patients, three experienced clinical improvement in presenting symptoms and no further complications. One patient developed an intermittent low-grade cerebrospinal fluid leak that resolved spontaneously 4 months after surgery. The remaining one patient developed a persistent low-grade cerebrospinal fluid leak and subsequent subdural empyema and cerebritis. This prompted a craniotomy for evacuation of the empyema and a protracted course of antibiotics including intrathecal gentamicin, after which he recovered to his pre-operative neurologic baseline. Of the three patients with neurologic deficits at presentation, two significantly improved after surgery and one was neurologically stable.

All patients were monitored with serial measures of serum sodium and urine specific gravity every 6 h during their post-operative hospital course. No patient presented with any occurrence of diabetes insipidus (defined as serum sodium values of >145 mg/dL, urine specific gravity of <1.003, or urine output greater than 200 mL per hour over three or more hours). One patient (case#2) developed hyponatremia (Na = 133 mEq/L) in the immediate

Table 1 Clinical presentation

Case	Age	Gender	Prior sellar surgery?	Days between original surgery and presentation	Symptoms	Focal neurologic deficits
1	32	F	Y	80	Headache	None
2	33	F	Y	20	Headache, meningismus, sepsis, fever	None
3	37	F	Y	74	Headache, diplopia	Left CN VI palsy
4	60	M	Y	311	Headache, progressive visual acuity loss	Left temporal hemianopsia, Right superior temporal quadrantanopsia
5	63	F	Y	26	Headache, fever, CSF leak, diplopia	Left CN III palsy

CN VI abducens nerve, *CN III* oculomotor nerve, *CSF* cerebrospinal fluid

Table 2 Preoperative radiologic and laboratory investigation

Case	Size (cm)	Other radiographic characteristics	ESR	CRP	WBC
1	2.0 × 1.7 × 1.3	Rim-enhancing, diffusion restriction	Normal	Normal	Normal
2	1.2 × 1.6 × 1.3	Rim-enhancing, no definite diffusion restriction	Normal	Elevated	Elevated
3	1.9 × 2.0 × 1.4	Mass effect on infundibulum and cavernous sinus, rim-enhancing, diffusion restriction	Normal	N/A	Normal
4	3.4 × 2.5 × 2.4	Mass effect on chiasm, rim-enhancing, no diffusion restriction	N/A	N/A	Normal
5	1.2 × 1.2 × 1.1	Rim-enhancing, no definite diffusion restriction	Elevated	Elevated	Normal

ESR erythrocyte sedimentation rate, *CRP* C-reactive protein, *WBC* white blood cell count

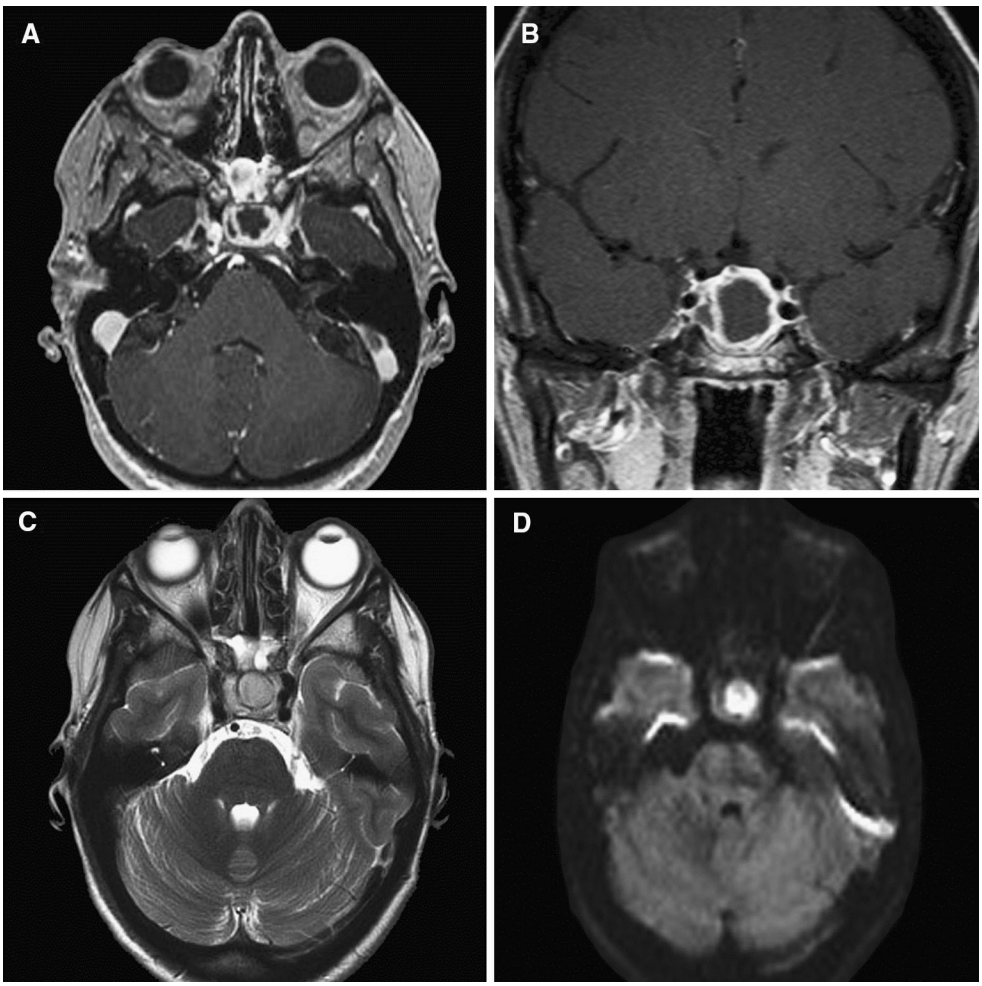

Fig. 1 Classic MRI findings in intrasellar abscess. **a** Axial and **b** coronal T1-weighted gadolinium-enhanced MRI demonstrating an intrasellar rim-enhancing lesion. **c** T2-weighted axial images show a well-defined oval lesion with a center that is hyperintense in relation to brain and a hypointense thin peripheral rim. **d** Avid diffusion restriction noted within the intrasellar lesion on DWI MRI sequence

post-operative period that was managed with a mild fluid restriction with subsequent resolution. In consultation with the endocrinology team, four of our five patients were placed on perioperative stress-dosed steroids. After the immediate post-operative period, none of our patients required either increase in dosage of pre-existing hormone replacement regimens or the initiation of new hormone replacement medications.

Pathologic analysis of surgical specimens revealed ubiquitous heavy inflammatory infiltrates. Bacterial cultures grew *Staphylococcus aureus* in four patients, with one harboring concomitant *Streptococcus pneuomoniae*. The

Table 3 Preoperative and post-operative endocrine status

		TSH (uIU/mL)	T3 (ng/dL)	Free T4 (ng/dL)	Cortisol (ug/dL)	LH (IU/L)	FSH (IU/L)	Estradiol (pg/mL)	Testosterone (ng/dL)	Prolactin (ng/mL)	HGH (ng/mL)
Normal ranges		0.5–5.7	80–200	0.9–1.7	8 am: 6.2–19.4 4 pm: 2.3–11.9	2.4–95.6 (dependent on ovulatory phase)	3.5–134.8 (dependent on ovulatory phase)	14–364 (dependent on ovulatory phase)	193–740	2.7–26.7	0.01–3.61
Case 1	Pre-Operative	1.90	89	0.9	14.8 (4 pm)	2.5	6.4	26	–	**100 (baseline elevation)**	0.16
	Post-Operative	2.44	70	1.2	16.7 (8 am)	–	–	–	–	**54.1**	–
Case 2	Pre-Operative	–	–	–	–	–	–	–	–	–	–
	Post-Operative	1.24	–	1.0	–	10.0	6.3	–	–	–	–
Case 3	Pre-Operative	–	–	–	–	–	–	–	–	–	–
	Post-Operative	2.41	–	1.1	17.11 (8 am)	–	–	–	–	19.4	–
Case 4	Pre-Operative	0.215		7.6	**0.9 (midnight)**	0.3	3.0	–	–	6.9	–
	Post-Operative	–	–	1.2	23 (8 am)	–	–	–	586 (on home replacement)	–	–
Case 5	Pre-Operative	**0.007** **(on home replacement)**	83	1.4	**1.44 (11 am)** **(on home replacement)**	–	–	–	–	–	–
	Post-Operative	**<0.004**	–	1.8	**3.01 (11 am)** **(on home replacement)**	–	–	–	–	–	–

All values not available have been left blank

Pre-operative results are only reported here if obtained while patient was symptomatic

Post-operative results obtained either during inpatient recovery or at immediate post-operative follow-up clinic

Abnormal lab values indicated by bold

TSH thyroid-stimulating hormone, *LH* luteinizing hormone, *FSH* follicle-stimulating hormone, *HGH* human growth hormone

Table 4 Treatment and Outcomes

Case	Operation	Pathology	Microbiology	Antibiotic Treatment	Complications	Follow-up Length (mo)	Clinical Outcome
1	Endoscopic transsphenoidal drainage	Mucosa, acute and chronic inflammation, granulation tissue	4+ *Staphylococcus aureus*	IV oxacillin × 6 wks	None	3	Return to baseline
2	Microscopic transsphenoidal drainage	Mucosa, adipose tissue, acute and chronic inflammation	2+ *Streptococcus pneumoniae*, 2+ *Staphylococcus aureus*	IV ceftriaxone × 4 wks + PO moxifloxacin × 2 wks	None	48	Return to baseline
3	Microscopic transsphenoidal drainage + placement of lumbar drain	Acute and chronic inflammation	4+ *Staphylococcus aureus*	IV nafcillin × 5 wks + PO rifampin and levofloxacin × 3 mo	None	72	6th nerve palsy improved
4	Endoscopic transsphenoidal drainage	Fibrinopurulent material, acute and chronic inflammation	3+ *Staphylococcus aureus*	IV nafcillin × 6 wks + PO levofloxacin and rifampin × 6 mo	Intermittent low-grade CSF leak; spontaneously resolved by 3 mo follow-up	60	Visual improvement, some residual upper left temporal quadrantanopsia
5	Microscopic transsphenoidal drainage + removal of infected fat graft	Necroinflammatory debris, acute inflammation	Delayed growth of *Enterobacter aerogenes*	IV vancomycin and meropenem × 2 wks + Intrathecal gentamicin + PO ciprofloxacin and meropenem × 6 wks	Persistent post-operative low-grade CSF leak; subsequent subdural abscess + cerebritis requiring craniotomy and drainage	60	Resolution of systemic infection, stable 3rd nerve palsy

CSF cerebrospinal fluid, *wks* weeks, *mo* months

remaining patient initially did not grow any organisms on cultures, but upon subsequent presentation for subdural abscess and cerebritis, cultures were positive for *Enterbacter aerogenes*.

Discussion

We present a consecutive series of culture-positive abscesses of the sella turcica. Data on these lesions remain limited, and much remains to be established in terms of their etiology and diagnosis. In particular, though many case reports and small case series exist in the literature, significant heterogeneity exists in the definition of these lesions. A significant number of previously reported cases represent culture-negative or so-called "sterile" abscesses, which as others have noted previously, may include Rathke's cleft cysts [9]. This is challenging, as the contents of these Rathke's cleft cysts are known to be highly inflammatory and are known to cause aseptic meningitis from leakage of cyst contents [10]. In contrast, our series is limited only to those cases with positive confirmation of infection and thus, may represent a better characterization of lesions of infectious etiology.

One prominent characteristic of our series was that all patients underwent prior pituitary surgery within 1 year of presentation with intrasellar abscess. This contrasts with some previously reported series, where many cases have no antecedent pituitary surgery [2, 11]. Notably, these series also feature a high reported rate of culture-negative lesions. The converse relationship between prior pituitary surgery and culture-positive abscesses has also been noted. One study of 12 patients reported only five cases of culture-positive abscess, though all 12 had a history of prior pituitary surgery [3]. Given the limits of data available through case series, it is not surprising that significant variation exists among various published series. Moreover, our review was limited to patients encountered by the neurosurgical service, which may have biased our data to include more patients with a previous history of surgery. With these limitations in mind, our data suggest that inoculation from prior sellar interventions contributes significantly to abscess formation and heightened suspicion for abscess should be exerted in symptomatic patients with a recent history of pituitary surgery.

Differentiation of abscesses from other cystic pituitary lesions remains a significant challenge, with studies reporting that the correct pre-operative diagnosis of pituitary abscess is made in only 21–50 % of cases [2, 11, 12]. Similarly, pituitary abscess was the clear leading diagnosis in only two of our cases, though abscess was high on the differential diagnosis in two others. The diagnosis of these lesions remains difficult not only because of the rarity of intrasellar abscess formation, but also the potential for other cystic lesions of the sella to present with similar radiologic findings [8, 10, 13]. Moreover, though previous reports have suggested that diffusion-weighted imaging can help identify and differentiate abscesses from other cystic lesions, three of our five patients lacked definite diffusion restriction in our series [14–16]. It is possible that signal artifact created by either nearby air-containing sinuses or surgically-inserted fat may make diffusion-weighted imaging less well-suited to identify intrasellar abscesses compared to those in other intracranial locations. It is also possible that timing of imaging may also confound the results. In one of our cases (patient#1), we were able to detect evolution of the abscess on serial imaging over time, with lack of definite restriction on diffusion-weighted imaging on initial presentation, but development of diffusion restriction on repeat imaging 10 days later. These results are consistent with the evolution of other intracranial abscesses, and illustrate that the timing of image acquisition may also affect the sensitivity of neuroimaging. Thus, despite significant advancement in imaging techniques over recent decades, care should nevertheless be exercised when interpreting neuroimaging evidence in suspected cases of abscess.

Gram-positive bacteria were the predominant causative organisms in our series, with involvement of *S. aureus* in four of our five cases (one with concomitant growth of *Streptococcus pneumoniae*) and *Enterobacter aerogenes* in the other case. This is in agreement with previous series, which consistently note gram-positive cocci as major drivers of intrasellar abscesses [2–4]. Alternatively, *Escherichia coli*, *Mycobacterium* species, *Neisseria* species, and various fungal species have also been reported [1–4, 17, 18]. Thus, although the microbiology of these lesions appears diverse, our data suggest that gram-positive cocci are common causative organisms, and that it is imperative for empiric treatment of intrasellar abscess to include adequate gram-positive coverage.

All of our patients were treated with surgical drainage followed by an aggressive antibiotic regimen. Any foreign body or devascularized tissue was removed during surgical exploration. In contrast to the high morbidity and mortality reported in some older series, we encountered no mortalities. All patients had either resolution or stabilization of their symptoms, though three harbored persistent neurologic deficits post-operatively [4, 5, 19]. Other contemporary series have also described significantly improved mortality and morbidity rates, which likely represent advances in diagnostic imaging and antibiotic regimens [2, 3]. We advocate surgical drainage and prolonged post-operative microbiology-guided antibiotic therapy as standard treatment for intrasellar abscesses.

Intrasellar abscess remains a diagnostic challenge and can mimic many other non-infectious intrasellar and parasellar lesions. Particular suspicion for infection should be raised in patients with a recent history of sellar surgery. When present, prompt treatment with surgical drainage and aggressive post-operative antibiotics can lead to a favorable outcome.

Conflict of interest The authors have no conflicts of interest or funding sources to disclose.

Ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. For this type of study formal consent is not required.

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