Case Report
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Metastatic Sinonasal Undifferentiated Carcinoma to the Temporal Bone: A Case Report and Literature Review

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Abstract

Introduction:

Sinonasal undifferentiated carcinoma (SNUC) is a rare malignancy of the nasal cavity and paranasal sinuses, with highly aggressive behaviour. Although a multimodal strategy is considered the standard treatment approach, recurrence remains common both locally and at distant metastatic sites. Temporal bone metastases represent a rare entity, with patients primarily manifesting otologic symptoms. Breast, lung, and prostate cancers are the most common primary malignancies associated with temporal bone metastases, whereas no cases originating from the nasal cavity or paranasal sinuses have previously been reported. Herein, we report a unique case of metastatic SNUC to the temporal bone, presented with facial nerve paralysis. A brief descriptive review of all cases of distant metastases in SNUC is also reported.

Case Report:

We report the case of a patient with SNUC who developed temporal bone recurrence three years after trimodal treatment (induction chemotherapy, surgery and adjuvant radiotherapy) performed with good oncological outcome. Moreover, we retrospectively reviewed our case series of patients surgically treated for sinonasal undifferentiated carcinoma from 2006 to 2023 and we also performed a search of the literature from January 1, 1980, to December 31, 2024.

Conclusion:

The incidence of recurrent metastasis from SNUC disease in patients treated surgically is variable. This case report represents the first case of SNUC metastasis on the temporal bone, highlighting the rare occurrence of a middle ear recurrence after multimodal treatment. Despite its rarity, temporal bone metastasis should be considered in oncological patients presenting with facial palsy or other persistent otologic symptoms.

Keywords: Sinonasal Undifferentiated Carcinoma, SNUC, Metastasis, Facial Nerve, Facial Paralysis, Temporal Bone, Mastoid

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Introduction

Sinonasal undifferentiated carcinoma (SNUC) is a rare and highly aggressive malignancy arising from the nasal cavity and paranasal sinuses, accounting for approximately 3–5% of all sinonasal cancers. Due to its tendency for extensive local invasion and early regional spread, SNUC is frequently diagnosed at an advanced stage, which contributes to its poor overall prognosis (1). There is currently no clear consensus regarding the optimal therapeutic management of SNUC. However, a multimodal treatment strategy is widely considered the standard approach. This typically includes a combination of chemotherapy, surgery, and radiotherapy, tailored according to the tumor characteristics and the patient's performance status. Despite aggressive treatment, the cumulative 5-year survival rate remains low, and recurrence is common, occurring both locoregionally and as distant metastases, most frequently involving the lungs, bones, brain and liver (2,3).

Temporal bone metastases (TBM) represent a rare clinical entity. Patients typically present with otologic symptoms, including facial nerve palsy and hearing loss, which are often initially misdiagnosed as benign conditions. According to a recent literature review by Jones et al. (4), a total of 255 cases of TBM originating from various primary tumors of different anatomical sites have been reported over the past century. The most common primary malignancies were breast, lung, and prostate cancers cases arising from the nasal cavity or paranasal sinuses were identified (4).

Herein, we report a unique case of SNUC metastasizing to the temporal bone, presenting with facial nerve paralysis and no evidence of locoregional disease recurrence at the primary sinonasal site. In addition, a brief descriptive review of previously reported cases of distant metastases in SNUC is provided.

Case Report

Twelve patients with sinonasal undifferentiated carcinoma (SNUC) were treated at our department between 2006 and 2023. In 2022, one of them developed a metastasis to the temporal bone. The metastatic lesion was successfully treated, and the patient remains under follow-up with no evidence of disease progression at 12 months. The patient provided informed consent for publication of the clinical case.

A 57-year-old man presented to our department with left-sided otalgia accompanied by facial droop, resulting in difficulty in smiling and closing his left eye. Otoscopic examination revealed a bulging and erythematous left tympanic membrane. Facial nerve paralysis (FNP) was graded V according to the House-Brackman (HB) grading system. Pure-tone audiometry demonstrated a moderately-severe mixed hearing loss in the left ear, predominantly affecting the higher frequencies, while speech audiometry showed a mildly increased speech reception threshold. Impedance audiometry revealed a type B tympanogram and absence of stapedial reflexes.

The patient's past medical history was notable for a SNUC diagnosed 4 years earlier. At that time, the tumor involved the right anterior and posterior ethmoid sinuses as well as the maxillary sinus, and it was staged as T3N0M0 according to the AJCC 8th edition staging system. He underwent a trimodality treatment consisting of induction chemotherapy, surgical resection and adjuvant radiotherapy. The chemotherapy regimen was three cycles of induction chemotherapy with docetaxel, cisplatin, and 5-fluorouracil (TPF scheme). This was followed by complete surgical resection with negative margins via a transnasal endoscopic bilateral craniectomy. Subsequently, hadrontherapy was administered to the primary tumor site and electively to the neck (bilateral levels I-III), consisting of an upfront 15 Gy carbon ion boost followed by 60 Gy of proton therapy.

At presentation, intravenous antibiotics and steroid therapy were administered; however, no clinical improvement was observed. A high-resolution temporal bone Computed Tomography (CT) scan demonstrated left mastoid opacification associated with bone erosion of the petrous apex and the anterior mastoid portion, with involvement of the Fallopian canal (Figure 1). Subsequent contrast-enhanced brain and maxillo-facial Magnetic Resonance Imaging (MRI) showed no evidence of tumor recurrence in the nasal or sinonasal regions. However, it confirmed the presence of heterogeneous enhancing tissue within the petrous bone, with extension along the tympanic and labyrinthine segments of the

left facial nerve, the geniculate ganglion region, and the proximal portion of the greater petrosal nerve (Figure 2).

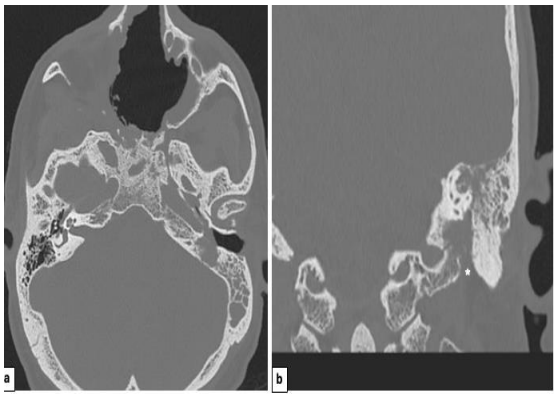

Fig 1. High-resolution temporal bone CT scan showing left mastoid opacification with bone erosion of the petrous apex and the anterior portion of the mastoid (a, axial view), with the involvement of the Fallopian canal (b, coronal view, asterisk).

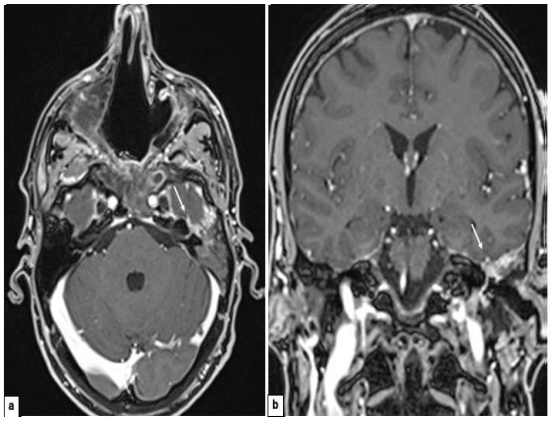

Fig 2. Brain and maxillo-facial MRI showing the absence of tumor relapse in the sinonasal compartment and confirming the presence of contrast-enhanced tissue within the petrous bone, involving the tympanic and labyrinthine segment of the left facial nerve, the geniculate ganglion region, and the proximal tract of the greater petrosal nerve (white arrow; a, axial view and b, coronal view).

Positron emission tomography (PET) revealed increased fluorodeoxyglucose (FDG) uptake in the same region, raising suspicion for neoplastic disease.

Multiple biopsies were obtained through a left combined transcanal- transmastoid approach. Intraoperatively, fibrous and highly vascularized tissue was found occupying the tympanic cavity, epitympanum, mastoid antrum, and mastoid process, extending along the course of the facial nerve, as illustrated in Figure 3.

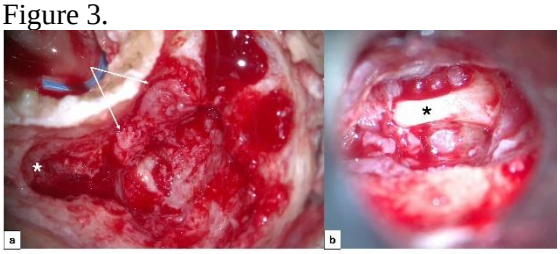

Fig 3. Intraoperative pictures showing the presence of fibrous and highly vascularized tissue within the left mastoid process (a) at the level of antrum and along the course of the facial nerve (white arrows); asterisk marks the mastoid tip. The same tissue was present in the tympanic cavity (b) surrounding the ossicular chain; asterisk marks the incus long process.

Frozen section analysis revealed fibrosclerotic tissue containing aggregates of atypical cells. Definitive histopathological examination, supported by immunohistochemical analysis (CKAE1/AE3 positive and Ki67 85% compatible with the previous sinonasal tumor), confirmed metastatic involvement consistent with localization of SNUC (Figure 4). In the immediate postoperative period, pure-tone audiometry thresholds remained stable, while FNP partially improved to HB grade II.

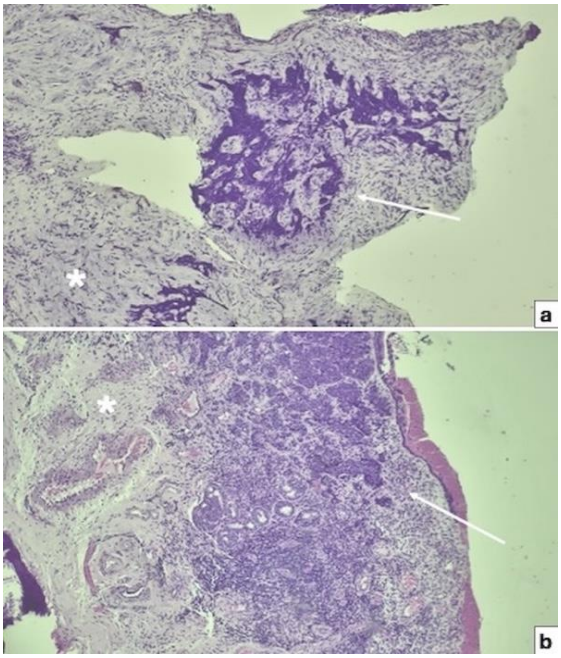

Fig 4. Histopathological image of mastoid biopsy showing areas of large pleomorphic cells with vesiculated nuclei (white arrow) within the middle ear epithelium (asterisk) indicative of nests of sinonasal undifferentiated carcinoma (**a**). In figure **b**

the histological sample of the previous sinonasal surgery: white arrow indicates the tumor cells, asterisk the nasal respiratory epithelium.

The case was then discussed at our hospital's Head and Neck Tumor Board and an indication for multisystemic treatment and Intensity-Modulated Proton Therapy (IMPT) was established. IMPT was delivered to the mastoid and petrous regions at a total dose of 54 Gy, and taxane- and platinum-based chemotherapy was administered.

After three cycles of systemic therapy, the left FNP resolved. No evidence of disease was detected on PET imaging performed after completion of IMRT and the sixth and final cycle of chemotherapy. Clinical and radiological findings remained stable at the last follow-up 12 months after the beginning of treatment.

Literature review

A search of the literature from January 1, 1980, to December 31, 2024, was conducted on the electronic databases PubMed, Web of Science and Scopus to identify original case series and/or case reports concerning distant metastases in SNUC. A manual review of the reference lists of retrieved articles was also performed to capture any additional relevant reports. A comprehensive summary of all reported cases of distant metastases in SNUC is provided in Table 1.

Table 1. Distant metastases from sinonasal undifferentiated carcinoma reported in literature and in our experience.

Author	N° of patients	N° of patients with distant failure.	Site of metastases
Tanzler et al.[5] (2008)	15	3 (20%)	Lung, bone
Chen et al.[6] (2008)	21	7 (33.3%)	Lung, central nervous system, bone
Mourad et al.[7] (2012)	18	3 (16.5%)	NR
Christopherson et al.[8] (2014)	23	6 (26%)	Bone, liver, chest, pancreas
Gamez et al.[1] (2017)	40	10 (25%)	Lung, liver, bones of the spine
Morand et al.[9] (2017)	11	5 (24.5%)	Lung, bone, liver
De Bonnecaze et al.[10] (2018)	54	10 (18.5%)	NR
Workman et al.[3] (2018)	27	8 (30%)	NR
Gray et al.[11] (2019)	19	2 (10,5%)	Liver, bone
Our series (2023)	12	1 (8,3%)	Facial nerve

NR: Not Reported

A total of 103 cases out of 688 reported patients are described in the literature, with ~~a~~ variable incidence rate across the analyzed series.

In our department, 12 patients with SNUC were surgically treated following induction chemotherapy, with or without radiotherapy (3 and 9 patients, respectively), in accordance with current guidelines and the existing literature. Postoperatively, 8 patients received adjuvant radiotherapy. At follow-up, 8 patients are alive without evidence of disease, while 3 died of disease. Two of them died ~~for~~ due to local recurrence (at 5 and 2 years after treatment, respectively), and the third died 9 months after treatment due to persistent disease ~~o~~ with extension to the cavernous sinus. Only the present patient developed distant metastasis.

Discussion

Sinonasal undifferentiated carcinoma (SNUC), first described by Frierson et al. (12) in 1986, is a rare and aggressive malignancy arising from the Schneiderian epithelium of the nasal cavity and paranasal sinuses, with an estimated incidence of 0.02 per 100000 individuals (13). At presentation, patients with SNUC generally manifest locally advanced disease, often with involvement of the orbit and skull base; cervical lymph node metastases are observed in approximately 10-30% of cases. Although distant metastases at diagnosis are

uncommon, SNUC demonstrates a higher tendency for distant spread compared with ~~to~~ other neuroendocrine malignancies. This behavior is likely related to the relatively high rates of vascular and perineural invasion (20–30%) and to the potential for cerebrospinal fluid dissemination, leading to so-called "drop metastases" (14). A trimodality treatment approach, consisting of induction chemotherapy followed by surgical resection and adjuvant radiotherapy, seems to provide better disease control and may reduce the risk of distant metastases (1,15,16). However, given the limited size of available series and the heterogeneity of chemotherapy regimens employed, the optimal therapeutic protocol has yet to be clearly defined. Overall, SNUC continues to be associated with a poor prognosis, with most series reporting a 5-year disease-specific survival rate below 50% (2). In particular, patients presenting with metastatic disease at diagnosis demonstrate significantly worse outcomes. A recent retrospective analysis of the American National Cancer Database (17) reported a 5-year survival rate of 18.6% in patients with metastatic disease at presentation, compared with 45.6% in those without distant metastases.

The reported incidence of distant metastases of SNUC varies across published series, as summarized in Table 1. In the retrospective study by Mourad et al. (7), 5 of 18 patients (28%) developed distant metastasis, while Christopherson et al. (8) reported metastatic progression in 6 of 23 patients (26%) during follow-up. A French retrospective study (10) including 54 patients with SNUC found that 10 of 40 evaluable patients (18.5%) developed distant metastases. Similarly, in the retrospective series by Gamez et al. (1), 10 of 40 patients (25%) experienced distant metastatic spread. Bone is the most common site of distant metastasis in SNUC, followed by the lungs, brain, and liver. In our institutional experience, 1 of 12 treated patients (8.3%) developed distant metastasis. To date, no cases of SNUC metastasizing to the facial nerve have been reported in the literature. In general, metastasis of solid tumors to the middle ear and temporal bone is exceedingly rare. A recent literature review by Jones et al. (4) reported temporal bone metastases as an uncommon entity arising from a wide spectrum of primary tumors of different sites and histological origins.

Although 255 cases were identified in the review, none originated from the nasal cavity or paranasal sinuses, thereby making the present case, to the best of our knowledge, the first to be reported.

A further peculiarity of the present case is that metastasis to the facial nerve occurred in the absence of local recurrence and on the contralateral side relative to the primary tumor origin, three years after the initial diagnosis. This unusual presentation makes it difficult to determine the exact route of tumor spread from the sinonasal site. In general, sinonasal malignancies may reach the temporal bone by direct extension through well-defined anatomical pathways, including the nasopharynx, Eustachian tube, pterygopalatine fossa, or parapharyngeal space.

As described by Jones at al (4) metastatic lesions often involve the petrous apex first, with subsequent spread to adjacent temporal bone structures. On the other hand, SNUC is known to exhibit a marked propensity for perineural invasion and metastatic spread (14,18); therefore, perineural dissemination was considered the most plausible mechanism of spread of the disease in the present case. This hypothesis is supported by the radiological evidence of involvement of the geniculate ganglion region and greater petrosal nerve.

As this report describes a single, exceptionally rare case, its findings are inherently limited, and firm conclusions regarding incidence, prognosis, or management cannot be made.

Conclusion

In conclusion, this case represents a delayed metastasis of sinonasal undifferentiated carcinoma (SNUC) to the mastoid and middle ear, likely occurring through perineural spread. To date, no cases of temporal bone metastasis without locally recurrent disease in the nasal or paranasal cavities have been reported in the literature. Systemic therapy resulted in complete remission at the 12-month follow-up, likely reflecting the intrinsic chemosensitivity of SNUC disease. Although metastases to the temporal bone are rare, it they should be considered in oncological patients presenting with facial palsy or other persistent otologic symptoms.

Declaration of Interests

The authors have no conflict of interest to declare.

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