Giant Epithelioid Malignant Perineural Nerve Sheath Tumor of the Head and Neck: A Case Report

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Abstract- Malignant peripheral nerve sheath tumor (MPNST) is a rare and aggressive soft tissue sarcoma, with the epithelioid subtype accounting for less than 5% of cases. Most MPNSTs are associated with neurofibromatosis type 1 (NF1), prior radiation exposure, or occur sporadically. Head and neck involvement is uncommon, especially in large tumors. We report a case of giant sporadic epithelioid MPNST in a 21-year-old male without NF1. The patient presented with a progressively enlarging left head and neck mass over two years. Imaging revealed a heterogeneous lesion with extensive soft tissue, bony, and neural involvement. Histopathology confirmed epithelioid MPNST with high-grade spindle cell sarcoma features, positive for S-100 and p53, and a Ki-67 index of 20%. The patient underwent wide local excision with neurosurgical assistance, preserving major cranial nerves but requiring sacrifice of the facial nerve and jugular vein. Postoperative recovery was uneventful, and no recurrence was observed at six months. This case highlights the diagnostic complexity, aggressive nature, and surgical challenges of giant epithelioid MPNST in the head and neck, underscoring the importance of complete excision with negative margins for improved outcomes.

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Introduction

Malignant peripheral nerve sheath tumor (MPNST) is a rare, highly aggressive soft tissue malignancy arising from peripheral nerves or their sheaths. With an estimated incidence of 1 in 100,000, it accounts for 5-10% of all soft tissue sarcomas (1). MPNST may occur in association with neurofibromatosis type 1 (NF1), secondary to radiation therapy, or sporadically (2,3).

In 2013, the World Health Organization (WHO) classified MPNST as a distinct soft tissue sarcoma subtype, further categorizing it into variants such as epithelioid MPNST, malignant triton tumor (MTT), and glandular MPNST (2,4). Among these, the epithelioid variant accounts for approximately 5% of all MPNSTs and is only rarely associated with NF1.

Anatomically, most MPNSTs arise in the trunk and extremities; head and neck presentations are uncommon, and reported lesions are typically less than 5 cm in size (5). This rarity, combined with overlapping histopathological features, makes diagnosis particularly challenging. Here, we present a case of a giant sporadic epithelioid MPNST of the head and neck—an exceptionally unusual presentation—adding to the limited literature and emphasizing diagnostic and management considerations.

Case Report

A 21-year-old man presented to the

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Otorhinolaryngology department with a two-year history of an enlarging mass on the left side of his head and neck. The patient had no past medical history or symptoms suggestive of neurofibromatosis or other relevant diseases. Physical examination revealed an oval-shaped mass measuring 23×12×8 cm, fixed to the underlying tissues and with limited mobility. Despite the significant mass size, the patient exhibited no neurological symptoms (lower cranial nerves were intact). Computed tomography (CT) showed a heterogeneously enhancing soft tissue mass involving the infratemporal space, parapharyngeal space, perivertebral space, and spinal canal. The lesion caused anteromedial deviation of the left internal and external carotid. CT scans also revealed erosion of the mandibular and petrosal bones on the left side. Magnetic resonance imaging (MRI) confirmed a large heterogeneous mass in the left parotid and lower temporal area, with extra-axial involvement. Additionally, there was evidence of vertebral involvement from C1 to C3, extending into the neural foramen and epidural space (Figure 1).

We decided to perform an incisional biopsy under general anesthesia. We performed a Blair incision and released the mass anterior to the sternocleidomastoid (SCM) muscle, with dissection posteriorly and inferiorly. We sent the tissue for a frozen-section biopsy, and the response suggested an adenoma. Due to the nerve's presence at the stylomastoid foramen's site and the nerve trunk's absence, the possibility of a nerve mass was raised. We consulted colleagues regarding the indication of denervation. To decide whether to cut the nerve, we chose to wait until the pathology results were ready. Then, we extended the incision posteriorly and excised the posterior part of the mass, which was very hemorrhagic. We sent the specimen for pathology. We applied SURGICEL and sutured the skin.

The incisional biopsy of the mass suggested epithelioid MPNST, with histologic features indicative of a high-grade spindle cell sarcoma. Immunohistochemistry (IHC) showed positivity for S-100 and P53, along with a Ki-67 index of 20%, increasing the likelihood of MPNST (Figure 2). One month later, for the main surgery, we performed a wide local excision of the mass on the left lateral neck and face based on the pathology results. After administering general anesthesia, we made an incision using the Fisch technique and dissected the mass from the inferior part. We managed to preserve the vagus nerve, the Accessory nerve, and the Hypoglossal nerve. Since the mass involved the jugular vein in the Jugular foramen area, we had to sacrifice the vein. The fascial nerve was also sacrificed. We dissected the mass from the infratemporal, parapharynx, and carotid artery, and we performed a total parotidectomy. Since the tumor also involved the base of the skull, the Jugular foramen, and the lateral part of the C1 to C3 vertebrae, a neurosurgeon separated the mass from the dura of the posterior fossa and vertebral artery. The neurosurgeon also excised the malignant tissue from the neural foramina under microscopic guidance. We used the sternocleidomastoid (SCM) muscle to cover the carotid artery, and we sutured the skin. At last, we performed a tracheostomy and tarsorrhaphy for the left eye. The patient received a blood transfusion and was admitted to the intensive care unit post-surgery (Figure 3).

The pathology results confirmed MPNST and reported that the left cervical lymph nodes were free of tumor. No complications or recurrence of malignancy were reported during the 6-month follow-up.

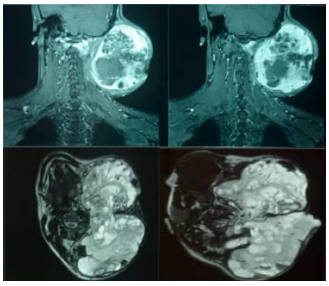

Figure 1. Magnetic resonance imaging (MRI) confirmed a large heterogeneous mass in the left parotid and lower temporal area, with extra-axial involvement

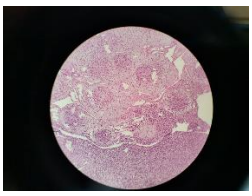

Figure 2. Pathology of the mass suggested epithelioid MPNST, with histologic features indicative of a high-grade spindle cell sarcoma

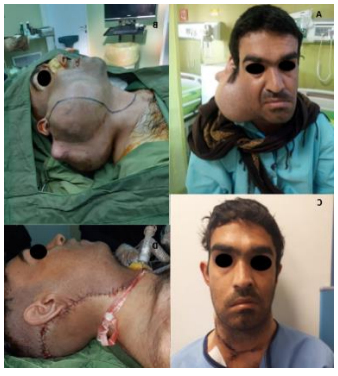

Figure 3. Pre- and post-operation imaging of the patient

Discussion

Malignant peripheral nerve sheath tumors (MPNSTs) are rare soft tissue sarcomas derived from Schwann cells or perineural fibroblasts. They primarily arise in the trunk and extremities, with only 12-19% of cases occurring in the head and neck region (2). Although the average age at diagnosis in this location is approximately 49 years, our patient was significantly younger, illustrating that MPNST can present aggressively in early adulthood (6,7). This age variation highlights the need for vigilance, as early-onset cases may behave differently and present unique surgical challenges.

Approximately 50% of MPNSTs are associated with neurofibromatosis type 1 (NF1), whereas the remainder occur sporadically or as a late complication of prior radiation therapy (8). NF1 is an autosomal dominant genetic disorder caused by mutations in the NF1 gene, leading to reduced neurofibromin activity. Loss of neurofibromin function increases susceptibility to both benign and malignant tumors. NF1-associated MPNSTs often develop from preexisting plexiform neurofibromas, which can invade surrounding tissues and carry a 10% risk of malignant transformation (9). In contrast, sporadic MPNSTs, like in our patient, arise de novo and may follow different biological pathways, making their clinical course more unpredictable.

Radiation-induced MPNSTs account for 10-13% of cases, most commonly developing after radiation therapy for lymphoma or breast cancer, with a median latency period of approximately 13.5 years (10). Understanding these etiologic variations is important because tumor biology, recurrence risk, and overall prognosis can differ based on the underlying mechanism of tumorigenesis.

Accurate diagnosis and surgical planning rely heavily on imaging. CT scans provide information on tumor density, enhancement patterns, calcifications, and bone involvement, while MRI offers superior soft-tissue contrast, allowing detailed evaluation of tumor margins, neurovascular relationships, and potential intracranial or spinal extension (11). In our case, imaging demonstrated extensive involvement of the infratemporal, parapharyngeal, and cervical spaces, underscoring the need for a multidisciplinary surgical approach.

Histopathology remains the diagnostic gold standard for MPNST. Typical microscopic features include spindle cells arranged in fascicular patterns, increased cellularity, nuclear pleomorphism, and areas of necrosis. However, histologic features can overlap with those of other spindle cell neoplasms, including sarcomas, melanomas, and carcinomas, making immunohistochemistry (IHC) essential for definitive classification. Negative staining for melanocytic markers such as Melan-A, MITF, and HMB45 helps exclude melanoma, while the absence of cytokeratin differentiates MPNST from carcinoma. Positive markers such as S100, H3K27me3, p53, and Ki-67 are informative: S100 indicates Schwann cell differentiation, H3K27me3 loss reflects PRC2 inactivation, p53 positivity correlates with tumor suppressor dysregulation, and an elevated Ki-67 index demonstrates high proliferative activity (12,13).

Genetic studies suggest that most MPNSTs, whether NF1-associated or sporadic, share mutations in NF1, CDKN2A/B, TP53, and components of the polycomb repressor complex 2 (PRC2), including SUZ12 and EED (14). Inactivation of these tumor suppressor genes contributes to high mitotic activity, aggressive behavior, and poorer outcomes. In addition to genetic factors, clinical and pathologic characteristics, such as tumor size, location (trunk vs. head and neck), histologic grade, Ki-67 proliferation index, and metastasis status, strongly influence prognosis (15). Overall, MPNST carries a relatively poor prognosis, with reported 5-year survival rates of 50-60% and local recurrence rates approaching 38% (15,16).

Treatment of MPNST is multimodal, with surgical excision being the cornerstone of therapy. Complete resection with negative margins offers the highest chance of long-term disease control and reduced recurrence (17). Adjuvant radiotherapy is often recommended for high-grade or large tumors (>5 cm) to achieve local control, although its impact on overall survival remains variable. Chemotherapy and targeted therapy may be considered in metastatic or unresectable cases, but their efficacy in improving survival is limited (16). In our patient, careful planning enabled complete resection while preserving critical neurovascular structures, followed by adjuvant radiotherapy to minimize the risk of recurrence. The favorable early outcome highlights the importance of a multidisciplinary approach involving head and neck surgery, neurosurgery, radiology, and pathology for managing complex head and neck MPNSTs.

This case underscores several important points for clinicians. First, MPNST should be considered in the differential diagnosis of large, rapidly growing head and neck masses, even in younger patients without NF1. Second, detailed preoperative imaging and careful surgical planning are crucial for achieving negative margins while minimizing morbidity. Finally, understanding the genetic and histopathologic characteristics of MPNST can inform prognosis and

guide follow-up strategies. Long-term surveillance is essential, given the potential for late recurrence and the aggressive nature of this malignancy.

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