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

Wen-Jing Gu[1], Peng-yu Chang[2],
Ling-Jing Wang[3], Wei Zhu[1] and
Hong-Wei Zhou[3,4] (iD)

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.

[1]Department of Otorhinolaryngology Head and Neck Surgery, the First Hospital of Jilin University, Changchun, China
[2]Department of Radiation Oncology, the First Hospital of Jilin University, Changchun, China
[3]Department of Radiology, the Third People's Hospital of Shenzhen, Shenzhen, China

[4]Department 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

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 neurilemomas, 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 hyper-attenuation in the prevertebral space of C1–C5, and it was approximately $2.0 \times 4.6 \times 3.4$ 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
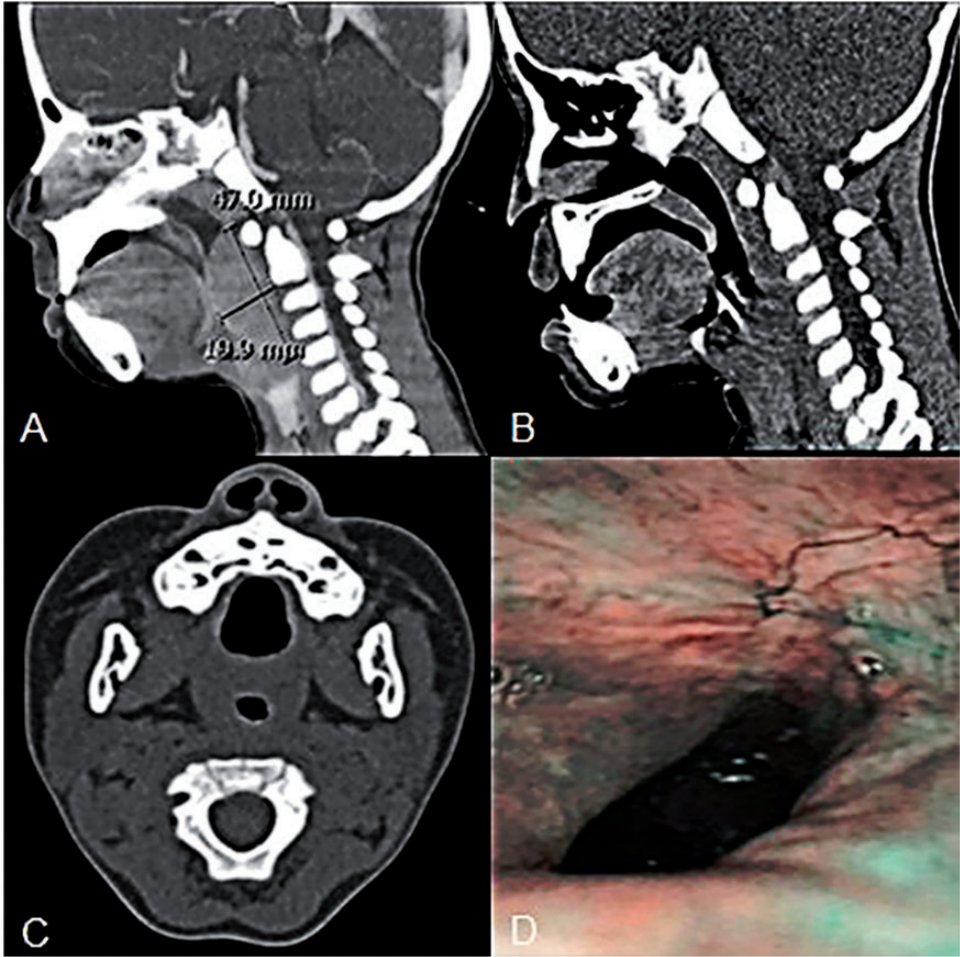
Figure 1. Imaging characteristics of computed tomography in our case. (a) Sagittal multiplanar reconstruction with contrast-enhanced computed tomography shows irregular hyperattenuation in the prevertebral space of C1–C5, approximately 2.0 × 4.6 × 3.4 cm, with heterogeneous enhancement. (b, c) Sagittal and axial non-contrast shows that the nasopharynx and oropharynx are normal. (d) Mild contracture can be seen between the nasopharynx and oropharynx 2 years after the operation. The narrow band imaging mode of laryngoscopy shows that the tumor area is normal.

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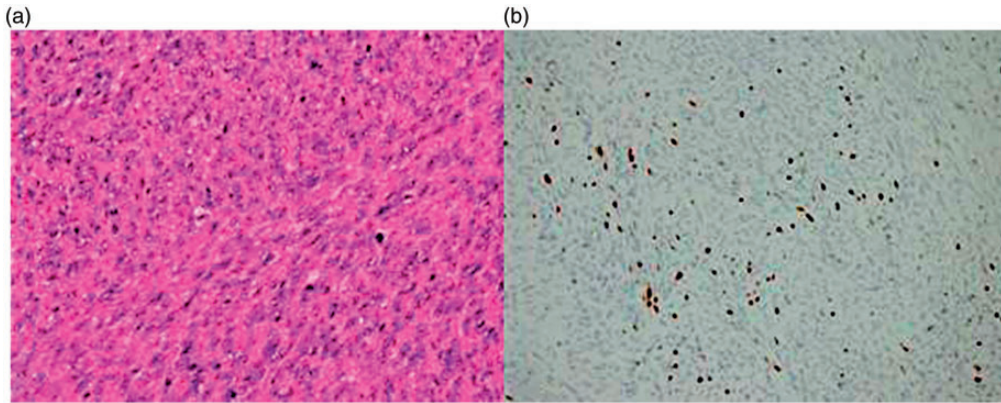
Figure 2. (a) Histology of a malignant peripheral nerve sheath tumor shows alternating dense cellular fascicles and myxoid regions, also called a marble pattern. The cells may have irregular contours and be spindle shaped, or may be fusiform or round in shape. Hematoxylin and eosin staining, ×400.
(b)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

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-catentin (+/−), 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.

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%[7] 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.[8,9] 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.[7] 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.[10] The main factor for improving overall survival and tumor relapse rates is believed to be the negative margin status.[1]

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.[11] 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.[12] H3K27me3, also known as loss of methylation of histone 3, is highly specific for MPNST and may be a useful diagnostic marker.[13] 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

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ORCID iD

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

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