Malignant peripheral nerve sheath tumor in the nasopharynx and oropharynx: a case report

Wen-Jing Gu¹, Peng-yu Chang², Ling-Jing Wang³, Wei Zhu¹ and Hong-Wei Zhou³,⁴

Abstract
Malignant peripheral nerve sheath tumor (MPNST) in the nasopharynx and oropharynx has not been reported. A 3-year-old boy was referred to hospital after experiencing intermittent inspiratory dyspnea for 3 years. Preoperative imaging showed that the lymph nodes were clear. Therefore, neck lymph node dissection was not performed during the operation. This could have reduced the collateral damage. Complete excision and radiotherapy were performed because of the pathological diagnosis of MPNST. Because of the high location of the tumor, we chose the transoral approach instead of the cervical approach, avoiding tracheotomy, and we effectively improved the quality of life of the child. A mass in the nasopharynx and oropharynx was diagnosed pathologically as an MPNST after surgery. The patient’s inspiratory dyspnea was resolved. No recurrence was observed during a 3-year follow-up. After review of our case, we found that postoperative recovery in our patient was closely related to accurate preoperative imaging assessment, the choice of operation methods, thorough resection, and postoperative neoadjuvant radiotherapy. Prevertebral fascia acted as a barrier to surround the mass and prevented it from growing further toward the vertebral body, which was important for a good prognosis. Children undergoing tracheotomy often have long tube management and difficult extubation.

¹Department of Otorhinolaryngology Head and Neck Surgery, the First Hospital of Jilin University, Changchun, China
²Department of Radiation Oncology, the First Hospital of Jilin University, Changchun, China
³Department of Radiology, the Third People’s Hospital of Shenzhen, Shenzhen, China
⁴Department of Radiology, the first hospital of Jilin University, Changchun, China

Corresponding author:
Hong-Wei Zhou, Department of Radiology, First Hospital, Jilin University, #71 Xinmin Street, 130021, Changchun, China.
Email: zhouhongweiris@163.com

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).
Keywords
Nasopharynx, oropharynx, malignant peripheral nerve sheath tumor, dyspnea, neoadjuvant radiotherapy, neurofibromatosis 1

Date received: 6 May 2019; accepted: 3 December 2019

Introduction
Among all sarcomas of soft tissues, 5% to 10% are malignant peripheral nerve sheath tumors (MPNSTs). MPNSTs include solitary (primary) tumors and neurofibromatosis 1 (NF-1). Approximately 50% of patients with an MPNST have NF-1 malignant transformation, but malignant transformation of schwannomas is rare. NF-1-related MPNSTs often occur in older men.1 MPNSTs, also known as malignant schwannomas, malignant neurilemmomas, neurogenic sarcomas, or neurofibrosarcomas, show differentiation into peripheral nerve sheath cells and generally occur in the trunks of major nerves. Additionally, 40% to 50% of cases of MPNSTs are associated with neurofibromatosis.2 In patients aged from 28 to 36 years, primary MPNSTs are usually detected, and their occurrence in children and adolescents is rare.3 To the best of our knowledge, MPNST in the nasopharynx and oropharynx has not been reported in the literature. There is no significant difference in the incidence of MPNST between men and women, and multiple sites of tumor occurrence have been found, such as in the trunk, retroperitoneal locations, lower limbs, upper limbs, head, and neck areas, oral cavity, and pelvis.4 5 Superficial MPNSTs may be less aggressive than deep-seated MPNSTs.6 We report a case of MPNST in the nasopharynx and oropharynx in a child. The previous history, family history, and related examination of the child suggested that MPNST was not related to NF-1 and it was a primary MPNST.

Case presentation
A boy (3 years old) was admitted to our hospital with a 2-year history of snoring and breathing through the mouth. The patient also had inspiratory dyspnea, especially during sleeping. The out-patient diagnosis was tonsil hypertrophy. Inspiratory dyspnea and three concavity signs were apparent, even when the child was calm. Nasoscopy showed adenoid hypertrophy, accounting for two thirds of the posterior nares. A tumor with a smooth surface, which was lying on the posterior wall between the nasopharynx and oropharynx, was also detected. A computed tomography scan with contrast showed irregular hyperattenuation in the prevertebral space of C1–C5, and it was approximately 2.0 × 4.6 × 3.4 cm in size, with heterogeneous enhancement (Figure 1a–c). After admission, the patient developed severe dyspnea. Because of the possibility of pulmonary infection, he was immediately transferred to the pediatric intensive care unit of our hospital. He was provided oral tracheal intubation and gastric tube implantation. After anti-infection and symptomatic treatment, his symptoms greatly improved and he underwent surgery. We wished to avoid tracheotomy because it can cause surgical injury and affect quality of life of the child. Because the inspiratory dyspnea was severe, we performed tracheal intubation
and operated under a mouth gag. During the operation, there was no clear gap between the tumor and pharynx mucosa. The tumor was excised together with the mucosa of the pharynx. The tumor easily bled. The tumor extended backwards, but there was a distinct gap between the tumor and prevertebral space. A rapid pathological examination during the operation showed a malignant tumor originating from mesenchymal tissue. Preoperative evaluation of lymph nodes was clear. No lymphadenectomy was performed because mesenchymal malignancy had spread mainly by the hematogenous route.

Tumor tissue was subjected to histopathological and immunohistochemical analyses (Figure 2a, b). The pathological results...
indicated an MPNST. Immunohistochemistry showed the following positive and negative results: Ki-67 (+10%), cytokeratin pan antibody CK-pan (−), vimentin (−), S-100 (focal +), smooth muscle actin (−), h-caldesmon (−), desmin (−), cluster of differentiation 117 (−), discovered on gastrointestinal stromal tumor 1(part +), cluster of differentiation 34 (−), β-catenin (+/−), cluster of differentiation 56 (−), and neuron-specific enolase (−).

An indwelling nasogastric tube was inserted and the patient was allowed to eat on the 13th day after surgery. The patient received radiotherapy 30 days after the operation. The dose at the posterior thickened area of the pharyngeal wall was 5600 cGy/33F and the tumor bed area dose was 4760 cGy/28F. Mild stenosis was found between the nasopharynx and oropharynx 3 years after the operation. The narrow band imaging mode of laryngoscopy showed that the area of the tumor was normal (Figure 1d).

Informed consent was obtained from the patient’s parents for publication, and this study received approval from the Research Ethics Committee of The First Hospital of Jilin University.

**Figure 2.** (a) Histology of a malignant peripheral nerve sheath tumor shows alternating dense cellular fascicles and myxoid regions, also called a marble pattern. The cells may have irregular contours and be spindle shaped, or may be fusiform or round in shape. Hematoxylin and eosin staining, ×400. (b) Immunohistochemical study of biopsy samples shows that tissue is positive for Ki-67 (×200).

**Discussion**

Complete surgical resection is the only potentially curative option for MPNST, but metastasis that is locally invasive and/or uncontrollable make this option non-feasible. Despite chemotherapy and radiotherapy, survival is not remarkably affected, with a 5-year survival rate of 20% to 50%. MPNSTs can resemble benign tumors, both histologically and radiologically. To make an early diagnosis of MPNST, evaluation by magnetic resonance imaging and a biopsy should be performed immediately when malignancy is suspected. Previous authors have suggested that diagnosis of MPNST is easy in patients without NF-1 who present with a palpable mass and pain. However, diagnosis is frequently delayed in patients with NF-1 because of misdiagnosis of these lesions as neurofibroma and/or plexiform neurofibroma. Our patient did not have NF1 malignant transformation. We did not consider the diagnosis of MPNST before the operation. Furthermore, magnetic resonance imaging data on this condition are scarce. Nevertheless, the treatment of choice for MPNST is complete surgical resection.
followed by postoperative chemotherapy. In MPNST, histone deacetylase inhibitor (HDACi)-induced autophagy increases cell survival by possibly opposing apoptosis, and blocking autophagy enhances proapoptotic effects of HDACis. This occurs not only in cells that are resistant to HDACis, but also in MPNST, thus showing relative sensitivity when blocking autophagy further enhances proapoptotic effects of HDACis. Chloroquine has been evaluated in human glioblastoma and lung cancer because of its anti-autophagy property, and its safety has been confirmed by initial studies. The main factor for improving overall survival and tumor relapse rates is believed to be the negative margin status.

The in vitro growth rate of MPNST cell lines is heterogeneous and leads to variation in the expression of retinoblastoma protein, tumor protein p53, alternate reading frame protein p14, and cyclin-dependent kinase inhibitor protein p16. MPNSTs are highly invasive and demonstrate rapid growth. In the early stages, these tumors can be transferred via blood. Even complete surgical resection is only reported to confer a <50% overall 5-year survival rate. H3K27me3, also known as loss of methylation of histone 3, is highly specific for MPNST and may be a useful diagnostic marker. H3K27me3 shows slightly better sensitivity than that of S-100 protein and sex determining region Y-box 10. S-100 protein is a specific marker of Schwann cells in the peripheral nervous system. S-100 can be expressed in most soft-tissue tumors, but it is obvious in fibrous tissue. This protein is often used as an important marker to distinguish between mesenchymal tumors and epithelial tumors. In our case, positive expression of S-100 protein was important for diagnosing MPNST.

Tumors of the nasopharynx and oropharynx, especially MTNST, are rarely encountered in children. Because of the rarity of these tumors, they tend to remain undiagnosed or are frequently misdiagnosed. For this reason, such cases need to be reported and physicians should be educated to help in efficient detection and management of MTNST.

Declaration of conflicting interest
The authors declare that there is no conflict of interest.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ORCID iD
Hong-Wei Zhou https://orcid.org/0000-0003-1831-2195

References
1. Anghileri M, Miceli R, Fiore M, et al. Malignant peripheral nerve sheath tumors: prognostic factors and survival in a series of patients treated as a single institution. Cancer 2006; 107: 1065–1074.
2. Weiss SGJ. Enzinger and Weiss’s Soft Tissue Tumors. 4th ed. St Louis, Mo, USA: Mosby, 2001.
3. Kleihues P, Louis DN, Scheithauer BW, et al. The WHO classification of tumors the nervous system. J Neuropathol Exp Neurol 2000; 61: 215–225.
4. Ziadi A and Saliba I. Malignant peripheral nerve sheath tumor of intracranial nerve: a case series review. Auris Nasus Larynx 2010; 37: 539–545.
5. Voznesensky MA, Yamase H and Taylor JA 3rd. Malignant peripheral nerve sheath tumor of the renal pelvis. Urol Int 2009; 83: 370–372.
6. Thomas C, Somani N, Owen LG, et al. Cutaneous malignant peripheral nerve sheath tumors. J Cutan Pathol 2009; 36: 896–900.
7. Lopez G, Torres K, Liu J, et al. Autophagic survival in resistance to histone deacetylase inhibitors: novel strategies to treat
malignant peripheral nerve sheath tumors. Cancer Res 2011; 71: 185–196.

8. Demir HA, Varan A, Yalcın B, et al. Malignant peripheral nerve sheath tumors in childhood: 13 cases from a single center. J Pediatr Hematol Oncol 2012; 34: 204–207.

9. Tosun HB, Serbest S, Turk BA, et al. Giant malignant peripheral nerve sheath tumor of thigh in an adolescent with neurofibromatosis type 1: a case report. Int Med Case Rep J 2015; 8: 267–271.

10. Solomon VR and Lee H. Chloroquine and its analogs: a new promise of an old drug for effective and safe cancer therapies. Eur J Pharmacol 2009; 625: 220–233.

11. Miller SJ, Rangwala F, Williams J, et al. Large-scale molecular comparison of human schwann cells to malignant peripheral nerve sheath tumor cell lines and tissues. Cancer Res 2006; 66: 2584–2591.

12. Minovi A, Basten O, Hunter B, et al. Malignant peripheral nerve sheath tumors of the head and neck: management of 10 cases and literature review. Head Neck 2007; 29: 439–445.

13. Schaefer IM, Fletcher CD and Hornick JL. Loss of H3K27 trimethylation distinguishes malignant peripheral nerve sheath tumors from histologic mimics. Mod Pathol 2016; 29: 4–13.