ESTHESIONEUROBLASTOMAS WITH INTRACRANIAL EXTENSION

PROLIFERATIVE POTENTIAL AND MANAGEMENT

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SUMMARY - A total of 15 patients with esthesioneuroblastomas were treated between 1978 and 1992 at the Neurosurgery Department, Nordstadt Hospital, Hannover. In 9 cases, the tumors invaded the anterior cranial fossa. One patient died before any surgical intervention. Eight tumors were operated by a combined paranasal and subfrontal approach. Gross total tumor removal was achieved in all cases. Apart from anosmia, the only postoperative complication was transient mental changes in one case. Immunohistochemical analyses with MIB 1 monoclonal antibodies, directed against recombinant parts of Ki-67 antigen, were performed to estimate the proliferative potential of the esthesioneuroblastomas. Most of the tumors showed high proliferating cell indexes, which ranged from 3 to 42% (mean, 16%). The proliferating cell index with MIB 1 showed a correlation with postoperative outcome, although this was not statistically significant. Esthesioneuroblastomas can be totally removed surgically. The proliferating cell index may reflect histologically the biological behavior of tumor. Long-term follow-up is mandatory, and imunohistochemical studies may be of help in predicting outcome.

KEY WORDS: anterior cranial base, MIB 1, neuroblastoma, olfactory nerve, paranasal sinuses, radiotherapy.

Estesioneuroblastomas com extensão intracraniana: análise do potencial proliferativo e conduta

RESUMO - O índice proliferativo celular tumoral de 8 casos cirúrgicos de estesioneuroblastomas com extensão intracraniana (9 com extensão intracraniana em um total de15, coletados de 1978 a 1992 no Hospital Nordstadt de Hannover, Alemanha) foi avaliado através do anticorpo monoclonal MIB-1, notando -se uma correlação prognóstica. A maioria dos tumores revelou índice proliferativo alto (3% a 42%, média de 16%) e a classificação histopatológica de Hyam foi utilizada. A ressecção foi radical em 100% dos casos e o acesso cirúrgico combinado (paranasal e subfrontal) o preconizado. Os autores apresentam revisão da literatura discutindo a sua casuística.

PALAVRAS-CHAVE: base craniana anterior, MIB 1,neuroblastoma, nervo olfatório, seios paranasais, radioterapia.

Esthesioneuroblastomas (olfactory neuroblastomas) are uncommon neoplasms probably derived from the neuroepithelial sensory cells of the olfactory mucosa[1,2]. They arise in the nasal vault, near the ethmoid sinus, usually presenting as masses in the nasal cavity[1,3]. The most common findings are unilateral nasal obstruction and epistaxis. These tumors frequently invade the paranasal sinuses, the nasopharynx, the palate, the orbit, the base of the cranium, and even the brain[4]. In

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approximately 20 to 25% of cases they produce neurological symptoms due to intracranial invasion[2,5]. Esthesioneuroblastomas are often slow growing tumors that do demonstrate a response to radiation therapy, but often have a tendency to reccur[1,6]. Metastases into the regional lymph nodes and to the lung occur in one-fifth of all patients[5,7]. The staging system of classification into three groups suggested by Kadish et al. (depending on the location of the tumor) and modified by Morita et al. has been of prognostic value[8,10]. Prognosis depends on the histological maturity and the degree of malignancy. However, a systematic evaluation of the proliferation activity of esthesioneuroblastomas using immunohistochemical techniques has not been described so far. The monoclonal antibody MIB 1 has the same sensitivity and specificity of Ki-67 with the major advantage of its utility in paraffin sections preserved for years[11].

We report on our experience in dealing with 8 cases of esthesioneuroblatomas presenting with intracranial extension. The diagnosis of esthesioneuroblastoma was made based on histopathological features and radiological localization of tumor. These cases were operated on via a combined craniofacial approach. The paraffin sections of 7 esthesioneuroblastomas were used for immunohistochemical tests that evaluate the proliferation activity of tumor cells. An attempt has been made to correlate the biological behavior of these tumors with the immunohistochemical studies.

MATERIAL AND METHODS

Between 1978 and 1992, 15 patients with olfactory neuroblastomas were treated in the Neurosurgery Department of Nordstadt Hospital. In 9 cases, the tumors invaded the anterior cranial fossa (Fig 1). One patient with a very large intracranial tumor extension died before any surgical intervention was attempted. Eight patients underwent tumor removal by a combined transfacial-subfrontal approach. These 8 cases constiute the object of this study. All patients underwent plain X-rays, nonenhanced and enhanced computed tomography (CT) with soft tissue and bone algorithms (Fig 2). Cerebral angiography was also performed in all cases in order to study the tumor vascularity, and the involvement of the major vessels. Embolization was not carried out in these
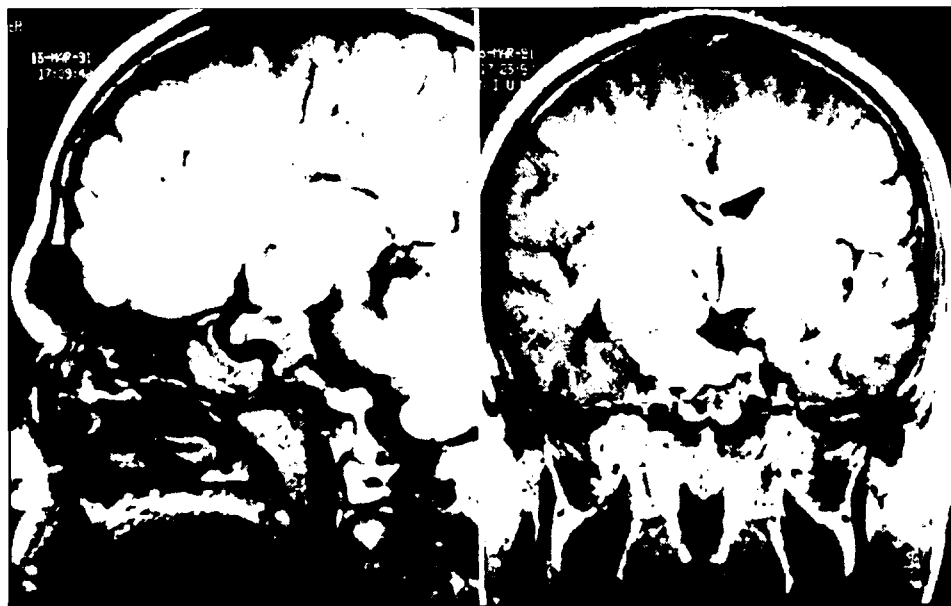

Fig. 1. Preoperative sagittal (left) and coronal (right) Gadolinum-enhanced MRI slices of the esthesioneuroblastoma of Case 8 showing the dorsal part of the tumor involving the ethmoid sinus, sphenoid sinus, and carotid artery. The tumor shows an isointense and a hyperintense portion with suprasellar extension.

Fig 2. Bone destruction is seen at bone window CT scan in the region of ethmoid sinus.

patients. In 3 most recent cases, magnetic resonance imaging (MRI) was also obtained.

Surgical approach

The surgical procedures usually involved first a paranasal approach and then a intradural subfrontal approach (Fig 3). For the extracranial tumor removal, a paranasal incision was performed extending from the medial third of the eyebrow to the base of the ala nasi. The maxillary process of the frontal bone, and the frontal process of the maxilla were exposed. After removal of bone, the tumor was exposed and was removed in piecemeal. For the intracranial part, the anterior skull base was exposed intradurally through a bifrontal craniotomy and later the tumor was removed with help of microscope and Cavitron Ultrasonic Surgical Aspirator (CUSA). For small tumors, the olfactory nerves were microsurgically dissected and resected. Since the bone resection usually involved the cribriform plate, the ethmoid roofs, and a portion of the planum sphenoidale, the skull base would be reconstructed in two-layers fashion consisting of a dural flap and a galeal pericranial flap. In case of large cranial defect, a methylmethacrylate plate was molded to the shape of the defect and placed between the dural and the galeal flaps.

Histopathological studies

Besides hematoxilin and eosin (H&E), electron microscopy or immuno-histochemistry studies (chromogranin, neuron specific enolase, S100, vimentin, and keratin) were performed in all cases. The following histological factors at H&E studies were considered: lobular architecture, mitosis,

Table 1. Hyams' grading system for esthesioneuroblastomas.

Histopathogical factors	Grade			
	1	2	3	4
Lobular architecture	+	+	±	±
Mitosis	-	+	++	+++
Nuclear pleomorphism	-	+	++	+++
Rosettes	HW ±	HW ±	Flexner ±	-
Necrosis	-	-	Occasional	Common

HW, Homer-Wright; - absent; +, present; ++, prominent; +++, marked; ± , present or absent

nuclear pleomorphism, necrosis, and rosettes. Based on these factors, a tumor grade from 1 to 4 was established according to the Hyam's Grading System[3] (Table 1).

Immunohistological studies with MIB 1

Formalin fixed paraffin sections of 7 consecutive esthesioneuroblastomas were available for immunohistochemical studies. The immunohistochemical staining was performed as described by Cattoretti et al[6]. In summary, the paraffin sections were dewaxed in xylene & acetone and rehydrated. They were then processed in a microwave with 10 mM citric acid buffered with 2M NaOH to pH 6.The sections were treated first with normal serum (rabbit against mouse) in 1:20 dilution, followed by primary antibody MIB 1 (Dianova, Hannover, Germany) in 1:10 dilution. These were stained with APAAP immunostaining technique. The immunostaining was controlled by histologic sections of tonsilla-tissue submitted to the same reactions.

The cell was classified as positive when either the entire nucleus or a portion of the nucleus was stained (Fig 4). The number of positive and negative cells were scored in a total of 500 cells per area (total of 6 areas) or 3000 cells per section. The labelling index (LI) or growth fraction was defined as the proportion of positive cells in relation to the total of 3000 cells evaluated (excluding labelled endothelial cells and lymphocytes). A total of 6 readings were performed. The average LI (LI mean) was obtained by adding all 6 readings and dividing by 6. The maximal LI (LI max) was the highest of the 6 readings.

Follow-up evaluation

Postoperatively, besides clinical evaluation all patients underwent endonasal endoscopy and enhanced CT scans at the time of discharge, in order to determine the completeness of the tumor removal. After discharge, clinical, endoscopical, and radiological (CT) follow up was regularly carried out to detect or to exclude tumor recurrence.

Postoperative treatment consisted of radiotherapy, either immediately after the first surgery or later on after detection and removal of tumor recurrence.
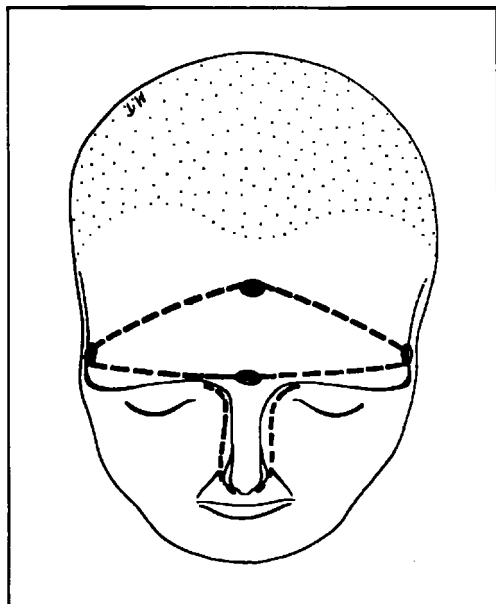

Fig 3. Drawing of combined surgical bifrontal-paranasal approach for craniofacial resection of esthesioneuroblastoma. The paranasal incision is performed in one or both sides depending on tumor extension in the nasal and paranasal cavities.

RESULTS

The esthesioneuroblastomas accounted for 0.3% of all 2800 intracranial tumors, which were operated upon in our Department in the same period. Six patients were women and 2 were men. The average age was 50 years, ranging from 29 to 70 years.

The time interval between beginning of symptoms and diagnosis of the disease varied considerably, ranging from 4 months to 10 years (mean 3 years). Most common symptoms and signs were sensation of nasal obstruction (63%), decrease of smell sensation (50%), epistaxis (38%), and visual loss (13%). One patient with a large intracranial involvement had signs of frontal lobe dysfunction.

In 7 cases, previous transnasal biopsy and extracranial ENT intervention indicated the diagnosis of esthesioneuroblastoma, which led to planning the definitive neurootological procedure. Craniofacial intervention was performed with "total" tumor resection in all cases. Postoperatively, 5 patients received radiotherapy which dosis ranged from 45 to 66 Gy.

Clinical, endoscopic and radiological follow up examinations showed that one patient has been free of disease 5-1/2 years after combined surgery and radiotherapy (Case 5). One patient has been free of tumor 4-1/2 years after surgery (Case 6). One patient presented with lymph node metastasis at the neck 7 years after the surgery, but she had no local recurrence of tumor (Case 1). One patient
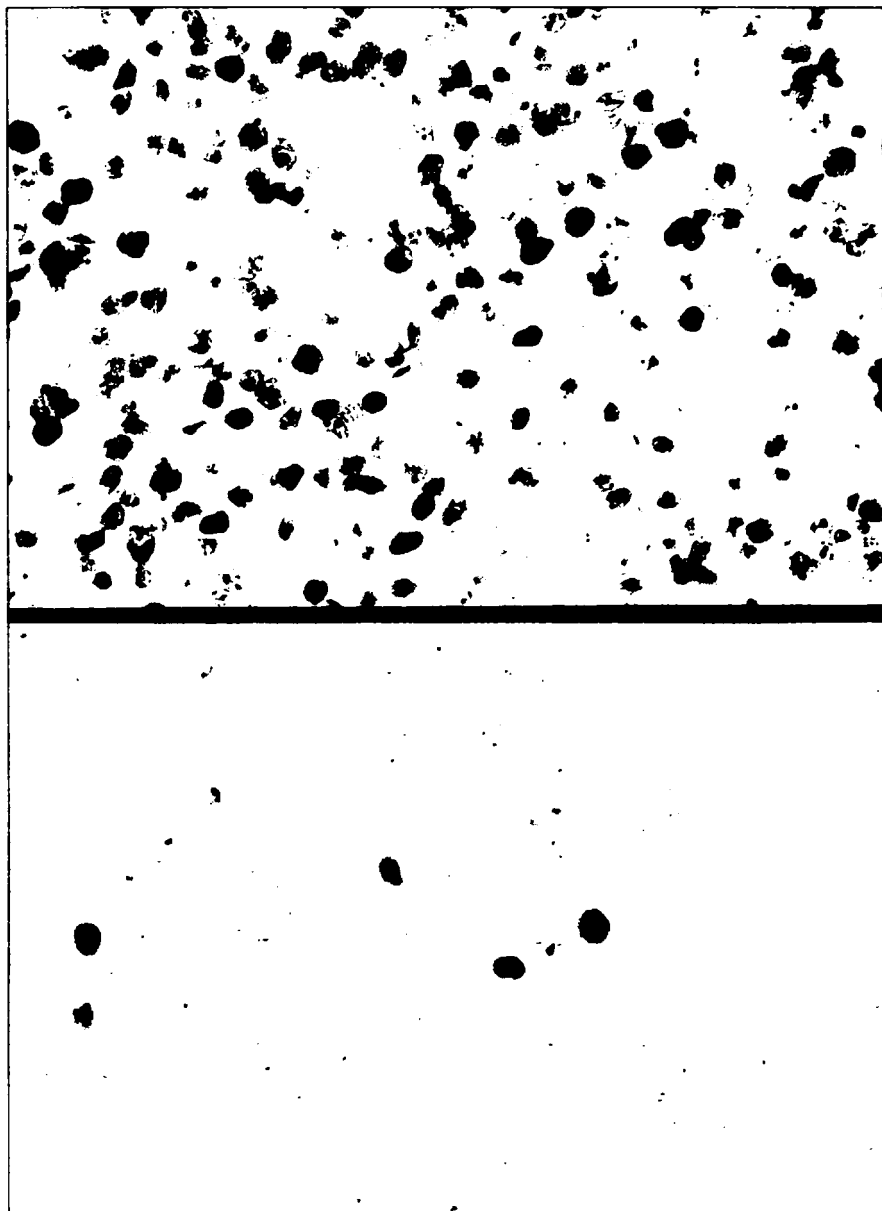

Fig 4. Above: MIB 1 immunohistochemical photomicrographs of Hyams grade 3 tumor, displaying strong immunoreactivity for MIB 1 with numerous red-stained nuclei (MIB 1, x 625). Below: MIB 1 immunohistochemical photomicrographs of grade 2 tumor, displaying slight immunoreactivity for MIB 1 with few red-stained nuclei (MIB 1, x 625)..

Table 2. Clinical presentation, therapy and follow up in 8 cases of esthesioneuroblastoma with invasion of the anterior cranial fossa.

Case N°	Sex & Age	Symptoms duration	Signs & symptoms	Prior treatment	Tumor removal	Radio therapy	Follow up (time)
1	F 50	5 years	ONR, anosmia	Biopsy	Total	45 Gy	Neck lymph node metastasis but no local recurrence (7 years)
2	M 70	2 years	Epistaxis, hyposmia	Biopsy	Total	no	Died of cardiovascular disease; autopsy: local recurrence and lymph node metastasis (18 months)
3	F 29	4 months	ONR epistaxis	Biopsy	Total	no	Recurrence (5 years)
4	F 47	2 years	Anosmia	ENT surgery	Total	45 Gy	Recurrence (6 months)
5	F 52	1 years	Epistaxis	Biposy + radiation	Total	66 Gy	No recurrence (5 1/2 years)
6	F 54	10 years	ONR anosmia	Biopsy	Total	No	No recurrence (4 1/2 years)
7	M 55	3 years	ONR visual deficit	Biopsy	Total	45 Gy	Spinal metastasis (18 months)
8	M 61	4 years	ONR	No	Total	50 Gy	No recurrence (4 1/2 years)

ONR, obstruction of nasal respiration; ENT surgery transethmoidal approach by ear, nose and throat surgeon

Table 3. Histopathological studies in 8 cases of esthesioneuroblastomas

Case N°	Electron microscopy	Immunohistochemisty						Hyams'grade
		NSE	Chromogranin	S100	Vimentin	Keratin	MIB1	
1	yes	n.d.	n.d.	n.d.	n.d.	n.d.	15%	2
2	yes	n.d.	n.d.	n.d.	n.d.	n.d.	20%	2
3	yes	n.d.	n.d.	n.d.	n.d.	n.d.	42%	3
4	yes	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	2
5	yes	n.d.	n.d.	n.d.	n.d.	n.d.	3%	2
6	n.d.	+	+	+	+	-	10%	2
7	n.d.	+	+	+	-	+	6%	2
8	n.d.	+	+	+	+	-	15%	2

NSE, neuron specific enolase; n.d., not done; +, positive; -, negative.

developed paraplegia due to spinal metastasis of the esthesioneuroblastoma at 1st thoracic vertebral level 18 months after surgery (Case 7) without local recurrence of tumor. One patient had local recurrence 6 months after tumor removal & radiotherapy (Case 4). One patient died of cardiovascular disease 18 months after tumor removal; autopsy demonstrated local tumor recurrence and lymph node metastasis (Case 2). One patient had local recurrence 5 years after surgery (Case 3) (Table 2).

Histopatological findings

The histopathological findings are summarized at Table 3. The proliferation activity of tumor cells at MIB 1 was considered high, ranging from 3% to 42% (average, 16%). Seven of the 8 tumors had Hyams' Grade 2; the only Grade 3 tumor had the highest proliferation activity of 42% (Fig 4).

COMMENTS

Esthesioneuroblastoma, which is also called by various names, namely olfactory neuroblastoma, olfactory neural neoplasm, olfactory esthesioneuroblastoma, olfactory esthesioneuroma, olfactory esthesioneuroepithelioma, esthesioneurocytoma, and neuroendocrine carcinoma, was first described by Berger and Luc in 1924 in French literature[1] and in 1951 by Schall and Linback[29] in American literature. These tumors are rare and the incidence has been estimated to be between 2-3% of all malignant intranasal neoplasm from olfactory mucosa in close proximity to the cribiform plate[4,8].

Clinical aspects

Esthesioneuroblastomas is a disease of young adults[32] or middle-aged people with two peaks, one at 10-20 years and another at 50-60 years. In our series, the youngest was 29 and oldest was 70 years with female predominance (M:F, 3:5). Some authors have noted male predominance[31,32], but thorough review of literature did not reveal any difference[18,23]. Reported duration of symptoms ranged from 1 month to 10 years[25,31]. The patients frequently present with nasal obstruction, epistaxis, and lacrimation[10,21]. Intracranial symptoms include anosmia, increased intracranial pressure, frontal syndrome, diplopia, sudden blindness, psychomotor seizures, optic atrophy, proptosis, retroorbital pain, and decreased sensation on the face[11,19,26,36].

Radiological investigations

Radiological investigations in the past have included plain X-rays, tomography and angiography. Currently, high resolution CT scan with bone windows and MRI are the investigation of choice. These have revolutionized the surgical management of the disease. Plain X-rays reveal soft tissue masses in the nasal and paranasal areas, mucosal thickening, opacification of sinuses along with bone destruction[18,32]. Occasionally calcification or hyperostosis may be seen[17]. Angiography is not mandatory but if performed it delineates a high vascularized mass in 59% of cases[3].

Thorough literature search revealed that CT scan with bone windows in 78% of patients showed bony changes representing either erosion or molding with occasional tumor calcification[17]. Typically these tumors are isodense in nonenhanced CT scan.

MRI is the investigation of choice for demonstration of tumor and the involvement of surrounding soft tissue[30]. In T1 weighted images, the tumor is seen as hypointense becoming hyperintense after intravenous Gadolinium administration. The ability to produce sagittal images and the ability to see the submucosal spread of the tumor, vascularity and displacement of vessels and visualization of dural involvement have made this investigation indispensable.

Spread of tumor

Esthesioneuroblastomas are locally invasive and have the tendency to spread submucosally in the nose and paranasal sinuses, and with time they may invade the skull base, may become intracranial, and by violating the meninges produce cerebral edema and increased intracranial pressure. Involvement of the CNS in 20-30% of cases[26], orbital extrusion in 17%, distant metastases in 30%,

and lymph node involvement in 8 to 17%[31,32] have been noted in literature. Distant metastases mainly invade bone, lungs, liver, mediastinum, spleen, adrenal glands.

Though these tumors histologically resemble lymphoma, undifferentiated carcinoma, plasmocytoma, Ewing's sarcoma, embryonal rhabdomyosarcoma, oat cell carcinoma, and melanomas, special staining methods, electron microscopy and immunohistochemistry usually distinguish these tumors from one another[18,33].

Biological behavior of these tumors is often difficult to predict due to the fact that there are no definite pathological features that would help prognosticate these tumors. Depending on the cell of origin, either sensory nerve cells or epithelial cells, these tumors are called olfactory neuroblastomas or olfactory neuroepitheliomas, respectively. There appears to be no exact correlation between histological variant and prognosis[18]. Based on mitotic activity, lobular architecture, nuclear pleomorphism, rosettes and necrosis, Hyams et al[16] suggested four grades of malignancy. This grading system was found to be a significant prognostic factor in 49 cases studied retrospectively by Morita et al[22]. Patients with grade 4 tumors had poorer prognosis than those with low grade tumors (grade 1-2). However, no significant difference in survival rate was found among patients with grade 1,2, or 3 tumors. In our series, 7 tumors were classified as Hyams' grade 2, and one tumor as grade 3. This particular patient with grade 3 tumor had local recurrence 5 years after surgery.

In our study, cell proliferation with MIB 1 has been carefully evaluated from a prognosis point of view. This showed great differences among the cases, with the highest proliferation index (42%) in the grade 3 tumor. In our series, the MIB 1 ranged from 3% to 42%. The patient who had Hyams' grade 3 tumor had MIB 1 of 42% and this patient had tumor recurrence in 5 years. Another patient (Case 5) had Hyams' grade 2 tumor and MIB 1 of 3%; this particular patient had been tumor free for 5-1/2 years. Other patients, though had low levels of MIB 1 (Case 1 and 7) eventually developed distant metastases in the absence of local recurrence. Though no conclusion could be drawn from these observations because of the small number of patients, it is likely that a higher level of MIB 1 seems to correlate with higher grade of malignancy.

Immunohistochemical tests that determine the proliferation of cell index appear to be more sensitive to differentiate the esthesioneuroblastomas than a simple histological classification based on only hematoxylin and eosin studies as used in the Hyams' Classification System. Further MIB 1 sudies with a larger number of cases are thus necessary to support this observation.

Treatment

There is a continous debate on various modes of management of the esthesioneuroblastomas: primary radiotherapy[18], primary surgical therapy[22,32], or a combination of these two[24] or chemotherapy[12,34,35]. Since these tumors are slow growing with local invasion and high local recurrence rate (46%-68%)[22,32], it is conceivable that the course of the disease can be changed by performing radical surgery. Review of literature suggests that combination of therapy is superior to single mode of treatment.

Currently the approach is multidisciplinary. In stage A and B, when the tumor is confined to nasal cavity and paranasal sinuses, surgical involvement is mandatory[7]. Till recently, there seems to be little controversy as to the mode of management of stage A and B where surgery, radiotherapy and combined therapy have been met with good results[7], though Newbill et al.[23], and Kadish et al.[18] favoured primarily radiation as the mainstay of treatment. Incomplete tumor resection by extracranial surgery alone is directly related to high rate of recurrence[25,32] which is not altered even when the patient received preoperatively radiotherapy. Biller et al. found that radiotherapy is not necessarily advantageous if adequate excision of tumor can be performed[2]. Since the incidence of metastasis may be related to radiation, these authors reserve radiation for patients with incomplete tumor resection, postoperative recurrence, or nonsurgical cases.

Most of the authors agree that stage C needs to have craniofacial tumor resection. Doyle in 1971 was the first to perform craniofacial resection even in cases where there was no involvement of the anterior cranial fossa[14]. Fahlbusch et al.[11] prefered the transfronto-transbasal approach without transfacial operation in stage C tumors, achieving total resection of tumors.

Harrison[15], and Biller et al.[2] have advocated craniofacial resection even in stage A and B. Their results stated that radiotherapy followed by extracranial surgery alone had a local recurrence rate of 60% compared to craniofacial resection with 12% recurrence in stage A and B patients. Cantrell[4] had better results with preoperative radiotherapy followed by craniofacial resections but Mack et al.[19], and our previous experience[28] indicate that craniofacial resection with or without radiotherapy made no difference in outcome.

We strongly believe adequate bifrontal craniotomy and resection of both olfactory bulbs along with dura covering the anterior skull base, ethmoidal roof and anterior part of planum sphenoidale, crista galli and repairing the cranial fossa floor in 3 layers, in association with lateral rhinotomy and en bloc resection of nasal tumor would give good surgical results.

Five year survival rate with esthesioneuroblastomas ranges from 18-71%[9,25,32]. Survival of these patients depends on the size of the tumor, intracranial extension and lymphonode involvement. In patients with stage C disease, 5 years survival was 60%, and with stage A 100%[9].

Postoperatively, these patients need to be followed up by frequent CT scan or MRI, and if necessary, endonasal endoscopy. Any recurrence needs to be intervened surgically. Long term survival is likely if radical surgical resection is combined with the postoperative radiation. The role of chemotherapy seems promising, particularly in those cases with distant metastases.

CONCLUSIONS

It is difficult to prognosticate the esthesioneuroblastomas by the tumor location or histological grading alone. Immunohistochemistry, especially MIB 1 antibody studies may in future help or at least complement the existing factors to prognosticate these tumors. Radical surgical resection with postoperative radiation and in cases of distant metastases (stage C) adjuvant chemotherapy would give optimal results and a longer survival.

REFERENCES

1. Berger L, Luc R. L'esthésioneuroepitheliome olfactif. Bull Assoc Franç Etude Cancer 1924, 13:410-421.
2. Biller HF, Lawson W, Sachdev VP, Som P. Esthesioneuroblastoma: surgical treatment without radiation. Laryngoscope 1990, 100:1199-1201.
3. Burke DP, Gabrielsen TO, Knake JE, Surger JF, Oberman HA. Radiology of olfactory neuroblastoma. Radiology 1980, 137:367-372.
4. Cantrell RW. Esthesioneuroblastoma. In Sekhar LN, Janecka IP (eds). Surgery of cranial base tumors. New York: Raven Press, 1993, p 471-476.
5. Canty P. Olfactory neuroblastoma: long-term survival. J Laryngol Otol 1979, 93:285.
6. Cattoretti G, Becker MHG, Key G, Duchrow M, Schlueter C, Galle J, Gerdes J. Monoclonal antibodies against recombinant parts of the Ki-67 antigen (MIB 1 and MIB 3) detect proliferating cells in microwave processed formalin-fixed paraffin sections. J Pathol 1992, 168:357-363.
7. Cheesman A, Lund VJ, Howard DJ. Craniofacial resection for tumors of the nasal cavity and paranasal sinuses. Head Neck Surg 1986, 8:429-435.
8. Cummings LW. Otolaryngology head and neck surgery. St. Louis: Mosby, 1986, p 3397-3398.
9. Doyle P, Payton H. Combined surgical approach to esthesioneuroepithelioma. Trans Pa Acad Ophthalmol Otolaryngol 1971, 75:526-531.
10. Durham JC. Olfactory neuroblastoma. Ear Nose Throat J 1989, 68:185-204.
11. Fahlbush R, Neubauer U, Wigand M, Weidenbecher M, Röckelein G, Thierauf P, Sauer R. Neuro-rhinosurgical treatment of aesthesioneuroblastoma. Acta Neurochir (Wien) 1989,100:93-100.
12. Garces LAR-N, Heiss E, Grote E. Sudden blindness by an esthesioneuroblastoma: case report. In Sheunemann H, Schürmann K, Helms J (eds). Tumors of the skull base: extra- and intracranial surgery of skull base tumors. Berlin: Walter de Gruyter, 1986, p 127-130.

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13. Goldsweig HG, Sundaresan N. Chemotherapy of recurrent esthesioneuroblastoma: case report and review of literature. Am J Clin Oncol 1990, 13:139-143.
14. Hamilton AE, Rubinstein LJ, Poole GJ. Primary intracranial esthesioneuroblastoma. J Neurosurg 1973, 39:548-556.
15. Harrison D. Surgical pathology of olfactory neuroblastoma. Head Neck Surg 1984, 7:60-64.
16. Hyams VJ, Batsakis JG, Michaels L. Tumors of the upper respiratory tract and ear, In Hyams VJ, Batsakis JG, Michaels L (eds). Atlas of tumor pathology, Second Series, Fascicle 25. Washington, DC: Armed Forces Institute of Pathology, 1988, p 240-248.
17. Hurst RW, Erickson S, Cail WS, Newman SA, Levine PA, Burke J, Cantrell RW. Computed tomographic features of esthesioneuroblastoma. Neuroradiology 1989, 31:253-257.
18. Kadish S, Goodmann M, Wang CC. Olfactory neuroblastoma. Cancer 1976, 37:1571-1576.
19. Mack EE, Prados MD, Wilson CB. Late manifestation of esthesioneuroblastomas in the central nervous system: report of two cases. Neurosurgery 1992,30:93-97.
20. Meneses MS, Thurel C, Mikol J, Ramina R, Maniglia JJ, Arruda WO, Cophignon J. Esthesioneuroblastoma with intracranial extension. Neurosurgery 1990, 27:813-820.
21. Mills SE, Frierson HF. Olfactory neuroblastoma: a clinicopathologic study of 21 cases. Am J Surg Pathol 1985, 9:317-327.
22. Morita A, Ebersold MJ, Olsen KD, Foote RL, Lewis JE, Quast LM. Esthesioneuroblastoma: prognosis and management. Neurosurgery 1993, 32: 706-715.
23. Newbill ET, Johns ME, Cantrell RW. Esthesioneuroblastomas: diagnosis and treatment. South Med J 1985, 78:275-282.
24. O'Connor TA, McLean P, Juillard GJF. Olfactory neuroblastomas. Cancer 1989, 63:2426-2428.
25. Olsen KD, De Santo LW. Olfactory neuroblastoma: biologic and clinical behaviour. Arch Otolaryng 1983,109:797-802.
26. Rodas RA, Erkman-Balis B, Cahill DW. Late intracranial metastasis from esthesioneuroblastoma: case report and review of the literature. Neurosurgery 1986, 19:622-627.
27. Russell DS, Rubinstein LJ. Pathology of tumours of the nervous system. Ed 5. London: Williams & Wilkins, 1989, p 915-920.
28. Samii M, Löblich HJ, Draf W. Esthesioneuroblastoma. In Sheunemann H, Schürmann K, Helms J (eds). Tumors of the skull base: extra- and intracranial surgery of skull base tumors. Berlin: Walter de Gruyter, 1986, p 53-57.
29. Schall LA, Linback M. Primary intranasal neuroblastoma. Ann Otol Rhinol Laryngol 1951, 60:221-229.
30. Schroth G, Gawehn J, Marquardt B, Schabet M. MR imaging of esthesioneuroblastoma: case report. J Comput Assist Tomogr 1986, 10:316-319.
31. Schwaab G, Micheau C, Le Guillou C, Marandas P, Pacheco L, Domenge C, Richard JM, Wibault P. Olfactory esthesioneuroma: a report of 40 cases. Laryngoscope 1988, 98:872-876.
32. Skolnik EM, Massari FS, Tenta LT. Olfactory neuroepithelioma: review of world literature and presentation of two cases. Arch Otolaryngol 1966, 84:644-653.
33. Taxy JB, Bharani NK, Mills SE, Frierson HF, Gould VE. The spectrum of olfactory neural tumors: a light microscopic immunohistochemical and ultrastructural analysis. Am J Surg Pathol 1986, 10:687-695.
34. Watne K, Hager B. Treatment of recurrent esthesioneuroblastoma with combined intracranial chemotherapy: a case report. J Neurooncol 197, 5:47-50.
35. Weiden PL, Yarington T, Richardson RG. Olfactory neuroblastoma: chemotherapy and radiotherapy for extensive disease. Arch Otoryngol 1984, 110:759-760.
36. Wilson WMG, Cullen G. Olfactory groove tumor causing sudden blindness: a case report. Can J Ophthalmol 1967, 2:133-138.
37. Zülch KJ. Brain tumors: their biology and pathology. Berlin: Springer, 1986, p 483-485.