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Case Report

Malignant Degeneration of Squamous Papilloma Involving the Temporal Bone

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We report a rare case of malignant degeneration of a squamous papilloma to squamous cell carcinoma. A 47-year-old female presented at our tertiary referral center with squamous papilloma of the middle ear that transformed into advanced-stage (T4N0M0) squamous cell carcinoma of the temporal bone, with involvement of the facial nerve, labyrinth, temporomandibular joint, sigmoid sinus, and dura of the middle and posterior cranial fossae. An extended subtotal temporal bone resection, selective neck dissection, and superficial parotidectomy were performed, followed by concurrent radiation therapy and chemotherapy. At 9 months post-surgery, a clinical exam and imaging suggested disease-free status. Although extremely rare, malignant transformation of a benign squamous papilloma of the temporal bone can occur. These lesions should be managed by gross total tumor resection, with judicious preservation of vital structures, followed by close tumor surveillance.

KEY WORDS: Papilloma, squamous cell, carcinoma, squamous cell, middle ear, case reports

INTRODUCTION

Squamous papilloma is a relatively common, benign epithelial lesion that is generally caused by infection with human papilloma virus (HPV). It is known to occur within the upper aerodigestive tract, with commonly affected sites including the larynx, pharynx, oral cavity, and sinonasal tract [1]. The middle and external ear have also been described as sites of potential involvement [1], often secondarily via direct extension through the Eustachian tube. Malignant transformation of squamous papilloma into squamous cell carcinoma is possible, with particular risk felt to be present when HPV subtypes 16, 18, 31, 33, or 45 are involved [2]. However, while an isolated benign squamous papilloma of the middle and/or external ear is not exceptionally rare, malignant transformation with extensive tumor spread throughout the temporal bone is extremely rare. In this report, we describe an unusual and unique case of primary middle ear squamous papilloma that underwent malignant transformation and destructive expansion.

CASE PRESENTATION

A 47-year-old African-American female presented with febrile illness that included acute retroauricular pain, erythema, and swelling. She had a history of left unilateral hearing loss since childhood but was otherwise healthy. A physical exam revealed an area of fluctuance over the left mastoid and a polypoid soft tissue lesion filling the external auditory canal entirely. An audiogram demonstrated conductive hearing loss with a 30-dB air-bone gap, and computed tomography (CT) of the temporal bones revealed acute coalescent mastoiditis. In addition to erosion of the mastoid cortex and bony septations, there were also mild erosion of the scutum and soft tissue noted within the middle ear. There was no CT evidence of neoplasm involving the Eustachian tube or nasopharynx. Thus, a preliminary diagnosis of a subperiosteal mastoid abscess, possibly secondary to cholesteatoma, was made.

The mastoid abscess was surgically drained through a postauricular incision, and the tympanomastoid compartment was explored; however, instead of cholesteatoma, the antrum was blocked by soft tissue. This was determined to be squamous papilloma by frozen section histopathology. Additionally, the soft tissue involving the external auditory canal was noted to originate from within the middle ear and protrude through a subtotal tympanic membrane perforation. Further exploration revealed extensive involvement of the middle ear cleft, which ultimately required disarticulation of the ossicular chain in order to achieve gross total resection of the adherent tumor and stripping of the underlying associated mucosa. These additional tympanomastoid specimens and the original specimen were evaluated with serial sectioning to confirm the presence of squamous papilloma. Although one specimen demonstrated some focal low-grade dysplasia, there was no high-grade dysplasia or carcinoma *in situ* (Figure 1). The tympanic membrane was reconstructed with a plan for a second-look surgery, including the possibility of partial temporal bone resection, in the future. Postoperatively, the tympanic membrane healed completely, and all symptoms resolved with antibiotic treatment except for hear-

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ing loss; however, the patient did not return for planned surveillance visits/second-look surgery. After having been lost to follow-up for 18 months, she returned to the clinic with a 3-day history of acute facial nerve weakness (House-Brackman 5/6), worsened hearing, and dizziness. The physical exam once again showed bulky soft tissue completely filling the external auditory canal, and a repeat biopsy found benign squamous papilloma with negative HPV 16 and 18 subtyping. A repeat CT scan showed extensive destructive changes throughout the temporal bone, including erosion into the cochlea, horizontal semicircular canal, temporomandibular joint, and cranial vault (Figure 2). An audiogram demonstrated profound unilateral sensorineural hearing loss.

Despite a previous benign biopsy and negative subtyping, the behavior of the lesion and worrisome radiologic changes raised high suspicion for a malignant lesion; therefore, a decision was made to pursue major surgical resection. An extended subtotal temporal bone resection was undertaken, during which only malignant tumor could be observed grossly. Intraoperative frozen section pathology confirmed the diagnosis of squamous cell carcinoma (Figure 3), including invasion of the facial nerve. This was sacrificed, and negative nerve margins were obtained at both the internal auditory canal and proximal extra-temporal aspect.

The adjacent dura of the middle and posterior cranial fossae was widely involved with the tumor in continuum with the sigmoid sinus (Figure 4), prompting wide dural and sigmoid resection (3x5 cm area) that ultimately yielded negative dural histopathologic margins.

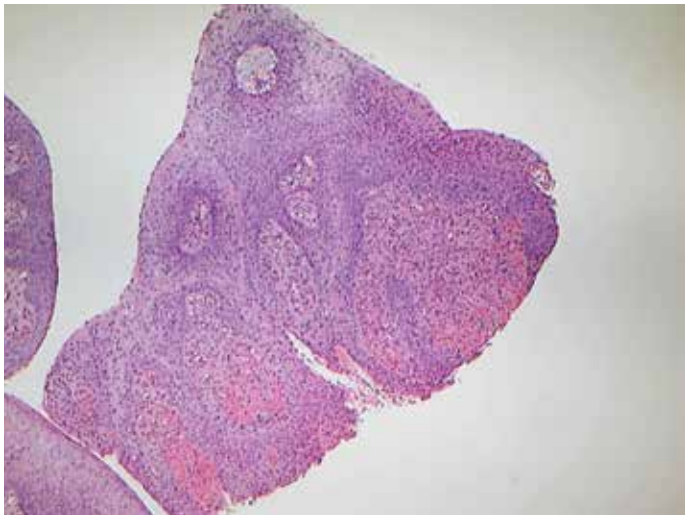

Figure 1. Frozen section biopsy. Image shows benign papillary projection of squamous epithelium. Stained with hematoxylin and eosin at 40x magnification

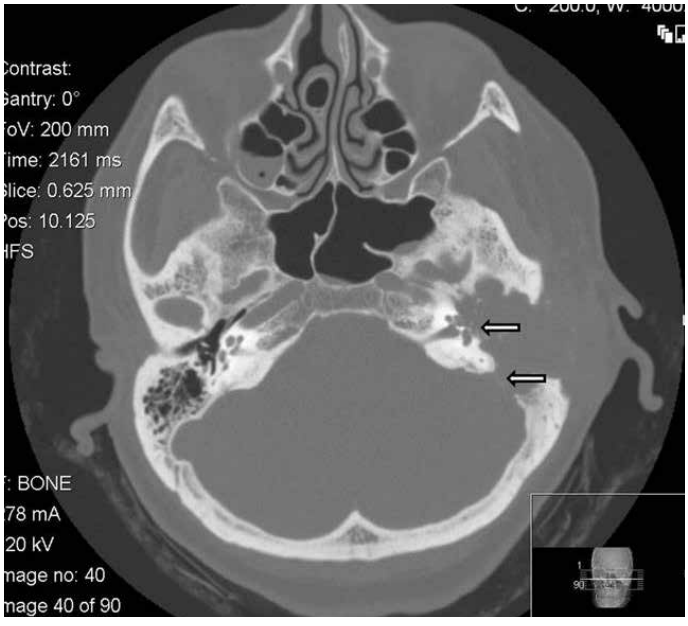

Figure 2. Postoperative axial CT scan. Arrows denote bony erosion of the cochlea and over the sigmoid sinus

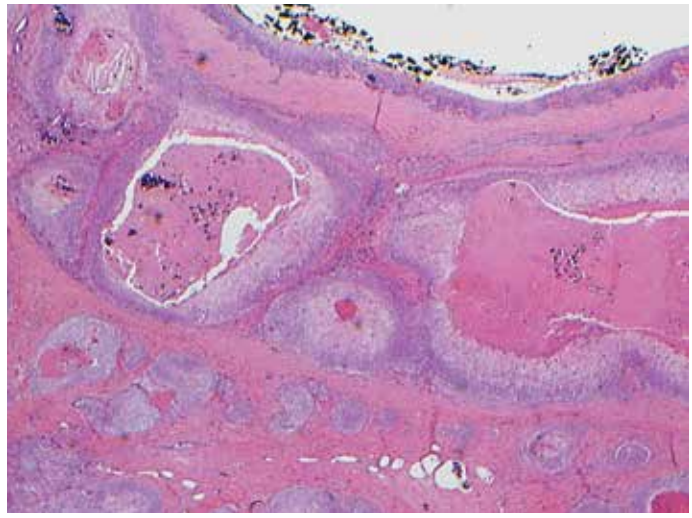

Figure 3. Frozen section biopsy after temporal bone resection. Biopsy shows invasive squamous cell carcinoma. The cells are only minimally atypical. The overlying epithelium is also minimally atypical, and the tumor presents as drop nests below the epithelium. Stained with hematoxylin and eosin at 100x magnification

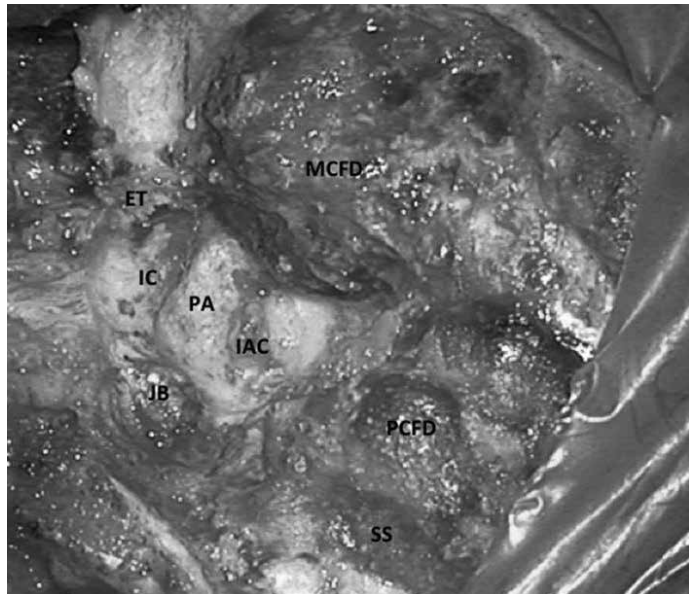

Figure 4. Left extended subtotal temporal bone resection prior to dura and sigmoid resection, demonstrating the extensive nature of dural involvement. Note the widespread involvement of the dura of the middle (MCFD) and posterior (PCFD) cranial fossae, which was resected in continuum with the sigmoid sinus (SS) with negative microscopic margins.
IC: internal carotid; JB: jugular bulb; ET: membranous eustachian tube orifice; PA: petrous apex; IAC: internal auditory canal

The brain itself was found to be uninvolved with the tumor. The temporomandibular joint and the mandibular condyle were resected in composite with the temporal bone specimen. The jugular bulb, intra-temporal carotid artery, petrous apex, mandibular branch of the trigeminal nerve (at foramen ovale), and membranous Eustachian tube were all tumor-free. Superficial parotidectomy and selective neck dissection (areas 2 and 3) did not show evidence of regional lymph node metastasis. The dura was reconstructed with DuraMatrix (Stryker Corporation; Kalamazoo, Michigan, USA), and the defect was filled with an anteriolateral thigh musculocutaneous free flap.

The final pathology report noted the presence of microvascular invasion, and Pittsburgh pathologic staging of the tumor was deemed to be $T_4N_0M_0$. The malignant portion of the tumor was well differentiated, as keratin was still being produced, and the cells were only minimally atypical; however, only 20% of the lesion was benign. Due to the requisitely vague subtotal temporal bone resection margins obtained by the drill throughout the involved temporal bone air cell tracts, the ultimate microscopic margin status was questionable.

Postoperatively, the surgical defect healed without complication. Adjuvant concurrent chemo-radiation therapy was initiated, consisting of weekly doses of cisplatin alongside a 6-week cycle of radiation at 6000 cGy. At the time of this writing, the patient was 9 months post-surgery, and the clinical exam and imaging suggested a disease-free status; however, close observation is planned for several years.

DISCUSSION

Malignant transformation of squamous papilloma involving the temporal bone is extremely rare, with only one other case in the English literature being reported by Miah et al. [3]. In their patient, the papilloma originated from the external auditory canal, as opposed to the middle ear cleft in our patient. However, due to the history of longstanding unilateral hearing loss since childhood in our patient, it is also feasible that the papilloma could have originated from within a longstanding retraction pocket. Similar to our case, their initial biopsy failed to demonstrate malignancy, and subtyping for HPV 16 and 18 was negative. Their subject was treated with radical mastoidectomy and postoperative radiation therapy and, similar to our subject at 9 months, was apparently disease-free at last follow-up (20 months post-surgery).

While generally considered benign, squamous papilloma within the head and neck region may undergo spontaneous degeneration into squamous cell carcinoma, and papillomas involved with HPV subtypes 16 and 18 have been shown to be particularly at risk. Several studies [4-6] of middle ear carcinoma have shown a high occurrence of oncogenic HPV material (≥78%) in sample tissue. A more recent study by Masterson et al. [7] reported a lower but well-verified occurrence rate of HPV in temporal bone carcinoma specimens (21%), but as previously mentioned, only a single other case exists, to our knowledge, of confirmed malignant degeneration of squamous papilloma in the ear [3].

The ideal management strategy for squamous papilloma of the ear and temporal bone is not certain, due to its relatively uncommon nature. However, given the apparent low incidence of malignant degeneration reported in the medical literature, it would seem reasonable to manage these lesions by gross total tumor resection, with judicious preservation of vital structures, such as the facial nerve and great vessels, followed by close tumor surveillance. A more aggressive approach may be justified in cases of bulky, chronically infected, and/or extensive recurrent tumor, as well as in cases judged to be at particular risk of malignant degeneration due to HPV subtyping.

In contrast to squamous papilloma, squamous cell carcinoma of the temporal bone should always be considered a potentially life-threatening condition that requires aggressive management that is tailored according to the tumor extent. Typically, a treatment regimen that involves some version of temporal bone resection is needed [8]. In early-stage disease confined to the external auditory canal, outstanding outcomes can be achieved with lateral temporal bone resection without adjuvant postoperative radiation therapy; however, the optimal management strategy for advanced-stage squamous cell carcinoma of the temporal bone is not clearly defined [9]. Radical surgery and postoperative radiation therapy for advanced-stage disease, such as the extended subtotal temporal bone resection with dural resection employed in our case, has been reported to result in 5-year survival rates falling roughly within the 30%-40% range [10, 11]. Whether or not the unique etiology of malignant degeneration from squamous papilloma and its associated tumor biology will impact the likelihood of tumor recurrence and patient survival in this case is unknown.

In conclusion, malignant degeneration of squamous papilloma of the ear and temporal bone can occur, but this appears to be exceptionally rare. In neither this nor the other reported case in the medical literature was subtyping for HPV 16 and 18 positive. Furthermore, the subjects in both cases had survived in the short term after combined management with surgery and radiation therapy; however, the long-term outlook for these patients is guarded.

Informed Consent: Written informed consent was obtained from the patients who participated in this case.

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Conflict of Interest: No conflict of interest was declared by the authors.

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