Objective: To present an uncommon case of squamous cell carcinoma (SCC) arising from severe recurrent respiratory papillomatosis (RRP) involving the upper and lower airway and temporal bone. Study Design: Case report and a review of the literature. Methods: We describe a case of a 24 year old woman with a history of human papilloma virus (HPV) type-11 since childhood originating in the larynx and trachea, then progressing to involve the distal pulmonary alveoli and right middle ear through the Eustachian tube. Papillomatous growth was treated with multiple surgeries including laser cytoreduction of laryngotracheal papillomatosis and radical mastoidectomy, followed by a trial of chemotherapy. Despite this aggressive treatment regimen, papillomatous growth progressed with recurrence in the right external auditory canal, middle ear and mastoid extending to involve the calvarium and scalp. Results: The patient underwent a composite resection of involved tissues, including the scalp, auricle and lateral temporal bone, with reconstruction using a latissimus dorsi free flap. Final pathologic analysis revealed an extensive infiltrative well-differentiated squamous cell carcinoma arising from the papilloma. A review of the literature on aggressive respiratory papillomatosis suggests that malignant transformation of juvenile-onset RRP occurs exclusively in cases positive for HPV-11. Conclusions: We report an unusual case of SCC originating from extensive RRP involving the airway, temporal bone and scalp and describe the medical and surgical management. Although the incidence of juvenile-onset RRP transformation to SCC is very low, the presence of HPV-11 as a risk factor for malignant transformation of RRP is becoming evident.

CASE REPORT

The patient is 24 year old Asian female diagnosed at the age of 2 with RRP primarily affecting her nasal cavity and nasopharynx. By the age of 10, however, she began to develop hoarseness and soon required regular laser ablations of laryngeal papillomas. Having undergone over 200 procedures without any episodes of dyspnea, shortness of breath or stridor, she was considered to have a chronic, stable form of RRP. However, at the age of 22, she experienced symptoms of airway distress and needed to be taken to the operating room for emergent laser treatment. Viral testing done at the time demonstrated HPV-11-associated RRP. Additional workup revealed extensive pulmonary involvement and accordingly the patient was started on intralesional cidofovir and subcutaneous interferon alpha-2b therapy. With subsequent further progression of disease, she was initiated on intravenous cidofovir, which reduced the average interval between surgeries but failed to bring about disease regression. Papillomatous extension into the Eustachian tube and trachea furthermore required regular medical therapy for recurrent acute oitis media on the right side and thoracic surgical involvement for tracheal disease debulking.

The patient later presented with a House-Brackmann grade II right-sided facial weakness, and computed tomographic (CT) imaging revealed complete opacification of the right mastoid with a soft tissue mass filling the medial one half of the external auditory canal (EAC). There was significant bony erosion and destruction present within the central mastoid air cells, along the tegmen, along the posterior wall of the EAC and within the middle ear. Expansion of the bony canal of the right Eustachian tube was also noted. Biopsies taken from the lesions within the EAC were consistent with papilloma and were without evidence of malignancy. A magnetic resonance imaging (MRI) scan to examine for evidence of intracranial involvement was requested, however the patient was unable to tolerate the scan. In an attempt to eradicate the otologic disease, she underwent a right radical mastoidectomy with removal of papilloma and tympanomastoid obliteration with an abdominal fat graft. Intraoperatively a small encephalocele in the tegmental defect was noted, and the dural defect was repaired with temporalis fascia. Post-operatively, the patient developed mild serous drainage from the wound and was started on oral antibiotic therapy. Subsequently, however, the patient was lost to follow up for six months.

She later re-presented with persistent serous drainage from the wound and a 4 cm post-auricular exophytic mass originating from the incision line and extending from the mastoid tip to several centimeters above the temporal line. CT scans revealed a large lesion centered in the area of the temporal bone.

DISCUSSION

• RRP transformation to a malignancy is a rare occurrence, with roughly 40 cases reported in the literature.
• Of those in which HPV genotyping was obtained, 100% demonstrated evidence of HPV-11 infection.
• Reidy and colleagues, moreover, have provided evidence demonstrating the ability of HPV-11 genes to integrate into the host genome, a known mechanism underlying the malignant conversion of “high risk” types of papillomavirus, including HPV-16 and 18. These authors suggest that RRP patients with HPV-11, currently considered a “low risk” virus, be closely followed due to their known more aggressive clinical course (Rabah) and emerging capacity for malignant transformation (Reidy).
• We also report the use of a wound vacuum to promote consistent and continuous apposition of a skin graft to the underlying free tissue flap, previously shown to be highly effective in these circumstances (Hanasono).
• Wound vacuums increase blood flow, improve tissue oxygenation and remove excess interstitial fluid (Argenta) and have been reported to increase the rate and extent of skin graft take when compared to bolster pressure dressings (Vidrine).
• The wound vacuum serves as an immobile, flat dressing resistant to shear forces that need not be changed until five to seven days post-operatively.
• Although we were able to successfully confirm flap perfusion routinely with handheld Doppler probing of the subcutaneous vascular pedicle in the neck, the benefits of negative pressure dressings will have to be considered in concert with this drawback on a case-by-case basis.

CONCLUSIONS

We present a unique case of SCC arising from RRP extending through an iatrogenic defect in the temporal bone and onto the auricle and scalp. Moreover, we contribute to the collection of reports of HPV-11-associated RRP malignant transformation. This case underscores the need for clinicians to have a low threshold to biopsy suspicious lesions of aggressive papillomatosis in the setting of HPV-11 infection. Principles of cancer-directed surgery are maintained in the medical and surgical management of these patients.

REFERENCES