The Role of Chemotherapy in the Management of Sinonasal and Ventral Skull Base Malignancies

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KEYWORDS

- Chemotherapy Sinonasal cancer Sinonasal tumor Multimodality therapy
- Systemic treatment Neoadjuvant chemotherapy

KEY POINTS

- In most cases of advanced sinonasal and ventral skull base cancer, a multimodal treatment approach provides the best chance for improved outcomes.
- Depending on the tumor type and extent of disease, systemic chemotherapy has been shown to play an important role in neoadjuvant, concomitant, and adjuvant settings.
- Prospective, high-quality studies are needed to understand ideal chemotherapeutic regimens and their role and sequential timing in sinonasal and ventral skull base cancer.

INTRODUCTION

Sinonasal cancer (SNC) represents less than 3% of all head and neck cancers with an overall incidence of less than 0.001%.¹ Although more than half of tumors originate in the nasal cavity, tumors may also frequently originate in the maxillary or ethmoid sinuses.² Due to the wide array of tumor histology and molecular profiles, as well as close proximity of vital structures, such as the brain and orbit, treatment planning can be complex. A multimodality therapeutic approach with complete surgical resection with postoperative radiotherapy remains standard of care.³ The advancement of

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endoscopic approaches as well as intensity-modulated radiation and proton therapy has improved survival and outcomes. $^{4\!-\!6}$

Despite these advances, the overall prognosis of patients with advanced SNC remains poor, with a reported 5-year survival rate of 30%.² Following the treatment paradigm of other head and neck cancers, physicians have investigated the hypothesis that the inclusion of chemotherapy in the treatment of SNC may improve locoregional control rates and reduce the frequency of metastasis, ultimately resulting in improved survival. Classically, the role of chemotherapy in SNC has been limited to palliative treatment of locally advanced or metastatic SNC.³ This role has expanded, however, to neoadjuvant, concurrent, or adjuvant settings in appropriate patient cohorts. This article explores the role of systemic therapy in the management of SNC.

NEOADJUVANT CHEMOTHERAPY

Due primarily to the rare nature of SNC, no prospective, randomized trials have been performed examining the efficacy of neoadjuvant chemotherapy. Single-center studies have used chemotherapy protocols extrapolated from the head and neck literature, such as the larynx preservation studies. In addition, interpretation of such studies has been complicated by the inclusion of patient cohorts with varying histologic tumor types.² As in all cases of neoadjuvant therapy, the potential benefit of optimal drug delivery through an intact tumor blood supply is weighed against the potential of delaying multimodal locoregional treatment due to systemic toxicity.⁷ Despite these limitations, single-center studies on neoadjuvant chemotherapy for advanced SNC have shown promising results (Table 1).

A 2003 study from Licitra and colleagues⁸ investigated neoadjuvant 5-fluorouracil, cisplatin, and leucovorin in 49 patients with resectable paranasal sinus tumors. Although the 3-year overall survival rate was 69% and the achievement of a pathologic complete response predicted a favorable outcome, significant morbidity was reported. Namely, 2 deaths due to thromboembolic events as well as 8 cases of cardiac complications resulting in discontinued therapy were reported. In 2011, Hanna and colleagues⁹ published a retrospective series of 46 patients with sinonasal squamous cell carcinoma treated with a combination of neoadjuvant platinum and taxane or taxane and 5-fluorouracil followed by either chemoradiation or surgery and radio-therapy; 80% of patients had stage IV disease. Despite this advanced disease stage at presentation, response to neoadjuvant chemotherapy was reported in 67% of patients and predicted treatment outcome and prognosis. This effect was independent of subsequent choice of locoregional therapy.

Although these studies analyzed SNCs with differing histologies, the results highlight the potential benefit of neoadjuvant chemotherapy in the multimodal treatment of advanced SNC. In the future, efforts should focus on elucidating the effect of induction chemotherapy on varying tumor types to allow for development of diseasespecific protocols.

CONCURRENT CHEMOTHERAPY

Advanced head and neck cancer has been successfully treated with concurrent chemoradiotherapy,¹⁰ but data regarding its use in SNC remain less robust. Recent evidence suggests that concomitant chemotherapy and radiotherapy can achieve promising survival and locoregional control rates in certain cases of SNC.¹¹ Protocols typically describe weekly carboplatin regimens.^{12–14} Individualized concurrent chemotherapy with cetuximab has been described in patients whose tumors overexpress epidermal growth factor receptor.¹⁵ Download English Version:

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