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Hermann Simo [1], Louis De Las Casas [2], Vasuki Anandan [2], Michal Preis [3] and Reginald Baugh [4]*

[1]The University of Toledo College of Medicine & Life Sciences, The University of Toledo Medical Center, Toledo, OH 43614, USA
[2]Department of Pathology, The University of Toledo Medical Center, The University of Toledo Medical Center, Toledo, OH 43614, USA
[3]Department of Otolaryngology, Maimonides Medical Center, The University of Toledo Medical Center, Toledo, OH 43614, USA
[4]Department of Surgery, Division of Otolaryngology, Head & Neck Surgery, University of Toledo Medical Center, The University of Toledo Medical Center Toledo, OH 43614, USA

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Introduction

Primary cutaneous squamous cell carcinoma tumors o en arise from the overlying epidermis or display an epidermal connection, the epidermis will show in-situ component or dysplasia, and the tumors will be located more super cially. In contrast squamous cell carcinoma tumors originating from a metastasis lack connection with the epidermis and the overlying epidermis will lack an in-situ component or dysplasia and they are o en located in the deeper dermis or subcutaneous fat. Once we know that the tumor is a metastatic squamous cell carcinoma, the next question we need to address is whether the metastasis is originating from the primary head and neck cancer, or is it a nodal presentation of a yet unknown primary tumor?

We report a rare presentation of delayed distant metastasis of tonsillar squamous cell carcinoma to the temporal scalp, eight years a er the primary tumor was treated and loco-regional control was achieved. Comparative immunehistochemical stain and in situ hybridization between the current tumor and the previous tumor eight years earlier showed similarities.

In light of patients clinical history of previous tonsilar carcinoma, combined with the facts that the current tumor has a similar morphology as the previous tonsilar tumor, immunohistochemical and In-situ hybridization studies (P16 and high risk HPV) of both tumors had similar pattern; we felt con dent concluding that we were dealing with a metastasis from the previous tonsil SCC tumor as opposed to a metastasis of a yet unknown primary.

is occurrence highlights the importance for identifying cancer stem cell lineage and the need for better methods and tools for testing and detection of sub-pathological distant metastases.

Case Report

A sixty- ve year old male was referred to our Otolaryngology clinic for follow-up a er being diagnosed with subcutaneous squamous cell carcinoma of the right temporal scalp at an outside facility.

e patient was originally diagnosed in 2003 with a 3cm keratinizing, moderately to poorly di erentiated squamous cell carcinoma of the le tonsil, which had spread to the le neck (Figure

*Corresponding author: Reginald F. Baugh, Department of Surgery, Division of Otolaryngology, The University of Toledo Medical Center, States3000 Arlington Avenue, Toledo, OH 43614, USA, Tel: 419-383-6834; E-mail: Reginald.Baugh@utoledo.edu

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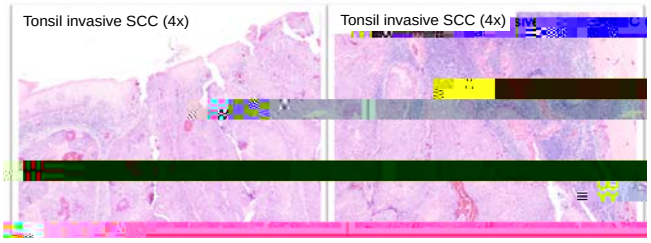

Figure 1: Tonsil Invasive squamous cell carcinoma with hematoxylin and eosin stain.

involving all surgical margins; consistent with metastasis (Figure 2). e patient was referred to our care, we completed a wide local excision with 2cm circumferential margin, the deep margin was super cial to the temporalis fascia by 3mm; the temporalis fascia was not involved but was removed as part of the specimen as an extra measure of protection. e pathology report showed SCC of similar histology as the primary tonsil tumor; a comparative immunohistochemical stain of p16 and high-risk HPV in situ hybridization between the current tumor and the previous tumor eight years ago showed similarities further supporting a distant metastasis from the original tonsil tumor (Figure 3). Both original tumor and supporting metastasis stained negative for high-risk HPV.

Discussion

e detection of a delayed distant metastasis in head and neck SCC poses a challenge to the physician: rst of all is it a primary cutaneous tumor or a metastatic tumor? Secondly is it a metastasis originating from the primary head and neck cancer, or is it a nodal presentation of a yet unknown primary tumor?

e tonsil is the most common primary site for carcinoma of the oropharynx. e incidence of distant metastasis for oropharyngeal cancer varies extensively in the literature, ranging between 4%-31% in clinical studies [1-5]. Metastases to the skin are extremely rare occurring in 1-2% of patients with head and neck SCC [6,7]. ey are o en associated with oral cavity cancers and have been reported to account between 10-15% of all distant metastatic lesions [2,5-9]. e incidence of metastasis is in uenced by various factors including location of primary tumor, initial staging, histological di erentiation and adequacy of loco-regional control at the primary site [1-5]. e occurrence of skin metastases a er treatment of head and neck SCC has been reported to be extremely rare, developing in less than 0.8% of patients with oropharyngeal head and neck SCC; with a time of occurrence between 1-36 months a er initial treatment [10].

Tumors with advanced loco-regional extension at the primary site carry an increased risk for distant metastatic spread [11]. Patients having achieved loco-regional control at the primary site are considered cured of the cancer. When they later develop distant metastases; poses a challenge to the physician- were these occult distant metastas present at the time of loco-regional treatment? What processes lea them to develop into clinically apparent disease?

For hematologic and lymphatic spread to occur so long a er the primary tumor was treated with curative intent is quite intriguing and unlikely. In our case, the fact that no enlarged lymph nodes were palpated and the PET scan did not show any lymph node involvemen leads to think of a hematogenous spread. Hematogenous spread would suggest that the circulating cancer cells used the blood to migrate from the primary site, then, hibernated for eight years before they began growing in the scalp to give rise to a cancer. Lymphatic spread would seem even less likely with the cancer cells passing through the regional lymph nodes to then enter the bloodstream to spread to the scalp. Even if these implausible events were to occur, metastases d not typically reproduce the entire spectrum of cancer subpopulations within the primary cancer. In fact, if it were not for the similarity in immunohistochemical staining as the primary tumor, this metastasis would have been mistaken for a second primary tumor. What triggered the development of cancer eight years a er the primary remains speculative; however, recent studies in cancer biology have linked Cancer Stem Cells (CSC) to tumor recurrence and metastatic spread in head and neck squamous cell carcinoma [12]. ese recent discoveries make cancer stem cells the most plausible and promising etiologic factor in our case.

Occult metastases could originate from cancer stem cells. Cancer Stem Cells (CSC) can either arise from normal stem cells or from mutated progenitor cells; and thus they possess characteristics similar to normal stem cells, speci cally the ability to give rise to all cell types found in a particular cancer sample [13,14]. erefore, due to their ability to generate tumors through the stem cell processes of self-renewal and di erentiation into multiple cell types, these cancer stem cells have been proposed to persist in tumors as a distinct population and to cause relapse and metastasis by giving rise to new tumors [14,15]. Normal adult stem cells are usually dormant undi erentiated cells that reside among di erentiated cells in an organ or tissue. When the need arises; they divide and di erentiate to replace the surrounding di erentiated cells. During the di erentiation process, they are not immune from mutation and could well give rise to a mutated cell that

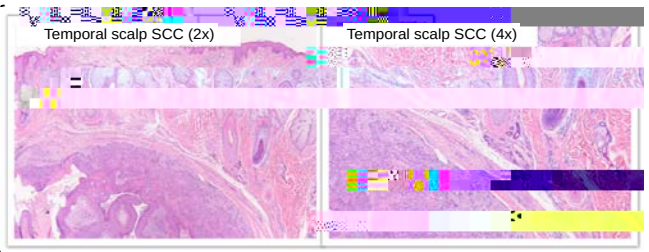

Figure 2: Temporal skin squamous cell carcinoma with hematoxylin and eosin stain.