



## Neurofibroma Transformation to Malignant Peripheral Nerve Sheath Tumor in the Parapharyngeal Space: A Case Report

Razan A. Aldhahri<sup>1,4</sup>, Rana A. AlJunidel<sup>1,4</sup>, Nasser A. Benomran<sup>1,4</sup>, Hussain M. Alkaff<sup>1,4</sup>, Nouf M. Aloraini<sup>1,4</sup>, Raghad A. Alotaibi<sup>1,4</sup>, Joon Seon Song<sup>2</sup>, Turki M. Almuhammad<sup>3,4\*</sup> and Soon Yuhl Nam<sup>4</sup>

<sup>1</sup> College of Medicine, King Saud University, Riyadh, Saudi Arabia

<sup>2</sup> Department of Pathology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea

<sup>3</sup> Department of Surgery, King Fahad Specialist Hospital, Dammam, Saudi Arabia

<sup>4</sup> Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

\*Corresponding e-mail: [dralmohimmed@yahoo.com](mailto:dralmohimmed@yahoo.com)

### ABSTRACT

The incidence of sporadic malignant peripheral nerve sheath tumors (MPNSTs) in general population is as low as 0.001%. Whereas in association with neurofibromatosis type 1 (NF1), the lifetime risk of MPNSTs is estimated to be 8-13%. MPNSTs are potentially found on the trunk and extremities. They are infrequently observed in the head and neck. Thus, they are extremely rare to arise from the para-pharyngeal space. Consequently, to the best of our knowledge, benign neurofibroma malignant transformation has never been reported in the para-pharyngeal space yet. Therefore, in this article, we report the first case of neurofibroma transformation into MPNST in the para-pharyngeal space of an NF1 patient. The cornerstone treatment is complete surgical excision of the tumor. In most cases, it is not possible to obtain clear margins in the head and neck region because of the lack of circumscription and anatomical complexity of the area. Recurrence rate ranges from 40% to 68%, whereas 5-year survival was reported ranging from 16% to 52%. Poor prognosis is linked with tumor size exceeding 5 cm, association with NF1, old age, distant metastases, inability to achieve tumor-free margins, high tumor grade, and poor differentiation. In conclusion, due to the rarity of this disease, only a few large studies investigated recurrence rate and survival. Poor outcomes are attributed to the rarity of the disease and complexity of the region. More cases shall be reported to improve our knowledge about the incidence, course, and prognosis of the disease, and allow for new effective management techniques discovery.

**Keywords:** Neurofibroma, Transformation, Malignant peripheral nerve sheath tumor, Parapharyngeal space

### INTRODUCTION

Malignant neurogenic sarcoma, also called malignant peripheral nerve sheath tumor (MPNST), malignant neurofibroma, malignant schwannoma, and neurofibrosarcoma, accounts for 5% of all soft tissue sarcomas, 8-14% of them affect head and neck region [1]. The incidence of sporadic MPNSTs in general population is as low as 0.001% [2]. Whereas in association with neurofibromatosis type 1 (NF1), the lifetime risk of MPNSTs is estimated to be 8-13%. Furthermore, 10% of MPNST cases were secondary tumors arising 10 to 20 years post radiotherapy treatment [3]. MPNSTs have equal male and female distribution and an age range of 20-50-year-old, whilst NF1 patients are affected at a younger mean age [4]. MPNSTs are potentially found in the trunk and extremities. They are infrequently observed in the head and neck region, thus, they are extremely rare to arise from the para-pharyngeal space. Consequently, to the best of our knowledge, benign neurofibroma malignant transformation has never been reported in the para-pharyngeal space yet. Therefore, in this article, we report the first case of neurofibroma malignant transformation into spindle cell MPNST in the para-pharyngeal space of an NF1 patient.

### Case History

A 23-year-old female patient who's a known case of NF1 and Moyamoya disease presented in February 2018 with a 3-month history of throat pain especially during mouth opening, and a 4-month history of dyspnea, and neck mass under the right ear. The patient was diagnosed with NF 1 since the age of 13 years and had been following up with neurology ever since. In October 2008, the patient underwent MRI/MRA brain for her Moyamoya disease and it incidentally revealed a right para-pharyngeal mass (neurofibroma) (Figure 1).



**Figure 1 T1 MRI coronal view showing increased size (3.3 cm to 5.3 cm) of presumed neurofibroma in right para-pharyngeal space without a change in morphology (October 2013)**

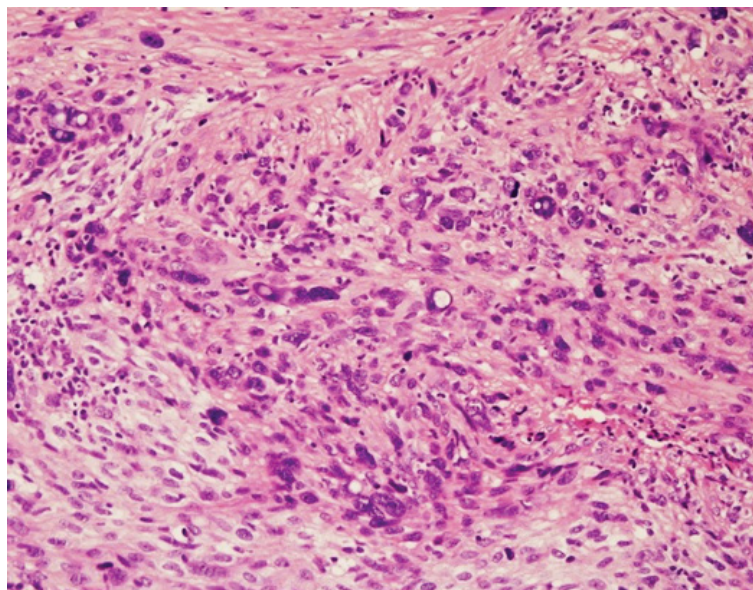
The initial mass size upon diagnosis was (3.3 × 1 cm) and the patient underwent follow up MRI annually since that time. In February 2018, the case was discussed with the patient and her parents since she started to show symptoms, mass bulging, and change in appearance and MRI of the whole body without enhancement was performed (Figure 2).



**Figure 2 MRI T2 coronal view showing increased size (5.3 to 6.3 × 4.4 cm) of the known mass in right para-pharyngeal space with slightly increased extent of perilesional T2 hyperintensity in superomedial aspect of the mass, heterogeneous cystic and solid components within the mass and increased solid portion within the mass since 2013-10-11 (MRI, whole spine)**

The patient was taken to surgery afterward. The preoperative plan was to do an excisional biopsy but intraoperative

gross negative margins were hard to obtain thus intraoral incisional biopsy of the mass was done to confirm the diagnosis and set the management plan. Biopsy results showed high-grade spindle cell sarcoma (Figure 3). A month after biopsy, the patient was diagnosed with many cervical lymph node metastases. PET scan of the whole body was done and showed multiple neurofibromas in the axillary areas. Bearing in mind the presence of multiple metastases and the complexity of the surgery the patient refused the surgery and preferred chemoradiotherapy alone. The patient underwent concurrent chemoradiotherapy using IMRT 35 cycles. Follow up of her 3 months later didn't show any regression or progression of the disease.



**Figure 3** Excision of para-pharyngeal mass was done. The mass is composed of highly cellular fascicles of spindle cells with a vaguely whorled growth pattern. The tumor cells show hyperchromatic nuclei with marked nuclear pleomorphism. Mitotic figures are frequently identified (21 mitoses per 10 high power fields). Multifocal necrosis is observed. (H and E, original magnification 200 X). On Immunohistochemistry, the tumor cells are focal positive for S100 protein

#### DISCUSSION

Commonly patients with MPNST in the para-pharyngeal space were present with rapidly enlarging neck mass or oropharyngeal bulge, severe pain, dysphagia, dyspnea, unilateral middle ear effusion, pulsatile tinnitus, bruit, thrill, otalgia, airway obstruction, foreign body sensation, and neurological deficits. The vagal nerve is the main nerve frequently involved in neck tumors, therefore, hoarseness is the main presentation but sometimes it includes true vocal cord palsy, Horner's syndrome, and dysarthria [5]. Whereas in our patient the tumor was incidentally found on the MRI/MRA, and she remained asymptomatic for about 10 years with a slow tumor growth rate. Ten years later, the patient started to show symptoms when the tumor size has increased. She began to have dyspnea, neck bulging and throat pain aggravated by mouth opening for the last 4 months. The patient did not show any signs of neurological deficit such as vagal nerve palsy.

MRI is considered the imaging modality of choice in cases of MPNSTs. The findings strongly suggestive of this malignant tumor usually include tumor size of more than 5 cm, fat planes invasion, heterogeneity, ill-defined margins and edema surrounding the lesion. Such tumors have a high tendency towards metastasizing to the lungs followed by bones. Therefore, it is vital to perform a chest CT scan after histological diagnosis [6]. To differentiate between benign and malignant tumors, a biopsy must be done and it's recommended to be open covering multiple tumor sections. However, CT-guided core-needle biopsy with a good histologic correlation with the final specimen obtained during surgery is a possible alternative that has fewer complications of exacerbated pain upon nerve distribution [7]. MPNSTs commonly appear white, large, solid in composition with areas of necrosis and hemorrhage. Microscopically, most MPNSTs are highly cellular, comprised of spindle cells reminiscent of Schwann cells. The cells are mitotically active and weakly S100 protein positive, consistent with dedifferentiation from Schwann cells [4,8]. In this case,

the diagnosis of the para-pharyngeal neurofibroma was initially done with only MRI which is enough to diagnose neurofibromas. The patient was followed with MRI\MRA annually, and the transformation from neurofibroma to MPNST was then confirmed by intraoral excisional biopsy results matching the criteria mentioned above.

Transformation of neurofibromas to MPNSTs is extremely rare with less than 20 cases reported in English literature. Total 6 patients of those were NF1 patients and one patient had Klippel-Trenaunay-Weber syndrome which is defined by a triad of port wine stain, varicose veins, and bony and soft tissue hypertrophy involving an extremity. The anatomical distribution of the tumors showed 7 cases arising from the trunk, 3 cases arising from the scalp, 6 cases arising from the extremities, 2 cases arising from the orbit and only 1 case arising from the neck region. Therefore, to the best of our knowledge, this case is the first reported case in the para-pharyngeal space and the second case in the neck region [9,10].

The differential diagnoses of a neoplastic mass in the para-pharyngeal space commonly include salivary gland tumors, neurogenic tumors, skull base, and vertebral tumors, and more rarely, Castleman's disease. Lesions of a non-neoplastic nature include branchial cleft cysts, lymphangiomas, arteriovenous malformations, and infective extensions arising from the odontogenic, submandibular gland, and pharyngeal tonsil sources [11].

The cornerstone treatment is complete surgical excision of the tumor [12]. In most cases, it is not possible to obtain clear margins in the head and neck region because of the lack of circumscription and the anatomical complexity of the para-pharyngeal area. MPNSTs are historically considered resistant to radiochemotherapy, therefore, the role that chemo and radiotherapy play is not clear yet. Nonetheless, the limited response concluded by old experiments may reflect older techniques rather than tumor behavior. Radiotherapy is definitely recommended nowadays at least as a palliative therapy and postoperative control of the tumor [13]. Due to the rarity of this disease, only a few large studies investigated the recurrence rate and survival. Recurrence rate has been described ranging from 40% to 68%. Whereas, 5-year survival was reported ranging from 16% to 52% [14]. Poor prognosis has been linked with tumor size exceeding 5 cm, high tumor grade, association with NF1, old age, distant metastasis, poor tumor differentiation, and inability to achieve tumor-free margins. The rate of distant metastasis is about 40% [15].

### CONCLUSION

In conclusion, the transformation of neurofibromas to MPNST's is considered very rare. Due to the anticipated rarity, further studies must be established and more cases shall be reported to improve our knowledge about the incidence, course, and prognosis of the disease, and allow for the discovery of new effective management techniques.

### DECLARATIONS

#### Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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