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Case Report

Ear, Nose and Throat Section

Ganglioneuroblastoma of Skull Base

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ABSTRACT

Neuroblastic tumours are common in childhood and adrenal glands are the most common site. Head and neck ganglioneuroblastomas are extremely rare and nose is a very uncommon site for a ganglioneuroblastoma. The management of this primitive sympathogonic tumour may vary depending on the age of the patient and stage of the tumour. We present a middle-aged man with a ganglioneuroblastoma of skull base, management of this tumour and a review of literature.

Keywords: Lateral rhinotomy, Medial maxillectomy, Neuroblastoma

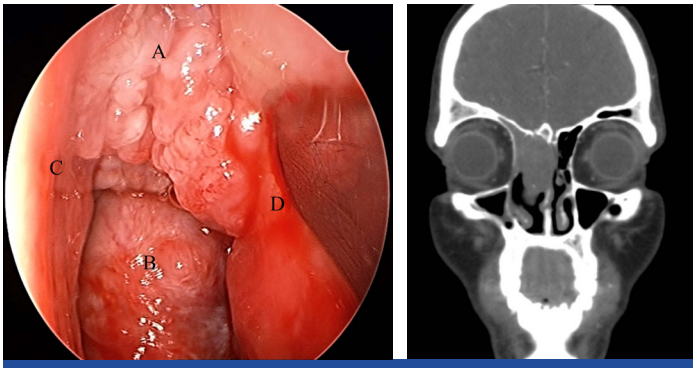
CASE REPORT

A 42-year-old hypertensive man presented with progressive right sided nasal obstruction, anosmia, intermittent, self-limiting epistaxis and right sided frontal headache of 6 months duration. He did not give history of visual disturbances, swelling in the oral cavity or fever. He did not have a swelling in the neck, loss of weight or appetite, breathlessness, abdominal pain or bone pain. His family history, past history and treatment history were unremarkable.

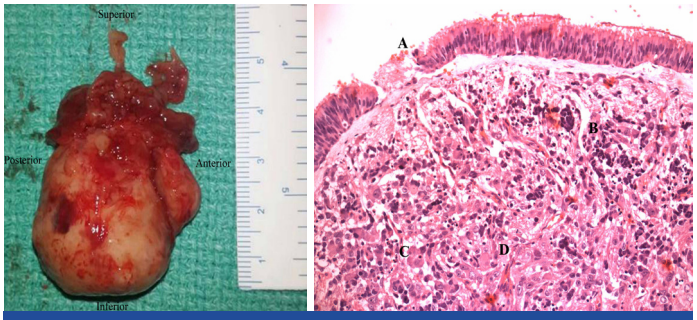
On clinical examination of the nose and the paranasal sinuses, an irregular firm mass appeared to arise from the roof of right nasal cavity extending medial to middle turbinate pushing the septum towards the left. It had prominent blood vessels on its surface, was insensitive to touch and bleed on probing [Table/Fig-1]. Ear, throat and neck examination were normal. Respiratory system, cardiovascular system, neurological system, per abdominal examination and general examination was normal.

Contrast enhanced CT scan (CECT) revealed an enhancing soft tissue mass measuring 4.0 x 0.2 x 3.2 cm arising from the roof of the nasal cavity and extending caudally. Bony landmarks were maintained and there was no breach of the skull base. There was soft tissue opacification of fronto-ethmoidal sinuses with blockage of the right frontal recess and maxillary sinus ostia [Table/Fig-2]. Biopsy from the nasal mass was reported as ganglioneuroblastoma. Urinary vanillyl mandelic acid was normal. Abdominal ultrasound was normal. Patient also underwent CECT chest, bone marrow biopsy, bone scan and MIBG scan to determine the presence of metastasis, however, they were normal.

Patient was planned for endoscopic excision of the tumour under general anaesthesia but torrential bleed was encountered during the endoscopic procedure, hence it was converted into medial maxillectomy by lateral rhinotomy approach followed by excision of right nasal mass in toto [Table/Fig-3]. Multiple feeding vessels from the internal and external carotid artery and their branches were ascertained as the cause for the bleeding. Intraoperatively, CSF leak was also noted in the cribriform plate which was closed in three layers using temporalis fascia, abdominal fat, and septal cartilage. Histopathological analysis revealed nests and sheets of neuroblasts in various stages of development ranging from small cells with hyperchromatic nuclei, scanty cytoplasm to large cells with hyperchromatic, pleomorphic nuclei with scanty to moderate cytoplasm. The ganglioneuromatous component comprised of sheets of ganglion cells with eosinophilic nucleus and stroma with spindle shaped Schwannian cells and neuropil along with areas of necrosis, calcification and proliferating blood vessels [Table/Fig-4].



[Table/Fig-1]: Endoscopic Image of the nasal mass showing:
a: Anterior friable polypoidal component
b: Posterior smooth globular component
c: Lateral nasal wall
d: Nasal Septum
[Table/Fig-2]: Contrast Enhanced coronal CT scan depicting the nasal mass arising from the roof of the nasal cavity pushing the septum to the left side with maintenance of skull base bony architecture



[Table/Fig-3]: Excised tumour in toto **[Table/Fig-4]:** Haemetoxyllin and eosin staining of 20X magnification demonstrating the following structures (a) Nasal epithelium (b) Neuroblasts arranged in nests and sheets (c) Large mature ganglion cells (d) Neuropil matrix

Hence, it was reported as ganglioneuroblastoma, intermixed type with negative margins. One month postoperatively, technetium 99m scintigraphy revealed an osteoblastic metastasis in L2 vertebra. He underwent postoperative external beam radiotherapy (36 Gy in 18 fractions over three and a half weeks) and isotretinoin based chemotherapy. Patient is on regular follow-up with no evidence of residual or recurrent tumour.

DISCUSSION

Tumours arising from the embryonic cells of the sympathetic nervous system have been termed as neuroblastic tumours [1,2].

In 1863, Virchow described neuroblastomas for the first time in world literature. In the early 20th century, Zuckerkandl and Kohn described its origin from the sympathetic tissue [3]. In 1927, various stages of differentiation of neuroblastic tumours were discovered [4]. Neuroblastic tumours have been subclassified into three different subtypes based on the stage of arrest of differentiation into neuroblastoma, ganglioneuroblastoma and ganglioneuroma. The degree of differentiation of the embryonic cells is primarily responsible for the potentially benign or malignant behaviour of the tumour [1,2,5].

Ganglioneuroblastoma is a primitive neuroectodermal tumour that can occur within the central nervous system or in peripheral sympathetic nervous system and contains both undifferentiated neuroblasts and mature ganglion cells [6]. Eighty percent of these tumours affect children less than 5 years of age. They rarely occur after the first decade and there is no gender predominance [7]. The most common site is the adrenal gland (35%). Approximately 1 to 5 percent of all neuroblastomas arise in the head and neck, however there is no report of ganglioneuroblastoma of skull base reported in literature. The other common locations are the retroperitoneal ganglia (30%), posterior mediastinum (20%) and pelvis (2-3%). Very rarely, they can arise from the thymus, cauda equina, kidney and lung. There has been association with genetic disorders like Von Recklinghausen disease, Hirschsprungs disease, Di George syndrome and Beckwith-Wiedemann syndrome [1,2].

The origin of ganglioneuroblastoma is likely to follow the distribution of sympathetic ganglia occupying the paramedian position in the head and neck and pelvis. This probably explains the site of origin of skull base ganglioneuroblastoma in the cribriform plate region in our particular case. Pippal et al., [8] and Squillaci [9] have described the occurrence of ganglioneuroblastoma in the maxillary sinus and ethmoid sinus respectively and the extremely variant behaviour of the tumour in the paranasal sinus and extracranial skull base region with respect to age and locoregional and distant spread of the tumour. In present case, a middle aged man presented with a short duration of symptoms and detection of spinal metastasis after surgery and complete remission after chemoradiation demonstrates the mystifying behaviour of ganglioneuroblastoma. The paucity of literature in ganglioneuroblastoma depicts that further long term case series studies are required to pin point the exact nature of ganglioneuroblastoma of skull base.

Symptoms mimic any other tumour in the nasal cavity. Non specific symptoms are widely present at onset like fever, sweating, pain and weight loss [1,2,5,10]. Presentation of metastasis is in the form of respiratory distress, bone pain and peripheral neurological deficit. Clinical examination may reveal a friable mass which bleeds on touch with extension into neighbouring structures. Metastasis of neuroblastic tumours is either by haematogenous or lymphatic dissemination. Common sites of metastasis are bone, liver, dura, lung, brain and skin. Literature shows that occasionally ganglioneuroblatomas may produce catecholamine's which may manifest clinically [1,2].

Histology of neuroblastic tumours reveals the presence of primary and secondary features. Neuroblasts along with the mature ganglion cells, Schwann cells and the surrounding stroma form the primary features. Neuropil which are neuritic extensions from neuroblasts are present in neuroblastomas. Central core of neuropil with an ovoid columnar or circular pattern arrangement of tumour cells represent a Homer Wright rosette which forms the characteristic feature of neuroblastoma which may not be always present. Karyorrhexis, mitosis, calcification, fibrosis, haemorrhage, necrosis and lymphocytic infiltrate form the secondary features of a neuroblastic tumour [1].

Shimada proposed a histological system for grading of tumours based on the presence of stroma, degree of differentiation of neuroblasts and patients age. Undifferentiated tumours and nodular tumours usually denote a poor prognosis whereas well differentiated tumours denote a good prognosis [11]. The presence of MYC-N, normal DNA, elevated neuron specific enolase and ferritin in the genetic make-up correlate with a poor outcome whereas the presence of hyper diploid DNA, elevated levels of CD 44 and expression of Trk-a correlates with a good outcome. Immunohistochemical analysis also plays a role in diagnosis. Chromogranin and synaptophysin have an affinity to neural tissue. CD 57, a neural marker for monoclonal antibody, Leu-7, a natural killer cell marker and CD 56, a marker for primitive cancer cells maybe positive in neuroblastic tumours [1].

CECT as an imaging modality in the nose and paranasal sinuses determines the skull base involvement, vascular infiltration, presence of lymphadenopathy, origin of the tumour and size. MRI is used for assessing intracranial and spinal involvement. It usually reveals a variable enhancement with low intensity on T1W and high intensity on T2W. Urinary catecholamine metabolite measurement and histopathology render definitive diagnosis. MIBG scintigraphy and Technetium 99m scintigraphy have set standards in metastatic evaluation of neuroblastic tumours. Bone marrow biopsy is warranted if there is suspicion of bony metastasis [1,2].

The treatment of ganglioneuroblastic tumours is multimodal. Low risk tumours can usually be treated by surgery alone. With risk of recurrence or neck node involvement, additional chemotherapy and radiation therapy maybe added. Intermediate risk tumours are treated with surgery and adjuvant chemotherapy. There are various studies which show the response of tumour to chemotherapy [12,13], however, the role of chemotherapy in nasal ganglioneuroblastoma has not been reported. Immunomodulators and retinoids are still under trial and show promise in the further treatment of neuroblastic tumours [1,2].

Prognosis of ganglioneuroblastoma is dependent on the age and stage of presentation. Early stage tumours with a young age group (less than 1 year) have a 3-year-survival rate of more than 75% whereas, children more than 1 year and late stage have a 3-year-survival of less than 50% [1].

CONCLUSION

Ganglioneuroblastoma of the skull base is intermediate risk tumour with a propensity to metastasize. There is little literature on the occurrence of ganglioneuroblastoma of the nose and the skull base. The management protocol for ganglioneuroblastoma varies when compared to an olfactory neuroblastoma. Accurate diagnosis and aggressive multimodality treatment of the tumour is required to propagate remission of the tumour. Surgery and chemoradiation form a pivotal role in treatment of this aggressive tumour with minimal risk of metastasis. Hence, early diagnosis of this pathology is extremely important in adequate management of this tumour.

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