Orbital Preservation in Patients with Esthesioneuroblastoma

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Abstract

Objectives Surgical resection in addition to adjuvant radiation with or without chemotherapy is the mainstay of treatment for esthesioneuroblastoma (ENB). However, management of patients with orbital involvement remains controversial. Historically, orbital exenteration has been advocated when there is evidence of periorbital invasion. Recently, the indications for orbital exenteration have become more selective and orbital preservation has been advocated. We report our experience with anterior craniofacial resection and orbital preservation in patients with ENB.

Design Retrospective review of all patients diagnosed with esthesioneuroblastoma who underwent traditional open anterior craniofacial resection at the Massachusetts General Hospital/Massachusetts Eye and Ear Infirmary Cranial Base Center from 1997 to 2008.

Results Sixteen patients were identified with a mean follow-up of 76 months. All patients underwent anterior craniofacial resection via an open approach and adjuvant proton beam radiation. Six of the 16 patients had evidence of either periorbital or lacrimal sac involvement at the time of surgery. All of these patients underwent periorbital resection to negative histologic margins with preservation of the orbit.

Conclusion In our study, patients with ENB and periorbital invasion—who were treated with anterior craniofacial resection and periorbital resection with orbital preservation—had no evidence of decreased survival. In all patients, negative histologic margins of the periorbital resection were achieved.

Keywords

- ▶ esthesioneuroblastoma
- ▶ anterior craniofacial resection
- ▶ orbital preservation
- ▶ skull base

Introduction

First described by Berger et al in 1924, esthesioneuroblastoma (ENB) is a rare malignant tumor of the sinonasal vault believed to arise from the olfactory epithelium.¹ Historically there have been several proposed strategies for management of ENB. In general, surgical resection with adjuvant postoper-

ative radiation therapy, with or without chemotherapy, has been the mainstay of treatment.^{2–8}

Because of the typical location of ENB within the superior nasal vault and sinonasal cavity, close approximation or frank involvement of the orbit is often seen at the time of initial assessment. Typically, surgical treatment for sinonasal tumors involving the periorbital or orbit included oncologic

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resection and orbital exenteration.⁹ More recently, the indications for orbital exenteration have become more selective, and orbital preservation has been advocated in a variety of settings.^{10–12}

The current treatment regimen for patients with ENB and orbital involvement at the Massachusetts General Hospital/Massachusetts Eye and Ear Infirmary Cranial Base Center consists of craniofacial resection (CFR) with orbital preservation followed by proton beam radiation therapy with or without chemotherapy.¹³ Previous review of this protocol demonstrated 5-year disease-free and overall survival (OS) rates of 90% and 87.5%, respectively—which compares favorably with those of other institutions.^{4,6,13,14} The goal of the present study is to review our experience with orbital preservation in patients with ENB and periorbital involvement who underwent treatment with an intent to cure.

Materials and Methods

The medical records of all patients diagnosed with ENB who underwent traditional anterior craniofacial resection at the Massachusetts General Hospital/Massachusetts Eye and Ear Infirmary Cranial Base Center between 1997 and 2008 were reviewed. Institutional review board (IRB) approval was obtained for this study. For the purpose of this study, orbital involvement was defined as histologic involvement of the periorbital. Sixteen patients were identified and included in the study.

Preoperative clinical data, imaging studies, operative notes, pathology reports, and follow-up medical records were reviewed for each patient. The patients were then divided into two categories: Group A, whose tumors did not invade the periorbital, and Group B, whose tumors did

invade the periorbital. The records were then examined to determine the long-term treatment results. The primary end point of the study was overall 5-year survival.

Surgical resection included traditional anterior craniofacial resection for all patients. During surgery the periorbital was inspected. If there was evidence of periorbital involvement, resection was performed with frozen sections utilized to confirm negative margins. All patients received postoperative proton beam radiation therapy. Seven patients received adjuvant chemotherapy.

Results

Our series included sixteen patients—eight women and eight men. Their mean age at diagnosis was 47 years, ranging from 11 to 77 years. Mean follow-up time was 76 months. Ten patients were found to have no periorbital involvement (Group A) (►Table 1) and six patients were found to have evidence of periorbital involvement (Group B) (►Table 2).

Four patients developed recurrences an average of 57.8 months after diagnosis. Two of these patients were in Group A and two were in Group B. In Group A, Patient 3 underwent CFR with postoperative proton beam radiation. He recurred locally at the edge of his frontal craniotomy bone flap 72 months after diagnosis. Recurrent tumor was managed with surgical excision and re-irradiation. He is currently alive without disease 125 months after his initial treatment. Patient 7 developed distant metastases to the brain and spine, which were managed with palliative chemotherapy. This patient ultimately succumbed to disease 31 months after diagnosis.

In Group B, patient 2 was treated with neoadjuvant chemotherapy, followed by CFR and mixed photon/proton

Table 1 Group A. Treatment and Outcomes: No Periorbital Involvement

Patient	Treatment	Total RT (Gy)	Chemo	Recurrence (months)	Final status	Total follow-up time (months)
1	CFR + proton/photon RT	66	None	No	NED	85
2	CFR + proton/photon RT	59.4	None	No	NED	106
3	CFR + proton/photon RT	59.2	None	Yes (72)	NED	125
4	CFR + proton RT	54	None	No	NED	113
5	CFR + proton RT	70	None	No	NED	75
6	Endoscopic resection (partial) → CFR + proton RT	54	None	No	NED	82
7	CT (NR) → CFR + proton/photon RT + CT	67.2	2 cycles cisplatin, etoposide → NR → 2 cycles carboplatin, etoposide	Yes (16)	DOD	31
8	CFR + proton RT + CT	68	4 cycles carboplatin	No	NED	30
9	CFR + proton RT	70	None	No	NED	65
10	CFR + proton RT	66	None	No	NED	35

Abbreviations: AWD, alive with disease; CFR, craniofacial resection; CT, chemotherapy; DOD, dead of disease; NED, no evidence of disease; NR, no response; RT, radiotherapy.

Table 2 Group B. Treatment and Outcomes: Positive Periorbital Involvement

Patient	Treatment	Total RT (Gy)	Chemo	Recurrence (months)	Final status	Total follow-up time (months)
1	CFR + proton/photon RT + CT	70.2	4 cycles cisplatin, etoposide	No	NED	77
2	CT (NR) → CFR + proton/photon RT	67	2 cycles cisplatin, etoposide	Yes (82)	AWD	176
3	CT (NR) → CFR + proton RT	60	2 cycles cisplatin, etoposide	Yes (61 & 143)	AWD	146
4	CFR + proton RT + CT	60	4 cycles cisplatin, etoposide	No	NED	33
5	CFR + proton RT + CT	60	4 cycles cisplatin, etoposide	No	NED	38
6	CFR + proton RT	66	None	No	NED	32

Abbreviations: AWD, alive with disease; CFR, craniofacial resection; CT, chemotherapy; DOD, dead of disease; NED, no evidence of disease; NR, no response; RT, radiotherapy.

irradiation. He recurred both regionally and distantly and was managed with surgical resection, chemotherapy, and re-irradiation. He is alive with probable disease 176 months after initial treatment. Patient 3 was also initially treated with chemotherapy followed by CFR and proton beam radiation. She recurred regionally 61 months after diagnosis and was managed with a parotidectomy and neck dissection. At 143 months following her diagnosis, she was found to have a second recurrence in the nasopharynx and cervical lymph nodes. She is currently undergoing proton beam radiation and concomitant weekly chemotherapy with carboplatin and Taxol (Bristol-Myers Squibb, New York, New York, USA).

Kaplan-Meier survival curves were constructed for 5-year OS rates (► **Fig. 1**). The calculated 5-year OS was 87.5%. There was no statistically significant difference in overall between Group A and Group B ($p = 0.4$).

Discussion

Since the early 1970s, several guidelines for orbital preservation in the setting of sinonasal malignancies have been proposed based on the degree of tumor involvement of the bony orbital wall and orbital structures.^{10–19} The evolution of treatment has been toward orbital preservation. Sisson in 1970 was one of the first to advocate orbital preservation, recommending preoperative radiation therapy followed by intraoperative evaluation.¹⁰ Harrison and Som later reported their experiences, with each recommending orbital exenter-

ation only in the setting of bone erosion determined at the time of surgical resection.^{11,12} In 1980, Weymuller et al reported that their series of patients—whose orbit was preserved in the face of bone erosion—had a similar prognosis to those who were treated with orbital exenteration.¹⁵

In 1988, Perry et al examined 41 patients with malignancies that abutted the orbital walls, 26 of which eroded through bone.¹⁶ In this study, if the tumor could be peeled from the periorbita, the eye was saved; if the periorbita was only minimally involved, it was locally resected with frozen-section control. Using this algorithm, they reported that preservation of the orbit did not alter local control or OS.

These findings were further supported by Imola et al in 2002.¹⁹ They reported on 66 patients undergoing treatment for sinonasal malignancy encroaching the orbit. Their indications for orbital exenteration included (1) involvement of the orbital apex, (2) nonresectable full-thickness invasion through periorbita into retrobulbar fat, (3) extension into the extraocular eye muscles, (4) invasion of the bulbar conjunctiva or sclera, and (5) lid involvement beyond a reasonable hope for reconstruction. The authors concluded that selective orbital preservation is oncologically safe and that consideration should be given to rigid orbital reconstruction in larger defects resulting from subtotal or total orbital floor resection or resections involving two or more orbital floors.

Unlike previous reports, our series reviewed a single disease entity. None of our 16 patients would have fulfilled Imola's criteria for orbital exenteration. The average time to recurrence of our four patients was 57.8 months, which is consistent with the late recurrences noted in the literature and reinforces the need for continued long-term follow-up. Of these four recurrences, two had gross periorbital invasion at the time of surgery and two did not. Of note, all three of the patients who underwent initial chemotherapy instead of upfront surgery recurred, whereas only one of 13 patients who underwent initial CFR recurred.

Overall, there was no statistically significant difference between Group A and Group B. In fact, the only death in our series occurred in a patient without periorbital involvement.

Fig. 1 Overall survival.

All patients in our series had preserved vision and extraocular motion after completion of treatment. The incidence of reported epiphora was equal in both groups.

Conclusion

In our series of patients treated for ENB, we believe that sparing the orbit in the face of gross or microscopic peri-orbital involvement is oncologically reasonable. Our experience with these 16 patients, 6 of whom had invasion of the periorbital, supports preservation of the orbit with resection of the periorbital utilizing frozen section control followed by proton beam radiotherapy with or without chemotherapy.

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