Induction Chemotherapy for Sinonasal Tumors in Patients Presenting with Brain Invasion and/or Neurological Deficits

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Abstract

Objective   The aim of this study was to investigate the safety of induction chemotherapy (IC) for patients with sinonasal malignancies with brain invasion or a neurological deficit.

Methods   We conducted a retrospective analysis of patients who underwent IC for sinonasal malignancies with intracranial invasion or a neurological deficit at a single tertiary cancer center from 1992 to 2020.

Results   In total, 460 patients with sinonasal malignancies were included in the study. Of the patients reviewed, 341 underwent IC and within this group 40 had brain invasion (BI) and 31 had a neurological deficit (ND) at presentation. The most prevalent malignancy was sinonasal undifferentiated carcinoma (BI 40%, ND 41.9%), followed by esthesioneuroblastoma (BI 27.5%, ND 9.7%). All tumors were stage T4 with the majority lacking nodal metastases (BI N0: 72.5%, ND N0: 77.5%). All patients completed at least two cycles of IC. Partial or complete response to IC was seen in 80% of BI and 71% of ND patients. No patients had cessation of treatment due to neurologic decline and none required urgent surgery. Five patients (12.5%) with BI and 2 (6.5%) with ND had interruption of IC for reasons other than neurological decline. In patients with ND, IC led to improvement of 54.5% NDs.

Conclusion   In patients with sinonasal malignancies with BI or ND who underwent IC, no patients had cessation of treatment due to neurologic decline. In contrast, most patients had improvement of neurologic symptoms with IC. IC was safely administered without interruption due to neurological decline or symptom progression.

Keywords

► induction chemotherapy
► sinonasal
► esthesioneuroblastoma
► squamous cell carcinoma
► sinonasal undifferentiated carcinoma
► brain invasion
► neurological deficits

Introduction

Sinonasal malignancies represent a histologically diverse group of pathologies with varying risks of local recurrence, regional spread, systemic metastases, and overall disease-related mortality. Despite the heterogenous diagnoses within this disease category, local invasion beyond the paranasal sinuses into the orbit and intracranial compartment is common.[1–4] While surgery plays an important role in achieving local control, histology-specific multimodal treatment

incorporating systemic therapy and radiation therapy is associated with improved long-term outcomes.[5–11]

For biologically aggressive malignancies that are either locally invasive or at high risk for metastatic spread, induction chemotherapy (IC) has emerged as an integral part of the multimodal treatment strategy. Examples of malignancies where neoadjuvant therapy is often considered includes high-grade neuroendocrine carcinomas, squamous cell carcinoma, sinonasal undifferentiated carcinomas (SNUCs), and higher grade esthesioneuroblastomas.[6,8,12–16] The use of IC for response-adjusted local therapy has been associated with improved survival, higher rate of organ preservation, and negative surgical margins.[6,12,13,17,18]

While IC plays an important role in the histology-specific treatment of patients with sinonasal malignancies, the treatment of patients who present with neurological deficits or brain invasion (BI) remains a challenge.[19–21] The specific questions in this patient population include whether IC exacerbates neurological decline, whether its use delays surgical resection leading to neurological decline, or whether up-front surgical resection is necessary to alleviate tumor mass effect. The aim of this study was to determine the neurological safety and efficacy of IC in patients with sinonasal malignancies who present with BI or neurological deficits.

Methods

This was an institutional review board-approved study for the retrospective analysis of patients with sinonasal pathologies treated at the University of Texas MD Anderson Cancer Center (protocol RCR04–0636). The database was queried for all patients with biopsy-proven sinonasal malignancies treated between 1992 and 2020. Our analytic cohort was composed of patients with BI or neurologic deficits (NDs), who were stratified by whether they received IC. The presence of BI with or without mass effect was identified based on radiologic screening with magnetic resonance imaging. Presentation with ND was identified based on documented neurologic exams prior to IC. All neurological deficits as well as symptoms attributed to frontal lobe or brain dysfunction were recorded. However, for the purpose of this study, subjective diplopia (without neuropathy), anosmia, and trigeminal dysfunction were not included under clinically relevant neurological deficits. For all patients, treatment was offered in a histology-specific manner at the discretion of the treating providers after multidisciplinary review; the treatment protocols used have been previously reported.[6] To account for potential selection bias in this study, during the same time period of this study, patients with similar histologic diagnoses who underwent upfront surgical resection without IC were identified. The data from this patient population were analyzed and characterized in the same manner.

A review of patients' charts was performed for key demographics. Pathology was reviewed and verified, along with tumor staging as outlined by the *American Joint Committee of Cancer (AJCC) Staging Manual,* seventh edition.[22] Anatomic

invasion was further divided into violation of skull base bone, orbit, extension to the dura, subdural space, BI, and BI with radiographic evidence of mass effect. A note was made of previous treatments, including radiation, chemotherapy, or surgery. For the cohort with NDs prior to IC, neurological deficits were classified as "frontal" denoting symptoms of personality changes, affect alterations, or seizures. If neurologic defects were due to an optic neuropathy, they were categorized in the "optic" group.

Details regarding IC (agents used, number of cycles, grade 3 and 4 hematologic and nonhematologic adverse events, and response to treatment) were recorded.[23] Based on Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria, radiographic response to IC was scored in four classifications: complete response, partial response, stable disease, and progressive disease.[13,24] Information regarding management of disease post-IC was collected. For patients where IC was interrupted, the rationale for treatment interruption was noted. The reasoning for and approach used during surgery was noted.

The primary outcome assessed for each cohort was interruption of IC secondary to neurologic decline, with or without progression of intracranial disease. We used descriptive statistics, and presented findings as a mean ± standard deviation (SD), for patient demographic data, tumor characteristics, histologic features, and treatment-related variables and outcomes. Statistical analysis was performed utilizing two-tailed t-test, significance set at 0.05 α (Microsoft Excel, Microsoft Corporation v16.65, 2019).

Results

Patient Demographics and Tumor Characteristics

A total of 460 patients were reviewed (►**Fig. 1**). Of the 341 patients undergoing IC, 40 patients were found to have BI and 31 with a ND at presentation, prior to IC. Within this cohort of patients, seven experienced both BI and ND. Of the 119 patients who underwent upfront surgery without IC, 16 patients had BI and mass effect, 8 patients with a ND, and a total of 3 patients presenting with both.

Induction Chemotherapy Cohort

The demographics for all patients with BI or ND are shown in ►**Table 1**. In the IC cohort with BI, the most prevalent histologic diagnoses were SNUC in 16 patients (40%), followed by esthesioneuroblastoma (Hyams 2–4) in 11 patients (27.5%), squamous cell carcinoma in 3 patients (7.5%), poorly differentiated carcinoma in 1 patient (2.5%), and endodermal sinus tumor in 1 patient (2.5%). All tumors were stage T4, a majority of which presented without nodal metastasis (N0 72.5%). Mass effect was found in 24 patients (60.0%). In the cohort with ND, the most prevalent pathology was SNUC in 12 patients (38.7%), followed by squamous cell carcinoma in 8 patients (25.8%), neuroendocrine carcinoma in 6 patients (19.4%), esthesioneuroblastoma (Hyams 2–4) in 3 patients (9.7%), and poorly differentiated carcinoma in 2 patients (6.5%). All tumors were stage T4 without nodal metastases in 24 patients (N0 77.4%). All tumors invaded the bony skull
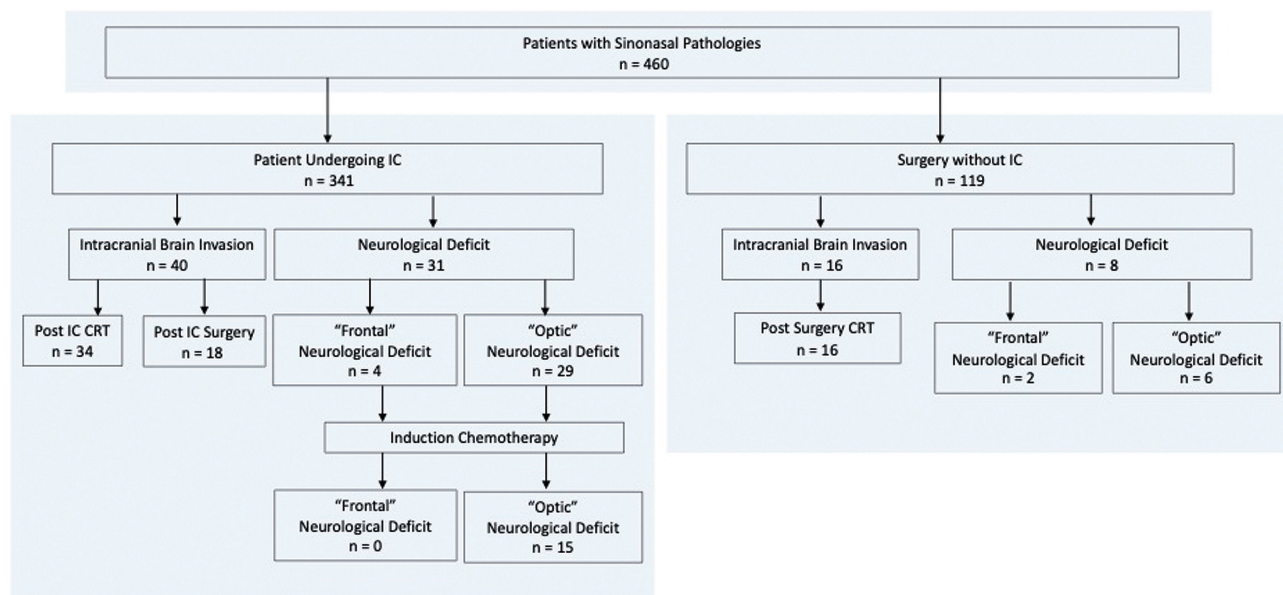
Fig. 1 Flow chart of the study population.

base and 26/31 patients (83.9%) showed orbital invasion. BI with mass effect was noted in seven patients (22.6%). Patients had previous treatment in 12.5% BI and 6.5% of the ND cohort.

Up-front Surgery Cohort

Of the 16 patients who underwent upfront surgery, the most common pathology in the BI group was esthesioneuroblastoma (Hyams 1–3) in 11 patients (68.8%) and the most common pathology in the ND group was adenocarcinoma in 3 patients (37.3%). Within the cohort of eight patients who presented with a ND, there was a nearly equal distribution of pathologies as outlined in ►**Table 1**. Among patients with ND, 6 patients had an "optic" ND, while 2 had "frontal" ND, including personality deficit/confusion in 1 patient and seizures in 1 patient. In both groups, all tumors were stage T4 without nodal metastases. Mass effect was seen in 2/16 patients (12.5%) of the BI group and 1/8 patients (12.5%) of the ND group. A quarter of patients who underwent upfront surgery had previous treatment.

Induction Chemotherapy Details

Consistent with clinical practice, the majority of patients were treated with platinum-based IC. Platinum plus etoposide was used in 23/40 patients (57.5%) and 15/31 patients (48.4%) of the BI and ND groups, respectively (►**Table 2**). The average number of treatment cycles was 3.2 (SD: 1.4) and 3.1 (SD: 0.9) in the BI and ND groups, respectively. Complete response to IC was observed in 5 (12.5%) BI and 3 (9.7%) ND patients. The majority of patients achieved a partial response to IC in both groups (67.5% BI, 61.3% ND), followed by patients who achieved stable disease (17.5% BI and 19.4% ND). Representative images of tumor response to chemotherapy of patients in the study are shown in ►**Fig. 2**. IC was interrupted in 5/40 BI patients (12.5%) and 2/31 ND patients (6.5%), but all patients were able to complete at least two

cycles. The cause for interruption of IC was adverse effects of chemotherapy in six patients, and one patient with BI elected to switch her care to Chinese herbal therapy. There were no instances of neurologic decline that merited interruption of IC in any patient in either group. Hematologic adverse events were experienced in 9/40 BI patients (22.5%) and 4/31 ND patients (12.9%), while nonhematologic symptoms were seen in 12/40 BI patients (30.0%) and 7/31 ND patients (22.9%).

Cohort Undergoing Induction Chemotherapy: Outcomes and Post-induction Chemotherapy Treatment

Consolidative radiation with or without concurrent chemotherapy was pursued post-induction in 34/40 patients (85.0%) with BI and 28/31 patients (90.3%) with ND (►**Table 3**). In the BI group, this was simultaneous chemotherapy and radiation (CRT) in 28/40 patients (70.0%). In total, 31 patients (77.5%) underwent chemotherapy and 30 patients (75%) underwent radiation, with an average dose of 66.3 Gy. Surgery was undertaken in 18/40 BI patients (45.0%) who underwent IC. The most common indication for surgery was residual disease after IC in 10/18 patients (55.5%), followed by poor or no response to IC in 5/18 patients (27.8%) and, lastly, recurrent disease after definitive CRT in 3/18 patients (16.7%). Gross total resection was achieved in 16/18 patients (88.9%), with negative margins in 13/18 patients (72.2%). Within this cohort with BI, the rate of disease recurrence was 16/40 patients (40%). The median progression-free survival was 24.8 months, and the overall survival was 55.7 months.

Of the patients who presented with ND, 21/31 (67.7%) underwent CRT. Again, the most common reason for surgery, which was performed in 11/31 patients (35.5%), was poor or no response to IC, or residual disease after treatment. The recurrence rate in this group was 51.6%, with median

Table 1 Patient demographics and tumor characteristics

	Induction chemotherapy		Upfront surgery	
	Brain invasion cohort	Induction cohort with neurological deficit	Brain invasion cohort	Neurologic deficit cohort
Total patients	40	31	16	8
Sex	26 (65%) male	18 (58.0%) male	11 (68.8%) male	5 (62.5%) male
	14 (35%) female	13 (42.0%) female	5 (31.2%) female	3 (37.5%) female
Age	48.6, SD: 17.0 y	55.1, SD: 12.8 y	59.2, SD: 11.4 y	69.1, SD: 14.0 y
Pathology				
Sinonasal undifferentiated carcinoma (SNUC)	16 (40%)	12 (38.7%)	1 (6.25%)	–
Esthesioneuroblastoma	11 (27.5%)	3 (9.7%)	11 (68.8%)	2 (25.0%)
Squamous cell carcinoma	3 (7.5%)	8 (25.8%)	1 (6.25%)	2 (25.0%)
Neuroendocrine carcinoma	–	6 (19.4%)		–
Adenocarcinoma	–	–	3 (18.8%)	3 (37.5%)
Poorly differentiated carcinoma	1 (2.5%)	2 (6.5%)	–	–
Endodermal sinus tumor	1 (2.5%)	–	–	–
Mucoepidermoid carcinoma	–	–	–	1 (12.5%)
Stage				
T4	40 (100%)	31 (100%)	16 (100%)	8 (100%)
N0	29 (72.5%)	24 (77.4%)	16 (100%)	8 (100%)
N1–3	11 (27.5%)	7 (22.6%%)	–	–
Tumor origin				
Nasal	17 (42.5%)	18 (58.0%)	4 (25.0%)	2 (25.0%)
Maxillary	2 (5%)	4 (12.9%)	–	1 (12.5%)
Ethmoid	20 (50%)	6 (19.4%)	12 (75%)	5 (62.5%)
Sphenoid	–	1 (3.2%)	–	–
Frontal	–	2 (6.5%)	–	–
Tumor extension				
Bone	40 (100%)	31 (100%)	16 (100%)	8 (100%)
Orbital	33 (82.5%)	26 (83.9%)	8 (50.0%)	5 (62.5%)
Dural	40 (100%)	25 (80.6%)	16 (100%)	5 (62.5%)
Subdural	40 (100%)	15 (48.4%)	16 (100%)	4 (50.0%)
Brain invasion	40 (100%)	7 (22.6%)	16 (100%)	3 (37.5%)
Brain invasion w/ mass effect	24 (60%)	7 (22.6%)	4 (25.0%)	1 (12.5%)
Previous treatment				
Initial treatment	35 (87.5%)	29 (93.5%)	12 (75%)	6 (75.0%)
Previous treatment	5 (12.5%)	2 (6.5%)	4 (25%)	2 (25.0%)

Abbreviation: SD, standard deviation.

progression-free and overall survival of 25.9 and 39.4 months, respectively.

Cohort Undergoing Induction Chemotherapy with Neurologic Deficits: Neurologic Outcomes

For patients presenting with ND, no patients experienced neurologic decline requiring interruption of IC. Of the 31 patients that presented with a ND, 2 had both an optic and a frontal ND. In total, 33 neurological deficits were analyzed. Eighteen of the 33 (54.5%) NDs improved after IC ($p < 0.05$) (►**Table 4).** Of all patients with ND, 29/33 (87.9%) patients had optic neuropathy prior to IC, compared with 15/29 (51.7%) after IC ($p < 0.05$). In addition, 4/33 (12.1%) NDs with a frontal etiology resolved after IC.
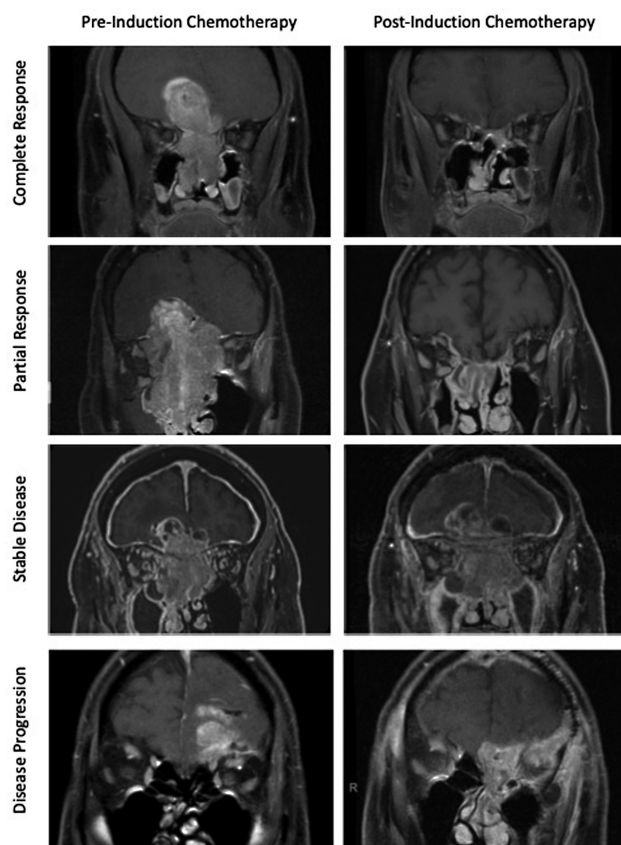
Fig. 2 Examples of sinonasal malignancies and their radiographic response to induction chemotherapy.

Cohort with Upfront Surgery: Outcomes and Postsurgical Treatment

Within the BI group, gross total resection was achieved in 11/16 patients (68.7%), with negative margins in 7/16 patients (43.7%). A transcranial surgical approach was used in 56.3% of patients and a combined transcranial, endoscopic, endonasal approach was used in 31.3%. The recurrence rate was 56.3%, with a median progression-free survival of 39.1 months and an overall survival of 84.9 months. The majority of these patients (69.7%) went on to undergo radiation, with 25% treated with CRT. In the ND group, the predominant surgical approach was a combined transcranial and trans-

facial approach (50.0%), followed by a transcranial approach alone (37.5%). A gross total resection was achieved in 6/8 patients (75%) with an equal number achieving negative margins. In this cohort, the recurrence rate was 62.5%, with a median progression-free survival of 34.2 months and overall survival of 87.1 months (►Table 5).

Discussion

Sinonasal malignancies present a challenge to clinicians due to their often-advanced stage at disease presentation. Further, their advanced stage not only denotes histopathological aggressiveness, but also a diffusely invasive tumor, extending beyond the nasal and paranasal sinuses, into the orbit and intracranial compartments.[1,2,25,26] Additionally, particular diagnoses carry elevated risks of regional and metastatic spread. A growing body of literature supports the role of IC for select diagnoses as an initial treatment as part of a larger multimodal strategy.[6,12,13] The current study demonstrates that upfront surgical resection may not be required for patients presenting with significant intracranial invasion with mass effect or a neurological deficit at presentation. Alternatively, IC is safe from a neurologic standpoint.

In a prior study, 123 patients with biopsy-proven squamous cell carcinomas who were treated with curative intent, response to neoadjuvant chemotherapy was associated with better outcomes and organ preservation.[12] Among the patients who showed at least a partial radiographic response to IC (56.9%), overall survival at 2 years was 68.2% compared with 33.3% in nonresponders. This study further provided support that IC could be utilized as an organ-sparing strategy, as a higher rate of orbital preservation was also observed. Response to neoadjuvant systemic therapy provides insight into the chemosensitivity of the tumor, and thus can aid in post-IC treatment planning. A prior study by Amit et al retrospectively reviewed data from patients diagnosed with SNUC who were treated with IC and provides further support for the use of IC; they found that a favorable response to IC was associated with better disease-specific and overall survival. A poor response to IC in this study, indicating a chemoresistant tumor, had a more surgically aggressive post-induction treatment course.[13] The multimodality management of sinonasal malignancies also includes that of

Table 2 Induction chemotherapy in patients with sinonasal malignancies with brain invasion and neurological deficits (5-FU: - 5-fluorouracil; IC: induction chemotherapy)

	Induction cohort with brain invasion	Induction cohort with neurological deficits
Induction chemotherapy agents		
Platinum + taxane	6 (15%)	4 (12.9%)
Platinum + 5-FU	1 (2.5%)	3 (9.7%)
Platinum + taxane + 5-FU	3 (7.5%)	2 (6.5%)
Platinum + taxane + ifosfamide	3 (7.5%)	4 (12.9%)

Table 2 (*Continued*)

	Induction cohort with brain invasion	Induction cohort with neurological deficits
Platinum + etoposide	23 (57.5%)	15 (48.4%)
Platinum + etoposide + ifosfamide	1 (2.5%)	1 (3.2%)
Platinum + etoposide + vincristine	1 (2.5%)	–
Adriamycin + ifosfamide + vincristine	1 (2.5%)	–
Irinotecan	1 (2.5%)	
Platinum + taxane + cetuximab	–	1 (3.2%)
Platinum + taxane + gemcitabine	–	1 (3.2%)
Cycles of IC	Avg: 3.2 (SD: 1.4), median: 3	Avg: 3.1 (SD: 0.9), median: 3
Radiographic response to induction chemotherapy		
Complete response	5 (12.5%)	3 (9.7%)
Partial response	27 (67.5%)	19 (61.3%)
Stable disease	7 (17.5%)	6 (19.4%)
Disease progression	1 (2.5%)	3 (9.7%)
Interruption in induction chemotherapy	5 (12.5%)	2 (6.5%)
Adverse events to systemic therapy		
Hematologic	9 (22.5%)	4 (12.9%)
Nonhematologic	12 (30%)	7 (22.6%)

Abbreviation: SD, standard deviation.

Table 3 Post-induction chemotherapy management and outcomes in patients with brain invasion and neurological deficit

	Brain invasion cohort	Neurologic deficit cohort
Post-induction chemotherapy treatment	34/40 (85%)	28/31 (90.3%)
Simultaneous CRT	28 (70.0%)	21/31 (67.7%)
Chemotherapy	31 (77.5%)	23/31 (74.2%)
Radiation	30 (75.0%) (Avg: 66.3 Gy)	25/31 (80.6%) (Avg: 61.1 Gy)
Post-induction chemotherapy surgery	18/40 (45.0%)_	11/31 (35.5%)
Indication		
Poor or no response to IC	5/18 (27.8%)	7/11 (63.6%)
Residual disease after IC	10/18 (55.6%)	3/11 (27.3%)
Recurrent disease after IC and CRT	3/18 (16.7%)	1/11 (9.10%)
Surgical approach		
Transcranial	3/18 (16.7%)	3/11 (27.3%)
Transcranial + transfacial	4/18 (22.2%)	2/11 (18.2%)
Transcranial + endoscopic	6/18 (33.3%)	3/11 (27.3%)
Endoscopic	4/18 (22.2%)	1/11 (9.10%)
transfacial	1/18 (5.60%)	2/11 (18.2%)
Extent of resection		
Gross total resection	16/18 (88.9%)	10/11 (90.9%)
Negative margins	13/18 (72.2%)	9/11 (81.8%)
Long-term disease control outcomes		
Recurrence	16/40 (40.0%)	16/31 (51.6%)
PFS (mo)	24.8 (SD: 27.4)	25.9 (SD: 32.9)
OS (mo)	55.7 (SD: 47.3)	34.9 (SD: 38.2)

Abbreviations: CRT, chemoradiation therapy; IC, induction chemotherapy; PFS, progression-free survival; OS, overall survival; SD, standard deviation.

Table 4 Neurological deficits and response to induction chemotherapy

	Prior to induction chemotherapy	Post-induction chemotherapy	
Total	33 (100%)	15 (45.5%)	$p < 0.05$
Frontal ND	4 (12.1%)	0	n/a
Optic ND	29 (87.9%)	15 (51.7%)	$p < 0.05$

Abbreviations: IC, induction chemotherapy; ND, neurological deficit.
Note: Of the 31 total patients that had a neurological deficit, 2 had both a frontal and optic deficits, thus a total of 33 neurological deficits included. Neurological frontal deficit (personality changes, impulsivity, seizures), optic neuropathy, or CN III, IV, VI deficit.

Table 5 Surgical approach and outcome of patients with sinonasal malignancy patients with brain invasion and neurological deficits who underwent upfront surgical resection without induction chemotherapy

	Surgical cohort with brain invasion	Surgical cohort with neurological deficit
Total patients	16	8
Surgical approach		
Anterior transcranial	9 (56.3%)	3 (37.5%)
Ant transcranial, transfacial	1 (6.25%	4 (50.0%)
Ant transcranial, endoscopic	5 (31.3%)	1 (12.5%)
Endoscopic	1 (6.25%)	–
Extent of resection		
GTR	11 (68.7%)	6 (75.0%)
Negative margins	7 (43.7%)	6 (75.0%)
Post-op adjuvant treatment		
Chemotherapy	5 (31.3%)	1 (12.5%)
Radiation	11 (68.7%)	3 (37.5%)
Chemotherapy + radiation	4 (25.0%)	0
Long-term disease control outcomes		
Recurrence rate	9 (56.3%)	5 (62.5%)
PFS (mo)	39.1, SD 35.7 mo	34.2, SD: 71.6 mo
OS (mo)	84.9, SD 69.5 mo	87.1, SD: 115 mo

Abbreviations: GTR, gross total resection; OS, overall survival; PFS, progression-free survival; SD, standard deviation.

esthesioneuroblastomas. While most authors reserve neoadjuvant chemotherapy for higher grade Hyams 2/3 or Kadish C tumors, a benefit has been shown in this patient population without an increase in complication rates.[16,27]

The relative safety and efficacy of IC in patients with advanced local disease at presentation with either ND or BI has not previously been established. In our study, we screened 460 patients in a prospectively maintained database of sinonasal malignancies to answer this question. The overall incidence of BI was 40/341 (11.7%), while the incidence of a ND at presentation was 31/341 (9.1%). To our knowledge, this is the first study to quantify these two important patient subsets within the sinonasal malignancy patient population. What remains unanswered in the literature, and a question that often arises within the treatment team, is that if there is a ND, or BI at presentation, should upfront surgical resection be pursued to address compressive etiologies causing the symptoms.

Our results show that our patient population matches well with previously published cohorts of patients with advanced locoregional sinonasal malignancies.[3] While this study was not designed to assess a specific pathology, SNUC, esthesioneuroblastoma, and squamous cell carcinoma together made up 75 and 77.4% of the BI and ND groups, respectively. All patients had stage T4 tumors, and a majority did not present with nodal metastases. Further, we extended our inclusion criteria for BI beyond simple dural, or extradural involvement to include intraparenchymal invasion, because in our opinion, this is most clinically significant. The neurological deficits included within the study were mainly composed of optic nerve neuropathies, and to a lesser extent, seizures and frontal lobe dysfunction. A platinum-based IC was utilized in the majority of patients in our study. All patients underwent at least two cycles of chemotherapy which is in keeping with the current standards of IC at our institution. The majority of patients showed a complete or

partial response to IC (80% in the BI group and 71% in the ND group) on a radiographic assessment.

Within the group of patients with ND, there were 33 total deficits in 31 patients. Two patients had both what we quantified as an "optic" and a "frontal" deficit. All of the frontal symptoms resolved after IC, prior to the initiation of further definitive treatment. Optic neuropathies improved in 14 patients, a 48.3% improvement ($p < 0.05$). Further, there were no patients in either the ND or BI cohort that experienced a neurological decline which necessitated the early termination of IC or surgical intervention to address progression of ND. Thus, our data not only support the safety of IC in patients presenting with a ND or BI, but also show a benefit in terms of improvement of neurological deficits, prior to any further definitive chemotherapy, radiation, or surgery.

During the same study period, we also report patients who underwent upfront surgical resection who had a ND or BI at presentation. Of the 119 patients who underwent direct surgical intervention, 16 presented with BI (13.4%), and 8 with a ND (6.7%). There was a higher proportion of esthesioneuroblastomas and adenocarcinomas within this patient cohort overall, which are less aggressive pathologies than squamous cell and SNUC. It is likely that the higher number of these etiologies in the surgical cohort is due to the current treatment practice that define sinonasal malignancies as a spectrum of pathologic aggressiveness, where Hyams 1/2 esthesioneuroblastomas and adenocarcinomas are typically considered less aggressive or less chemoresponsive and are more favorable surgical targets.[4,6,28] Further, the gross total resection rates were higher in the patients who underwent surgical resection after IC as compared with upfront surgical resection, (88.9 vs. 68.7%, respectively), highlighting another potential benefit of neoadjuvant chemotherapy in sinonasal malignances.

Limitations of our study include those inherent in a retrospective study design. This is not a pathology-specific analysis due to the relative rarity of the pathologies discussed, thus our results are represented in aggregate. Given this heterogeneity, we did not feel it was appropriate for a direct comparison of up-front surgery versus IC, as the distribution of pathologies was also different between these groups. However, the strength of our work is that it provides important information for clinicians and surgeons faced with patients presenting with BI or ND. The study supports the continued use and safety of IC in patients with select sinonasal malignances with BI or ND without the need for urgent upfront surgical resection and allows patients to benefit from neoadjuvant treatment.

Conclusion

Sinonasal malignancies represent an aggressive and clinically challenging problem for multidisciplinary treatment teams. In recent years, retrospective studies suggest IC is associated with an increased disease-free and overall survival. Our study further delves into the safety and efficacy of sinonasal malignancies in patients who present with BI or ND. We conclude that undergoing IC in this patient population is both safe and efficacious. This may allow patients to obtain the previously published benefits of neoadjuvant systemic therapy toward improved clinical outcomes.

Conflict of Interest
None declared.

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