Tongue Squamous Cell Carcinoma in Younger Adult Female with a History of Breast Cancer: A Rare Case Report

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ABSTRACT
Tongue squamous cell carcinoma (TSCC) is the most common presentation of oral cancer (OC). Risk factor traditionally associated with tobacco smoking and alcohol consumption affecting both sexes starting in four decades. Current case report highlights the associated risk factors from this patient and among younger age population. A 39 years old women with history of 3 years breast cancer (BC) had underwent surgery and chemotherapy, came to Ear, Nose, and Throat (ENT) clinic with pain while swallowing for 2 weeks. Examination shows redness on her right pharyngeal arch and right side of the tongue. During follow up, she presented with persisted swollen tongue. We suspected a tongue mass with inflammation of right palatine tonsil and a differential diagnosis of neoplasm was held. Apart from imaging modalities (endoscopy and head computed tomography scan), biopsy revealed a well differentiated squamous cell carcinoma without lymphovascular invasion, thus was referred to ENT subspecialist for further multidisciplinary treatment approach. To our knowledge, this is the first case of TSCC in patient with history of BC, in younger age population, and no family history. While the reported cases of TSCC in young adult are increasing, however previous studies demonstrated contradictive risk factors. Regardless the possibility of the case in younger adult population, the pathogenesis knowledge in TSCC is sparse. We proposed that our patient was most likely to develop oral SCC by chemotherapy-induced immunosuppression and carcinogenesis, as well as poor oral hygiene status of our patient.

Keywords: *oral cancer, tongue squamous cell carcinoma, breast cancer, risk factor.*

1. INTRODUCTION

Tongue squamous cell carcinoma (TSCC) is the most common oral cancer (OC), approximately 45% of all OC are TSCC. It is the eighth most frequent cancer-related death worldwide and prevalence profound high in Central and Southeast Asian countries [1-4]. The incidence and mortality rates of OC vary globally and are higher in developing countries. Tobacco use and alcohol consumption traditionally are the primary risk factors for head and neck cancers [4,5].

Head and neck squamous cell carcinoma (SCC) primarily is a disease of adults age 45 and older [6]. However data from developed countries showed that 6% of all OC occurred in young people under the age of 45 years in both men and women, and the incidence of this population is steadily increasing [4,6,7]. It was also demonstrated that younger patients do not show the typical exposures of tobacco and alcohol drinking as they are a well-known risk factors for older adult patients [2,6].

About 90–95% of all intraoral malignancies is oral squamous cell carcinoma (OSCC) [7], and grade vary from well-differentiated to poorly-differentiated [5]. Some authors reported that well-differentiated tumors were relatively more prevalent in the younger age group, despite it is not known whether the degree of tumor differentiation could represent a marker of poor prognosis for young patients [8].

2. CASE REPORT

A women 39 years old, with history of 3 years breast cancer had undergone surgery and chemotherapy, came to Ear, Nose, and Throat (ENT) clinic with chief complaint of pain while swallowing on her right side radiating to right ear for 2 weeks. She went to general practitioner (GP) one week prior and was prescribed

Ciprofloxacin, Diclofenac and Methylprednisolone, and reported a temporary improvement. The patient denied any history of smoking and alcohol, and none has similar history in her family.

Examination shows redness on the right side of the pharyngeal arch and tongue. She then diagnosed as Glossitis with Right Acute Tonsillitis on our initial assessment and was prescribed three times 300 mg Clindamycin, three times daily a combination of 500 mg Acetaminophen and 200 mg N-Acetylcysteine, also three times daily of anti-inflammatory agents, along with Iodine-based mouthwash two times daily.

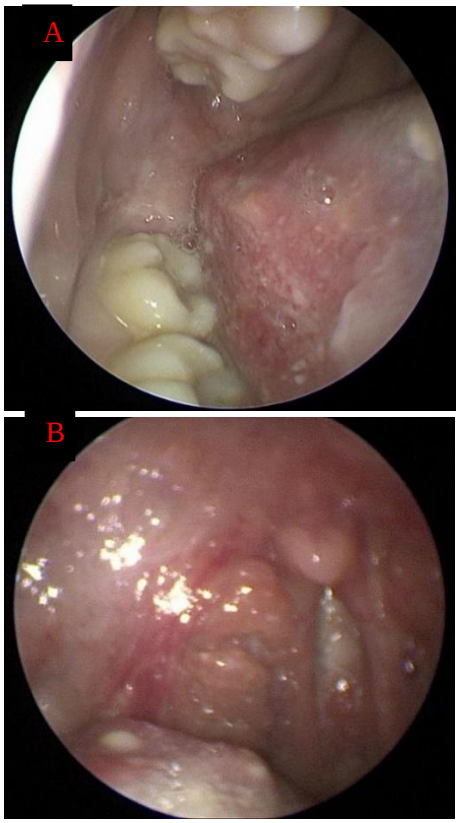

Figure 1 Endoscopic result from the first (A) and second (B) clinic visit

Five days later she returned to the clinic with the same swollen on her tongue, with reduced pain. From her medical record, we revealed the patient visited dentist clinic for a root canal treatment on dental number 46, a few days before her second visit to ENT clinic. We suspected a tongue mass with inflammation of right palatine tonsil and therefore, a differential diagnosis of neoplasm was held.

Four days later, she was admitted to the hospital for a biopsy plan. During admission she was given Levofloxacin, Methylprednisolone and Omeprazole each was once daily, intravenously. Head, neck and oral contrast-enhanced computed tomography (CT) scan was done during admission with result suggestive of malignant space-occupying lesion (SOL) on posterior right of tongue approximately 3.1 x 2.9 x 2,75 cm, with involvement of intrinsic and extrinsic muscles including musculus (M.) genioglossus, M. hyoglossus, M. palatoglossus, and right side of M. styloglossus, and slightly pass the midline. Also showed, level-II of right-side cervical lymph node with the biggest size of 23 x 12 x 10 mm, not showing malignant typical at the moment. Incisional biopsy was done and revealed a lesion of well differentiated SCC with no lymphovascular invasion. No abnormality found on heart, lungs and chest structure of the chest postero-anterior imaging. Laboratory test was done with no significant result. Based on 2020 National Comprehensive Cancer Network (NCCN) TNM staging, she was classified into T4aN1Mx and referred to the oncology ENT subspecialist for the next therapy plan.

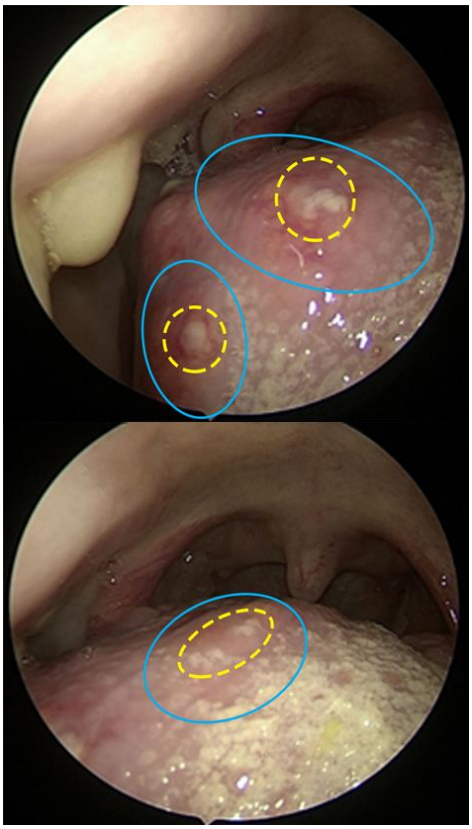

Figure 2 Endoscopic result from third clinic visit, two days before biopsy done. Yellow dashed-circle show ulcerative part of the mass, whereas blue circle show the induration area

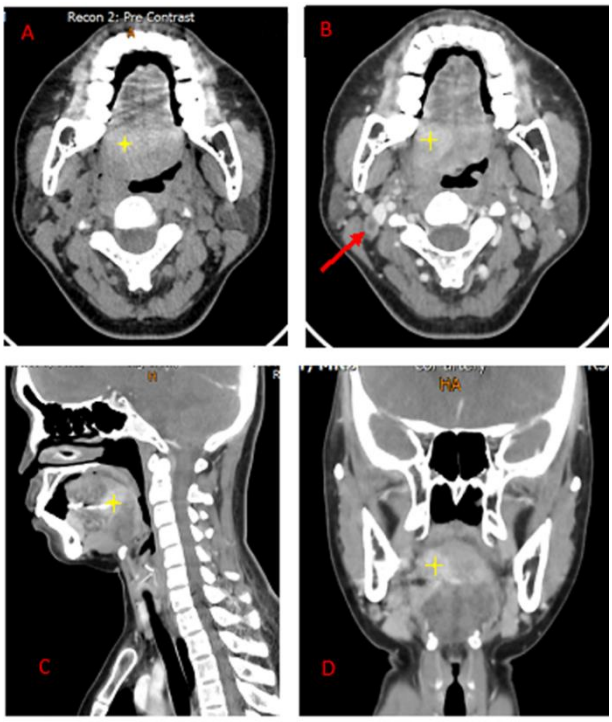

Figure 3 Head CT Scan with contrast showing a well-defined mass on the right tongue, a pre-contrast image on axial plane showing lesion (A), with contrast showing enhancement on lesion (B). Also shown the involvement of intrinsic and extrinsic muscles including musculus (M.) genioglossus, M. hyoglossus, M. palatoglossus, and right side of M. styloglossus, and slightly pass the midline. Level-II of right side cervical lymph node with biggest size 23 x 12 x 10 mm on the contrast view shown a hypo-dense lesion inside the node, showing abscess inside cervical lymph node (red arrow), which suggestive malignancy. No intracranial mass identified suggestive metastasis on the current CT scan. Figure (C) showing sagittal plane and (D) coronal plane

3. RESULT AND DISCUSSION

OSCC incidences are high in middle and low-income countries such in Central and Southeast Asia. It has been widely linked to habits, with exposure to smoke and alcohol drinking, and for some countries are tobacco or betel quid chewing. It is usually found in an older age population, also male sex majority. Young population in reported studies defined for age group between 35-to-45-year of age [3,4,7].

We present a women 39 years with T4aN1Mx TSCC according to 2020 NCCN. She has no history of oral and oropharyngeal cancer in her family and has a history of breast cancer diagnosed 3 years ago which had completed surgery also chemotherapy. Mohideen *et al.* in their meta-analysis of TSCC in young adults released on 2019, reports male predominance in young adult tongue SCC, in contrast to our case which is female [7]. Nevertheless, increasing incidence of young adult female TSCC are reported in some publications in the last few years. Among young population of OSCC, tongue is the most frequently affected site [7], as in our patient. Numerous cases reported metastasis from the breast cancer to the tongue, forming gland-like appearance in the biopsy. Although, in our case it was found to be SCC on the biopsy [9].

In the younger adult population, traditional risk factors of alcohol drinking and/ or tobacco exposure were not found. This leads researchers to find another potential agent that may implicate as cofactor in the genesis of tongue cancer such as genetic factors, immune deficiency, viral infections, iron deficiency, occupation and environmental exposure, and behavioural risk factors especially dietary factors [6,7].

We highlighted that our patient has no history of smoking nor alcohol drinking, which are the most frequent risk factor for OSCC. We found only one case of OSCC on patient with history of breast cancer reported. Addeo *et al*. reported a case in Italy of women with breast cancer underwent chemotherapy and hormonal therapy. The patient presented with painful nodule on her tongue then progressed to involve the floor of the mouth and the left border of the tongue, and which histologically present as a moderately differentiated SCC. However, it was not originated as a result of metastasis from the breast [10]. They proposed the previous chemotherapeutic treatment may have been involved to predispose the second neoplasm in the tongue. Similarly, previous articles demonstrated, chemotherapy-induced immunosuppression promotes carcinogenesis causing skin tumors particularly SCC [10,11]. Many anticancer drugs cause damage to the DNA of cells, and may act as carcinogens after long term treatments. Besides chemotherapy, radiation therapy also known for their long-term carcinogenic effects. Patients that underwent continuous chemotherapy are at a greater risk of presenting with a secondary malignancy, arising two to six years after the beginning of the treatment [6,12]. However, in the reported case by Addeo *et al.*, the patient was an elderly and has a history of smoking, which much likely to be another risk factor to develop OSCC. In accordance with Addeo *et al.*'s report, we suspected that our patient might develop SCC as the second neoplasm because of immune suppression after chemotherapy. Our argument supported by previous meta-analysis that immunodeficiency plays a role in the development of tongue cancer. Predominantly, the tongue and floor of the mouth cancers are not associated with carcinogenic factors, despite other sites of the oral cavity may have previous exposure history to carcinogens [7].

It is of known that chemotherapy leads to some oral complication, and one of them was viral infection. Another etiological factor is associated with viral infections involving Epstein - Barr virus (EBV) and Human Papillomavirus (HPV). It is possible that the viral infections are not related in the predisposing factor to develop SCC after chemotherapy, as the commonly oral viral infections occur approximately 18 days from the beginning of chemotherapy. The viral involved also different, which are herpes simplex virus type 1 (HSV-1) and herpes zoster [7,13].

Another possible risk factor was dental status of our patient. Recent meta-analysis demonstrated that chronic trauma in the form of denture flanges, broken dental restorations, and the position of the mandibular second molar may also play a vital role in the initiation and stimulation of neoplastic progression [7]. Thus, may promote or stimulate the TSCC in our patient.

In the term of outcomes, more recent studies reported no significant differences between the outcomes of SCC in younger vs. older adults. Previous cohort reported the outcome of young age TSCC and found higher locoregional recurrence and distant metastasis in young patients in comparison to older patients. Overall survival, five-year disease-free, and five-year distant metastasis-free rate were all lower in young age compared to the older age [2]. However, studied reported were not from patients with previous history of other carcinomas and already undergone chemotherapy, and the outcome may or may not differ.

4. CONCLUSION

Over any possible risk factors, we concluded that our patient is most likely to develop OSCC by chemotherapy-induced immunosuppression and that chemotherapy may act as carcinogens after long term treatments, besides the oral hygiene status of our patient.

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ETHICAL APPROVAL AND CONSENT

The patient has given consent for the case to be published.

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