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Case Report

ADVANCED OLFACTORY NEUROBLASTOMA: A CASE REPORT

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ABSTRACT

Olfactory neuroblastoma (ONB) is originated from the olfactory neuroepithelial cells of the nasal cavity and it accounts for <3% of tumors originating in the nasal cavity and paranasal sinus. Intracranial extension and orbital involvement have been shown to be independent risk factors associated with poorer outcomes. Treatment options are surgical excision or surgery combined with a radiotherapy (RT) and/or chemotherapy. The present study reports the case of a 57-year-old patient with a mass in the left nasal cavity since 6 months that was presented as progressive nasal obstruction and intermittent left-sided epistaxis associated with anosmia and loss of vision. A biopsy and immunohistochemistry of this mass was confirmed high grade olfactory neuroblastoma. A decision was made to start neoadjuvant chemotherapy with cisplatin and etoposide and had good response. This case report illustrate that neoadjuvant chemotherapy is effective treatment for high grade olfactory neuroblastoma. The literature for ONB and the treatment of the tumor are also discussed.

INTRODUCTION

Olfactory neuroblastoma (ONB), is also known as esthesioneuro-blastoma, is a rare malignant tumor of the olfactory neuroepithelium in the upper nasal cavity and accounts for 3% of all tumors of the nasal cavity and paranasal sinus.[1]The olfactory epithelium contains three cell types, which can be histologically identified in the tumor: basal cells, olfactory neurosensory cells, and supporting sustentacular cells. The basal cells are the stem cell compartment, continuously replacing the neurosensory cells throughout adult life, both physiologically and as a response to injury.

The most common symptoms at the time of presentation are nasal obstruction (52%), epistaxis (42%), exophthalmos (19%), and headache (19%). The age distribution of patients is unimodal with the majority of patients presenting at diagnosis in the 4th and5th decades of life yet presentation in patients under 30 years of age is not uncommon.[2]

A‘‘dumbbell-shaped’’ mass extending across the cribriform plate is one of the most characteristic imaging findings for this tumor. The observation depends on the size of the tumor and the duration of symptoms. The upper portion is a mass in the intracranial fossa, while the lower portion is in the nasal cavity, with the ‘‘waist’’ at the cribriform plate. CT will show speckled calcifications and bone erosion of the lamina papyracea, cribriform plate and/or the fovea ethmoidalis by non-contrast methods. Contrast enhanced CT will show homogenously enhancing mass, with non-enhancing areas suggesting regions of necrosis. MRI images with and without contrast will delineate the extent of the disease[4].

The two most important factors influencing prognosis in patients with olfactory neuroblastoma are extent of disease at diagnosis and histologic grade.

There is no universally accepted staging system for olfactory neuroblastoma. Kadish *et al* were the first to propose a staging system based on a series of 17 patients. Patients were classified into 3 stages: stage A, tumor confined to nasal cavity; stage B, tumor extends to one or more of the paranasal sinuses; and stage C, where the tumor extends beyond the nasal cavity and paranasal sinuses[6]. Morita *et al* modified the Kadish staging system by re-classifying patients with lymph node or distant metastases as stage D[7].

Treatment modalities for ONB are en bloc resection, extracranial resection or surgery combined with radiotherapy (RT) and/or chemotherapy. Both the Hyams grading and Kadish staging systems have been used to guide treatment decisions, including the appropriate use of neoadjuvant or adjuvant therapies[9].

CASE REPORT

A 57year old male presented with an 6- month history of progressive nasal obstruction and intermittent left-sided epistaxis. He had experienced several weeks of anosmia and increased pressure sensation in and around the left eye with decreased visual acuity and then vision loss.

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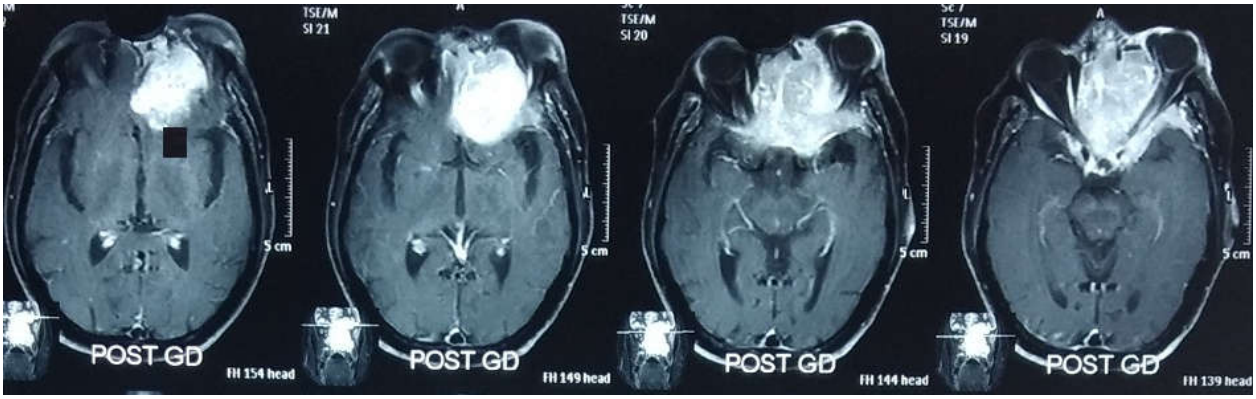

Figure 1 T1 MRI of the sinuses and brain

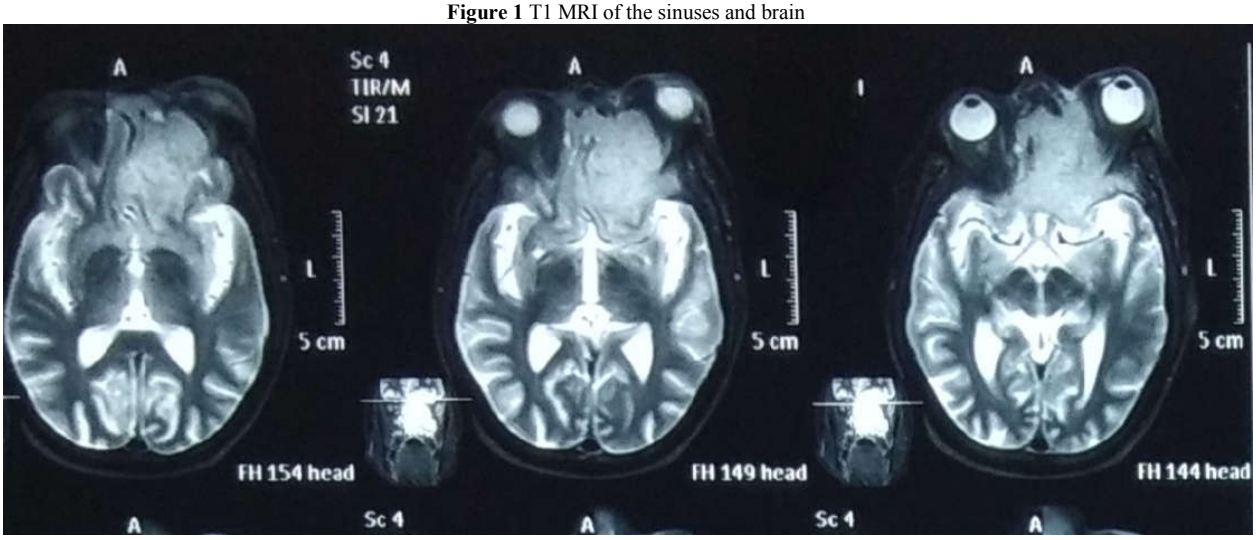

Figure 2 T2 MRI of the sinuses and brain

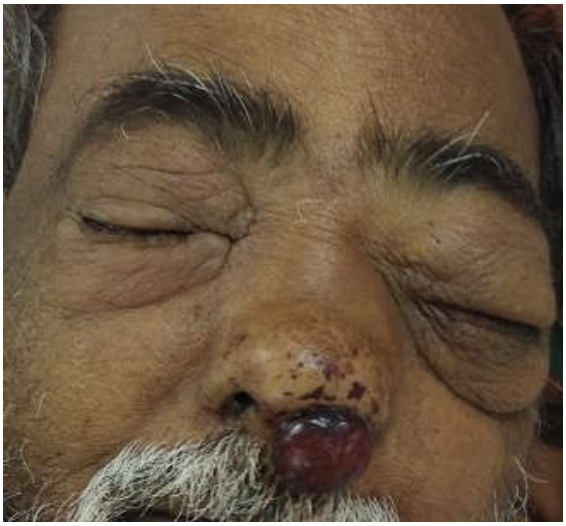

Figure 3

He was suffered from hypothyroidism and was taking tab. thyroxin 100 microgram daily since 2 years. On examination, nasal mass was present, protruding from left side of nostrils which was red, smooth not bleed on touch. Nasal root was widened due to mass effect. Left orbit was protruded out, eyelid was closed. An MRI of the sinuses showed a large soft tissue mass was seen in left nasal cavity extended OM complex leading to retention sinusitis, superiorly extended into ethmoid sinuses, infiltrated into the floor of anterior cranial fossa, lifted adjacent brain parenchyma, laterally the mass was infiltrated into the medial wall of left orbit, leaded proptosis of left eye ball. Size of mass was 45mm length, 90mm width, 60 mm depth.

A biopsy of the mass revealed no diagnostic information, showed fragments of neoplastic cells composed of round to oval cells. Immunohistochemical staining confirmed the tumor was positive for synaptophysin, EMA with rare cell expressed cytokeratine and chromogrannin A with a MIB-1 of approximately 45-50%. and negative for TTF-1, CD99,desmin and NKX2. The tumor was considered to be Olfactory neuroblastoma Hyam's grade III over a small cell neuroendocrinal carcinoma. Because of the local advancement and patient refusal surgical option was left and decision was made for neoadjuvent chemotherapy and radiotherapy. Patient was received three cycle of chemotherapy cisplatin and etoposide comfortably and had good response but he was not come for further treatment and follow up was tracked off.

DISCUSSION

ON is a rare locally aggressive tumor. Although it can be found in all age groups, it occurs more commonly in the 3rd and 6th decades of life, and is present equally in each gender. First being described in the literature in 1924 by Berger *et al*, there is still a limited collective experience with these tumors[3].

In microscopy, One of the most important histologic features is a lobular architecture comprised of "primitive" neuroblastoma cells. The tumor cells are ''small, round, blue'' cells slightly larger than mature lymphocytes, with a very high nuclear to cytoplasmic ratio. The nuclei are small and uniform with hyperchromatic, albeit delicate, uniform, ''salt-and-

pepper'' nuclear chromatin distribution. In immunohistochemistry ONBs are positive for synaptophysin, chromogranin, CD56, neuron specific enolase, NFP and S-100 protein. The small round cells are usually positive for the first five markers whereas the S-100 protein-positive cells are found at the periphery of the tumor lobules and correspond to Schwann (sustentacular) cells[4,5].

Kadish *et al* were the first to propose a staging system based on a series of 17 patients. Patients were classified into 3 stages: stage A, tumor confined to nasal cavity; stage B, tumor extends to one or more of the paranasal sinuses; and stage C, where the tumor extends beyond the nasal cavity and paranasal sinuses[6]. Morita *et al* modified the Kadish staging system by re-classifying patients with lymph node or distant metastases as stage D[7]. The optimal treatment modality for olfactory neuroblastoma continues to be debate because of limited previously reported medical literature.

Earlier staged lesions (Kadish A & B) have typically been described as being treated with a monomodality regimen such as surgery or radiation. Radical surgical resection has been shown to result in improved 5-year survival rates (76.2% vs. 14.3%) when compared to radiation alone when monomodality therapy is performed.[8] Tumor grade, low versus high, has been used to direct the indication for adjuvant therapy after surgical resection[9]. Radiation therapy has been advocated for low-grade lesions with close margins, residual and recurrent disease and in all patients with high-grade tumors[10]. Kadish stage C patients have typically been advocated to receive combination therapy such as surgery with adjuvant radiation therapy.

The use of combined modality treatment with surgery, radiotherapy and chemotherapy in various combinations has been increasingly adopted over the last two decades[10,11,12].

The use of neoadjuvant chemotherapy for Kadish stage C disease has been reported in retrospective cohort studies. Various chemotherapeutic combination regimens have been used involving alkylating agents and anthracylines with significant toxicities. Response to chemotherapy may be dependent upon the Hyam's grading of the original tumor[I2].

Turano S *et al*. treated advanced adult esthesioneuroblastoma successfully. After debulking surgery disease recurrence was treated with cisplatin and etoposide alternated with doxorubicin, ifosfamide and vincristine with granulocyte colony-stimulating factor (G-CSF) support after every cycle. Soon after the first cycle, an important reduction of pain and decrease of the exophthalmos and vertigos was observed[13].

Mishima *et al*. achieved a complete response in eight out of 12 patients with an aggressive multi agent chemotherapy schedule[14].

Sarah Boby Thomas, *et al*. published a case of Esthesioneuroblastoma with intracranial extension and cured with non-surgical approach. Patient received neoadjuvant chemotherapy with VAdrC-IE protocol (Vincristine 2 mg/m ^{2} Day 1, Adriamycin 75 mg/m ^{2} Day 1, Cyclophosphamide 1200 mg/m ^{2} Day 1, alternating with Ifosfamide 1800 mg/m ^{2} D1-D5, Etoposide 100 mg/m ^{2} Day 1-day 5 Q 3 weekly), after six cycles, which revealed near complete response then Radiation was delivered , total dose of 6000 cGy in 30 fractions. With 60 months of follow-up she continues to be disease free without any delayed complications of therapy[15].

In our patient tumor was considered to be Olfactory neuroblastoma Hyam's grade III and Kadish stage C over a small cell neuroendocrinal carcinoma with anterior cranial fossa infilteration, planned chemotherapy schedule as neoadjuvant setting. He was received first cycle of chemotherapy cisplatin and etoposide comfortably and discharged in stable condition but he was not come for next cycle and follow up was tracked off. This case report highlights the use of neoadjuvant chemotherapy in advanced Esthesioneuroblastoma. Further avenues of research are needed to demonstrate the efficacy of neoadjuvant chemotherapy in this rare neuronal cancer.

Conflict of Interest- None

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