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Case Report

Oral cavity and a second primary cancer in the larynx

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ABSTRACT

Head and neck cancer represents the sixth most common cancer in the world. Men are affected two to three times more than women, possibly as a result of higher tobacco and alcohol consumption. Oral cavity tumors have the highest rate of developing second primary malignancies. In patients with malignancies associated with alcohol and tobacco consumption, 80% of second primary tumors appear in the oral cavity, oropharynx, and larynx. Second primary tumors are usually invasive in nature with early metastasis and should be treated with aggressive therapy. Herein, we report a rare case of a second primary cancer in the larynx after a gingival squamous cell carcinoma.

Keywords: Head and neck cancer, larynx cancer, oral cavity cancer, second primary malignancy, squamous cell carcinoma.

Head and neck cancer is a widespread problem in several countries of the world. This type of malignancy represents the sixth most common cancer worldwide with more than 650,000 cases and 350,000 deaths annually.[1] These include malignant tumors of the oral cavity, particularly the lips, tongue, floor of the mouth, palate, cheeks or salivary glands, nasal cavity, paranasal sinuses, pharynx, larynx, and thyroid gland.[2] With a male-to-female ratio ranging from 2:1 to 4:1, males are significantly more affected than females.[3] However, the incidence by sex differs with anatomic location and has been changing as the number of female smokers has increased in recent years.[4]

Patients with a previous history of head and neck cancer have a higher potentiality to develop a second primary tumor. These second primary tumors appear at a yearly rate of 3 to 7% and, 50 to 75% of them are localized in the upper aerodigestive tract or lungs.[5] The high incidence of second primary malignancies results from the same carcinogenic exposure responsible for the initial primary process, called field cancerization. The idea of field cancerization was first established by Slaughter et al.[6] in 1953 while studying the presence of histologically atypical tissue surrounding oral squamous cell carcinoma (SCC). Second primary malignancies may present simultaneously or after the diagnosis of an index tumor. Synchronous second primary malignancies are usually discovered concurrently or within six months of the index tumor, whereas metachronous second primary malignancies are often identified beyond six months after the index tumor.[7] It is of great significance to differentiate second primary malignancies from local recurrences or metastasis of the primary tumor. Second primary malignancies are the most common cause of death in patients with head and neck SCC following cardiovascular and chronic obstructive pulmonary disease.[8]

In this article, we report a rare case of a second primary cancer in the larynx after a gingival squamous cell carcinoma.

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CASE REPORT

A 72-year-old male patient from Georgia suffered from a neck mass about two years ago, which was treated with medication. The patient had noticed a swelling of the floor of his mouth, which he first thought was caused by his dental prothesis. His past medical history was specific for tonsillectomy and hypertension. The patient was a regular alcohol consumer and smoker. He had a >100 pack-year smoking history (two packs a day for more than 50 years). Currently, he was taking antihypertensive drugs. On his physical examination, he presented a tumoral lesion on the alveolar process. The surface of this lesion was ulcerated (Figures 1, 2).

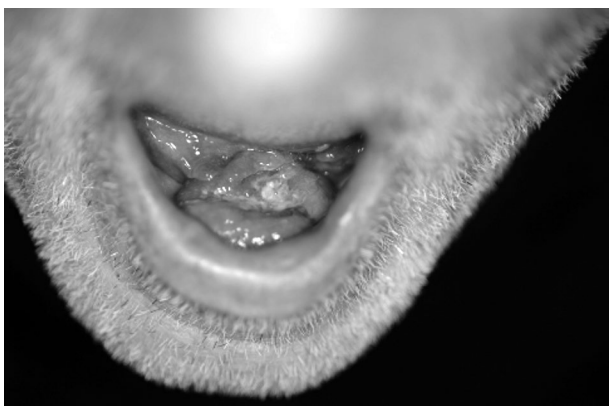

Figure 1. A 72-year old male patient with an oral cavity tumor.

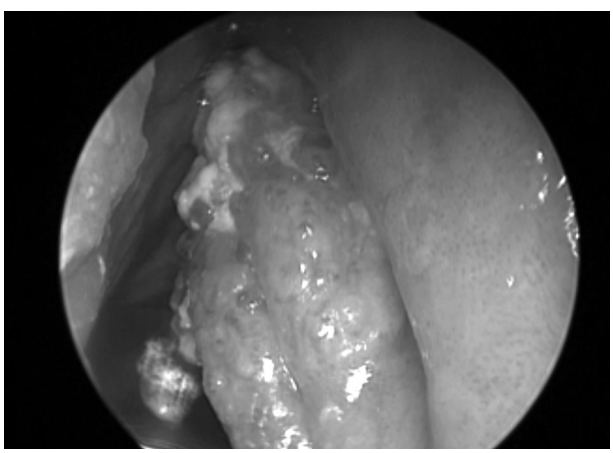

Figure 2. A direct laryngoscopic view of the laryngeal tumor.

The positron emission tomography-computed tomography (PET-CT) scan showed an increased fluorodeoxyglucose (FDG) uptake within a 45×35-mm tumor mass located in the middle and left lateral side of the mandibula (Figure 3). Another lesion of malignant nature was found on the left vocal cord with a size of 20×20 mm (Figure 4). Besides, there were some lymph nodes ranging from the left submandibular area to the right posterior cervical area. The thoracic sections demonstrated an increased FDG uptake in the posterior segment of the upper lobe of the right

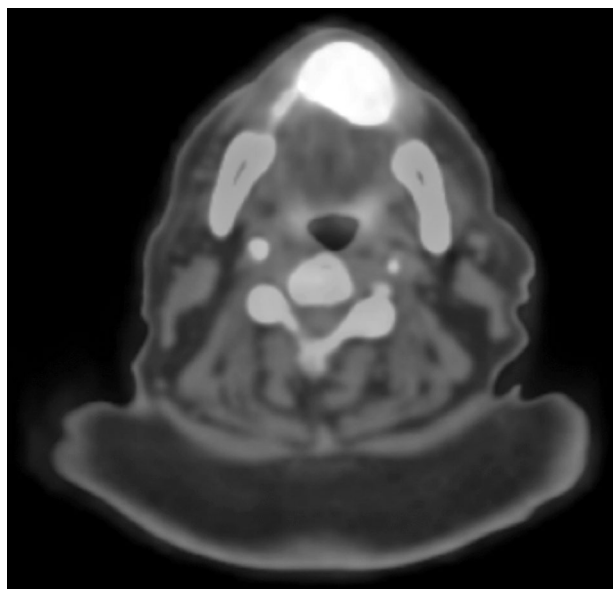

Figure 3. A positron emission tomography-computed tomography scan showing a high fluorodeoxyglucose uptake in lesion of anterior mandible.

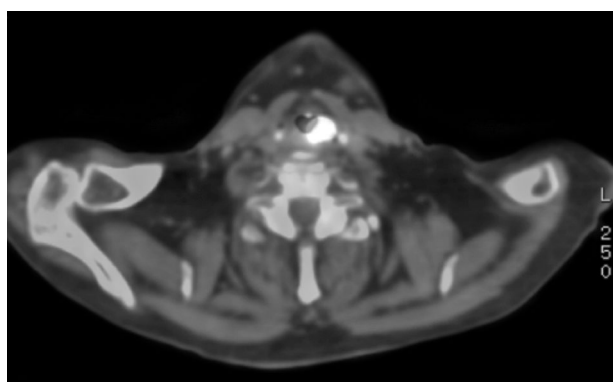

Figure 4. A positron emission tomography-computed tomography scan showing a high fluorodeoxyglucose uptake in left vocal cord.

lung. The other lesion with a high FDG uptake was located in the apicoposterior segment of the upper lobe of the left lung. Based on these findings, we decided to proceed with a tissue biopsy. A written informed consent was obtained from the patient.

During direct laryngoscopy, an ulcero-vegetative lesion was found in the medial side of the left aryepiglottic fold (Figure 5a-c). This lesion extended to the ventricle, but did not penetrate it. It did not turn around the lateral side of the aryepiglottic fold and did not extend into the posterior hypopharynx. In addition, a similar lesion involving the upper medial and caudal side of the right vocal cord was detected. The arytenoids were mobile, but there was a restriction of movement on the left side due to the lesion. It entered the ventricle and reached the anterior commissure. The laryngeal inlet was found to be significantly narrowed, due to the tumor mass and the position of the laryngeal structures (Figure 5a-c). There was an ulcero-vegetative lesion of the anterior mandibular gingiva of a diameter of 4.5 to 5 cm in width, widely infiltrating into the mandibular bone. The subglottic area, the piriform fossa, the vallecula, the superior part of the epiglottis, and the other parts of the larynx were intact. Biopsy was performed from both sides of the larynx and incisional biopsies were done from the gingival lesion. According to the pathological report, the lesions of the left ventricle and right vocal cord were inflicted with well-differentiated SCCs, whereas the lesion of the lower gingiva was a moderately differentiated SCC.

Magnetic resonance imaging (MRI) showed a tumor in the mid-portion of the anterior mandibular segment, infiltrating into the mandibular cortex. After the injection of intravenous contrast medium, the lobulated contour of the mass was recognizable. The mass was found to be more pronounced on the left side. It invaded the anterosuperior mandibula at the level of the attachments of bilateral mylohyoid muscles (Figure 6a, b). In addition, multiple lymph nodes were present in bilateral cervical chains (Level I-II). The CT scan was also performed (Figure 7a, b). The tumor infiltrated into the arytenoid cartilage and left aryepiglottic fold in the left supraglottic area, extending to the anterior commissure and leading to narrowing of the rima glottidis at a superior level (Figure 7a). Moreover,

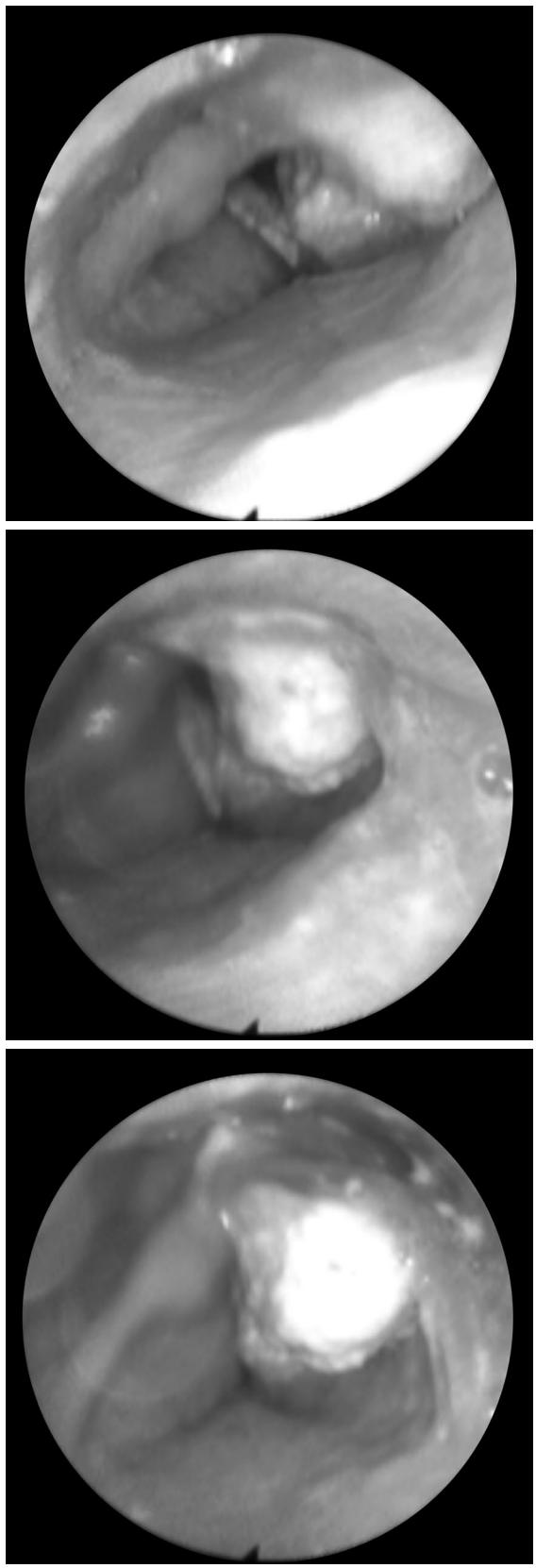

Figure 5. A laryngoscopic view of the tumor on left aryepiglottic fold.

the tumor expanded to the superior cornu of the thyroid cartilage (Figure 7b). These findings were discussed in the Tumor Council. A treatment plan consisting of surgical resection of the oral cavity lesion and defect reconstruction with a pedicled flap to be followed with external irradiation of the laryngeal primary, as well as of the oral cavity and both neck sides. As a result, a composite resection and a partial glossectomy were implemented. Intraoperative consultation was done to identify the diagnosis. During the operation, a wide local excision was done for the gingival lesion involving the ventral surface of the tongue and the floor of the mouth. Surgical margins were reported to be free of tumor according to the frozen-section analysis. Additionally, a tracheotomy was done prior to the oral tumor's resection. Then, the reconstruction was done with a pectoralis major myocutaneous flap. The patient tolerated the operation very well. The permanent section was reported as a carcinoma cuniculatum. The tumor made a focal cortical invasion into the mandible and the tumor showed microscopic continuity at the surgical margin. According to the Tumor, Node and Metastasis (TNM) staging system, the final diagnosis was T4N0M0 gingival SCC and a T2N0M0 second primary supraglottic laryngeal SCC.

After surgery, the patient was kept in the hospital for 10 days, at which he was first

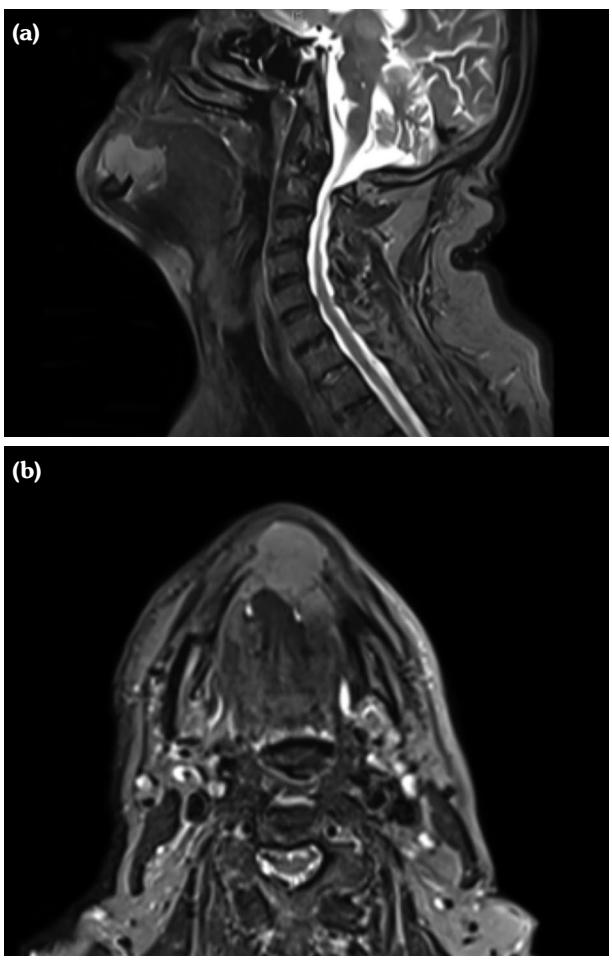

Figure 6. (a) Sagittal and **(b)** axial T1-weighted magnetic resonance imaging of the tumor located in anterior segment of mandible.

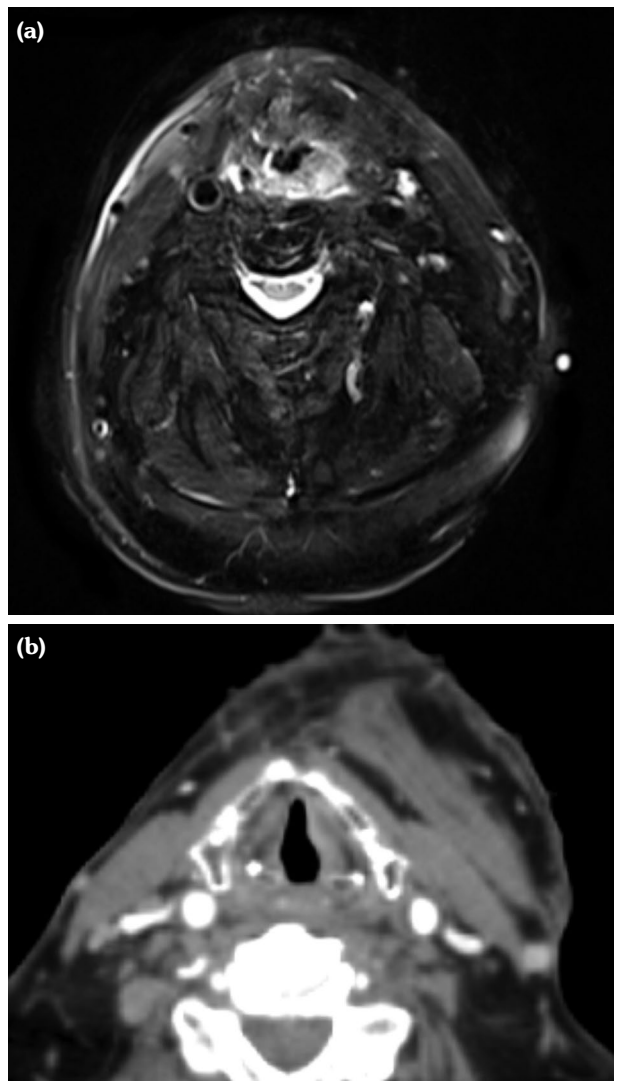

Figure 7. Axial computed tomography scan of the laryngeal tumor. **(a)** The tumor infiltrates into arytenoid cartilage and left aryepiglottic fold in left supraglottic area. **(b)** The tumor enters superior cornu of the thyroid cartilage.

fed through a nasogastric tube. Following decannulation on Day 7, he was discharged with enteral feeding. Within 20 days, the patient was able to have a full oral intake and his nasogastric tube was removed. Four weeks after surgery, he was scheduled for radiation therapy and he received chemoradiotherapy.

DISCUSSION

Oral cavity cancers are the second most common neoplasms among the head and neck malignancies, following laryngeal cancers. The tumors of oral cavity are divided into subregions such as tongue, floor of the mouth, buccal mucosa, hard palate, retromolar trigon, and gingiva, according to their anatomical location and different histological characteristics.[1] More than 90% of cancers in the oral cavity and oropharynx represent SCCs. Other types of cancers of the oral cavity include cancers of the salivary glands such as mucoepidermoid carcinoma and adenoid cystic carcinoma, sarcomas, and melanomas.[9]

Frequently, oral cancer is only discovered, when cancer has metastasized to another area, particularly the lymph nodes of the neck. Prognosis at this stage of discovery is notably worse than when it is found in a localized intraoral region. Apart from the metastasis, the primary tumor has time to invade deep into local structures.[10]

A number of premalignant lesions have been linked to the progress of SCCs (Table 1). Head and neck cancer can cause different types of symptoms (Table 2).[11] In particular, oral cancer is a treacherous form of cancer, as it expands without causing any pain or symptoms, and it has a high risk of being associated with second primary tumors.[10] The major risk factors for developing SCCs are tobacco use and alcohol consumption. Betel nut and tobacco chewing are also popular habits of the Asian population, leading to oral cavity cancers (Table 3).[11] Despite a simple self-examination and physical examination method, patients often present with advanced-stage disease. Head and neck examination is essential in patients with suspected oral cavity cancer. Visual inspection and palpation allow an accurate impression of the extent of the disease, the third dimension of tumor, the existence of bone invasion, or skin breakdown.[12]

In head and neck cancers, MRI and CT scan are essential in detecting both mass and regional metastases. Depending on the location of the mass, endoscopic procedures can be performed and a biopsy can be taken from the lesion or where it is likely to be malignant.[11] The PET-CT scan is another useful radiological technique for tumor staging, evaluation of the treatment response, and examining its origin in cervical lymph node metastasis.[13]

Table 1. Four main typical premalignant lesions of oral cavity and their specific features

	Age/Sex	Etiology	Localization	Histopathological + Clinical findings
Leukoplakia	30-60/M=F	Tobacco, alcohol, chronic irritation	Buccal mucosa, hard palate, retromolar trigone	White patch, not painful, irregular shape, cannot be scraped away, hyperkeratosis
Erythroplakia	50-70/M=F	Tobacco, alcohol, chronic irritation	Soft palate, floor of the mouth, tongue, retromolar trigone	Red macule or plaque with well-demarcated borders, texture is soft, velvety
Oral lichen planes	40-70/F>M	T-cell mediated autoimmune defects	Bilateral on the buccal mucosa, tongue, gingiva, palate	Reticular form: White keratotic lines ("Wickham's striae") with an erythematous border, bullous, reticular, papular. Erosive form: A mix of erythematous and ulcerated areas surrounded by keratotic striae
Oral submucous fibrosis	20-40/F>M	Betel nut chewing, ingestion of chilies	Pharynx, esophagus, palate, buccal mucosa, lips	Palpable fibrotic bands, stiff and blanched mucosa

The clinical TNM stage should be recorded instantly and modified as the evaluation progresses. The initial work-up consists of diagnosis by biopsy. Reachable lesions may be adequately biopsied in the clinic setting using punch forceps, core needle, or fine-needle aspiration. Clinical staging of the oral cavity tumors consists of primary tumor characteristics, the neck, and assessment for distant metastasis. The basic elements in staging of the primary site are the tumor size and invasion of deep structures.[11]

The standard of care for oral cavity cancers is primary surgical resection with or without postoperative adjuvant therapy. The first-line treatment of choice is surgical resection. It enables exact pathological staging and provides information about the status of margins, tumor spread, and histopathological characteristics of the tumor.[11]

Oral cancer patients have a high risk of locoregional recurrence and developing future new primary cancers; however, the risk of distant recurrence is low.[14] Clinical examination, high suspicion, and the control of risk factors form the basis of early diagnosis and treatment success.

In 90% of cases, laryngeal cancer is a SCC. The main risk factors of laryngeal cancer are smoking, alcohol abuse, low socioeconomic status, male sex, and advanced age. Hoarseness usually develops from the very beginning; therefore, vocal cord tumors are often diagnosed early. However, tumors in the supraglottic and subglottic area

Table 2. Different cancer localizations with possible signs and symptoms

Localization	Signs and symptoms
Oral cavity	• Persistent ulcer, pain • A lump or thickening in the cheek • Erythroplakia, leukoplakia • Lichen planus/lichenoid mucositis • Dysphagia, halitosis, lingual paresthesia • Trouble moving the jaw or tongue • Otalgia
Nasopharynx	• Epistaxis, nasal congestion • Lymphadenopathy in the neck • Hearing loss, tinnitus • Headache, diplopia • Unilateral or bilateral otitis media infections
Oropharynx	• Dysphagia, halitosis, hemoptysis • Cervical mass • Otalgia • Difficulties during opening the mouth or tongue movements • Weight loss
Hypopharynx	• Aspiration, dysphagia, globus hystericus, ptyalism • Trachyphonia, dyspnea • Otalgia during swallowing
Larynx	• Trachyphonia, dyspnea • Bleeding • Odynophagia, halitosis • Otalgia (tumor located in the supraglottic area)
Paranasal sinuses	• Blockage of sinuses and congestion • Headache, anosmia, epistaxis • Numbness or pain (face, ears, or teeth) • Diplopia, swollen eyes • Dysphagia
Salivary glands	• Swelling or lump on or near the jaw, neck, or mouth • Numbness • Unilateral muscle weakness of the face • Dysphagia • Persistent pain • Restricted mouth opening

Table 3. The risk factors of head and neck cancer

Risk factors of head and neck cancer
Tobacco products: Smoking tobacco, cigarettes, cigars, pipes, chewing tobacco, snuff
Alcohol consumption
Betel-quid chewing ("Paan")
Viruses: Human papillomavirus (HPV) → HPV type 16, Epstein-Barr virus infection (EBV)
Poor oral hygiene
Preserved or salted foods
Occupational exposure: Asbestos, chromium, nickel, arsenic, formaldehyde, radium, wood dust, vinyl chloride
Immunodeficiency
Radiation exposure
Sex: Men are 2 to 3 times more affected than women
Diseases: Gastroesophageal reflux disease (GERD), Fanconi anemia, Plummer-Vinson syndrome, scleroderma, xeroderma pigmentosum
Age >40 years
Previous history of head and neck cancer

often become apparent at an advanced stage and may persist asymptomatic for a long time.[15] About 60% of patients are admitted with a locally limited disease stage. Nearly 25% of patients have regional lymph node metastases in addition to the local tumor, whereas 15% only present in an advanced stage with or without distant metastases.[15]

Supraglottic and subglottic tumors have a high probability of lymph node metastases than glottic cancers due to minimal lymphatic drainage from the glottis. Furthermore, distant metastases are typical in the lungs or liver.[15] The tumor appears more often in the vocal folds and supraglottic larynx. The rarest localization is the subglottic larynx with 1% chance. Verrucous carcinoma, a single variant of SCC usually located in the glottic area, is characterized by locally invasive, exophytic warty growth.[15]

Laryngoscopy and biopsy are essential tools for the diagnosis of a laryngeal tumor. The treatment of choice for tumors at an early stage is surgery or radiation. Chemotherapy and radiation therapy are treatment options for advanced malignancies, which otherwise would require total laryngectomy. Surgery is intended for salvage therapy or for lesions with extralaryngeal expansion or cartilage destruction. After total laryngectomy, the ability to speak can be restored.[15] Current guidelines recommend a follow-up period of at least five years after curative therapy.[15]

In conclusion, the number of patients with multiple cancers in the head and neck area has increased rapidly due to high life expectancy and population survival. Tobacco smoking and alcohol consumption are the main risk factors for developing a second malignancy in the head and neck area. Patients having oral SCCs still have a high risk for developing regional or local recurrence, second primary malignancies, or distant metastases after primary curative treatment. Multidisciplinary treatment approach is crucial to improve the oncological and functional results in patients with multiple cancers.

Declaration of conflicting interests

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