Repetitive syncope caused by a rare massive sporadic malignant peripheral nerve sheath tumor involving carotid arteries

A case report

Tiehao Wang, MDa, Jiarong Wang, MDa, Jichun Zhao, MD, PhDa,∗, Ding Yuan, MD, PhDa,∗, Wenqing Yao, MDb

Abstract

Rationale: Malignant peripheral nerve sheath tumors (MPNSTs) are rare sarcomas arising from peripheral nerves. MPNSTs are uncommon in the head and neck, and various clinical manifestation often make the diagnosis challenging.

Patient concerns: A 67-year-old female was referred for evaluation of repetitive syncope with a massive mass in the neck. Preoperative evaluation revealed potential neuroendocrine activity of the mass and enhanced computed tomography showed carotid artery was involved.

Diagnosis: According to the preoperative imaging, intraoperative finding and postoperative pathological examination, the diagnosis of left neck MPNST involving left carotid arteries was made.

Interventions: Volume expansion therapy with phenoxybenzamine started one week before surgery. Complete surgical resection of the mass was performed and pathological analysis suggested the diagnosis of MPNST. The postoperative radiotherapy was not given due to her poor nutrition.

Outcomes: This patient recovered well after surgery and no sign of recurrence was noted at 2-year follow-up.

Lessons: Though the involvement of carotid artery with neuroendocrine activity is rare in sporadic MPNST, preoperative scanning of blood and urine catecholamine is crucial for intraoperative hemodynamic stability, especially when carotid artery is involved.

Abbreviations: CCA = common carotid artery, CTA = computed tomography angiography, ECA = external carotid artery, HN-MPNST = MPNST in the head and neck, ICA = internal carotid artery, MPNST = Malignant peripheral nerve sheath tumor, NF1 = neurofibromatosis type 1, other-MPNST = MPNST at other body sites.

Keywords: carotid artery, malignant peripheral nerve sheath tumors, neck mass, neuroendocrine activity, syncope

1. Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) are uncommon and biologically aggressive sarcomas which originate from peripheral nerves or from cells associated with the nerve sheath. As MPNSTs can arise from multiple cell types similar with other spindle cell sarcomas, the various clinical manifestation and histopathological appearance often make diagnosis and classification somewhat challenging.[1,2] In addition, the prognoses are generally poor, attributed to high rates of recurrence in the early stage and low response rate to chemotherapy in advanced stages.[3] MPNSTs accounts for approximately 2% of all sarcomas, with an estimated incidence of 5 people per million per year.[4] Compared to other genomically complex sarcomas, MPNSTs tend to present earlier in life and are mostly prevalent between 20 and 30 years.[5] Though large peripheral nerves in the extremities (i.e., sciatic nerve, brachial plexus, etc.) are typically affected, it was reported that, in rare conditions, 4% of the primary MPNSTs can arise in the head and neck.[6] We report a case of huge primary malignant peripheral nerve sheath tumor in the neck with carotid artery involvement, presenting with repetitive syncope and negative local nerve symptoms.

2. Case report

A 67-year-old female was initially seen in local hospital for evaluation of repetitive dizziness 10 years ago, and a 1×2 cm small mass was found in her left neck by ultrasound. After initial
diagnose with hypertension, standard antihypertensive drugs were prescribed. Due to its silent character and small diameter, the mass was left for surveillance. The symptom was temporarily relieved and the patient did not come back during the follow-up until one year before admission to our hospital, the mass in the left neck started growing rapidly and repetitive syncope occurred.

On admission, the patient complained of left frontier pain and repetitive syncope, with negative local nerve dysfunctions (i.e., hoarseness, difficulty in swallowing). No signs or symptoms of neurofibromatosis type 1 (i.e., cafe au lait spots, Lisch nodules, neurofibromas, bone deformities, etc.) was noted. Physical examination revealed a huge mass in the left neck, with the “Y” shape carotid artery bifurcation visible (Fig. 1A). The computed tomography angiography (CTA) showed the diameter of the mass was 20 cm × 17 cm × 15 cm, with the upper border reaching the level of temporomandibular joint and the lower border reaching the upper chest wall (Fig. 1B); left common carotid artery (CCA), internal carotid artery (ICA) and external carotid artery (ECA) were compressed and translocated by the mass (Fig. 1C); no obvious boundary between arteries and the mass (Fig. 1D). Due to repetitive syncope and relatively poor physical condition, neoadjuvant radiation or chemotherapy was inapplicable and surgical removal of the mass was assessed. Preoperative blood test revealed an elevated level of urinary norepinephrine at 101.97 μg/24h urine (16.3–41.5 μg/24h urine), which suggested potential neuroendocrine activity. Thus, volume expansion therapy with phenoxybenzamine started one week before surgery.

A longitudinal incision was adopted and the mass was gradually mobilized by blunt dissection. Change of blood pressure was noted when manipulating the mass. Left common carotid artery (CCA) and external carotid artery (ECA) were totally wrapped in the mass and internal carotid artery (ICA) was partially involved. After intravenous usage of heparin, intermittent clamp of the CCA facilitated dissection and mobilization of the CCA and carotid bifurcation following the proximal-distal route. Careful dissection and control of the ICA and ECA were obtained from the distal part. The involved vessel walls were partially excised and repaired by 6-0 prolene. The nourishing vessels from ECA were ligated and the mass was further mobilized and completely excised after careful dissection from the vagus trunk (Fig. 2A). The patient stayed in intensive care unit for 2 days and postoperative urine norepinephrine returned to normal level. The patient was discharged on postoperative day 5 without any adverse events.

The cross section of the mass showed pleomorphic pattern (Fig. 2B) and pathological analysis of the specimen revealed spindle cell sarcoma with myxoid degeneration and necrosis, accompanied with focal observation of rhabdomyoblast-like cell and chondroid differentiation. Immunohistochemical staining demonstrated strong positivity of nestin and focal positivity of S-100, CD34 and myoD1, while STAT6, desmin, myogenin, SMA, CR, EMA, HMB45, β-C, ALK-1 immunostaining were all negative (Fig. 3). The histomorphology and results of immunohistochemical staining supported the diagnosis of MPNST. Given the potential benefit from adjuvant radiotherapy in MPNST, the patient was referred to cancer radiotherapy outpatient clinic, however, the patient did not receive the regimen due to poor nutrition. At 2-year follow-up, the patient had no signs of nerve symptom and tumor recurrence, and CTA showed carotid arteries were distorted and patent (Fig. 4). Moreover, syncope or dizziness didn’t occur during the follow-up.

3. Discussion

The causes of syncope are diverse, among which malignancy in head and neck is relatively rare, less than one in 250 patients in a screen of approximately 4500 cases.[7] Malignancy-related syncope is commonly attributed to involvement of vasodepressor or vagal reflex arch, which were reported in pharyngeal or laryngeal carcinoma or carotid body tumor.[7,8] By comparison, few evidence is available regarding the relationship between MPNST and syncope. MPNSTs are groups of soft tissue sarcomas that originate from peripheral nerves or differentiate along the lines from various elements of the nerve
sheath (i.e. fibroblast, schwann cells, etc.), commonly presented in large peripheral nerves in the extremities and trunks. Unlike benign schwannomas, MPNSTs are seldom found in the head or neck area, comprising only 4% of all head and neck sarcomas.[9] MPNSTs in the head and neck (HN-MPNSTs) can be either sporadic or associated with neurofibromatosis type 1 (NF1), an autosomal dominant disorder affecting neurofibromin 1 suppressor gene.[3,10] It was reported that 20% MPNST patients were accompanied with neurofibromatosis and MPNST occurred in 40% to 50% of patients with neurofibromatosis,[4] but our case did not find any signs or symptoms of neurofibromatosis. Published case series of HN-MPNSTs suggested the most common onset symptom was a painless, rapidly growing cervical mass without nerve palsy,[11] while local compression or nerve symptoms may also occur, like airway obstruction, dysphagia and hoarseness.[12] However, sporadic MPNST with a long silent period followed by a rapid enlarging period is less common, involvement of carotid bifurcation causing repetitive dizziness and syncope as the onset syndrome is exceptionally rare.

It is known that MPNSTs can present in various differentiation patterns, generally characterized by commutative hypo- and hyper-cell areas or asystematic growth pattern of spindle-shaped cells.[13] Besides, epithelioid or other heterogeneous components could be found in approximately 15% of MPNSTs,[14] other components consisted of rhabdomyoblasts,[14,15] cartilaginous,[16] osseous,[17] smooth muscle,[17] neuroendocrine and liposarcomatous components.[16] A single MPNST rarely has two or more different differentiations,[18] and our case presented two heterogeneous components, namely, rhabdomyoblasts and cartilaginous components. Interestingly, no glandular or neuroendocrine differentiation component was observed in pathological analysis, but preoperative urine catecholamine test showed a high level of norepinephrine, indicating potential neuroendocrine activity of the tumor. Thus, we scheduled volume expansion therapy assisted with phenoxybenzamine one week before the surgery, which reduce the risk of dramatic change of intraoperative blood pressure when manipulating the mass. It was reported that neuroendocrine differentiation was rare and only observed in glandular MPNSTs in vast majority of instance.[15]
Our case suggested a preoperative test of blood and urine catecholamine is necessary to identify potential neuroendocrine activity of MPNST, in case of sudden change of blood pressure during the surgery, which is especially catastrophic when the tumor involved carotid artery bifurcation.

The diagnosis of MPNST simply based on histomorphology was difficult to differentiate from other sarcomas. Some neural markers, like S-100 and CD56, were proved to be sensitive markers for peripheral nerve sheath tumors. S-100 was classically regarded as the best marker for MPNST and was positive in about 50% to 90% of the tumors. Recent studies proposed combined immunostaining of nestin could reach a high sensitivity than other neural markers in MPNST. And focal S-100 positivity help to differentiate from schwannoma which show diffuse S-100 positivity. In addition, combination staining with SMA and HMB-45 can assist in distinguishing MPNST from leiomyosarcoma and malignant melanoma.

In the case of our patient, the patient had a high-grade malignancy with a high rate of recurrence. The preoperative management plan. Though a minority of HN-MPNSTs had a higher 5-year disease-specific survival of 19.3% versus 8.7 cm for other-MPNSTs, and HN-MPNSTs revealed average tumor size for HN-MPNSTs was 4.9 cm, compared with 8.7 cm for other-MPNSTs, and HN-MPNSTs had a higher 5-year disease-specific survival than other-MPNSTs (65.1% vs 57.4%). Therefore, though MPNSTs in the head and neck area share the same histology, these specific clinical patterns and prognosis of the tumor may have specific clinical pattern and prognosis. Our case also did not undergo adjuvant radiotherapy and no recurrence was observed at 2-year follow-up.

Involvement of carotid artery with neuroendocrine activity is a rare manifestation of sporadic MPNST. Early diagnosis based on CT scan and biopsy is important to schedule perioperative management plan. Though a minority of HN-MPNSTs have neuroendocrine activity, preoperative scanning of blood and urine catecholamine is crucial for intraoperative hemodynamic stability. In addition, evidence concerning the role of adjuvant radiotherapy in HN-MPNSTs is inadequate.

### Author contributions

Conceptualization: Jichun Zhao, Ding Yuan.

Data curation: Tiehao Wang, Jiarong Wang.

Investigation: Tiehao Wang, Wening Xiong.

Supervision: Bing Yuan.

Writing – original draft: Tiehao Wang, Jiarong Wang.

Writing – review & editing: Tiehao Wang, Jiarong Wang, Jichun Zhao.

### References

[1] Wanebo JE, Malik JM, Vandenberg SR, et al. Malignant peripheral nerve sheath tumors. A clinicopathologic study of 28 cases. Cancer 1993;71:1247–33.
[2] Duscharman BS, Schenauer BW, Piepgras DG, et al. Malignant peripheral nerve sheath tumors. A clinicopathologic study of 120 cases. Cancer 1986;57:2006–21.
[3] Farid M, Demicco EG, Garcia R, et al. Malignant peripheral nerve sheath tumors. Oncologist 2014;19:193–201.
[4] Ng VY, Scharschmidt TJ, Mayerson HL, et al. Incidence and survival in sarcoma in the United States: a focus on musculoskeletal lesions. Anticancer Res 2013;33:2597–604.
[5] Widemann BC. Current status of sporadic and neurofibromatosis type 1-associated malignant peripheral nerve sheath tumors. Curr Oncol Rep 2009;11:322–8.
[6] Kar M, Deo SV, Shukla NK, et al. Malignant peripheral nerve sheath tumors (MPNST)-clinicopathological study and treatment outcome of twenty-four cases. World J Surg Oncol 2006;4:55.
[7] Janda PH, Veerappan V, McKenzie ME, et al. Carotid body tumor as a reversible cause of syncope. J Am Osteopath Assoc 2011;111:638–44.
[8] Nakahira M, Nakatani H, Takeda T. Syncope as a sign of occult malignant recurrence in the retropharyngeal and parapharyngeal space: CT and MR imaging findings in four cases. AJNR Am J Neuroradiol 2002;23:1257–60.
[9] Peng KA, Grogan T, Wang MB. Head and neck sarcomas: analysis of the SEER database. Otolaryngol Head Neck Surg 2014;151:627–33.
[10] Tora MS, Xenos D, Texakalidis P, et al. Treatment of neurofibromatosis 1-associated malignant peripheral nerve sheath tumors: a systematic review. Neurosurg Rev 2019.
[11] 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;29:439–45.
[12] Lorenz TR, North JH, Werners BA, et al. Malignant peripheral nerve sheath tumors of the head and neck: analysis of prognostic factors. Otolaryngol Head Neck Surg 2000;122:667–72.
[13] Allison KH, Patel RM, Goldblum JR, et al. Superficial malignant peripheral nerve sheath tumor: a rare and challenging diagnosis. Am J Clin Pathol 2005;124:685–92.
[14] Rodriguez FJ, Folpe AL, Giannini C, et al. Pathology of peripheral nerve sheath tumors: diagnostic overview and update on selected diagnostic problems. Acta Neuropathol 2012;123:295–319.
[15] Guo A, Liu A, Wei L, et al. Malignant peripheral nerve sheath tumors: differentiation patterns and immunohistochemical features - a mini-review and our new findings. J Cancer 2012;3:303–9.
[16] Tirabosco R, Galloway M, Bradford R, et al. Liposarcomatous differentiation in malignant peripheral nerve sheath tumor: a case report. Pathol Res Pract 2010;206:138–42.
[17] Janczar K, Tybor K, Jezewicz M, et al. Low grade malignant peripheral nerve sheath tumor with mesenchymal differentiation: a case report. Pol J Pathol 2011;62:278–81.
[18] Suresh TN, Harendra Kumar ML, Prasad CS, et al. Malignant peripheral nerve sheath tumor with divergent differentiation. Indian J Pathol Microbiol 2009;52:74–6.
[19] Steck CJ, Tawalkar O. Malignant peripheral nerve sheath tumor with rhabdomyosarcomatous differentiation (malignant triton tumor). Arch Pathol Lab Med 2006;130:1878–81.
[20] Shimada S, Tsuzuki T, Kuroda M, et al. Nestin expression as a new marker in malignant peripheral nerve sheath tumors. Pathol Int 2007;57:60–7.
[21] Ralli M, Singh S, Hasija S, et al. Intrathoracic Malignant Peripheral Nerve Sheath Tumor: Histopathological and Immunohistochemical Features. Iran J Pathol 2015;10:74–8.
[22] Bradford D, Kim A. Current treatment options for malignant peripheral nerve sheath tumors. Curr Treat Options Oncol 2015;16:328.
[23] Kahn J, Gillespie A, Tsokos M, et al. Radiation therapy in management of sporadic and neurofibromatosis type 1-associated malignant peripheral nerve sheath tumors. Front Oncol 2014;4:324.
[24] Patel TD, Shaigany K, Fang CH, et al. Comparative Analysis of Head and Neck and Non-Head and Neck Malignant Peripheral Nerve Sheath Tumors. Otolaryngol Head Neck Surg 2016;154:113–20.