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Case Report

Malignant Cerebellopontine Angle Peripheral Nerve Sheath Tumor with Divergent Mesenchymal (Cartilaginous) Differentiation Presenting with Catastrophic Hemorrhage: Case Report and Review

Carolyn Lai[1], Demir Bajin[2], Joseph M. Chen[2], Brendan C. Dickson[3], Julia Keith[4], Farhad Pirouzmand[1]

[1]Division of Neurosurgery, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada
[2]Department of Otolaryngology–Head & Neck Surgery, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada
[3]Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada
[4]Department of Laboratory Medicine and Molecular Diagnostics, Sunnybrook Health Sciences Centre, Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada

ORCID IDs of the authors: C.L. 0000-0002-8025-4195, D.B. 0000-0003-1088-4367, J.M.C. 0000-0001-6378-4840, B.C.D. 0000-0003-2269-6216, J.K. 0000-0003-1519-6731, F.P; 0000-0001-8507-5391.

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Malignant peripheral nerve sheath tumors of the cerebellopontine angle are rare, especially even outside of the context of neurofibromatosis or malignant transformation of previously radiated vestibular schwannomas. This case report describes a case of a presumed vestibular schwannoma without previous radiation or history of neurofibromatosis presenting with progressive hearing loss, facial weakness, growth, and ultimately catastrophic hemorrhage requiring urgent surgery. Histopathology revealed an exceptionally rare malignant peripheral nerve sheath tumor with divergent mesenchymal (chondrosarcomatous) differentiation with few rigorously interrogated cases in the literature. In retrospect, facial weakness, growth, and early intratumoral hemorrhage were harbingers of atypical malignant pathology. We advocate for a heightened index of suspicion, shorter interval follow-up, and consideration of early surgery in such cases in hopes of preventing potentially catastrophic outcomes.

KEY WORDS: Cerebellopontine angle tumor, malignant peripheral nerve sheath tumor

INTRODUCTION

Vestibular schwannomas are benign tumors located at the cerebellopontine angle (CPA) and are relatively common, particularly in type 2 neurofibromatosis (NF2). Neurofibromas and their malignant counterpart, malignant peripheral nerve sheath tumors (MPNSTs), are uncommon at this location; the latter is typically associated with prior radiosurgery or type 1 neurofibromatosis (NF1).[1] Herein, we present the case of a woman with progressive hearing loss and facial weakness associated with intratumoral hemorrhage that subsequently necessitated emergent surgery. Histopathologic assessment of the debulked mass revealed an MPNST with divergent mesenchymal (chondrosarcomatous) differentiation.

CASE PRESENTATION

A 53-year-old woman presented with a 6-month history of transient right-sided tinnitus followed by sudden right-sided hearing loss and a 3-month history of progressive right facial weakness. Magnetic resonance imaging (MRI) revealed a 1.9 cm right CPA tumor (Figure 1A) on T2 weighted imaging (T2WI) without intratumoral hemorrhage. She was seen by radiation oncology with plans for hypofractionated radiosurgery. However, her planning MRI (Figure 1B) revealed new intratumoral hemorrhage as evidenced by the

Corresponding author: Carolyn Lai, e-mail: Carolyn.Lai@medportal.ca
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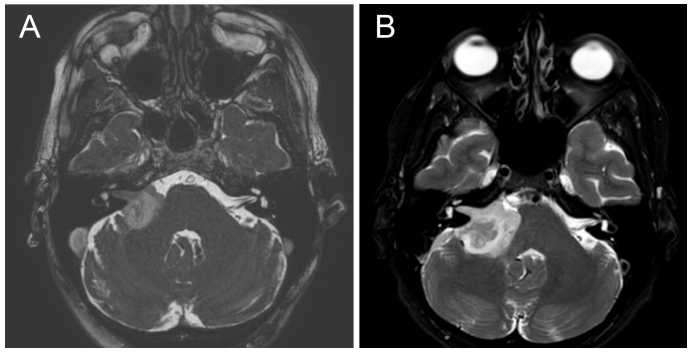

Figure 1. (A) Initial diagnostic MRI (T2WI) revealing a 1.6 × 1.9 cm right CPA tumor without intratumoral hemorrhage. (B) MRI T2WI planning scan 7 weeks later showing the right CPA 2.7 × 3.2 cm tumor with intratumoral hemorrhage and growth as evidenced by the new volume of hyperintense signal on T2WI within the tumor. CPA, cerebellopontine angle; MRI, magnetic resonance imaging.

new volume of hyperintense signal on T2WI within the tumor, associated with worsening of her facial weakness (House Brackmann 4) in addition to paresthesias in the V2-V3 distribution. Her functional status remained stable without dysmetria or gait difficulties. Her medical and family history revealed no instances of neurofibromatosis.

Given the intratumoral hemorrhage and expansion, the decision was made to proceed directly to surgery on a semi-urgent basis. The differential diagnosis at the time included a hemorrhagic vestibular schwannoma or a facial schwannoma given her facial weakness.

Unfortunately, shortly before surgery about 5 weeks after initial bleeding, she presented to the emergency room with a Glasgow Coma Scale (GCS) of 7 and a blown right pupil. Computed tomography (CT) scan revealed significant re-hemorrhage of her CPA tumor with severe mass effect (Figure 2).

The patient was taken for emergent decompression and tumor resection. Intraoperatively, the tumor was hemorrhagic and heterogeneous in consistency with firm solid components admixed with softer friable tumor (Figure 3). The tumor was intimately associated with the facial nerve in the region of the porus acusticus. In addition to growth and hemorrhage, this likely contributed to her early facial weakness. Hemorrhagic material was also found to have disrupted the tumor capsule violating the surrounding cerebellum and brainstem.

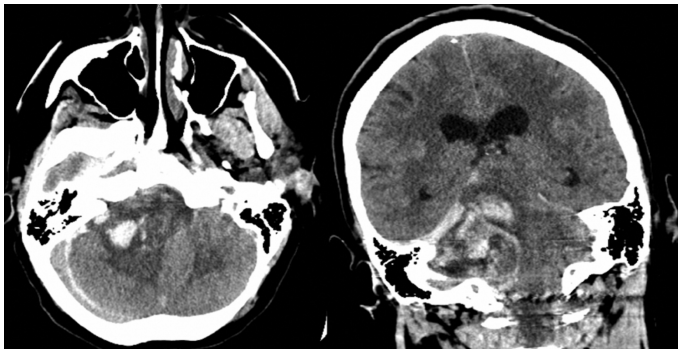

Figure 2. CT scan corresponding to her presentation in emergency room with GCS 7 and a right blown pupil revealing significant hemorrhage of her CPA tumor. CPA, cerebellopontine angle; CT, computed tomography; GCS, Glasgow Coma Scale

Given her guarded prognosis and critical condition, her posterior fossa was well decompressed and the tumor significantly debulked. Unfortunately, despite maximal treatment efforts, she did not make neurologic recovery and passed away days later.

Informed consent was obtained prior to the writing of this case report.

Pathology

Histologic sections demonstrated a biphasic neoplasm. Most of the tumor was composed of lobules of moderately cellular chondroid matrix. The lacunae contained chondrocytes with round ovoid hyperchromatic nuclei, occasional binucleation, and moderate pleomorphism; mitotic activity was inconspicuous. Interspersed were spindle cells with a so-called "marbled" pattern; there were cellular regions with a herringbone pattern, as well as hypocellular regions with a loose fascicular pattern. The nuclei were ovoid with moderate pleomorphism and brisk mitotic activity (>20 mitoses per 10 high power fields). Morphologically the differential diagnosis included malignant peripheral nerve sheath tumor, dedifferentiated chondrosarcoma, and mesenchymal chondrosarcoma. Ancillary immunohistochemical testing revealed expression of S100 in the chondroid regions; there was patchy and/or focal immunoreactivity for both S100 and SOX10, with loss of H3K27me3 expression, within the spindle cell component. Targeted RNA sequencing (TruSight RNAFusion, Illumina, Calif, USA) did not identify any fusion products associated with mesenchyme chondrosarcoma. Overall, the findings ultimately supported classification as a malignant peripheral nerve sheath tumor with divergent mesenchymal (cartilaginous) differentiation (Figures 4 and 5).[2]

DISCUSSION

Malignant peripheral nerve sheath tumors of the eighth cranial nerve have an exceedingly rare incidence of 0.017 per 1 million persons per year.[1] Our case of MPNST is unique in several aspects. First, the patient presented with intratumoral hemorrhage associated with a stepwise decline in facial function and a subsequent catastrophic hemorrhage which has not previously been reported in the literature. The tumor also demonstrated growth and progressive facial weakness. The clinical impression of benignancy was presupposed by the clinical-radiologic impression of vestibular schwannoma which, by definition, is benign. The clinical differential diagnosis also included the possibility of a facial schwannoma given her facial weakness; however the geniculate ganglion was not involved radiographically. Second, sporadic MPNSTs of the vestibular nerve are exceptionally rare; these are typically associated with either underlying NF1 or secondary to prior radiation. Finally, while divergent differentiation is relatively common in MPNST (e.g., rhabdomyoblastic differentiation in malignant triton tumor), cartilaginous differentiation is exceptionally rare in this context, with few rigorously interrogated examples in the medical literature.

Non-radiated, Non-neurofibromatosis Malignant Peripheral Nerve Sheath Tumors

Even though vestibular schwannomas are the most common CPA tumors, de novo MPNSTs in this location are exceedingly rare with only 2 case series reported covering 30 cases.[1,3] Cases include benign vestibular schwannomas that transform years later with pathologically confirmed benign and malignant components, those suspected

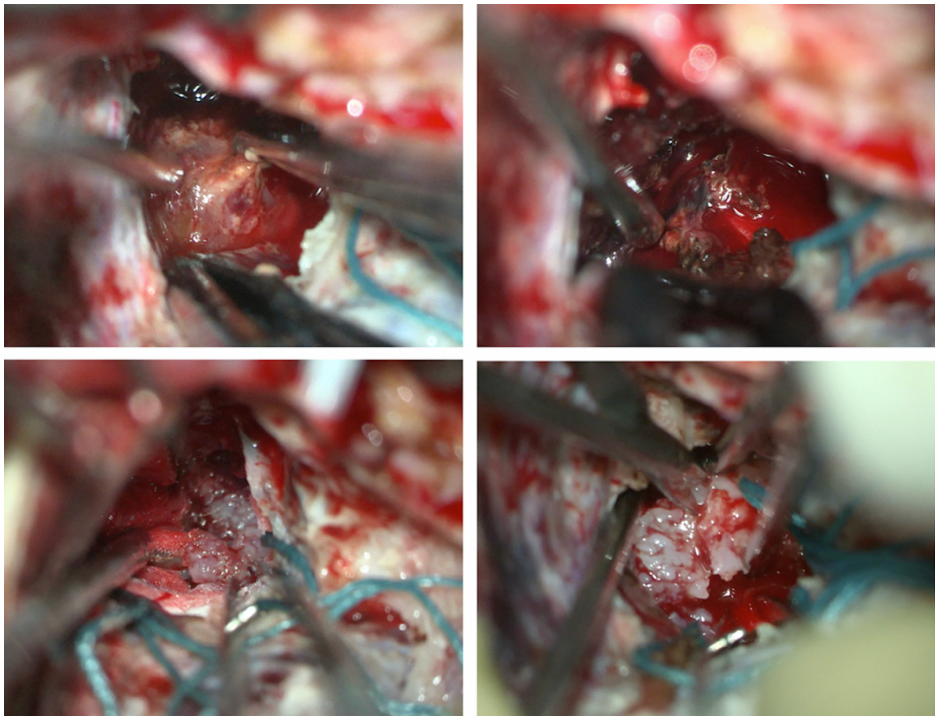

Figure 3. Intraoperative images depicting heterogeneous components of the tumor including solid portions requiring sharp dissection and careful piecemeal resection.

to be malignant at onset with rapid growth and cases diagnosed upon autopsy.[1,4,5] Only half of the cases present with facial weakness or atypical radiographic features (i.e., brainstem edema, internal necrosis, or ill-defined margins).[1]

Hemorrhage as a Possible Indicator of Malignancy

Unique to our case, hemorrhage has yet to be reported as a feature of an intracranial MPNST, potentially signaling a higher-grade characteristic. Our case demonstrated 2 instances of hemorrhage. The first was an intratumoral hemorrhage detected on planning MRI, which the patient in retrospect admitted to a decline in facial function. Shortly after, the tumor demonstrated a massive hemorrhage with additional extratumoral hemorrhage spilling outside of the capsule into the surrounding brain. The higher grade or malignant nature of the tumor could contribute to intratumoral hemorrhage as the proliferation of thin-walled, immature vasculature may be the culprit for this increased hemorrhagic risk.

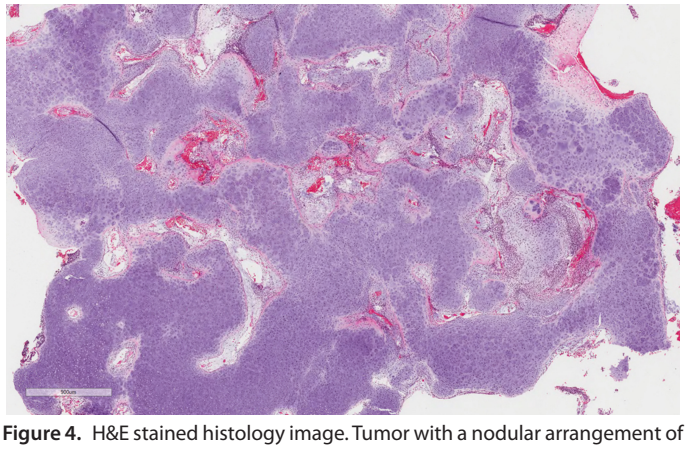

Figure 4. H&E stained histology image. Tumor with a nodular arrangement of predominantly chondroid tumor at low power.H&E, hematoxylin & eosin.

Treatment of intracranial MPNST

Management of intracranial MPNST involves multimodal strategies including surgery, radiotherapy, and chemotherapy.[6] Mainstays of treatment include radical surgical resection, adjuvant radiation, and chemotherapy.[3,7] Gross total resection is associated with improved disease-specific survival.[1] The inaccessibility of cranial MPNST to achieve wide margins may confer a poorer prognosis due to subtotal resection.[1] Although prior radiation can be a predisposing factor to malignant transformation, the survival rate is better with radiotherapy in the setting of MPNST.[3] Despite maximal aggressive treatment, prognosis is unfavorable and metastases to the spine are common.[1,3,8] Carlson et al reported a 54% mortality rate due to disease progression at a median of 3 months following diagnosis in their series.[1]

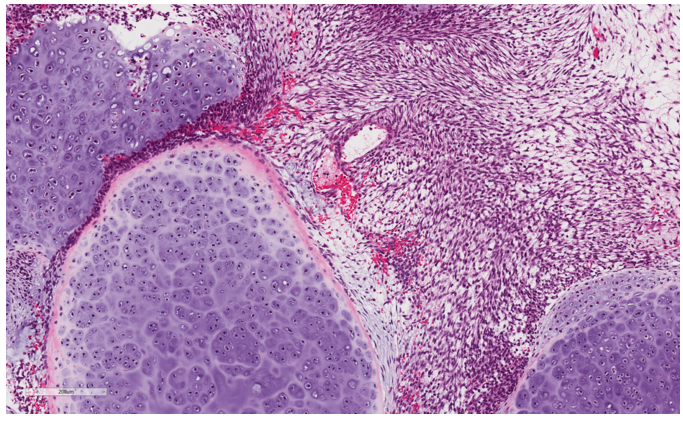

Figure 5. H&E stained histology image. Higher magnification demonstrating a biphasic tumor comprised of both chondroid nodules and intervening densely cellular spindled tumor with a fascicular and herringbone architecture. H&E, hematoxylin & eosin.

Malignant Peripheral Nerve sheath tumors with Divergent Mesenchymal differentiation

Divergent mesenchymal differentiation in an MPNST is a very rare phenomenon and usually takes the form of rhabdomyosarcomatous or angiosarcomatous differentiation.[9] There is a single case report of divergent chondroid differentiation in an MPNST of the acoustic nerve.[10]

Lessons Learned

Our unique case adds breadth to the limited number of cases in the literature reporting MPNST in the CPA location. In retrospect, the combinations of (a) facial weakness, (b) rapid growth, and (c) intratumoral hemorrhage were signs of malignant pathology in our case. Early suspicion can be challenging given the rarity with nearly half of the patients initially presenting with findings consistent with a benign vestibular schwannoma but should warrant earlier radiographic follow-up if atypical features are present (i.e., 3-month MRI).[1]

CONCLUSION

Malignant peripheral nerve sheath tumors of the CPA are exceedingly rare. Although they may present with features indistinct from the overwhelmingly more common benign vestibular schwannoma, clinical and radiographic characteristics that may be a harbinger of a malignant entity include facial weakness, rapid growth, and hemorrhage. We advocate for a heightened suspicion, which if present, should warrant a closer follow-up and consideration of early surgery.

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