

Head and Neck Cancer

Experiences and Outcomes in Olfactory Neuroblastoma Over A Decade at a Tertiary Cancer Center

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Abstract



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Background Olfactory neuroblastoma is a rare epithelial malignancy arising from the odorant receptors in the nasal mucosa or along the cribriform plate of the ethmoid bone. Clinical presentation includes nasal stuffiness, local pain, epistaxis, anosmia, visual impairment, proptosis, headache, and seizures. Radiologic imaging with CT or MRI, an ophthalmic evaluation, and histopathologic confirmation with immunohistochemistry are parts of the initial diagnostic workup. Although surgery, chemotherapy, and radiation have an equally important role in the management, earlier stages may preferably be treated with surgery or radiotherapy and the later stages with a multimodality approach.

Materials and Methods We conducted a retrospective review of 13 patients diagnosed with olfactory neuroblastoma, registered at Mehdi Nawaz Jung Regional Cancer Center over a decade (2010–2019). We analyzed the age and sex distribution, performance status at presentation, clinical symptomatology, and the Kadish stage. In addition, the therapeutic aspects of patients were studied.

Results The most common presentation noted was nasal stuffiness, followed by epistaxis and proptosis. The majority of patients had good performance status at presentation. Ten patients presented with a Kadish stage C, while the remaining patients presented with Kadish stage B. Cervical nodal metastasis was seen in three patients, four patients received multimodality treatment with neoadjuvant chemoradiotherapy followed by surgery, two patients received neoadjuvant chemotherapy followed by radiation, two patients received only surgery, and one patient received surgery followed by adjuvant radiation. Conformal radiation techniques were used to deliver doses as high as 50 to 66 Gy in 2 Gy per fraction. Two patients presented with distant metastasis during follow-up, one with bone metastasis, and the other with retroperitoneal nodal metastasis; they received palliative chemotherapy and conformal radiation to the primary site.

Conclusion This study concludes that neoadjuvant chemotherapy followed by radiation gives the best outcomes. It has been observed that in multi-modality treatment, radiotherapy played a significant role in improving overall survival and better outcomes. Multidisciplinary discussions provide a better sequencing of management.

Keywords

- ▶ Olfactory neuroblastoma
- ▶ Kadish staging
- ▶ Paranasal sinuses
- ▶ Cribriform plate
- ▶ Odorant receptors
- ▶ Nasal cavity
- ▶ Intensity-modulated radiation therapy

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Introduction

Olfactory neuroblastoma is a rare epithelial malignancy arising from the odorant receptors in the nasal mucosa or along the cribriform plate of the ethmoid bone. The purpose of this study was to assess the importance of neoadjuvant chemotherapy and radiotherapy in the management of olfactory neuroblastoma.

Materials and Methods

We conducted a retrospective review of 13 patients diagnosed with olfactory neuroblastoma, registered at the Mehdi Nawaz Jung Regional Cancer Center, over a decade (2010–2019). We analyzed the age and sex distribution, performance status at presentation, clinical symptomatology, and the Kadish stage. Several staging and grading systems have been developed to assess esthesioneuroblastoma (ENB). The Hyams grading system is used for prognosis and grading, while the Kadish system is used for staging the disease. These are the most widely used systems in modern-day literature. The difficulty in validating any staging system in the case of ENB is due to the low incidence of disease among other variables.^{1,2} In addition, the therapeutic aspects of patients were studied. We ensured follow-ups for all cases and collected the data regarding the survival of patients.

Management of Olfactory Neuroblastoma

In modern practice, multimodality/multidisciplinary therapy appears to be the best approach for olfactory neuroblastoma.³

Kadish A

Surgery alone with clear margins is sufficient in “Kadish A”-staged tumors. Adjuvant RT is indicated in close and positive margins or with residual disease. There is no role of adjuvant chemotherapy. The benefits of surgery are tumor removal, immediate relief in compressive symptoms, and proper tissue for histopathological and prognostic evaluation. An international collaborative study of 17 centers reported the role of craniofacial resection in esthesioneuroblastoma in 2012. The 5-year overall survival was 78% and the 5-year recurrence-free survival was 64%.⁴

Kadish B

Surgery followed by adjuvant RT is the treatment of choice. The role of adjuvant CT is controversial. Recent reports show the use of adjuvant CT. Neoadjuvant CT or RT can be used in inoperable cases.

Kadish C

Kadish C-staged tumors require all three modalities. Neoadjuvant approach (CT/RT/concurrent CT-RT) is preferred. An example of a challenging outcome is described by Yin et al. (2016) who used radiation therapy before surgical resection and found the results to be superior to using it after surgery in terms of disease-free survival.⁵

Intracranial extension and close proximity to the cribriform plate and ethmoidal roof requires a combined trans-

facial and neurosurgical approach.⁶ The role of chemotherapy is not clear in adjuvant settings in early tumors; however, it plays a definitive role in locally advanced and metastatic tumors. It decreases the chances of systemic failure by acting on systemic micrometastasis.⁷

In neoadjuvant settings, it decreases the size of the tumor, reduces compressive symptoms, and helps in further complete removal of the tumor. It can be combined with RT in both neoadjuvant and adjuvant settings for better results.⁸

Kadish D

Systemic chemotherapy and palliative RT to local and metastatic sites are advised. Palliative care should be incorporated for improving the quality of life.

RT is delivered to the tumor bed and local extension with nodal irradiation reserved for involved nodes. Elective nodal irradiation is not practiced routinely. The RT doses vary from 50 to 60 Gy in the literature.⁹

In small local recurrences, stereotactic radiosurgery and stereotactic radiotherapy can be used even for reirradiation.¹⁰

Results

In this study, we noticed a near bimodal age distribution with the youngest at 14 years and the eldest at 65 years. There was a female preponderance with a male to female ratio of 5:8. The most common presentation noted was nasal stuffiness, followed by epistaxis and proptosis. The majority of patients had a good performance status at presentation. Ten patients presented with a Kadish stage C, while the remaining patients presented with Kadish stage B. Cervical nodal metastasis was seen in three patients. In this study, four patients received multimodality treatment with neoadjuvant chemoradiotherapy followed by surgery, two patients received neoadjuvant chemotherapy followed by radiation only, two patients received only surgery, and one patient received surgery followed by adjuvant radiation. Conformal radiation techniques were used to deliver doses as high as 50 to 66 Gy in 2 Gy per fraction. Two patients presented with distant metastasis during follow-up, one with bone metastasis and the other with retroperitoneal nodal metastasis; they received palliative chemotherapy and conformal radiation to the primary site (→ [Table 1](#)).

Discussion

Being a rare malignancy, treatment protocols for olfactory neuroblastoma need to be constructed after reviewing many institutional experiences. In developing countries such as India, most of the cases of olfactory neuroblastoma presented at an advanced stage, that is with cervical metastases and Kadish stage C. Thus, it is necessary to decide on management options.

In this study, four patients received multimodality treatment with neoadjuvant chemoradiotherapy followed by surgery, two patients received neoadjuvant chemotherapy followed by radiation only, two patients received only surgery, one patient received surgery followed by adjuvant

Table 1 Patients' characteristics, staging, and treatment given in this study

Patient Number	Age (y)	Gender	Kadish stage	Chemotherapy	Radiation	Surgery	Metastasis	Survival (months)
1	60	F	C	NACT: VAC IE	50 Gy IMRT	Subtotal resection	—	7
2	60	M	C	NACT: 2 cycles cisplatin + etoposide	50 Gy IMRT	Subtotal resection	—	13
3	35	M	C	NACT: 2 cycles cisplatin + etoposide	54 Gy IMRT	Subtotal resection	—	24
4	16	F	C	Neoadjuvant CT-RT with cisplatin	54 Gy VMAT	Subtotal resection	—	26
5	14	F	C	NACT: 6 cycles CAP	50 Gy 25# IMRT	—	—	10
6	17	F	C	NACT: 6 cycles CAP	60 Gy IMRT	—	—	60
7	20	F	B	—	Adjuvant RT 66 Gy IMRT	Left medial maxillectomy	—	58
8	31	M	C	—	—	Bifrontal craniotomy, excision	—	22
9	65	M	C	—	—	Subtotal resection	—	3
10	16	M	C	Concurrent cisplatin, palliative chemotherapy VAC IE	66 Gy IMRT	—	Retroperitoneal nodes, left supra clavicular nodes	30
11	65	F	B	Palliative chemotherapy: zole-dronic acid	66 Gy IMRT	—	Bone metastasis, 30 Gy to lumbar spine, sternum	25
12	55	F	B	—	—	—	—	—
13	35	F	C	—	—	—	—	—

Abbreviations: CT, chemotherapy; IMRT, intensity-modulated radiation therapy; NACT, neoadjuvant chemotherapy; RT, radiotherapy; VAC IE, vincristine, Adriamycin, cyclophosphamide, ifosfamide, etoposide.

radiation. Conformal radiation techniques were used to deliver doses as high as 50 to 66 Gy in 2 Gy per fraction. Two patients presented with distant metastasis during follow-up, one with bone metastasis and the other with retroperitoneal nodal metastasis; they received palliative chemotherapy and conformal radiation to the primary site. As we observed, multimodality treatment such as neoadjuvant chemotherapy and radiation achieved surgical resection without affecting the critical organs. However, the outcomes and survival also improved with the multimodality management in the advanced stage (Kadish stage C). The neoadjuvant chemotherapy schedules were used such as VAC IE (vincristine, Adriamycin, cyclophosphamide, ifosfamide, etoposide), CAP (cyclophosphamide, Adriamycin, carboplatin), and cisplatin–etoposide.

Due to the rarity of the disease and different treatment modalities in different centers, generalizations about single-center experiences are difficult. Moreover, there is heterogeneity that comes with the findings that must be kept into consideration while evaluating the results.

Conclusion

Being a rare malignancy, treatment protocols for olfactory neuroblastoma need to be constructed after reviewing many institutional experiences. This study concludes that neoadjuvant chemotherapy followed by radiation gives the best outcomes and feasibility for surgery, as most of the patients presented with advanced disease (Kadish C). Doses of 50 to 66 Gy can be delivered using conformal radiation techniques while respecting the doses to organs at risk, especially the eye, optic nerve, optic chiasm, brain, and pituitary gland. It has been observed that, in multi-modality treatment, radiotherapy played a significant role in improving the overall survival and better outcomes. Multidisciplinary discussions can provide a better solution to the sequencing of management.

Abbreviations

MNJ	Mehdi Nawaz Jung
Gy	Gray
CT	Chemo Therapy
MRI	Magnetic Resonance Imaging

IMRT	Intensity Modulated Radiation Therapy
RT	Radio Therapy
ENB	Esthesio Neuroblastoma
Yrs	Years
NACT	Neoadjuvant Chemo Therapy
VAC IE	Vincristine, Adriamycin, Cyclophosphamide, Ifosfamide, Etoposide
CAP	Cyclophosphamide, Adriamycin, Carboplatin
PALL	Palliative
VMAT	Volume Modulated Arc Therapy

Conflict of Interest

None declared.

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