



## Olfactory Neuroblastoma with Metastasis to Parotid Gland: A case report

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### Abstract

*Olfactory neuroblastoma also known as esthesioneuroblastoma is uncommon malignant neoplasm usually occur at roof of nasal cavity. It usually metastasize to lymph node and rarely metastatise to parotid gland. There has been only one case reported regarding metastasis of ONB to parotid gland in 2005 [7]. We report a case of elderly women with diagnosis of olfactory neuroblastoma presented with parotid swelling 2 months after the operation which is progressively increases in size. Histopathology and immunohistochemistry confirm the diagnosis of olfactory neuroblastoma metastasize to parotid gland. The patient underwent total parotidectomy, tumour debulking, left cervical lymph node removal with preservation of facial nerve branches and left selective neck dissection was performed. Patient is planned for further chemotherapy and palliative care*

### Introduction

Olfactory neuroblastoma is uncommon malignancy of olfactory sensory epithelium of nasal cavity, neural in origin arising from olfactory neuroblastoma first described by Berger et al in 1942 [5, 6, 15]. Now the tumour is established as neuroectodermal tumour arises from roof of latera lwall of the nose. The olfactory neuroblastoma exhibiting wide range of hitopathological findings and give difficulty in the diagnosis. [5, 6, 15]. Clinical finding, radilogical and immunohistochemistry correlation is very important to reach to the diagnsois. Patient usually presented with nasal obstruction, epistaxis, rhinorrhea, headache and visual disturbance. The tumour is known to be locally invasive tend to spread to surrounding strucures and frequent locall

recurrent is reported. Isolated metastasize to parotid gland without continuous extension is very rare. [1]

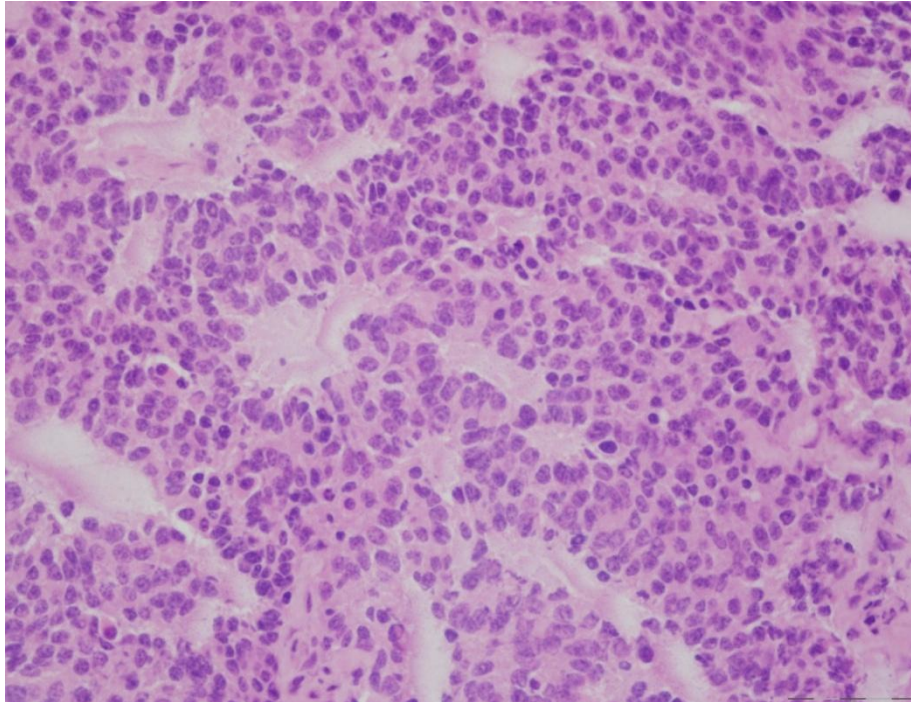
### Case Report

A—58 years postmenopausal woman, with underlying hypertension and type 2 Diabetes Mellitus known case of olfactory neuroblastoma was referred from another centre for further treatment. At first presentation, she complained of bilateral epistaxis and anosmia associated with memory impairment, lost of vision, headache, intermittent fever, lethargy, loss of appetite and loss of weight for 6 months duration. Initial examination revealed a mass arising from the left middle turbinate measuring 4x4 cm. Fossa of Rosenmuller was normal and no lymph node was

palpable. CT scan of paranasal sinus showed superior ethmoidal aggressive tumour with local infiltration to bilateral frontal lobes and possible subfalcine herniation.

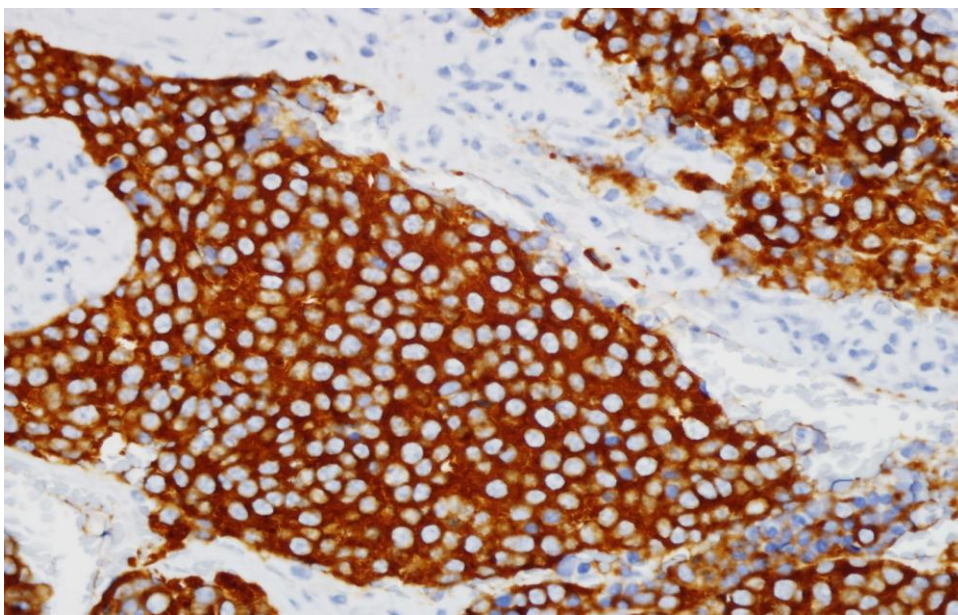
Diagnosis of olfactory neuroblastoma was made from the tumour excision specimen. Histopathologically, the tumour exhibiting organoid fashion, in a group of small monotonous

cells with round nuclei, salt and pepper chromatin, occasional prominent nucleoli, indistinct nuclear membrane and prominent fibrillary background. Immunohistochemistry show positivity towards chromogranin, synaptophysin NSE and negative for epithelial marker. S100 shows positivity of sustentacular cells in the background.

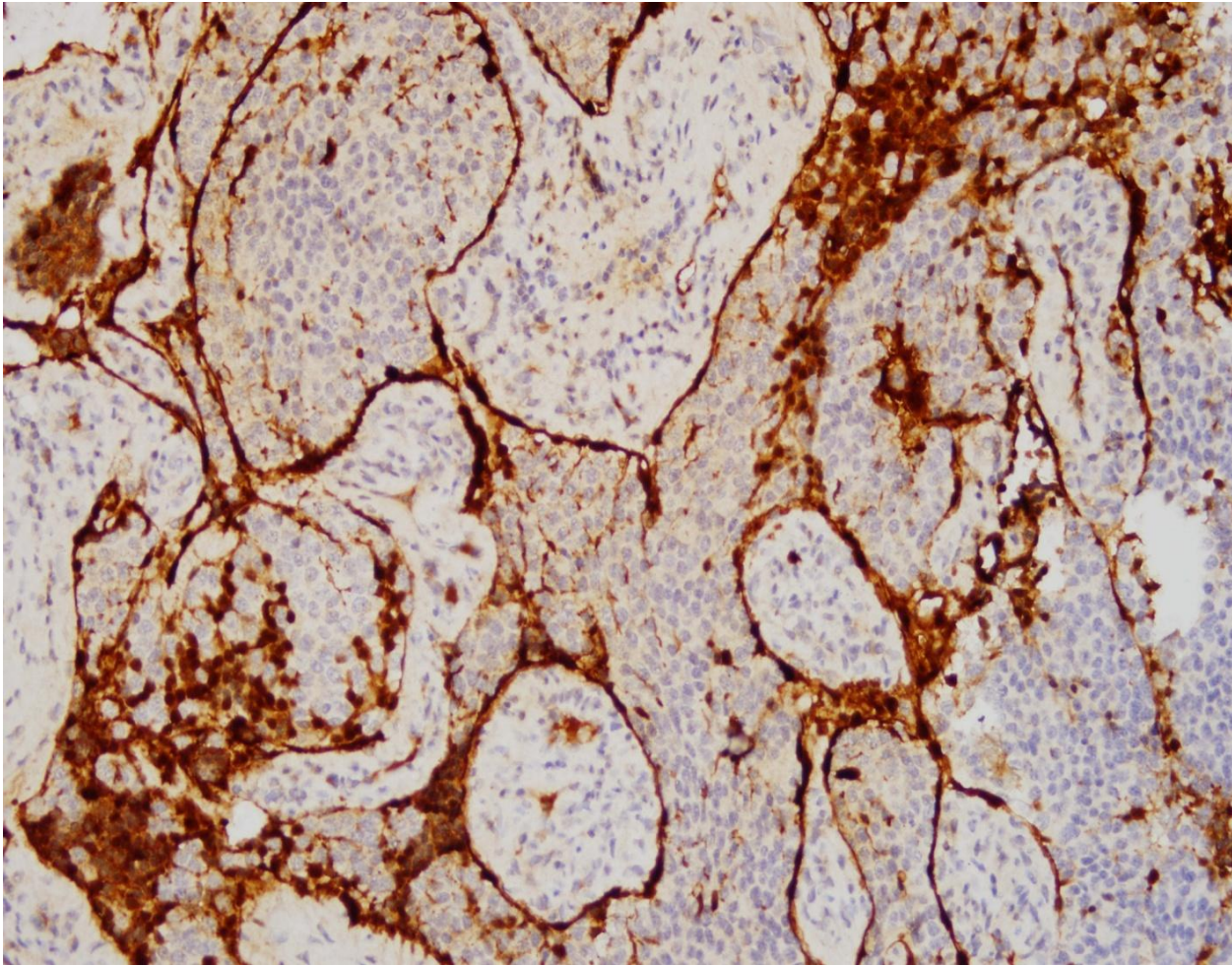


The tumour cells arranged in organoid pattern, having monotonous nuclei with salt and pepper chromatin pattern, some prominent nucleoli and

indistinct eosinophilic cytoplasm. Some of them foaming vague rosette pattern.



SYN 9184 x40



## S100 9184B x20

Repeat CT scan 1 month later showed smaller size postoperative intranasal tumour. Follow up 2 months post operation showed presence of left parotid region node 2.5 x 2.5 cm without any continuous extension from primary tumour.

FNA was performed on the nodes and revealed atypical cells suggestive of olfactory neuroblastoma. During presentation at our centre, the parotid swelling measured 3x 4cm, mobile, non-tender with no skin change. There were also bilateral level II nodes 2x1 cm each. Total parotidectomy, tumour debulking and left cervical lymph node removal with preservation of facial nerve branches and left selective neck dissection was performed. The facial nerve is found closely embedded into the tumour. Histopathological finding confirm the diagnosis metastatic olfactory neuroblastoma to the parotid gland.

### Discussion

Olfactory neuroblastoma (ONB) (also called esthesioneuroblastoma, olfactory placode tumour, esthesio-neurocytoma, esthesioneuroepithelioma, esthesioneuroma) is an uncommon sinonasal tract tumor affecting one person in ten million populations. It arises from the specialized sensory neuroepithelial cells (olfactory) cells in the upper part of nasal cavity.

It can occur at any age without any gender predilection. Most cases occur in the 2<sup>nd</sup> and 6<sup>th</sup> decade of life. Patient usually presented with nasal obstruction and epistaxis. Less common symptoms are headache, pain, excessive lacrimation, rhinorrhea, anosmia and visual disturbances. Interestingly anosmia is not common despite the tumor arising from olfactory neuroepithelium <sup>[1]</sup>

On CT scan the tumor shows marked tumor enhancement after gadolinium. It can present with only an intracranial mass. The tumour usually appears as a unilateral, polypoid, glistening, soft, red–grey mass with an intact mucosa. There is no specific appearance. The surface is grey-tan to pink-red and hypervascular. The size range from 1 cm up to large mass involving the nasal cavity and intracranial region and expanding into the adjacent paranasal sinuses, orbits and cranial vault.<sup>[1]</sup>

Histologically the tumor comprised of ‘primitive’ neuroblastoma cells arranged in lobular pattern. These circumscribed lobules or nests are seen below an intact mucosa separated by vascularized fibrous stroma. In situ tumor is possible, but not appreciated as the tumor usually progresses and exhibit symptoms. 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 and delicate, uniform, ‘salt and pepper’ chromatin. Nucleoli are inconspicuous. Neuronal processes form the background. Fine fibrovascular septae surround the cellular nests in an organoid fashion.

According to Hyams grading system. ONBs are graded (from I to IV) based on a combination of cytoarchitectural features, including lobularity, nuclear uniformity, mitotic figures, calcification, necrosis, fibrillarity, and Homer Wright and Flexner-Wintersteiner rosettes<sup>[2]</sup>.

The Kadish et al. proposed staging system from 1976 is still used, despite the presence of TNM-type classification for ONBs<sup>[3]</sup>. The Kadish system includes: A: tumor limited to nasal cavity; B: nasal cavity and paranasal sinuses; C: beyond nasal cavity and sinuses. Increase in grade and stage is associated with decrease in survival<sup>[4]</sup>.

The differential diagnosis include sinonasal undifferentiated carcinoma (SNUC), extranodal NK/T cell lymphoma, nasal type, rhabdomyosarcoma, Ewing/ Primitive neuroendocrine tumour (PNET). Other tumours like mucosal malignant melanoma, neuroendocrine carcinomas (NEC) and squamous cell carcinoma have to be considered as

well. Less likely are paraganglioma, extramedullary plasmacytoma, pituitary adenoma, extracranial meningioma, mesenchymal chondrosarcoma, and granulocytic sarcoma. In addition, metastatic adrenal gland neuroblastoma to the sinonasal tract would be difficult to distinguish as it present with histologically identical finding recognized only by the lack of MYCN.<sup>[1]</sup>

NEC in comparison to ONB tends to be high-grade lesions, with necrosis, high mitotic figures, and apoptosis. NEC shows a punctate paranuclear cyokeratin immunoreactivity not seen in the cases of ONB that react with keratin. ONB is non-reactive with TTF-1, while NEC can be positive. SNUCs cytologically share the features of a poorly differentiated carcinoma. Comparatively, ONBs generally lower-grade tumors with cytological evidence of neuroectodermal differentiation. Nuclei in ONB tended to be smaller, with smoother nuclear contours and more even chromatin. Fibrillary cytoplasm or Homer Wright rosettes were identified. The presence of cytoplasmic vacuoles, ‘signet ring’-like cells, or extracellular lumina in the majority of SNUCs allow it to be distinguished from ONB.

A panel of immunohistochemical stains can help differentiate difficult cases. Appropriate clinical context, and a prior histologic diagnosis, made a specific cytologic diagnosis possible<sup>[13, 14]</sup>.

Olfactory neuroblastoma of grade I & II (Hyams grade) resemble other neuroblastomas with small round cells arranged in rosettes and an abundant neurofibrillary background. Grade III & IV (Hyams grade) have little or no neurofibrillary background with few or no rosette formations. Small cell neuroendocrine carcinoma should be considered when tumor cells showed rosette arrangement with absent of neurofibrillary background.<sup>[1]</sup>

Small biopsy with crush artifact poses a diagnostic dilemma. Edge effect and diffuse artifacts with immunohistochemistry may not resolve the differential, and might lead to misdiagnosis.

Making an interpretation on such limited material have to be done with extra caution.<sup>[14]</sup>

Literature search for reported cases of ONB with emphasis on parotid gland metastasis showed only a one reported case before. This could be due to the fact that there are numerous lymph nodes in the parotid gland that replace the entire gland. Continuous extension of the tumour from primary site also can occur. ONB has the potential to spread regionally<sup>[5]</sup>. Neck metastasis can occur either early in the disease or many years later. Metastasis usually is by lymphatic spread to cervical lymph nodes<sup>[6]</sup>. Haematogenous metastases are rare but may occur in bone, bone marrow, lung or skin at the time of relapse. Metastasis to parotid gland is not common. The majority of metastases to the parotid gland being melanomas and squamous cell carcinomas<sup>[7]</sup>. Other malignant tumors that involve the parotid gland were also reported by including cylindromas of the ear canal, from the cheek and thyroid, basal cell carcinoma of the brow and mucoepidermoid carcinoma. A case of esthesioneuroblastoma metastasized to the paraglandular nodes was also reported. A study of cytology smears by Mahooti et al. failed to specify whether their neck metastasis in their series were to parotid gland or other structures<sup>[8]</sup>

To understand how metastasis to the parotid gland happens it is important to look at the anatomy.

The parotid gland is supplied by the transverse facial artery that branches from superficial temporal artery originating from branches of the external carotid artery. The transverse facial artery also supplied the parotid duct, and the masseter muscle. Venous blood drains from the superficial temporal vein that runs through the parotid gland just deep to the facial nerve to join the external jugular vein. There is a high density of lymph nodes within and around the parotid gland. The parotid is the only salivary gland that has two nodal layers, both draining into the superficial and deep cervical lymph systems. Approximately 90% of the nodes are located in the superficial layer between the glandular tissue and its capsule.

These superficial nodes drain The parotid gland, external auditory canal, pinna, scalp, eyelids, and lacrimal glands whereas the deep layer of nodes drains the gland, external auditory canal, middle ear, nasopharynx, and soft palate<sup>[9]</sup>. The normal parotid gland contains an average of 20 lymph nodes with capsules and sinuses without including aggregates of lymphocytes and lymphoid tissues<sup>[7, 10]</sup>. Metastasis may occur from lymphatic spread, hematogenous dissemination or by direct extension (more common with primary in the parotid region). Lymphatic metastases may be direct without paraglandular or extraglandular lymph nodes involvement or may be secondary from a paraglandular lymph node, as well as retrograde extension from metastases in the neck. Unless tumor cells overrun the lymph node, the identification of its capsule and circumscription from the parotid parenchyma point to a lymphatic metastasis.<sup>[11]</sup>

Diagnosis becomes difficult if there was no previous histological diagnosis and the main presentation is parotid swelling. Cytologic diagnosis is made possible by proper clinical correlation and immunohisto chemistry. The pathologist needs to be aware of the possibility of ONB and distinguish it from other malignancies of the neck.<sup>[5, 6, 15]</sup>

Treatment includes complete surgical elimination by a bicranial-facial approach (trephination), which removes the cribriform plate, and is usually followed by a course of radiotherapy to achieve the best long-term outcome. Occasionally, endoscopic resection for limited tumor is also carried out. An elective neck dissection is not warranted. Palliation with chemotherapy is reserved for advanced unresectable tumors or for disseminated disease.<sup>[4]</sup>

Overall survival is adversely affected by female gender, age less than 20 or more than 50 years at initial presentation, high tumor grade, extensive intracranial spread, distant metastases, tumor recurrence, a high proliferation index, and polyploidy or aneuploidy. The presence of

metastasis to parotid gland is a grave prognosis factor, associated with disseminated disease<sup>[12]</sup>

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