Olfactory Neuroblastoma - Our Experience

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Abstract

The authors present six cases of olfactory neuroblastoma with or without intracranial extension operated on by the team headed by Otolaryngologists and Neurosurgeons. Data was analysed with respect to age group, sex, presenting symptoms and signs, stage, and results of combined modality of treatment. The author's experience suggests excellent local control can be achieved by combined craniofacial resection followed by radiation therapy. Hence the authors recommend planned combined radical treatment for all the resectable lesions and routine use of nasal endoscope along with other conventional methods for comprehensive follow-up of all cases.

Key Words

Esthesioneuroblastoma, Olfactory Neuroblastoma

Olfactory neuroblastoma is an extremely rare malignant tumour originating in the olfactory epithelium, often misdiagnosed in rhinology practice. Originally described by Berger et al (1) in 1924 as esthesioneuroepithelioma olfactif, fewer than three hundred cases have been reported in the English literature. The highest series of 39 cases was reported by Jackson et al, in 1984 (2). Various terminology has been used to describe this tumour, but olfactory neuroblastoma is the most commonly accepted term used all over the globe.

Its biologic behaviour, morphology, aggressiveness and propensity for intracranial extension make this tumour a challenge for the surgical team. Different treatment modalities have been mentioned in the English literature, from the days of lateral rhinotomy approach to the present anterior craniofacial resection.

Meneses et al (3) advocated craniofacial resection followed by radiotherapy as the appropriate treatment modality for maximum local control of these tumours with intracranial extension. This paper reveals our experience with this unusual tumour, with or without intracranial extension. It is the purpose of this paper to emphasize that combined modality of treatment (craniofacial resection followed by external radiotherapy) gives the best local control rates,

although this does not preclude against distant metastasis. The use of nasal endoscope has a great role in follow up care.

Materials & Methods

Since 1985, twenty five cases of anterior craniofacial resection have been performed for varying pathology in the Department of E.N.T. and Head & Neck Surgery, K.M.C., Manipal. Of these, six cases were olfactory neuroblastomas and thus taken up for the present study. All cases were investigated thoroughly, with Diagnostic nasal endoscopy, CT scanning and serial section histopathological studies. Digital subtraction angiography was carried out in selected cases.

Staging of the tumour was according to the Kadisch's classification. Surgery was performed by two surgical teams, the E.N.T. surgeons and neurosurgeons. Initial mobilization of the tumour was carried out by the E.N.T. surgeon via the facial route, followed by the neurosurgeon, except in one case where the extradural extension of the tumour was removed en bloc from below via the medial maxillectomy approach under the operating microscope. All the cases were operated by the same surgical team headed by the senior consultants.

Details of the clinical features, staging, nasal

Fig. 1. Showing lateral rhinotomy & bifrontal craniotomy incision

endoscopic and operative findings, complications and metastasis, treatment and follow up are depicted in Table 1. Right maxillo-ethmoidal complex was involved more often than left in our series.

The surgical approaches adopted by the E.N.T. surgeon were medial maxillectomy or total maxillectomy using the lateral rhinotomy incision with Link's extension (Fig. 1). The conventional bifrontal craniotomy flap approach was adopted by the neurosurgeons (Fig. 2). All the resected tumours were further evaluated by histopathological studies (Fig. 3).

Results and Discussion

The tumour was first reported in the English literature by Schall and Lineback at the Massachusetts Eye & Ear Infirmary in 1951, when they described three cases of "primary intranasal neuroblastoma" (4). Since

then, less than three hundred cases have been reported and no single author has accumulated enough experience in the therapeutic management of these patients. Most authors have shown a female predominance in their series (2). In our series also, there were 4 females and 2 males. Four of our six patients were below the age of 25 years, showing a predilection for the younger age group. Five of our six patients showed involvement of the right side.

This tumour mostly originates from the neural crest, which is evident from the various terms used to describe it. It arises from the olfactory region of the nasal cavity, which constitutes the upper third of the nasal septum, the cribriform plate and the corresponding areas of the lateral wall (superior and supreme turbinates).

The three most common symptoms were nasal obstruction, proptosis and epistaxis. Also recorded were diminished vision, headache, anosmia and epiphora. These are similar to those reported by most authors. Physical findings consisted of an intranasal mass in all cases, usually with orbital signs and, in one case, lateral rectus palsy. The tumour has a gross appearance similar to a nasal polyp, and patients may give histories of previous biopsies or polypectomies. The neuroblastoma presents as a greyish, oedematous, friable, fleshy, polypoidal mass, which is quite vascular and bleeds easily on biopsy.

Microscopic appearance shows nests of neurocytes or undifferentiated neuroblasts, and neurofibrils, occasionally arranged into true neuroepithelial rosettes

Fig. 2 Complete ethmoidectomy seen from craniotomy site

Table I

Case No.	Age (Yrs)	Sex	Kadisch Staging	Presenting Features	Diagnostic Endoscopy Findings	Nasal Findings	Operative Findings (Extent)	Treatment (Other than Surgery)	Complications & Metastasis	Follow up & Prognosis
1	25	M	C	Left nasal obstruction Epistaxis Intercanthal widening Left diminished vision	Irregular fleshy mass arising from the roof of the Nasal cavity		Tumour invading the left frontal, anterior & middle ethmoids & maxillary sinus. No Intracranial extension	6000 rads & 3 courses of chemotherapy (5FU) Radical neck dissection done	1st month- Orbital recurrence Upper left cervical lymph nodes 2½ yrs. later	Surviving 4½ yrs NED
2	17	F	C	Right nasal obstruction Proptosis	Slough covered fleshy mass occupying right nasal cavity arising from the lateral wall		Tumour invading medial wall of maxilla, frontal sinus, ethmoid labyrinth & sphenoid sinus roof of the orbit and adherent to the basal dura.	4000 rads given Bone flap removal under general anaesthesia	2nd month- frontal osteomyelitis 3rd month - epistaxis & multiple discharging sinuses over the forehead, Recurrent neuroblastoma,	Dead Survival 5 months
3	66	M	C	Right nasal obstruction Proptosis Diminished vision Right VI cranial nerve palsy Anosmia	Polypoid granular mass from right middle meatus		Tumour involving nasal bones, right ethmoid, lamina papyracea orbital periosteum, right medial maxillary antrum, sphenoid sinus & posterior end of the septum, No Intracranial extension.	5600 rads given	No complications or metastasis	Surviving 4¼ yrs.

Table I (Contd.)

Case No.	Age (Yrs)	Sex	Kadisch Staging	Presenting Features	Diagnostic Endoscopy Findings	Nasal Findings	Operative Findings (Extent)	Treatment (Other than Surgery)	Complications & Metastasis	Follow up & Prognosis
4	17	F	C	Right proptosis Nasal obstruction	Polypoid granular mass arising from right middle meatus		Tumour invading right medial wall of maxilla, ethmoids lamina papyracea, orbit, floor of the cranial fossa and basal dura of the right frontal lobe.	6000 rads given Additio- nal 2000 arising from right radiotherapy, 3 courses of chemotherapy were given.	5th month- swelling rads of palliative forehead & right hip tenderness, X-ray showed distension of head of left femur.	Surviving with disease 4 $\frac{1}{3}$ yrs.
5	19	F	C	Right nasal obstruction Epistaxis.	Polypoid mass with ulcerations, bleeds on touch arising from right lateral wall.		Tumour invading right ethmoid labyrinth & right sphenoid with ? intracranial extension	5000 rads and nine courses of chemotherapy given (CCNU, VCR) Frontal bone flap excised. Palliative radiotherapy 2000 rads given	2nd month- survival Right eye showed first 2 $\frac{1}{2}$ yrs. degree optic atrophy 9th month-patient developed osteomyelitis of frontal bone, 2 yrs-generalised weakness with inability to pass urine & weakness of lower limbs. Chest X-ray (PA view) showed superior mediastinal widening. Spinal metastasis present.	Dead Survival 2 $\frac{1}{2}$ yrs
6	55	F	C	Right nasal obstruction Proptosis	Right fleshy granular mass arising from lateral wall		Tumour invading medial wall of right maxilla, ethmoid, lamina papyracea and orbit.	6000 rads given	None	Lost to follow up after 3 yrs survival (NED)

Fig 3 Microphotograph (High Power) showing true neuroepithelial rosettes and pseudorosettes.

and pseudorosettes. The presence of neurofibrils is said to be diagnostic under light microscopy, however, electron microscopy may be necessary in order to firmly establish the diagnosis (2). Schenck and Ogura (5) have referred to this tumour as the "great impostor", as it has been mistaken for lymphoma, melanoma, transitional cell carcinoma, undifferentiated carcinoma, sarcoma, plasmocytoma, rhabdomyosarcoma and rhinosporidiosis.

Investigations like Diagnostic nasal endoscopy, Digital subtraction angiography, C.T. scanning and M.R.I. scanning along with histopathological examination by an experienced pathologist are most helpful in coming to a diagnosis, and also in planning the line of management in these cases, especially in those with intracranial extensions. C.T. scans give an accurate indication of orbital and intracranial spread. Bony destruction is clearly seen, though on occasion, intact bony planes may be seen in spite of extension of the tumour beyond the bone. Post operative C.T. scans are also valuable to detect early recurrence of tumour.

Kadisch proposed a classification system based on the clinical extent of the disease at presentation. All our patients' belonged to group C. Hence, radical excision was planned and anterior craniofacial resection was carried out in five patients and medial maxillectomy without bifrontal craniotomy in one patient. Post operative radiotherapy from 50 to 60 Grays was administered to all the cases.

Distant metastasis rates ranging from 18% to 62% (6) have been reported in the literature. Three of our cases developed distant metastasis (50%) and one case

cervical lymph node metastasis (17%), thus indicating that olfactory neuroblastoma is an aggressive tumour, with a high risk of distant metastasis. These were seen in the spinal cord, brain and head of femur. A local recurrence rate as high as 50% has also been reported. However, we noted only 1 case with local recurrence (17%). This may be due to two reasons. Firstly, Chapman et al (7) and Shah et al (8) found tumour extension along the olfactory nerves in nearly all their cases despite radiological evidence to the contrary. This may explain our low local recurrence rate as we performed craniofacial resection for all our cases, even when the radiological investigation did not show intracranial spread. Secondly, if the surgical excision is confined to a lateral rhinotomy approach, the surgeon is operating through the tumour field and there is a risk of tumour implantation at the skull base, which may explain the previously reported high rates of local recurrence at this site.

The role of chemotherapy for metastatic esthesioneuroblastoma, especially in the paediatric age group has been well documented, but adjuvant chemotherapy for advanced stage (B and C) disease is still under evaluation (9). Two of our cases received palliative chemotherapy for distant metastasis and one received post operative chemotherapy as there was dural and frontal lobe involvement. Two of our six patients have so far died from their disease, one with local recurrence who died after 5 months and the other with distant metastasis who survived for two and a half years. One patient survived for 3 years and was then lost to follow up. The other three surviving patients are being regularly followed up, and show no evidence of disease.

Conclusion

Our series shows that Kadisch group C are extremely aggressive tumours which in spite of combined modality of therapy show a high rate of distant metastasis, which in turn may be amenable to palliative chemotherapy. A low rate of local recurrence if wide excision of the olfactory neuroblastoma has been carried out by combined anterior craniofacial resection. Hence, we recommend combined craniofacial resection followed by post operative radiotherapy as the ideal treatment for all cases of olfactory neuroblastoma. Further studies with long term follow-up and the evaluation of adjuvant chemotherapy for advanced tumours to prevent distant failures are recommended.

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