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Case Report

Pre-operative chemoradiation for sinonasal undifferentiated carcinoma of the anterior nasal cavity resected through a lateral nasal flap approach☆

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ABSTRACT

Introduction: Sinonasal undifferentiated carcinoma (SNUC) is an exceedingly rare and aggressive tumor that carries a poor prognosis due to its non-specific presentation and advanced stage at time of diagnosis. Early detection and treatment are vital, with chemotherapy, radiation, and surgery all being viable options. The literature is sparse and there is no consensus for optimal treatment. In surgical candidates, the otolaryngologist must have a vast skill set in order to resect the tumor with wide margins and reconstruct the defect in hopes of returning the patient to their pre-morbid state.

Methods: A 74-year-old female presented with a growing left nasal mass which was biopsied and found to be a sinonasal undifferentiated carcinoma originating from the anterior nasal cavity between the septum and upper lateral cartilage. The patient was treated with neo-adjuvant carboplatin with concurrent radiation, followed by resection through a lateral nasal flap. The defect was reconstructed with a contralateral septal hinge flap and septal cartilage graft with primary closure of the lateral nasal flap.

Results: Intraoperatively, no skin or cartilage invasion was noted and as such, nasal skin was spared and utilized for primary closure. At a follow-up of 3 months, the patient had no evidence of recurrence and had a well healing repair site with satisfactory cosmesis.

Conclusions: Despite the aggressive nature of SNUC tumors, neo-adjuvant chemo-radiation and surgical intervention with functionally and aesthetically minded reconstruction can provide patients with improved outcomes and decreased morbidity.

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1. Case presentation

A 75-year-old otherwise healthy female presented to the office complaining of an enlarging left nasal mass over the past 1 year. She stated that she was having increasing difficulty breathing from the left nasal passage and also noticed that the left side of her nose was beginning to appear swollen and distorted. She denied weight loss, nasal discharge, epistaxis, changes in vision and cognition, or any other constitutional symptoms.

A complete head and neck examination was performed including fiberoptic nasopharyngolaryngoscopy, revealing a large grayish polypoid mass protruding from the left nasal vestibule. The mass appeared to be originating from the superior vestibular mucosa in the region between the septum and the left upper lateral cartilage. There was no evidence of posterior extension or invasion of regional structures. The remainder of the examination was unremarkable and revealed no adenopathy, masses, or gross abnormalities.

A fine-needle-aspiration of the nasal mass revealed an undifferentiated carcinoma in the background of inflammation. Tumor specific stains were performed and found to be positive for p16, Ki-67, p63, and CK (AE1/AE3), conferring the diagnosis of sinonasal undifferentiated carcinoma. The pathology findings from the biopsy can be seen in Fig. 1.

The patient was evaluated by medical and radiation oncology, and began treatment with cisplatin and concurrent external beam radiation. After the first week of cisplatin, the patient had an elevation in creatinine so therapy was changed to weekly carboplatin, which was continued for an additional 6 weeks. Following completion of treatment, the tumor was grossly decreased in size and repeat imaging was performed as shown in Fig. 2. Computed tomography (CT) and magnetic resonance imaging (MRI) revealed residual tumor in the anterior nasal cavity with questionable involvement of the cartilage and nasal skin.

Following a thorough discussion with the patient, the decision was made to surgically extirpate the remaining tumor followed with primary reconstruction. As imaging suggested possible involvement of the nasal skin, the decision was made to access the tumor through a lateral nasal flap and reconstruct with a paramedian forehead flap. Following incision and elevation of the nasal flap, the soft-tissue envelope of the nose appeared to be uninvolved. Repeat examination suggested that the tumor was wedged between the left septal mucosa and upper lateral cartilage. The tumor was resected *en bloc* with septal cartilage, left septal mucoperichondrium, and the left upper lateral cartilage. Frozen section analysis of the surgical margins was negative.

As nasal skin was not resected, a paramedian forehead flap was not performed. The septal mucosa on the right side was raised as a hinge flap and used to recreate the inner lining of the anterior left nasal cavity. With the remaining septal cartilage, a large graft was taken for dorsal support and

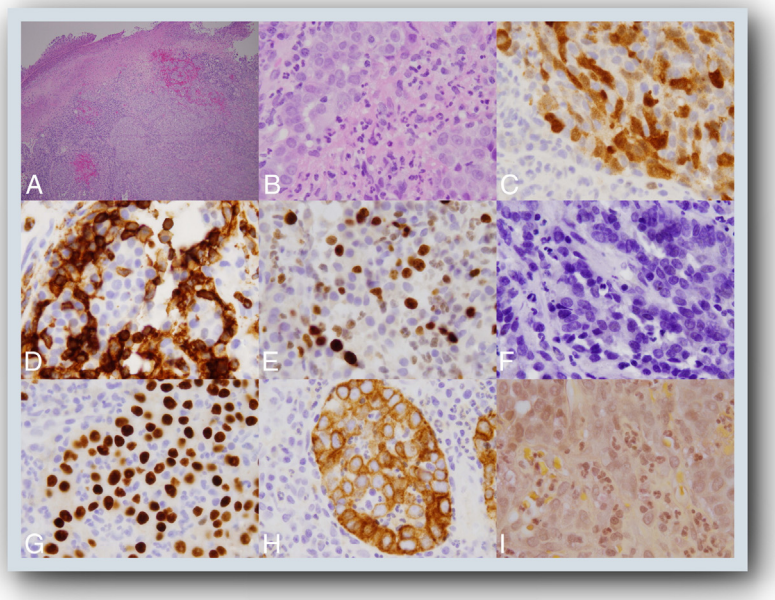

Fig. 1 – Pathology slides from fine needle biopsy of left nasal mass revealing sinonasal undifferentiated carcinoma. (A) Hematoxylin and eosin stain, 10×. (B) Hematoxylin and eosin stain, 100×. (C) Partial positivity to p16, 100×. (D) Negative staining for CD45, 100×. (E) 30% positivity to Ki-67 in proliferating carcinomatous cells, 100×. (F) Negative staining for EBER (*in situ* hybridization for Epstein–Barr virus), 100×. (G) Positive p63 stain, 100×. (H) Positive CK (AE1/AE3 cytokeratin cocktail), 100×. (I) Negative staining for mucicarmine, 100×. Courtesy of Dr. Codrin Iacob, Department of Pathology at New York Eye and Ear Infirmary of Mount Sinai.

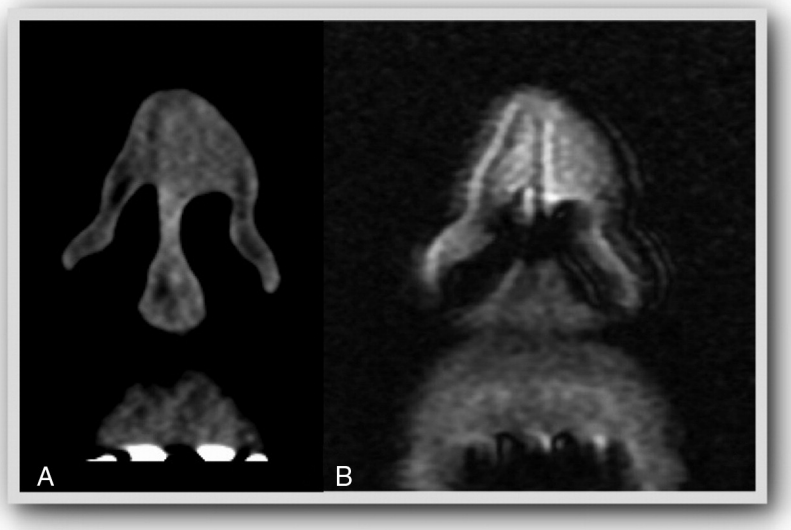

Fig. 2 – Imaging following pre-operative chemotherapy and external beam radiation showing anterior nasal tumor with suggestive of cartilage and skin involvement. (A) Non-contrast coronal CT showing anterior nasal mass. (B) T1 coronal MRI with contrast showing enhancement of nasal mass. Compared to the right side, the plane between cartilage and nasal skin is not well preserved suggesting chondrocutaneous involvement. Courtesy of Dr. Roy Holliday, Department of Radiology at New York Eye and Ear Infirmary of Mount Sinai.

secured overlying the hinge flap. The lateral nasal flap was closed primarily, and the surgery was concluded at that time. The steps of the resection and reconstruction are displayed in Fig. 3.

Post-operatively, the patient had no surgical complication and has been healing well thus far. Endoscopic examination of the left nasal cavity at three-months revealed an intact reconstruction without evidence of disease recurrence (Fig. 4).

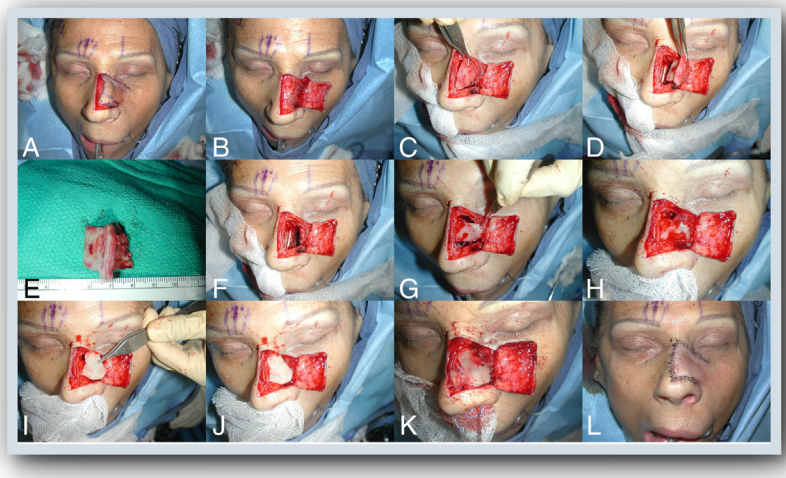

Fig. 3 – En bloc resection of lesion through lateral nasal flap approach with reconstruction using septal hinge flap and septal cartilage graft. (A) Left lateral nasal flap incised and raised. (B) Lateral nasal flap reflected laterally to reveal underlying tissue. (C) Resection lesion held in place to demonstrate orientation. (D) Resected lesion partially removed from nasal cavity. (E) Resected lesion revealing tumor, septal cartilage, and upper lateral cartilage. (F) Post-resection defect. (G) Septal hinge flap raised on right septal mucosa. (H) Septal hinge flap secured to recreate nasal lining. (I) Septal cartilage graft held over proposed placement site. (J) Septal cartilage placed over hinge flap. (K) Cartilage secured to recreate dorsal support and contour. (L) Primary closure of nasal flap. Patient photographs used with permission.

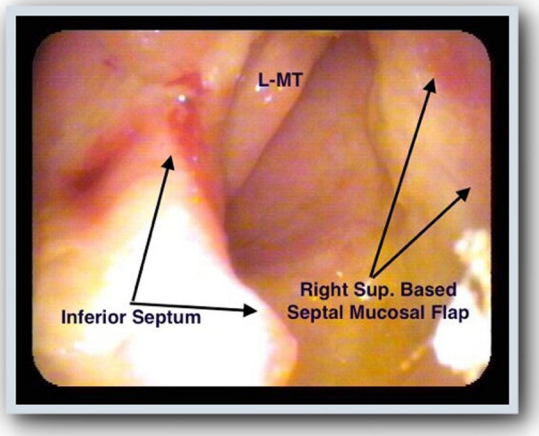

Fig. 4 – Endoscopic view of left nasal cavity at three months post-op revealing well healing repair and no evidence of recurrence.

2. Discussion

First reported in 1986 by Frierson et al. [1], SNUC is a rare tumor with a reported incidence of 0.02 per 100,000 [2]. These masses are hypothesized to develop from Schneiderian epithelium of the sinonasal tract and are further subcategorized into exophytic, inverted, and oncocytic papillomas. [3] Symptoms develop rapidly in the weeks preceding diagnosis. Epistaxis, facial swelling, nasal obstruction, proptosis, vision changes, and pain are common complaints. In a large retrospective epidemiologic survey, Chambers et al. [2] concluded that SNUC shows a three times greater predilection for men than for women and mean age at time of diagnosis is 57.8 years. Diagnosis at age greater than 60 years, intracranial extension, and presence of neck disease portends an unfavorable prognosis [2,4]. In order of likely incidence, primary tumor site include the maxillary sinus, nasal cavity, ethmoid sinus, and frontal and sphenoid sinus [5]. A link to human papillomavirus (HPV) has been reported and for uncertain reasons, patients with HPV positive tumors have better survival rates than their HPV negative counterparts [6]. HPV negative, p16 positive cases have also been identified [7].

The rarity of SNUC and non-specific nature of symptoms at time of presentation often delays diagnosis. As defined by the American Joint Committee on Cancer, an estimated 84% to 92% of patients are initially diagnosed with T4 disease [8]. Detailed immunohistochemical analysis of a tissue specimen is the gold standard for diagnosis. The aggressive nature of these tumors, with local invasion of the orbit and skull base, makes management a formidable challenge for the otolaryngologist [9]. Median survival time following diagnosis is 22.1 months [2]. Overall disease-free survival rate after treatment is 26.3% between both genders [4].

Presently, there is no consensus on staging or treatment regimens for SNUC. Current literature focuses on comparing the survival probabilities of patients who undergo surgery, radiation, chemotherapy, and a multi-modal approach. When a single-modality treatment is utilized, surgery alone confers the highest survival rate [10]. Musy et al. [11] report a 64% survival rate in patients who underwent surgery compared with a 25% survival rate in those who received definitive radiotherapy ± chemotherapy. As with all oncologic resection, the goal of surgery should be gross total resection with negative margins. Subtotal resection is associated with lower local control rates and earlier times to recurrence [12]. Unresectable tumors, such as those that invade the optic pathway or cavernous sinus, encase the carotid artery, or extend in the cranium, are best addressed with definitive radiation ± chemotherapy [13]. There is no consensus on the optimal radiotherapy dose for SNUC, although doses ranging from 50 to 60 Gy resulted in appreciable disease regression [14]. Cyclophosphamide, doxorubicin, vincristine, and platinum based treatments are the most cited chemotherapies in the management of SNUC.

The timing and optimal order of multi-modal treatment and the methods employed to surgically debulk these tumors remain unclear. The type and extension of the surgery are dictated by the spread of disease. The trend has been toward wide craniofacial resection with maxillectomy, orbital exenteration ± neurosurgical involvement followed by adjuvant chemotherapy.

To our knowledge, this is the first reported case of SNUC treated with neoadjuvant chemoradiation followed by resection through a lateral nasal flap. Based on our experience, we propose neoadjuvant therapy as a strong consideration for the treatment of SNUC tumors at the time of diagnosis to improve mortality and promote feasibility of cosmetic and functionally minded surgical resection. Adjuvant radiotherapy ± chemotherapy should be considered when advanced local or regional disease is present [4]. Intensity modulated radiotherapy ± proton beam therapy is recommended in such cases to reduce late toxicity events and visual impairment [4].

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