Case Report

NEUROLOGY

Aseptic meningitis after 20 years of endoscopic transsphenoidal pituitary surgery: a rare complication

Syed Zohaib Maroof Hussain[1], Muhammad Osama Anwer[1], Syeda Marsha Noor[2], Salman Hashmi[3], Sanam Anwer[4], Uzair Yaqoob[5]

1) Aga Khan University Hospital, Karachi, Pakistan

2) Jinnah Post-graduate Medical Centre, Karachi, Pakistan

3) Peterborough City Hospital, United Kingdom

4) Central Southside Community Hospital, Chicago, United States of America

5) Dow University of Health Sciences, Karachi, Pakistan

Abstract

A transsphenoidal surgical (TSS) approach is used for pituitary gland surgery involving pituitary adenomas, as well as for the biopsy of various neurosurgical tumors. TSS, although a relatively safe procedure, can lead to complications like hypopituitarism, visual impairment, nasal septal perforation, diabetes insipidus, carotid artery injury, and cerebrospinal fluid (CSF) leaks. Aseptic meningitis is also one of the complications of this procedure with an incidence of 1-2%, presenting with symptoms similar to bacterial meningitis, but with a low-grade fever of <102 F or even apyrexia. Here, we present a rare case of aseptic meningitis due to CSF leakage, presenting after 20 years of endoscopic surgery. A ventriculoperitoneal shunt was placed to stem the leak after two unsuccessful attempts of endonasal repair.

Keywords: transsphenoidal surgery, aseptic meningitis, pituitary adenoma

Introduction

A transsphenoidal surgical (TSS) approach is used for pituitary gland surgery involving pituitary adenomas, as well as for the resection or biopsy of meningiomas, aspergillomas, and debulking of large brain tumors. Documented complications of this approach are hypopituitarism, visual impairment, nasal septal perforation, diabetes insipidus, carotid artery injury, and cerebrospinal fluid (CSF) leaks. TSS is a relatively safe procedure with a low incidence rate of complications. Aseptic meningitis occurred at an incidence rate of 1-2% in a cross-sectional survey of 958 neurosurgeons reporting their own experience [1–3].

Bacterial meningitis is a rare but potentially life-threatening complication of endoscopic skull base surgery, occurring usually in fewer than 5% of all cases [4]. Bacterial meningitis most commonly presents with symptoms of meningismus which include; fever of 102 Fahrenheit (F), headache, nuchal rigidity, and photophobia. Aseptic meningitis usually presents with more or less similar symptoms, but the patient has a fever of less than 102 F or even apyrexia. It represents 50 to 75% of all post-surgical cases of meningitis [5,6].

Here, we present a rare case of aseptic meningitis, delayed by twenty years. After a thorough literature review, we did not find any reported cases of aseptic meningitis from around the world which presented 20 years after endoscopic surgery.

Case report

A 47-year-old woman came to the emergency department with a complaint of severe holocranial headache and neck stiffness for 2 days. The patient was alert and well oriented to time, place, and person on presentation with stable vital signs. Physical examination revealed mild to moderate neck stiffness, no neurological deficit, and negative Kernig/Brudzinski signs. She received intravenous (IV) fluid, magnesium, metoclopramide,

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Address for correspondence:
ozair_91393@hotmail.com

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and ketorolac in the emergency department and her headache subsided. After 12 hours, she became febrile and hypotensive and it was suspected that she has developed acute adrenal insufficiency. She was given IV hydrocortisone 100 mg immediately and fluid boluses after which she was admitted to the inpatient neurology service. She underwent imaging studies including computerized tomographic angiography of the head and neck and magnetic resonance imaging of the brain which ruled out any acute or chronic intracranial pathology. During hospitalization, the patient again became febrile and hypotensive, prompting an infectious disease consultation and evaluation. Blood and urine cultures revealed no pathogen growth. Lumbar puncture (LP) done under fluoroscopic guidance yielded CSF with RBCs: 42/mm^3 (reference range, <1/mm^3), WBCs: 365 cells/µL (59% monocytes, 41% polymorphic neutrophils) (reference range, ≤5 cells/µL), glucose: 48 mg/dL (reference range, 45-80 mg/dL), and protein: 74 mg/dL (reference range, 15-45 mg/dL). The opening pressure was normal (reference range, 8-15 mmHg). Gram stain of the CSF also yielded no growth of the organism. Bacterial and viral cultures both came out to be negative. The patient was examined by the Ear Nose and Throat (ENT) department of the hospital. The ENT exam revealed a normal external nose and anterior nares.

However, when the patient was asked to lean forward, clear fluid appeared at her nares. Upon further data gathering, the patient revealed that he was diagnosed with pituitary adenoma in 1994 for which transsphenoidal removal was done. She just had the discharge card with her according to which the surgery was performed by a consultant neurosurgeon under general anesthesia. A horizontal sublabial (under the upper lip) incision was made and Sella was approached through the sphenoid sinus. Under the endoscopic view, the tumor was removed and it was made sure that there was no residual tumor. A fascial autologous graft from the right femur was used to close the sellar defect made during the surgery and connected to the remaining nasal bony septum. The cartilaginous septum and nasal mucosa that was retracted was brought to the normal position and the cavity was filled with gauze (soaked in the ointment) for three days to heal the mucosa. The buccal cavity was then sutured at the incision site. According to the card, there was no postoperative complication. However, the patient complains that since the surgery, she had to postnasal drip but since it never bothered her, she never asked for medical advice.

Rigid nasal endoscopy was performed immediately and a large anterior to posterior septal perforation with clear fluid lying within the sphenoid sinus, that appeared to be pulsating, was found. The fluid tested positive for Beta-2 transferrin, identifying it as CSF. According to the ENT specialist, the source was most likely the transsphenoidal hypophysectomy incision done 20 years ago.

Hence, the diagnosis of aseptic meningitis was made. The patient underwent two endonasal endoscopic repairs (with an anterior to posterior nasal septal perforation visualized on endoscopy to be corrected using endoscopic nasal approach) but the CSF leak persisted. Eventually, ventriculoperitoneal (VP) shunt placement by neurosurgery was required to stem the leak. A fixed differential pressure valve was used in the procedure. The patient reported having no rhinorrhea or postnasal drip after the procedure was complete.

Figure 1 shows the patient's sphenoid sinus obtained after rigid nasal endoscopy. Here we can visualize the sphenoid sinus through the septal perforation along with some traces of a clear fluid that was initially suspected to be CSF, which was later confirmed with the Beta 2 transferrin test to be true. Informed consent was obtained from the patient both for the procedure and the possible publication after explaining all the management steps throughout the course.

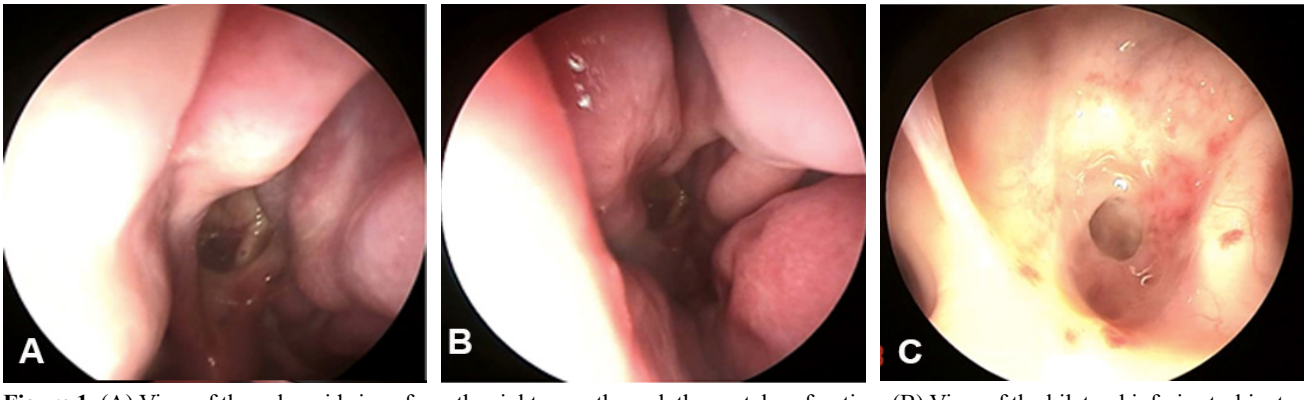

Figure 1. (A) View of the sphenoid sinus from the right nare, through the septal perforation, (B) View of the bilateral inferior turbinates through the perforation, (C) View of the sphenoid sinus, with clear fluid and minimal pooling.

Post VP shunt the case was thoroughly investigated and followed up by the ENT team and the neurosurgeons as this was a new case to all of them. The fistula closed on itself on day 8th post shunt and all the blood tests and observation showed that patient had no signs of infection. Moreover patient also didn't complain of any symptoms as she was told all the red flag signs and was educated to follow up if any occurred. The first follow-up was after a month then at the third month, a CT scan was done to ensure that everything is stable. Then the patient was followed up every six months.

Discussion

Aseptic meningitis from CSF leak after 20 years is an extremely rare complication, never reported in the literature. The incidence of postoperative CSF leaks from TSS ranges from 0.5%-15% [7]. Leaks are more common after revision surgery rather than primary surgery with intraoperative CSF leak statistically being the most significant risk factor [8], requiring multidisciplinary management. In the setting of meningitis and post-infectious hydrocephalus, a VP shunt may be necessary [9]. All these risks and complications are usually seen in the immediate postoperative period ranging from few days to few months [10]. Unlike, in our case, in which the patient presented 20 years postoperatively.

The laboratory workup of meningitis includes baseline studies, CSF analysis, culture, and sometimes imaging as well. In contrast to bacterial and viral meningitis, CSF findings in aseptic meningitis reveal normal glucose level, normal or slightly increased protein, negative gram stain/culture, and CSF cell count of 100-1000 cells/mm3 (usually with a lymphocytic or monocytic predominance). These features are consistent with a study in which 70 percent of their patients developed an "aseptic meningeal syndrome". Examination of their CSF revealed leukocytosis, elevated protein, low glucose, and sterile cultures [11]. In contrast to other studies, it is suggested that polymorphonuclear neutrophils (PMNs) can be the most predominant cell in early aseptic meningitis followed by shifts to mononuclear cells within 24 hours. Another review has reported that CSF glucose is remarkably decreased in patients with bacterial meningitis, while CSF and serum white blood cells are notably higher [12]. These inconsistent results may lead to uncertainty in the diagnosis and treatment of meningitis.

It is important that along with laboratory findings we need to do a complete patient's assessment and physical exam to devise the best treatment plan. Van de Beek et al. reported that bacterial or infectious meningitis may reveal the sterile or negative culture, especially when empiric antibiotics are started before acquiring culture samples [13]. In bacterial meningitis, gram stain is only 56 to 86% sensitive [14]. Therefore, clinical assessment is crucial for diagnosis and appropriate management.

Sakushima et al. described CSF lactate, as a reliable new biomarker in the early differentiation of bacterial and aseptic meningitis, with one meta-analysis describing sensitivity and specificity of 93 and 96% respectively. The recommended clinical value for the CSF lactate level is 35 mg/dl [7]. Therefore, patients with low-grade fever, normal CSF glucose, low CSF lactate level, and serum leukocytosis are suspected most probably of having aseptic meningitis. However, bacterial meningitis shows CSF pleocytosis or positive culture of the CSF or blood. Meningitis after TSS is usually caused by gram-negative microorganisms and is associated with hypoglycorrhachia, pleocytosis, and hyperproteinemia in CSF analysis [15].

In terms of treatment of aseptic meningitis, conservative management with steroids is preferable instead of prolonged courses of antibiotics or further surgical intervention [16]. However, due to initial similar symptoms of aseptic meningitis and bacterial meningitis, The British Society of Chemotherapy and other authors have suggested treatment with empirical antibiotics for post-surgical meningitis, but treatment withdrawal must be done when culture turns negative in 48 to 72 hours [16]. Once the exact leakage site is identified, surgical repair should not be delayed. Primary reconstruction can be done using autologous grafts (like fascia lata) or pedicled nasoseptal flaps [17]. In our patient, we used the autologous graft as this is the most common practice in the region. Due to a lack of sophisticated and advanced instruments, the endoscopic approach failed. Some of the main reasons for the failure of the endoscopic approach are residual air cells, adhesions in the ethmoid area, human error, or unavailability of appropriate equipment [18].

Our patient had a VP shunt placement, by neurosurgery after which there was no reported rhinorrhea or postnasal drip and aseptic meningitis resolved after antibiotic treatment.

Conclusion

Although the development of meningitis from cerebrospinal fluid leakage after TSS is a well-documented complication, a delayed presentation of almost two decades such as in the above case is very unique in itself. Further research and studies need to be carried out to have a much more clearer perspective about the underlying pathology and cause responsible for the delayed presentation of this life-threatening complication so that we will be able to manage such incidents in the future in a much better way.

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