

# Analysis of the Bacterial Flora in the Nasal Cavity and the Sphenoid Sinus Mucosa in Patients Operated on with an Endoscopic Endonasal Transsphenoidal Approach

Shunsuke SHIBAO,<sup>1</sup> Masahiro TODA,<sup>1</sup> Toshiki TOMITA,<sup>2</sup> Kaoru OGAWA,<sup>2</sup> and Kazunari YOSHIDA<sup>1</sup>

Departments of <sup>1</sup>Neurosurgery, <sup>2</sup>Otorhinolaryngology, Head and Neck Surgery, Keio University Graduate School of Medicine, Tokyo

## Abstract

The aim of this study was to analyze the bacterial flora in the nasal cavity and sphenoid sinus and evaluate the sensitivity of these bacteria to antibiotics that can be used to prevent postoperative meningitis. Bacteria of the preoperative nasal cavity and intraoperative sphenoid sinus mucosa were cultured and analyzed in 40 patients (20 men and 20 women; mean age, 52.2 years) who underwent endoscopic transsphenoidal surgery. The sensitivity of these bacteria to cephalosporin, a representative prophylactic antibiotic, was examined. *Staphylococcus epidermidis* was the most frequently detected species in both spaces; 24 (38.7%) of 62 isolates in the nasal cavity and 26 (37.1%) of 70 isolates in the sphenoid sinus. In contrast, *Corynebacterium* species were found mainly in the nasal cavity, and anaerobic bacteria were found only in the sphenoid sinus. Bacteria that were resistant to cephalosporin were found in the nasal cavity in 3.2% of patients and in the sphenoid sinus in 20% of patients. In conclusion, the composition of bacterial flora, including bacteria that are resistant to prophylactic antibiotics, differs between the nasal cavity and the sphenoid sinus.

Key words: endoscopic endonasal transsphenoidal approach, bacterial flora, nasal cavity, sphenoid sinus, postoperative meningitis

## Introduction

The endoscopic endonasal transsphenoidal approach (EEA) has recently become the preferred surgical technique for lesions in the sellar and clival regions, including pituitary adenomas,<sup>1)</sup> Rathke's cysts,<sup>2)</sup> craniopharyngiomas,<sup>3)</sup> and chordomas.<sup>4)</sup> Although EEA is safe with low morbidity and mortality, it is a "clean-contaminated" procedure. Therefore, steps must be taken to prevent postoperative infections such as meningitis and sinusitis. However, the protocol for antibiotic prophylaxis has not been clarified in the context of EEA. In fact, only a few papers on this topic have been published in recent years, and they largely refer to patients undergoing conventional transsphenoidal surgery.<sup>5–7)</sup> According to these reports, the rates of meningitis and sinusitis after transsphenoidal surgery range from 0.5% to 14% and from 3.6% to 9.6%, respectively. Postoperative

meningitis is one of the most critical complications of EEA, especially in procedures involving the subdural space. Orlando et al. retrospectively evaluated the rate of postsurgical infection in 170 patients who underwent EEA and showed that a third-generation cephalosporin was an appropriate prophylactic antibiotic.<sup>8)</sup> In this study, we analyzed the bacterial flora of the preoperative nasal cavity and the intraoperative sphenoid sinus mucosa in patients undergoing EEA, and we discuss the use of prophylactic antibiotics in such patients.

## Materials and Methods

The research ethics board of Keio University Hospital approved the study without the need to obtain written informed consent from patients.

Bacterial cultures of the preoperative nasal cavity and the intraoperative sphenoid sinus mucosa were established for 40 patients (20 men and 20 women; mean age, 52.2 years) who underwent EEA between

May 2011 and May 2013 in the Department of Neurosurgery, Keio University Graduate School of Medicine. Nasal swabs were obtained before surgery, and mucosa of the sphenoid sinus was taken for culture after opening the anterior wall of the sphenoid sinus during surgery. The composition of the bacterial flora and the rates of sensitivity to cephalosporins were compared between the anatomical spaces. The most common reason for a transsphenoidal operation was a pituitary adenoma (72.5%) followed by a Rathke's cyst (10%), chordoma (7.5%), meningioma (5%), cholesterol granuloma (2.5%), and giant cell tumor (2.5%) (Table 1). Twelve patients (30%) developed major intraoperative cerebrospinal fluid (CSF) leakage, and two patients (5%) developed postoperative CSF leakage that required reoperation. A subdural procedure was performed in two patients (5%). Postoperative meningitis or sinusitis did not occur in any patient in this series. Administration of antibiotics was based on the amount of intraoperative CSF leakage; in cases with a large amount of CSF leakage (subdural procedure and wide fenestration of the diaphragm, in which subdural structures were visible), a third-generation cephalosporin was administered for prophylaxis of postoperative meningitis, and in cases with little or no CSF leakage (minor fenestration of the diaphragm, in which subdural structures were not visible), a first- or second-generation cephalosporin was selected. Antibiotics were administered for at least 2 days after operation; the administration of antibiotics was extended up to 1 week depending on the amount of intraoperative CSF leakage. Intensive irrigation with saline was performed in all surgeries.

**Table 1 Clinical features of 40 patients who underwent endoscopic transsphenoidal surgery**

Sex	
Male (n)	20
Female (n)	20
Age	
Average (y)	52.2
Range (y)	15–77
Disease	
Pituitary adenoma	29
Rathke's cyst	4
Chordoma	3
Meningioma	2
Cholesterol granuloma	1
Giant cell tumor	1
Total patients (n)	40

## Results

The species composition of the preoperative nasal cavity cultures and the intraoperative sphenoid sinus cultures is shown in Table 2. The most frequently detected species in both spaces was *Staphylococcus epidermidis*; 24 (38.7%) of 62 isolates in the nasal cavity and 26 (37.1%) of 70 isolates in the sphenoid sinus.

In the nasal cavity cultures, *Staphylococcus* and *Corynebacterium* species were found most frequently. Among the 62 isolates detected in nasal cavity cultures, two (3.2%) were resistant to cephalosporins (*S. epidermidis* and *Enterobacter aerogenes*). Three patients (7.5%) had no bacteria in the nasal cavity.

In the sphenoid sinus cultures, anaerobic bacteria were found in addition to *Staphylococcus* species. More isolates were resistant to cephalosporins in the sphenoid sinus cultures (20%) than in the nasal cavity cultures (3.2%). Furthermore, the percentage of isolates in the sphenoid sinus cultures that were resistant to first-generation cephalosporins (20%) was higher than that of those resistant to third-generation cephalosporins (5.7%). Two out of 40 patients (5%) had no bacteria in the sphenoid sinus. Three of 12 cases with intraoperative CSF leakage had *S. epidermidis* that was resistant to cephalosporins. An additional 13 cases had minor CSF leakage.

In six patients, the species composition of the nasal cavity culture was identical to that of the sphenoid sinus culture. In all six cases, the species composition included *S. epidermidis*. Fifteen patients had no species in common between the nasal cavity and sphenoid sinus cultures. Among the remaining 19 patients, 17 had cultures that contained *Staphylococcus* species, and in 16 cases these species included *S. epidermidis* (Table 3).

## Discussion

EEA should be considered a procedure that exposes at-risk patients to infectious complications including meningitis and sinusitis. The risk of meningitis is reported to be associated with the incidence of CSF leakage and its incidence ranges from 0.5% to 14%, as reported in the literature.<sup>6,9–14)</sup> On the other hand, the rate of the sinusitis ranges from 3.6% to 9.6%.<sup>7)</sup> Prophylaxis of postoperative infections is important, and we present the first report of the species composition and antibiotic sensitivity of bacteria in the endonasal transsphenoidal corridor.

Preoperative nasal cavity culture is meaningless for prediction of the bacteria of the sphenoid sinus. This study showed that the bacterial species composition often differed between the nasal cavity and the

**Table 2** Distribution of microorganisms in cultures of the preoperative nasal cavity and the intraoperative sphenoid sinus

Microorganisms	Nasal cavity culture			Sphenoid sinus culture		
	Total number (n)	First-generation cephalosporin resistance (n)	Third-generation cephalosporin resistance (n)	Total number (n)	First-generation cephalosporin resistance (n)	Third-generation cephalosporin resistance (n)
<i>Staphylococcus epidermidis</i>	24	1	1	26	12	4
<i>S. aureus</i>	10	0	0	3	0	0
<i>Staphylococcus</i> spp.	4	0	0	3	0	0
<i>S. lugdunensis</i>	0	0	0	1	1	0
<i>Gamma streptococcus</i>	0	0	0	2	0	0
<i>Alpha-streptococcus</i>	3	0	0	3	0	0
<i>Aerobic G-pos. cocci</i> ,	5	0	0	0	0	0
<i>Propionibacterium acnes</i>	0	0	0	12	0	0
<i>Propionibacterium</i> spp.	0	0	0	12	0	0
<i>Anaerobic G-pos. cocci</i>	0	0	0	2	0	0
<i>Anaerobic G-pos. rods</i>	0	0	0	1	0	0
<i>Corynebacterium</i> spp.	12	0	0	3	0	0
<i>Klebsiella oxytoca</i>	1	0	0	1	0	0
<i>Enterobacteraero</i> genes	1	1	0	1	1	0
<i>Haemophilus influenzae</i>	1	0	0	0	0	0
<i>Moraxella</i> spp.	1	0	0	0	0	0
<i>Branhamella catarrhalis</i>	2	0	0	0	0	0
Total	62	2 (3.2%)	1 (1.6%)	70	14 (20%)	4 (5.7%)

sphenoid sinus. This suggests that prophylactic use of antibiotics may be problematic when based on results from preoperative nasal cavity cultures. The environments of the two anatomical spaces differ. Whereas drug-resistant bacteria readily drain from the open nasal cavity, resistant bacteria are easily stored in the nearly closed sphenoid sinus. Therefore, if infections such as meningitis persist despite the administration of third-generation cephalosporins, results from intraoperative sphenoid sinus cultures need to be considered when selecting antibiotics.

The choice of prophylactic antibiotic usually depends on the pharmacokinetic profile of the drug and the local bacterial flora.<sup>8)</sup> Cephalosporins tend to be administered to prevent postoperative meningitis.<sup>15)</sup> Orland et al. described the usefulness of a third-generation cephalosporin as a prophylactic antibiotic.<sup>8)</sup> Third-generation cephalosporins reach the levels in the CSF that are sufficient to inhibit *Staphylococcus* species and gram-negative bacilli,<sup>16)</sup> and they are useful for reducing the risk of meningitis. In this study, bacteria that were sensitive to cephalosporins represented 96.8% of the isolates in the nasal cavity and 80% of those in the sphenoid sinus. Furthermore, in the sphenoid

sinus, the percentage of isolates that were resistant to first-generation cephalosporins (20%) was higher than the percentage of isolates that were resistant to third-generation cephalosporins (5.7%). Considering these facts, third-generation cephalosporins should be recommended for preventing postoperative infections, especially when subdural procedures are performed. In fact, Orland et al. applied a prophylactic antibiotic regimen including a third-generation cephalosporin and found low incidences of meningitis (0.58%) and sinusitis (1.17%).<sup>8)</sup> Despite the existence of bacteria resistant to third-generation cephalosporins, no meningitis occurred in our series. We believe that intensive irrigation with saline, in addition to postoperative antibiotics, may be effective for preventing postoperative meningitis.<sup>17)</sup> Considering the prevalence of resistant bacteria, intraoperative washing of the nasal cavity and the sphenoid sinus before cutting of the dura is recommended.

## Conclusion

Bacterial flora differs between the nasal cavity and the sphenoid sinus. Therefore, the use of preoperative

**Table 3 Contents of bacteria in each case**

Case No.	Nasal cavity	Sphenoid sinus
1	<i>Staphylococcus epidermidis</i>	<i>S. epidermidis</i>
2	<i>S. epidermidis</i>	<i>S. epidermidis</i>
3	<i>S. epidermidis</i>	<i>S. epidermidis</i> *
4	<i>S. epidermidis</i>	<i>S. epidermidis</i> * **
5	<i>S. epidermidis</i> * **	<i>S. epidermidis</i> * **
6	<i>S. epidermidis</i> , <i>Alpha-streptococcus</i> , <i>K. oxytoca</i>	<i>S. epidermidis</i> , <i>Alpha-streptococcus</i> , <i>K. oxytoca</i>
7	<i>S. epidermidis</i>	<i>S. epidermidis</i> *, <i>Propionibacterium</i> spp.
8	<i>S. epidermidis</i>	<i>S. epidermidis</i> *, <i>Propionibacterium</i> spp.
9	<i>S. epidermidis</i>	<i>S. epidermidis</i> , <i>Propionibacterium</i> spp.
10	<i>S. epidermidis</i>	<i>S. epidermidis</i> *, <i>P. acnes</i> , <i>Propionibacterium</i> spp., <i>Alpha-hemo. streptococcus</i>
11	<i>S. epidermidis</i>	<i>S. epidermidis</i> , <i>Prevotella</i> spp.
12	<i>S. epidermidis</i> , <i>S. aureus</i>	<i>S. epidermidis</i>
13	<i>S. epidermidis</i> , <i>S. aureus</i>	<i>S. epidermidis</i> , <i>Anaerobic G-pos. rods</i> , <i>Propionibacterium</i> spp.
14	<i>S. epidermidis</i> , <i>S. aureus</i> , <i>Haemophilus influenzae</i> , <i>Moraxella</i> spp.	<i>S. epidermidis</i> , <i>S. aureus</i> , <i>P. acnes</i> , <i>Alpha-hemo. streptococcus</i> , <i>Gamma-hemo. streptococcus</i>
15	<i>S. epidermidis</i> , <i>Corynebacterium</i> spp.	<i>S. epidermidis</i> , <i>Propionibacterium</i> spp.
16	<i>S. epidermidis</i> , <i>Corynebacterium</i> spp.	<i>S. epidermidis</i> *, <i>Propionibacterium</i> spp.
17	<i>S. epidermidis</i> , <i>Corynebacterium</i> spp.	<i>S. epidermidis</i> *, <i>Propionibacterium</i> spp., <i>Gamma-hemo streptococcus</i>
18	<i>Staphylococcus</i> spp.	<i>S. epidermidis</i> , <i>P. acnes</i>
19	<i>Staphylococcus</i> spp.	<i>S. epidermidis</i> , <i>P. acnes</i>
20	<i>Staphylococcus</i> spp., <i>S. aureus</i> , <i>Corynebacterium</i> spp., <i>Aerobic G-pos. cocci</i> , <i>B. catarrhalis</i>	<i>S. epidermidis</i> , <i>Propionibacterium</i> spp.
21	<i>S. epidermidis</i> , <i>S. aureus</i> , <i>Corynebacterium</i> spp.	<i>Staphylococcus</i> spp., <i>Propionibacterium</i> spp.
22	<i>S. epidermidis</i> , <i>Corynebacterium</i> spp.	<i>Staphylococcus</i> spp., <i>Enterobacter aerogenes</i> *, <i>P. acnes</i>
23	<i>Staphylococcus</i> spp., <i>S. epidermidis</i>	<i>S. aureus</i> , <i>S. lugdunensis</i> *
24	<i>S. epidermidis</i> , <i>Corynebacterium</i> spp., <i>Aerobic G-pos. cocci</i>	<i>Corynebacterium</i> spp., <i>P. acnes</i>
25	<i>Aerobic G-pos. cocci</i> , <i>Alpha-hemo. streptococcus</i>	<i>S. epidermidis</i> * **, <i>Aerobic G-pos. cocci</i>
26	<i>Staphylococcus</i> spp., <i>S. aureus</i> , <i>Alpha-hemo streptococcus</i>	<i>Anaerobic G-pos. rods</i> , <i>Anaerobic G-pos. cocci</i>
27	<i>Staphylococcus</i> spp., <i>enterobacteraerogenes</i> *	Negative
28	<i>S. epidermidis</i> , <i>S. aureus</i> , <i>Corynebacterium</i> spp.	<i>Propionibacterium</i> spp.
29	<i>S. epidermidis</i> , <i>S. aureus</i>	<i>Propionibacterium</i> spp., <i>Corynebacterium</i> spp.
30	<i>S. epidermidis</i> , <i>Corynebacterium</i> spp., <i>B. catarrhalis</i>	<i>P. acnes</i>
31	<i>S. aureus</i>	<i>S. epidermidis</i>
32	<i>S. aureus</i> , <i>Aerobic G-pos. cocci</i>	<i>Corynebacterium</i> spp.
33	<i>Corynebacterium</i> spp.	<i>Staphylococcus</i> spp., <i>Propionibacterium</i> spp.
34	<i>Corynebacterium</i> spp.	<i>S. epidermidis</i> * **
35	<i>Corynebacterium</i> spp., <i>Aerobic G-pos, cocci</i> , <i>B. catarrhalis</i>	Negative
36	Negative	<i>S. epidermidis</i>
37	Negative	<i>S. epidermidis</i> *, <i>Propionibacterium</i> spp.
38	Negative	<i>S. epidermidis</i> *, <i>P. acnes</i>
39	Negative	<i>S. aureus</i> , <i>P. acnes</i>
40	Negative	<i>P. acnes</i>

1–6: completely matched, 7–25: partially matched, 25–40: not matched, \*: resistant to first-generation cephalosporin, \*\*: resistant to third-generation cephalosporin.

nasal cavity cultures as the basis for selecting the correct antibiotic for prevention of meningitis is problematic. Third-generation cephalosporins are a reasonable choice for preventing meningitis after EEA. Intraoperative irrigation should be performed because of the existence of third-generation cephalosporin-resistant bacteria in the sphenoid sinus.

### Conflicts of Interest Disclosure

The authors have no personal or institutional financial interest in any of the drugs, materials, or devices described in this article.

### References

- 1) Laws E, Jane JA Jr: Pituitary tumors—long-term outcomes and expectations. *Clin Neurosurg* 48: 306–319, 2001
- 2) Aho C, Liu C, Zelman V: Surgical outcomes in 118 patients with Rathke cleft cysts. *J Neurosurg* 102(2): 189–193, 2005
- 3) Jane JA, Kiehna E, Payne SC, Early SV, Laws ER Jr: Early outcomes of endoscopic transsphenoidal surgery for adult craniopharyngiomas. *Neurosurg Focus* 28(4): E9, 2010
- 4) Carrabba G, Dehdashti AR, Gentili F: Surgery for clival lesions: open resection versus the expanded endoscopic endonasal approach. *Neurosurg Focus* 25(6): E7, 2008
- 5) van Aken MO, de Marie S, van der Lely AJ, Singh R, van den Berge JH, Poublon RM, Fokkens WJ, Lamberts SW, de Herder WW: Risk factors for meningitis after transsphenoidal surgery. *Clin Infect Dis* 25(4): 852–856, 1997
- 6) van Aken MO, Feelders RA, de Marie S, van de Berge JH, Dallenga AH, Delwel EJ, Poublon RM, Romijn JA, van der Lely AJ, Lamberts SW, de Herder WW: Cerebrospinal fluid leakage during transsphenoidal surgery: postoperative external lumbar drainage reduces the risk for meningitis. *Pituitary* 7(2): 89–93, 2004
- 7) Ciric I, Ragin A, Baumgartner C, Pierce D: Complications of transsphenoidal surgery: results of a national survey, review of the literature, and personal experience. *Neurosurgery* 40: 225–236; discussion 236–237, 1997
- 8) Orlando R, Cappabianca P, Tosone G, Esposito F, Piazza M, de Divitiis E: Retrospective analysis of a new antibiotic chemoprophylaxis regimen in 170 patients undergoing endoscopic endonasal transsphenoidal surgery. *Surg Neurol* 68(2): 145–148; discussion 148, 2007
- 9) Cappabianca P, Cavallo L: Surgical complications associated with the endoscopic endonasal transsphenoidal approach for pituitary adenomas. *J Neurosurg* 97(2): 293–298, 2002
- 10) Ciric I, Ragin A, Baumgartner C, Pierce D: Complications of transsphenoidal surgery: results of a national survey, review of the literature, and personal experience. *Neurosurgery* 40(2): 225–236; discussion 236–237, 1997
- 11) Dumont AS, Nemergut EC, Jane JA, Laws ER: Postoperative care following pituitary surgery. *J Intensive Care Med* 20(3): 127–140, 2005
- 12) Dusick J, Esposito F, Kelly D: The extended direct endonasal transsphenoidal approach for nonadenomatous suprasellar tumors. *J Neurosurg* 102(5): 832–841, 2005
- 13) Gaillard T, Gilsbach J: Intra-operative antibiotic prophylaxis in neurosurgery. A prospective, randomized, controlled study on cefotiam. *Acta Neurochir (Wien)* 113(3–4): 103–109, 1991
- 14) Kaptain GJ, Vincent DA, Sheehan JP, Laws ER: Transsphenoidal approaches for the extracapsular resection of midline suprasellar and anterior cranial base lesions. *Neurosurgery* 62(6 Suppl 3): 1264–1271, 2008
- 15) Little AS, White WL: Prophylactic antibiotic trends in transsphenoidal surgery for pituitary lesions. *Pituitary* 14(2): 99–104, 2011
- 16) Kernodle D, Kaiser A: Postoperative infections and antimicrobial prophylaxis. In Gerald L. Mandell, John E. Bennett, Raphael Dolin (eds). *Principles and Practice of Infectious Diseases, 4th Edition*. New York, Churchill Livingstone Inc., 1995, pp 2742–2756
- 17) Mori H, Kobara H, Rafiq K, Nishiyama N, Fujihara S, Oryu M, Masaki T: Effects of gastric irrigation on bacterial counts before endoscopic submucosal dissection: a randomized case control prospective study. *PLoS One* 8: e65377, 2013

---

Address reprint requests to: Shunsuke Shibao, MD, Department of Neurosurgery, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan.  
e-mail: pochisuke616@mac.com