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Case Report

Pneumocephalus with Inverted Papilloma in the Frontoethmoidal Sinus: Case Report and Literature Review

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Here, we describe the unique case of a pneumocephalus originating from an inverted papilloma (IP) in the frontoethmoidal sinus. A 71-year-old man with diabetes presented with headaches and altered consciousness. Imaging revealed the pneumocephalus together with bone destruction in the left frontal sinus. He underwent simultaneous endoscopic endonasal and transcranial surgery using an ORBEYE exoscope. Pathological diagnosis of the tumor confirmed IP. Post-surgery, the pneumocephalus was significantly resolved and the squamous cell carcinoma antigen level, which had been elevated, decreased. This case underscores the importance of a multidisciplinary approach and innovative surgical methods in treating complex sinonasal pathologies.

Key words: pneumocephalus, inverted papilloma, frontoethmoidal sinus, endoscopic endonasal and transcranial surgery

Pneumocephalus is characterized by air accumulation within the epidural, subdural, or intraventricular regions of the brain. Neurotrauma is the predominant etiology, particularly when associated with skull base fractures, contributing to approximately 75% of pneumocephalus cases. Other contributing factors include neoplasms, infectious agents, and events resulting from medical interventions such as cranial, spinal, or lumbar procedures [1].

Inverted papilloma (IP) is a benign lesion with a prevalence of up to 4% among all sinonasal tumors; however, invasive growth and varying malignancy tendencies have been reported [2]. These tumors tend to destroy bone and invade adjacent structures such as the orbit and central nervous system, even without malignancy [3]. To the best of our knowledge, no other cases of pneumocephalus attributable to sinonasal IP have been documented. Herein, we present a unique case of pneumocephalus resulting from IP of the frontoethmoidal sinus and its successful treatment.

Case Report

A 71-year-old male patient with a history of diabetes mellitus was admitted to a nearby hospital with headaches and impaired consciousness. At age 63, he had developed a subarachnoid hemorrhage due to a rup-

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tured anterior communicating artery aneurysm, which was treated by clipping and ventriculoperitoneal shunt placement. There was no history of head trauma in his medical records. Cranial computed tomography and contrast-enhanced magnetic resonance imaging revealed a pneumocephalus — a discernible soft-tissue shadow spanning from the left frontal sinus to the anterior ethmoidal sinus — and marked bone destruction of the posterior wall of the left frontal sinus (Fig. 1). No overt cerebrospinal fluid (CSF) leakage was observed. Serum squamous cell carcinoma antigen (SCCA), beta-D-glucan, and C-reactive protein levels were 3.97 ng/ml (normal range, 0-2 ng/ml), 8 pg/ml (< 11 pg/ml), and 5.25 mg/dl (< 0.3 mg/dl), respectively. A provisional diagnosis of tumor or infection of the left frontoethmoidal sinus was made, and a dual therapeutic regimen of antibiotics and antifungals was initiated for potential meningitis, together with complete bed rest.

The patient was transferred to our hospital after five days of this conservative treatment, having failed to show improvement in his pneumocephalus. It was then that we determined the need for a definitive surgical repair. The patient underwent combined and simultaneous endoscopic endonasal and transcranial surgery (EETS). The transcranial technique was performed using an Olympus ORBEYE exoscope with a 4K endoscopic camera system (Olympus VISERA ELITE III, Tokyo), facilitating an endonasal approach. Otolaryngologists performed the endoscopic endonasal procedure, including Draf type III. Simultaneously, neurosurgeons performed a bifrontal craniotomy and a coronal skin incision (Fig. 2), while plastic surgeons harvested an anterolateral thigh (ALT) flap.

After the craniotomy, the frontal sinus was opened to reveal abscesses and tumors. The posterior wall of the frontal sinus was destroyed, and the tumor and abscess were found attached to the dura. There was also a 4-cm × 4-cm defect in the attachment site of the dura. Fortunately, attachment of the tumor to the dural defect appeared to have prevented continuous CSF leakage. Intraoperative histodiagnosis of the tumor suggested benign papilloma. The neoplastic growth was completely excised, and the compromised left frontal lobe was carefully debrided. Following this, we used two perforators to elevate the ALT flap as a vascularized free adipofascial flap and divided it into two paddles. One adipofascial flap was used for dural repair, and the other was used for filling the cranial base defects. Vascular anastomosis was performed on the superficial temporal artery and vein. Postoperatively, optimal viability of the free vascularized flap, absence of CSF leakage, and marked resolution of the pneumocephalus were confirmed on CT (Fig. 3).

In the resected dura mater, isolated areas of inflam-

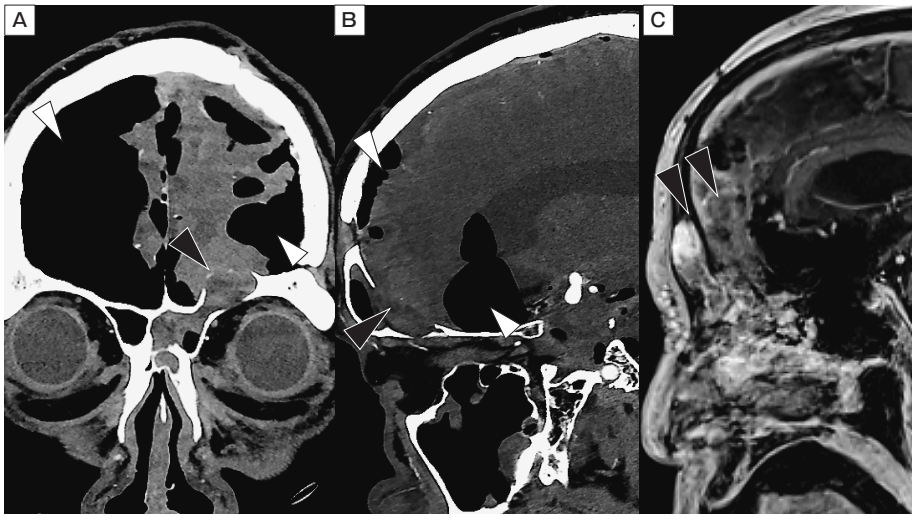

Fig. 1 Preoperative cranial computed tomography (CT) and contrast-enhanced magnetic resonance imaging (MRI) results. Bone window coronal (A) and sagittal (B) CT images reveal pneumocephalus (white arrowhead) and marked bone destruction of the left frontal sinus posterior wall with a soft tissue shadow spanning from the left frontal sinus to the anterior ethmoidal sinus (black arrowhead). (C) Contrast-enhanced MRI reveals a contrast effect over the frontal sinus and base of the frontal lobe, suggesting the presence of inflammation.

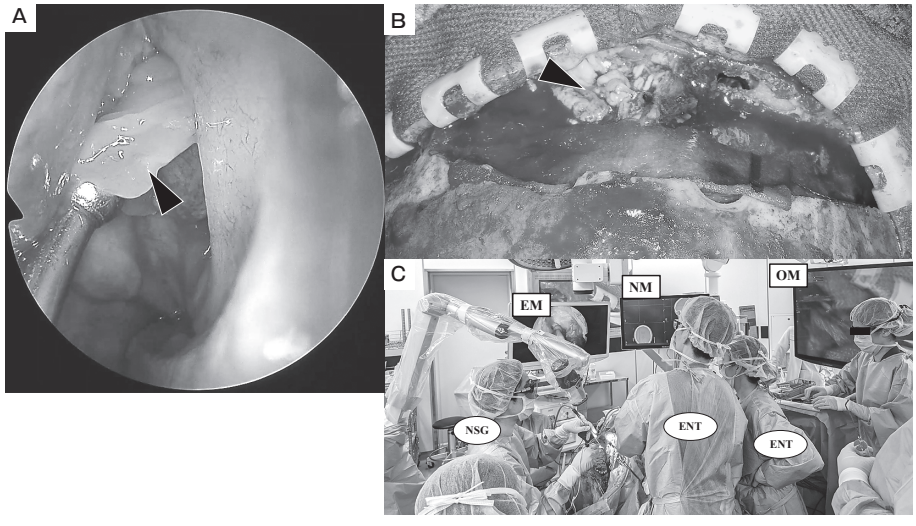

Fig. 2 Intraoperative photographs. (**A**) Endoscopic view showing a tumor in the anterior ethmoid sinus (black arrowhead). Intraoperative histodiagnosis suggested a papilloma devoid of malignant attributes. (**B**) Exoscopic view showing the left frontal sinus filled with tumor and pus (black arrowhead) and a dural defect consistent with a skull base bone defect. (**C**) A neurosurgeon (NSG) and team of otolaryngologists (ENTs) simultaneously performed transcranial and transnasal surgeries.
EM, endoscope monitor; OM, ORBEYE monitor; NM, navigation monitor.

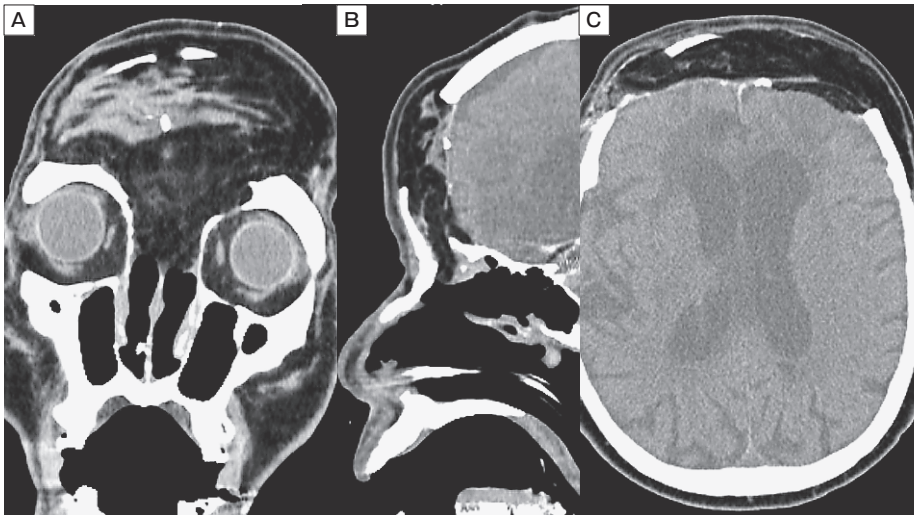

Fig. 3 Postoperative cranial computed tomography images showing frontal sinus cranialization using a free vascularized adipofascial flap, with a marked resolution of the pneumocephalus.

mation were found with no evidence of invasive malignant components (Fig. 4A). Histiocyte-dominant inflammatory cells were observed (Fig. 4B). Inverted and papillary growth of the tumor was found and it was accordingly diagnosed as IP (Fig. 4C). The stroma of the IP showed extensive and severe histiocyte-predominant inflammation (Fig. 4D). No bacteria or fungi were identified in IP by special stains such as Gram stain, periodic acid-Schiff stain, acid-fast stain, and Warthin–Starry stain. The postoperative serum SCCA level was 1.34 ng/ml, lower than the preoperative level. On postoperative day 23, the patient was transferred to the original hospital for rehabilitation, still unconscious owing to meningitis. Nevertheless, he gradually

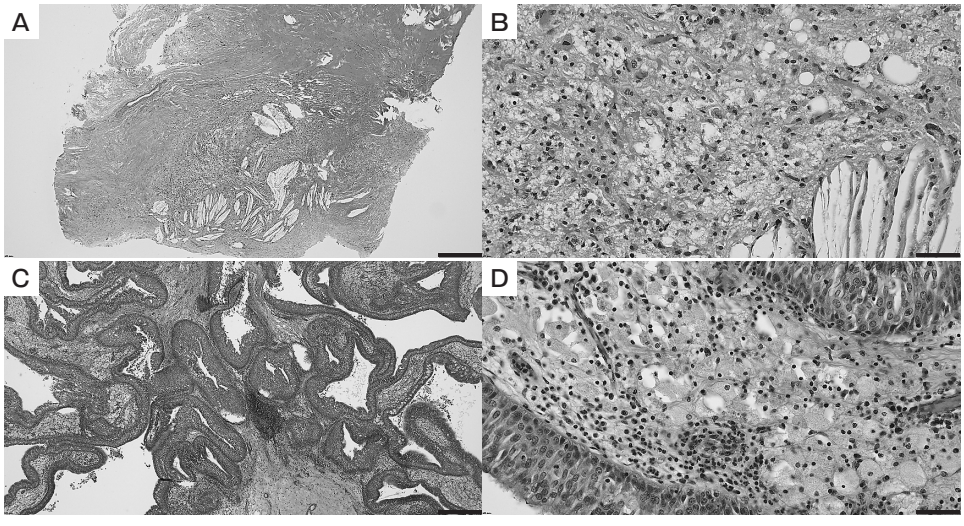

Fig. 4 Histological findings of the resected dura (A, B) and the tumor (C, D). Hematoxylin–eosin (HE) staining (A-D). Bars, 500 μm (A, C) and 50 μm (B, D). (A) Focal inflammation with cholesterol crystals was observed in parts of the dura. (B) Inflammatory cells such as histiocytes and lymphocytes were found, together with hemosiderin deposition. (C) The tumor showed inverted papillary growth. (D) The stroma of the tumor revealed prominent inflammatory cells, including histiocytes and neutrophils.

recovered over the next two months.

All procedures performed in this patient's treatment and its write-up were in accordance with the ethical standards of the Okayama University Hospital research committee (IRB # 2010026), which adheres to the 1964 Helsinki Declaration and its later amendments. Written informed consent to publish this study was obtained from the patient. All procedures were carried out with the adequate understanding and written consent of the participant.

Discussion

Pneumocephalus is frequently observed after skull base surgery for sinonasal tumors; however, spontaneous pneumocephalus due to sinonasal tumors is uncommon. Since 1992, 34 documented cases of sinonasal tumor accompanied by pneumocephalus have been reported, including those described herein. A review of these cases (Table 1) revealed a mean patient age of 44.4 years (range: 14-84 years) and more frequent manifestations in men (88.2%).

Sinus osteomas are the predominant tumor type involved in pneumocephalus (28 of 34 cases). Other associated pathologies have included squamous cell carcinoma, epidermoid tumor, ossifying fibroma, benign fibro-osseous lesion, and osteoma with osteoblastoma-like histology; to the best of our knowledge, this case may be the first reported pneumocephalus case due to IP of the frontal sinus. In all patients, the tumor has been located near the skull base, sometimes with intracranial invasion. Among the 34 cases, the primary extracranial sites of the tumor were the frontal sinus in 10 cases, the ethmoid sinus in 10 cases, and the frontoethmoidal sinus in 8 cases. In previous studies, frontal craniotomy was the most frequent surgical intervention although transnasal endoscopic resection was performed in some patients.

Two central theories on the mechanism of nontraumatic pneumocephalus that are commonly postulated are the "inverted bottle" and "ball valve" mechanisms [4, 5]. The former implies that CSF drainage reduces intracranial pressure, allowing air to flow through the compromised dura. The latter, which is potentially more applicable to our patient, emphasizes a "ball valve" movement arising from the mass lesion breaching the subfrontal dura. Actions that increase extracranial pressure, such as sneezing, prompt brief air movement into the intracranial space. Once this amplified intranasal pressure reverts to its normal level, superior intracranial pressure is reinstated, causing the mass lesion to function as a sealing valve, closing the dural flaw and retaining the introduced air [5]. Hence, the rapid onset or worsening of symptoms has often been

Table 1 Summary of literature on sinonasal tumors with pneumocephalus

Authors	Year	Age (years), Sex	Pathology	Extracranial location of tumor	Surgical approach	After-effects
This study	2023	71, M	Inverted papilloma	Frontoethmoidal sinus	Craniotomy, transnasal resection	Persistent unconsciousness from meningitis
Takahashi et al.	1992	49, M	SCC	Maxillary sinus and sphenoid bone invasion	(−)	Death
Kinsley and Dougherty	1993	37, M	Epidermoid tumor	Ethmoid sinus	N/A	None
Holness and Attia	1994	62, M	Osteoma	Frontoethmoidal sinus	Craniotomy	None
Rappaport and Attia	1994	70, M	Osteoma	Frontal sinus	Craniotomy	None
Brunori et al.	1996	63, M	Osteoma	Frontal sinus	Craniotomy	None
Tobey et al.	1996	51, M	Ossifying fibroma	Ethmoid sinus, maxillary sinus, and orbit	N/A	None
Marras et al.	1998	40, M	Osteoma	Frontoethmoidal sinus	Craniotomy	None
Nakayama et al.	1998	35, F	Osteoma	Ethmoid sinus	Craniotomy	None
Saito et al.	1998	15, M	BFL	Paranasal sinuses and nasal cavity	Craniotomy	Anosmia, visual obscuration
Bramley and Ghosh	2001	63, M	Osteoma	Ethmoid sinus and orbit	Craniotomy, rhinotomy	Anosmia
Johnson and Tan	2002	62, M	Osteoma	Frontal sinus	Craniotomy	None
Gezici et al.	2004	29, F	Osteoma	Frontal, ethmoid, maxillary sinuses, and orbit	Craniotomy	None
Gezici et al.	2004	53, M	Osteoma	Frontal sinus	Craniotomy	None
Mahabir et al.	2004	68, M	Osteoma	Ethmoid sinus	Craniotomy	None
Onal et al.	2006	26, M	Osteoma	Frontal sinus	Craniotomy	None
Nelson et al.	2007	56, F	Osteoma	Ethmoid sinus	Craniotomy	None
Park et al.	2008	68, M	Osteoma	Ethmoid sinus	Craniotomy, transnasal resection	None
Kamide et al.	2009	57, M	Osteoma	Ethmoid sinus	Craniotomy	None
Ahmet et al.	2009	31, M	Osteoma	Ethmoid sinus	Craniotomy, transnasal resection	Anosmia
Guedes et al.	2011	33, M	Osteoma	Frontoethmoidal sinus	Transnasal resection	None
Wu et al.	2011	14, M	Osteoma	Ethmoid sinus	Craniotomy	None
Lehmer et al.	2012	30, M	Osteoma with OBLH	Frontal sinus	Craniotomy	None
Harasaki et al.	2013	61, F	Osteoma	Frontoethmoidal sinus	BHD, transnasal resection	None
Mikals et al.	2013	21, M	Osteoma	Frontoethmoidal sinus	Transnasal resection	None
Kendre et al.	2013	42, M	Osteoma	Frontal sinus	Craniotomy	None
Ruddick and Tomlin	2015	21, M	Osteoma	Ethmoid sinus and orbit	Transnasal and transorbital resection	None
Umredkar et al.	2017	22, M	Osteoma	Frontal sinus	N/A	None
Hackenbroch et al.	2017	24, M	Osteoma	Frontal sinus	BHD, tumor resection[a]	None
Brown and Vahidassr	2018	84, M	Osteoma	Ethmoid sinus	Craniotomy[a]	None
Licci et al.	2018	49, M	Osteoma	Frontoethmoidal sinus	Craniotomy	None
Iplikcioglu and Karabag	2019	24, M	Osteoma	Frontoethmoidal sinus	Craniotomy	None
Pathak et al.	2020	45, M	Osteoma	Ethmoid sinus	(−)	Death
Ali et al.	2021	35, M	Osteoma	Frontal sinus	Craniotomy	None

SCC, squamous cell carcinoma; BFL, benign fibro-osseous lesion; OBLH, osteoblastoma-like histology; BHD, burr-hole decompression of the pneumocephalus; M, male; F, female; N/A, not applicable; [a]Details were not described.

correlated with abrupt changes in extracranial pressure caused by activities such as sneezing, nose blowing, or exposure to pressure changes during flights [5-8]. In malignant tumors, radiation-induced osteonecrosis of the skull base is a plausible contributing factor to pneumocephalus [9]. Here, we postulate that the invasive characteristics of IP together with inflammation culminated in the skull-base bone and dura defects.

Our patient underwent combined simultaneous EETS using a high-definition three-dimensional exoscopic instrument, the ORBEYE. Various reports have detailed combined EETS application for the excision of anterior skull base malignancies [10-12]. Approaches that provide optimum maneuverability and a clear visual perspective are typically selected for tumor excision. The transcranial approach relies mainly on microscopic visualization. Simultaneous execution of the transcranial technique with microscopic guidance and an endoscopic endonasal procedure presents inherent complexities for otolaryngologists and neurosurgeons. This complexity arises from the large dimensions of the surgical microscope, which is positioned directly in the operative region. When the transcranial and nasal methodologies are performed consecutively, the total duration of surgery is often protracted [13]. The ORBEYE has attributes such as a depth of field and visual range that transcend those of conventional operative microscopes [14]. Moreover, using a compact exoscope during simultaneous EETS creates an additional spatial domain above the surgical site, enabling concurrent endoscope insertion [13]. This configuration ensures uninterrupted continuity of concomitant surgical protocols.

Following the decision to proceed with combined and simultaneous EETS, we considered various reconstruction options. While an anterior craniofacial resection could have been repaired using a pericranial flap, the feasibility of harvesting such a flap in this case was questionable due to the patient's past craniotomy. Additionally, considering the presence of infection, a more robust reconstruction was deemed necessary. Therefore, we opted for a vascularized adipofascial anterolateral thigh (ALT) free flap for reconstruction [15]. The versatility of an ALT and its potential to be divided into multiple sections made it an ideal choice for this complex reconstruction. In this case, we used two perforators to elevate the ALT flap as a vascularized free adipofascial flap and divided it into two paddles. One paddle was used for dural repair and the other for filling the cranial base defects. This approach not only allowed for a more robust and adaptable repair but also considered the potential aesthetic outcomes and the need for reliable separation of anatomical structures. Our case demonstrates the efficacy of using an ALT flap for cranial base reconstruction, especially in cases with a history of craniotomy and the presence of infection.

Here, the preoperative increased serum SCCA level reverted to the normal level following surgical intervention. As described in our previous study, serum SCCA concentrations tend to be elevated in individuals with sinonasal IP [16]. These levels are significantly reduced after surgical tumor excision, making this metric a potent tool for identifying recurrent IP. Although there was a significant reduction of the pneumocephalus, this patient will undergo periodic imaging and serum SCCA level evaluations to monitor for potential relapse. In light of the high recurrence rate and the potential for malignant transformation of IP, it is generally recommended that patients undergo regular follow-up visits with imaging studies, such as CT or MRI, for several years post-surgery [17, 18]. However, there is no established standard for the exact frequency of these follow-ups, including SCCA checks and imaging examinations. A specific follow-up schedule should be tailored by the treating physician based on the individual risk factors and clinical course of each patient. We have started the patient on every-six-month visits and plan to adjust as needed.

This is a unique case of pneumocephalus associated with IP in the frontoethmoidal sinus, and its specific conditions may make our methods and assumptions non-translatable to other cases. Pathological findings showed similarly severe inflammatory foci in the IP and the dura mater. While we inferred that the inflammation associated with IP caused the pneumocephalus, the causal relationship between IP and the development of pneumocephalus could not be conclusively established. Furthermore, the successful use of the ORBEYE exoscope and the monitoring of serum SCCA levels in this particular case provide promising strategies for treatment and postoperative monitoring. However, these findings are based on a single case; thus, generalizing the outcomes may not be appropriate without further accumulation of these extremely rare cases. These limitations underline the need for cautious interpretation of our findings and suggest areas for future

research. It is essential to further investigate the complex dynamics between sinonasal pathologies, like IP, and rare complications, such as pneumocephalus, to better understand their interactions and to develop more effective diagnostic and treatment strategies.

In conclusion, this case highlights the complex interplay between pneumocephalus and IP in the frontoethmoidal sinus. The successful outcome can be attributed to careful decision-making, multidisciplinary collaboration, and the application of advanced surgical techniques. The selection of EETS, enhanced by the use of the ORBEYE exoscope, proved crucial in managing this challenging case effectively. Additionally, the monitoring of serum SCCA levels has played a significant role in the postoperative period.

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