CASE REPORT

Once in a Blue Moon: Second Primary P16-Negative Tonsillar Carcinoma after Temporal Bone Squamous Cell Carcinoma

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ABSTRAK

Kanser utama kedua (KUK) dikenali sebagai penyebab kematian yang berjangka panjang di kalangan pesakit kanser kepala leher (KKL). Kejadian KUK kepala leher selepas KKL dikaitkan dengan radioterapi, rokok dan alcohol. Rawatan susulan jangka panjang adalah penting bukan sahaja untuk menilai kewujudan kanser berulang tetapi juga untuk memastikan tiadaka KUK. Pengesahan awal KUK membolehkan rawatan yang sepatutnya dan dapat memberikan hasil kelangsungan hidup yang terbaik. Ujian genetik diperlukan di masa hadapan untuk lebih memahami risiko dan menambahbaik hasil perubatan pesakit KUK. Kami melaporkan kes KUK tonsil setelah 16 tahun di diagnosis kanser tulang temporal pada pesakit yang tidak merokok.

Kata kunci: kanser; kanser utama kedua; kanser sel skuamosa tulang temporal; kepala leher; tonsil

ABSTRACT

Second primary malignancy (SPM) is a well-known long-term cause of mortality in head and neck squamous cell carcinoma (HNSCC). The high incidence of head and neck SPM after HNSCC is related to field cancerisation, tobacco and alcohol exposure. Early detection of head and neck SPM is paramount to allow

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appropriate treatment and have better functional and survival outcomes. Further genomic study is warranted for better understanding about the risk, outcome and to improve survival of SPM. We reported the first case of second primary tonsillar carcinoma that was presented sixteen years after diagnosis of temporal bone squamous cell carcinoma (SCC) in a non-smoker patient. We highlighted the importance of having a long-term surveillance follow up in HNSCC, not only to look for locoregional recurrence and metastases but also to asses for SPM.

Keywords: Carcinoma; head and neck; second primary malignancy; temporal bone squamous cell carcinoma; tonsil

INTRODUCTION

Second primary malignancy (SPM) is a well-known long-term cause of mortality in patients with head and neck squamous cell carcinoma (HNSCC). Almost one third of HNSCC deaths are attributable to SPM, triple the number of deaths due to metastasis (Morris et al. 2011). The incidence of head and neck SPM in patients with HNSCC index tumour is not uncommon (12-24%) with the median time to develop SPM in six years (Diaz et al. 2016; Yamashita et al. 2017). Numerous studies support the concept of field cancerisation in SPM whereby prolonged carcinogens exposure such as tobacco and alcohol result in molecular alterations in surrounding mucosa and elevate the risk of malignant changes (Morris et al. 2011; Ng et al. 2019). A large population-based cohort study by Morris et al. (2011) reported hypopharynx squamous cell carcinoma (SCC) has the highest risk for SPM, followed by oropharynx SCC. Temporal bone SCC is rare and constitutes only 0.2% of all HNSCC. To the best of our knowledge, the incidence of SPM in temporal bone SCC has never been reported (Moody et al. 2000). We reported the first case of SPM of tonsils in a non-smoker patient, sixteen years after being diagnosed with temporal bone SCC.

CASE REPORT

A 65-year-old non-smoker male was diagnosed with stage 3 right temporal bone SCC and underwent lateral temporal bone resection with superficial parotidectomy and 30 fractions of adjuvant radiotherapy. Regular surveillance follow-up showed no clinical or endoscopic evidence of locoregional recurrence. Sixteen years later, he complained of odynophagia with painless right neck swelling for two months duration. Intraoral examination revealed ulcerative lesion at the superior pole of right tonsil. There was presence of ipsilateral level II swelling measuring 4 x 5 cm. Biopsy of right tonsil reported as P16 negative non-keratinising squamous cell carcinoma (SCC). Computed tomography (CT) scan showed enhancing mass in right

tonsillar region measuring 2.3 cm x 2.1 cm x 3.4 cm, abutting the right tongue base and the prevertebral space (Figure 1) with presence of lymphadenopathy at right level II (Figure 2). There was no radiological evidence to suggest recurrence at the right temporal region. Patient was diagnosed with right tonsillar SCC T2N2M0 and underwent radical tonsillectomy with right modified radical neck dissection. Frozen section of tissue from right tonsillar bed was negative for malignancy. Histopathological examination concluded non-keratinising squamous cell carcinoma of right tonsil with metastatic carcinoma of level II lymph nodes (Figure 3). He received adjuvant radiotherapy and free from recurrence up to 3-year follow-up.

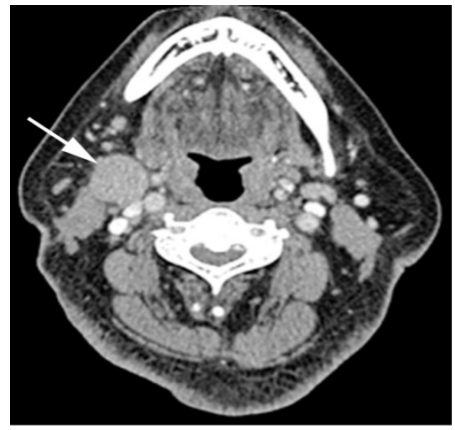

FIGURE 2: Axial CT image at a more inferior level of the palatine tonsils showed an enlarged right level IIA adenopathy (white arrow), abutting the right sternocleidomastoid muscle posterolaterally. No encasement of the ipsilateral carotid sheath was found. Few smaller subcentimetre nodes may be observed at the adjacent right level IB in this image

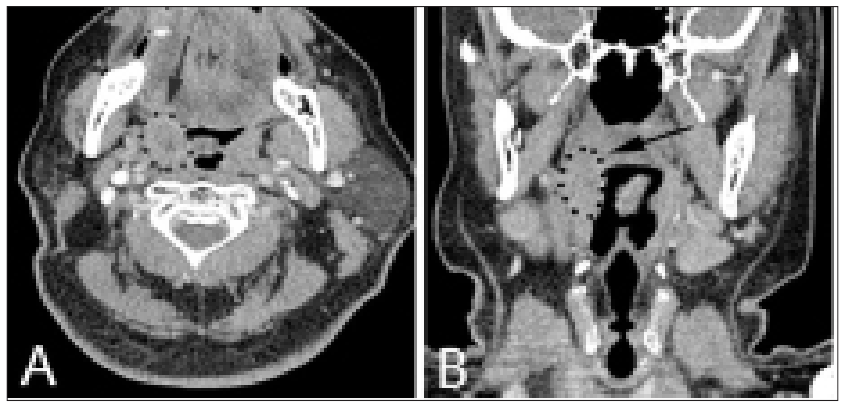

FIGURE 1: Contrast enhanced computed tomography (CT) of the neck in axial plane at level of palatine tonsils (A) and coronal plane (B) showcasing the mass (black arrows) with its margins outlined by dotted lines. On this axial image, subtle hypodense core was observed within said mass probably representing necrotic soft tissue centrally. The normal left palatine tonsil can be identified on both images. Anteriorly and posteriorly, the mass abutted the right tongue base and the prevertebral space respectively. No significant effacement of ipsilateral parapharyngeal space was seen. No vascular encasement of the right carotid sheath was indicated. The coronal image (B) showed part of the right soft palate is involved

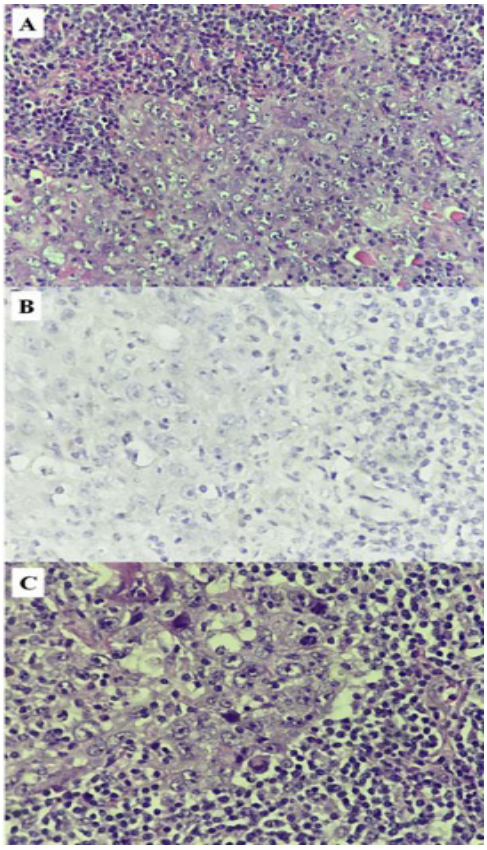

FIGURE 3: (A) The tumour composed of malignant cells arranged in sheets and exhibited large, pleomorphic and vesicular nuclei with prominent nucleoli and eosinophilic cytoplasm; (B) These cells were negative toward P16 immunohistochemistry; (C) The level II cervical lymph node demonstrated metastatic carcinoma

DISCUSSION

SPM is defined as histologically proven malignancies in both index and secondary tumour which both anatomically separated by normal mucosa and the circumstance of SPM being a metastasis from the index tumour must be eliminated (Warren & Ehrenreich 1944). On the other hand, a second malignancy that occurs at the previous site of index tumour can only be defined as SPM if it presents at least 3 years after the index tumour (Schwartz et al. 1994). SPM can be of two types. Synchronous SPM is when the lesion is detected within two to six months of diagnosis of index tumour. Contrarily, metachronous SPM occurs at least six months or more after first primary (Schwartz et al. 1994). Several studies revealed 30% to 35% of SPM in patients with a head and neck index tumour are located again in the head and neck with oral cavity and oropharynx being the most frequent sites (Morris et al. 2011; Yamashita et al. 2017). The median time for HNSCC to develop SPM in head and neck is 6 years (Yamashita et al. 2017). The five-year survival rates decreased progressively with every new head and neck tumour albeit the second tumours usually have lower stage compared to the index tumour (Morris et al. 2011), similar to our case.

Temporal bone SCC is a rare tumour among head and neck malignancies. By reason of anatomic complexity, surgical margin of advanced temporal bone SCC is difficult to be estimated during surgery and radical surgery often results in unfavourable quality of life. Thus, a combination of surgery and post-operative adjuvant radiotherapy has been recommended in advanced temporal bone SCC (Ng et al. 2019). Disastrously, the rate of radiation-related neoplasm has been estimated at 15% within five years of radiotherapy in treatment of HNSCC (Moody et al. 2000). To the best of our knowledge, there is no reported case of SPM after advanced temporal bone

SCC.

Low dose radiation is associated with higher risk of SPM as limitation in conventional beam delivery techniques in low dose radiation results in scatter dose to tissues at distance from the primary treatment volume, which may initiate carcinogenesis (Diaz et al. 2016). Another theory is field cancerisation where environmental carcinogens such as tobacco and alcohol exposure may induce field carcinogenesis causing precancerous disease and increase epithelial cancer risk throughout upper aerodigestive tract (Adjei Boakye et al. 2018). However, this was inconsistent with our patient as he was not a smoker nor alcohol consumer. This warrants further study to explore genetic susceptibility and other risk factors for SPM in HNSCC. Recently, Hoxhaj et al. (2021) identified nucleotide polymorphisms in fifty one genes with increased the risk of developing SPM in HNSCC, with p21C70T, FASLG -844C>T, P21 C98A GST-M1 and GST-T1 being the most significant. These genes were involved in pathways of carcinogenesis, including detoxification, DNA repair, apoptosis or cell cycle regulation, developmental pathway and cell adhesion (Hoxhaj et al. 2021)

This report had implications to temporal bone SCC survivors, surgeons, oncologist and public health practitioners. Therapeutic decision especially for metachronous SPM is challenging as extensive radical surgery and second radiotherapy results in unfavourable outcome. Thus, having a long-term follow up with high index of suspicion among clinicians is paramount to ensure early detection of SPM to reduce morbidity and mortality. Cancer survivors may reduce the risk of SPM by eliminating exposure to carcinogens such as tobacco and alcohol. Furthermore, future genomic study is beneficial for better understanding in identifying the risk, improving survival and influencing clinical guidelines in treating SPM in HNSCC.

CONCLUSION

In conclusion, SPM is associated with worse prognosis and high mortality. Furthermore, therapeutic decision for SPM in HNSCC is challenging as patients would have received full treatment including surgery, radiotherapy or chemotherapy. It is not a secret that early detection of SPM would reduce the mortality rate. Thus, we would like to emphasise the importance of long-term clinical surveillance not only to assess for recurrence but also to detect SPM in HNSCC including temporal bone SCC.

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