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Original Article

Esthesioneuroblastoma Treatment Results From a Tertiary Care Center

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Abstract

Background: Esthesioneuroblastomas (ENB) or olfactory neuroblastomas are extremely rare malignant tumors of the head and neck region. Surgery is the primary modality of treatment. Adjuvant radiotherapy (RT) is used from Kadish stage B onward. RT is used as a single modality whenever surgery is not possible. Chemotherapy is used in residual, inoperable, advanced, and metastatic diseases.

Materials and Methods: Patients diagnosed with ENB between January 2012 and December 2017 in our institute were analyzed retrospectively.

Results: Five patients were treated in the study period (5 years). The median age of the patients was 54 years with M:F ratio of 1.5. Most of the patients had nasal block as presenting symptom followed by epistaxis. All the patients presented in the advanced stage (Kadish C and D). Surgery was possible in only two-third of patients in stage C, and they received adjuvant RT. One-third of patients in stage C received radical RT. Half of the patients in stage D were fit for palliative RT alone, and the other 1/2 received radical RT dose. Chemotherapy was given for four patients with four cycles of cisplatin and etoposide. After chemotherapy, there was partial response in two patients, complete response in one patient, and progressive disease in one patient.

Conclusion: Since ENBs are rare, the standard of care and chemotherapy role remains to be explored a lot. Radiation and chemotherapy help in many patients, especially as palliation.

Key words: Esthesioneuroblastoma, Hyams pathological grading, Kadish stage, Olfactory neuroblastoma

INTRODUCTION

Esthesioneuroblastomas (ENB) or olfactory neuroblastomas are uncommon malignant tumors of the head and neck region and were first described by Berger and Luc.[1] They usually arise from nasal mucosa and cribriform plate and the cell of origin is thought to be olfactory receptors. Due to proximity to the central nervous system and locally aggressive nature,[1] they become inoperable or complete excision that is difficult, and many patients require radical or adjuvant radiotherapy (RT). The incidence is very rare, and it forms 3% of endonasal neoplasms. The median age of the patient is 53 years, and bimodal distribution is seen with most patients presenting in the 4th–6th decade and some cases in the 2nd decade.[2-6] Male predominance is seen. The presentation can include nasal block, epistaxis, nasal discharge, pain, and nodal spread or distant metastasis can occur rarely. Special staging system, known as the Kadish system and its modification,[7,8] is used unlike other head and neck malignancies, where AJCC system is used. The most commonly computed tomography (CT) scan is performed to find the bony extension, and magnetic resonance imaging (MRI) gives the detailed picture of intracranial extension and orbital invasion of disease, and both are complementary to each other. Since this is a neuroendocrine tumor octreotide scan and positron emission, tomography/CT has a role and can be useful in picking up nodal or distant metastasis. A pathological examination only will confirm the diagnosis. Whenever surgery is possible, it should be done first with a craniofacial approach yielding superior local control and survival than transfacial approach.[9] Combined surgery and adjuvant RT improved survival over surgery or RT

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alone.[9] The role of adjuvant chemotherapy is unclear. Chemotherapy with cisplatin and etoposide combination is used in disseminated and locally advanced disease with or without local treatment.[10]

MATERIALS AND METHODS

This manuscript was written to find the presentation and treatment outcome of this uncommon malignancy in our population and also the treatment outcome. Details of all head and neck cancer patients registered between January 2012 and December 2017 were searched, and those who were histologically proven to be ENB were identified and analyzed. Six patients were identified, and details of one patient were incomplete, and hence, those five patients were analyzed individually. Statistical analysis was made with the help of SPSS software version 23. Mean, mean, mode, standard deviation, range, percentage, and disease response at the end of primary and subsequent treatment were analyzed.

RESULTS

Five patients with a diagnosis of ENB were analyzed. Three were male and two were female. The median age of presentation was 54 years (range 39–62 years). The median follow-up period was 61 months (range 33–83 months). Symptom duration ranged from 1 month to 26 months. About 80% (n = 5) of the patients had nasal block (right side being more common) and 60% (n = 3) patients had bleeding from nose. Other symptoms and signs and their median duration of time are depicted in Table 1. The median duration for diagnosis after the presenting complaint was 35 days (range 20–48 days). Three (60%) patients had Kadish stage C and 2(40%) patients had Kadish D stage. Eastern cooperative oncology group (ECOG) performance score was 1 for 2 patients, score 2 for 2 patients, and score 3 for 1 patient. Hyams' grading system was used for histopathological reporting. Grade of the individual patient is shown in table 3, and 1 patient's grading could not be done (Patient 1), as slides and blocks could not be traced. All the patients were worked up initially with CT and MRI, and the feasibility of surgery was assessed in tumor board with head and neck team and neurosurgeons. CT and MRI of two patients are shown in Figure 1a and b, respectively. Only two patients with Kadish stage C were taken up for surgery, and both of them had residual disease after surgery (Patient 1 and 4), and they received adjuvant RT. Patient 2 was in poor ECOG and, hence, received only palliative RT of 30 Gy followed by palliative care. The other two patients (Patient 3 and 5) received a radical radiation dose of 66 Gy. Four patients received chemotherapy after radiation was completed with cisplatin 100 mg/m^2 D1 and etoposide 100 mg/m^2 D1-D3q21 days. Three patients received four cycles, and one patient could receive two cycles only and stopped due to disease progression. A complete response could be achieved in only one patient, and he received all three modalities of treatment. Individual patient responses to initial treatment and subsequent treatment with chemotherapy are shown in Tables 3 and 4, respectively.

DISCUSSION

All five patients presented in an advanced stage (Kadish stage C or D) which makes complete excision difficult. Surgery being the primary modality of treatment, when not adequate, it leads to poor treatment outcome. RT, when used after surgery as an adjuvant treatment, will produce better treatment outcome than surgery alone for Kadish stage B onward.[11] Doses <54 Gy usually produce inferior local control.[12] Radiation alone usually has poor survival, as shown in the literature.[11] RT helped in palliation of

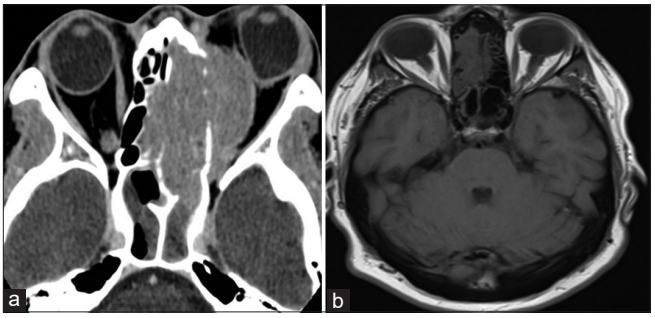

Figure 1: (a and b) Computed tomography and magnetic resonance imaging of Patient 3 and 4, respectively

Table 1: Kadish staging of olfactory neuroblastomas

Stage	Definition
A	Confined to nasal cavity
B	Involves the nasal cavity and one or more paranasal sinuses
C	Extending beyond the nasal cavity or paranasal sinuses
D	Regional lymph node or distant metastasis

Table 2: Presentation

Signs/Symptom	Number (%) n=5	Median duration (months)
Nasal obstruction	4 (80)	21
Epistaxis	3 (60)	1.5
Right:Left:Bilateral	2:1:1	
Nasal discharge	3(60)	9
Loss of smell (anosmia)	2(40)	5
Neck swelling	3 (60)	26
Nasal swelling	4 (80)	7
Pain	-	-
Visual disturbance	1 (20)	2
Diplopia	1(20)	1
Epiphora	1(20)	3
Otalgia	-	-

Table 3: Hyams' grading system

Grade	Lobular preservation	Mitotic index	Nuclear polymorphism	Fibrillary matrix	Rosettes	Necrosis
1	+	None	None	Prominent	HW rosettes	None
2	+	Low	Moderate	Present	HW rosettes	None
3	±	Moderate	Prominent	Low	HW rosettes	Rare
4	±	High	Marked	Absent	None	Frequent

Table 4: Initial treatment

P. No.	Age	Sex	Grade	Stage	Initial treatment	RT dose	Response
1	54	M	NR	C	SX + RT	54 Gy/30#	SD
2	62	M	3	D	RT	30 Gy/10#	PD
3	58	F	2	C	RT	66 Gy/33#	SD
4	51	M	2	C	SX + RT	55.8 Gy/31#	PR
5	39	F	4	D	RT	66 GY/33#	PR

P. No: Patient number, M: Male, F: Female, NR: Not recorded, SX: Surgery, RT: Radiotherapy, SD: Stable disease, PD, Progressive disease, PR: Partial response

Table 5: Subsequent treatment

P. No.	Subsequent treatment	Number of cycles	Response
1	CIS+ETO	2	PD
2	PALLIATIVE CARE	-	-
3	CIS+ETO	4	PR
4	CIS+ETO	4	CR
5	CIS+ETO	4	PR

P. No: Patient number, PD: Progressive disease, PR: Partial response, CR: Complete response, PR: Partial response

symptoms such as nasal block, epistaxis, nasal discharge, and pain, especially when debulking is not possible and in patients with poor performance status. The mode of RT is very important due to the presence of critical structures such as optic nerve, optic chiasma, and brain stem since more than 54 Gy is required in the adjuvant setting and 66–70 Gy in radical setting for better disease control. Intensity-modulated RT and proton therapy will be helpful in this scenario. Concurrent chemo is not a standard of care, unlike squamous cell carcinoma of head and region, where it is given routinely along with RT. Chemotherapy is given only as an adjunct to surgery and RT and not helpful as a single modality as these tumors are not much chemosensitive. The most commonly used drugs are cisplatin, etoposide, vincristine, cyclophosphamide, and Adriamycin. There are no large randomized control trials comparing various drug combinations as its extremely difficult to recruit the patients due to the rarity of incidence. Each institution has various policies of choosing chemotherapy schedule. In our institute, cisplatin and etoposide are given for residual disease and inoperable setting after RT. It produced partial response in 50% of patients and some patients poorly respond to chemotherapy. Hence, disease response after two cycles is important both clinically and by imaging to avoid cisplatin toxicity for non-responders.

CONCLUSION

Esthesioneuroblastomas are still challenging, due to the rarity of the tumor and proximity to critical structures. More Indian data are required to compare results from different institutions and will help in developing the standard of care.

ETHICAL APPROVAL

Obtained as per the institution protocol.

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