INTRODUCTION

The first total laryngectomy for a malignant laryngeal tumor was performed by Billroth in Vienna on the last day of 1873. Over the last 140 years, and especially nowadays with surgical strategies for malignant tumors being focused on the principle of preservation of organ and function, total laryngectomy is a well-established surgical procedure with still reliable indications: This modality is reserved for advanced laryngeal or hypopharyngeal malignancies with cartilage infiltration, invasion of adjacent structures (eg, thyroid, skin), bilateral laryngeal tumors, recurrence after definitive radiochemotherapy, perichondritis of the laryngeal framework after partial laryngectomy, histopathological subtypes resistant to radiotherapy as well as persistent aspiration endangering the patient’s life.

Despite its oncologic safety, total laryngectomy has dramatic consequences on the patient’s social function, mainly through the loss of normal speech and the presence of a tracheostoma. Moreover, laryngectomy leads to a loss of nasal function with elimination of olfaction and impairment in the possibility of heating, humidifying, and filtering the inhaled air. A question that emerges is whether this postlaryngectomy loss of nasal function could additionally predispose to metachronous sinonasal cancer. Several literature reports have described in detail the significant alterations in the physiology and histology of the nasal mucosa following complete resection of the larynx. Our report describes two cases of postlaryngectomy sinonasal cancer and points to the potential coexistence of more than one carcinogenetic mechanism for this tumor constellation.

CASE REPORT

2.1 Case 1

A 60-year-old man presented to our department with dysphagia, a foreign-body sensation, and hoarseness. His medical
history was remarkable with respect to diabetes mellitus type II and nicotine abuse of 40 pack years. In the panendoscopy, an exophytic vulnerable lesion in the supraglottic larynx could be seen and histology revealed a G2 squamous cell carcinoma. This was well-resectable without any functional (swallowing) deficits for the patient and was subsequently managed by means of transoral laser resection with bilateral neck dissection. Histology showed a pT2 pN0 G2 supraglottic squamous cell carcinoma. Thirteen years later, he relapsed with a supraglottic larynx carcinoma on the same side, with infiltration of the ipsilateral arytenoid cartilage and fixation of the ipsilateral vocal cord. After presentation of this case to our interdisciplinary tumor board, both therapeutic modalities (definitive radiochemotherapy with 74 Gy, cisplatin and 5-fluorouracil or total laryngectomy) were discussed thoroughly, but surgical therapy was primarily recommended because of the cartilage infiltration through the tumor, which does not offer ideal conditions for organ presentation protocols. Definitive histology after total laryngectomy showed a pT3 ycN0 G2 squamous cell carcinoma. The patient was examined at regular follow-up appointments (every 6 weeks for 6 months, followed by 3 months in the first two years, and every 6 months thereafter). A PET-CT scan 6 months later showed no signs of tumor recurrence in the head and neck region (Figure 1). Three years later, nasal endoscopy at the regular check-up examination showed a suspicious lesion arising from the left inferior nasal concha. Biopsy showed a poorly differentiated squamous cell carcinoma (G3) (Figure 2). A CT scan demonstrated a diffuse soft tissue plus on the inferior turbinate on the left side with infiltration of the paranasal soft tissues and an asymmetric absorption of contrast medium (Figure 3). After presentation of this case to our interdisciplinary tumor board, both possibilities (surgical management or definitive radiochemotherapy with 74 Gy, Cisplatin and 5-FU) were again recommended and the patient opted for the nonsurgical modality. Therefore, definitive radiochemotherapy was performed at the patient’s wish and request, and was also possible as the patient had not been managed with radiation until then.

2.2 | Case 2

A 58-year-old man presented to our department with dysphagia, foreign-body sensation, and referral otalgia. Hypertension and nicotine abuse of 30 pack years were mentioned in his medical history. Panendoscopy detected an exophytic lesion in the left supraglottis and histology revealed a G3 squamous cell carcinoma. Taking the endoscopic and imaging findings into consideration, the disease was staged as cT2cN2b cM0 and was managed by primary radiochemotherapy because of the location of the tumor (arytenoid cartilage—aryepiglottic fold) and the expected swallowing dysfunction. One year later, the patient presented with a local recurrence infiltrating a large part of the left supraglottis (arytenoid cartilage, aryepiglottic fold, left part of the laryngeal epiglottis). Considering the localization of the recurrence and the previous radiochemotherapy, our interdisciplinary tumor board recommended management in the form of salvage total laryngectomy and bilateral neck dissection. Histological analysis showed a pT3 pN1 L0 V0 Pn0 R0 G3 squamous cell carcinoma of the left supraglottis. Two years later, the patient presented with recurrent episodes of haemoptysis and dyspnea as well as recurrent episodes of persistent bleeding from the right nasal cavity over the past year. Computer tomography of the thorax demonstrated a suspicious solitary nodule in the middle lobe of the right lung. Bronchoscopy confirmed pulmonary metastasis of a moderately differentiated squamous cell carcinoma (G2). On nasal endoscopy, a small, exophytic, vulnerable lesion arising from the right inferior turbinate was seen. Histologic analysis showed a poorly differentiated squamous cell carcinoma (G3) of the nasal mucosa (Figure 4). A PET-CT scan showed a suspicious lung nodule as well as an FDG uptake in the right nasal cavity (Figure 5). In this case, the tumorous lesion on the inferior turbinate was smaller than in case 1, well-localized and easily accessible, and an endonasal endoscopic-controlled resection of the lesion was recommended by our interdisciplinary tumor board. Surgical resection of the tumorous lesion was performed and followed by immunotherapy with PD-1 inhibitors every 3 weeks due to the pulmonary metastasis (intravenous administration of pembrolizumab 200 mg).
According to the literature, most treatment failures after total laryngectomy are attributed to distant metastases, whereas local recurrences after total laryngectomy are most often seen in the tracheostoma or the neopharynx. It is accepted that secondary malignancies occur frequently in patients with head and neck carcinomas. This may be caused by a generalized exposure to the same risk factors (eg, nicotine), resulting in “field cancerization” of the mucosa or to the individuals’ generalized susceptibility to cancer. However, the sinonasal cavity is not commonly included in the sites considered at risk for this process. Furthermore, the sinonasal tract has been identified as a potential “hotspot” for HPV-related malignancies, with up to 25% of sinonasal carcinomas harboring transcriptionally active high-risk HPV. Our study cases led to the reasonable line of thought that another factor could also play a role in the pathogenesis of the disease in laryngectomized patients. Regarding altered physiology, several studies have pointed out the increase in endonasal temperature and moisture, the disappearance of the nasal cycle, as well as the decrease in endonasal blood flow and mucociliary activity following laryngectomy. Histologically, the loss of nasal function leads to atrophic rhinitis with destruction of the goblet cells and cilia, myxoid degeneration, fibrosis, neovascularization, and squamous metaplasia. This possible mechanism is sustained by the observation that squamous metaplastic change in the nasal mucosa is seen in more than 80% of cases with atrophic rhinitis. Furthermore,
this theory is also based on the fact that the vast majority of malignant sinonasal tract tumors represent squamous cell carcinomas. In our view, an association between the postlaryngectomy status and secondary sinonasal cancer appears to be more than coincidental. Notably, the sinonasal tumors in both cases were closely associated with dysplastic sinonasal mucosa, pointing to their primary origin from nasal mucosa. We assume that metastasis from the previous laryngeal cancer is unlikely. The variable time between laryngectomy and nasal cancer (3 years in case “1,” 2 years in case “2”) does not allow specific conclusions to be drawn and perhaps points to a multifactorial oncogenesis in these cases.

**CONCLUSION**

Postlaryngectomy sinonasal squamous cell carcinoma is rare and has not been reported before. It could be explained either by exposure to the same risk factors (in the sense of a field effect) or by the development of precancerous histologic alterations in the nasal mucosa due to postlaryngectomy loss of nasal function and/or altered physiology of the nasal cavity. These first cases of postlaryngectomy sinonasal cancer in the literature point to the need for a thorough examination of the whole head and neck region, including the sinonasal cavities, even long after the occurrence of the primary tumor. A second message regarding clinical management could lie in the need for local care of the nasal mucosa in order to delay postlaryngectomy alterations, which could theoretically represent the additional danger of secondary carcinogenesis. Meanwhile, we are intensively examining the nasal mucosa in the laryngectomized patients of our department in order to detect further histologic alterations or even precancerous lesions.

**CONFLICT OF INTEREST**

None declared.
AUTHOR CONTRIBUTIONS
Konstantinos Mantsopoulos: involved in conception and design of study, literature search, analysis of data, drafting of article, and final approval. Lava Taha: involved in design of manuscript, literature search, analysis of patients’ data, drafting of article, and final approval. Abbas Agaimy: involved in providing of histologic specimens, interpretation of pathologic findings, drafting of article, and final approval. Heinrich Iro: involved in design of manuscript, drafting of article, and final approval.

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