Int. J Med. Pharm. Res. (P-ISSN: 2958-3675 | E-ISSN: 2958-3683)
Available on: https://ijmpr.in/
DOI:

International Journal
of Medical and
Pharmaceutical Research

ORIGINAL ARTICLE OPEN ACCESS

Malignant Peripheral Nerve Sheath Tumour Of Hypoglossal Nerve: A Case Report

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OPEN ACCESS

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Received: 14-04-2024
Accepted: 15-05-2024
Available online: 20-05-2024

A B S T R A C T

A 55-year-old woman presented with symptomatic malignant peripheral nerve sheath tumor (MPNST) of the right hypoglossal nerve, characterized by six months of pain radiating to the right ear, headaches, and swelling over the submandibular region. Initial diagnosis was confirmed through a biopsy, and the treatment regimen included surgical resection followed by radiation therapy.

About half of MPNSTs, an uncommon kind of soft tissue sarcoma, are linked to a mutation in Neurofibromatosis type 1 (NF1), with the remaining cases being random. Because these tumors are rare and aggressive, they frequently pose difficulties for diagnosis and treatment. This case presents a unique clinical setting due to the unusual involvement of the hypoglossal nerve.

A multidisciplinary strategy is usually used in the therapy of MPNST, with surgery serving as the main treatment to establish local control. In order to lower the chance of recurrence, radiation therapy is frequently used after surgery. Depending on the patient's state and the behavior of the tumor, chemotherapy might be considered in some circumstances.

This case highlights the necessity of considering MPNST in differential diagnoses for patients with similar symptoms, particularly in those with NF1. Early detection and comprehensive treatment are essential for improving patient outcomes in such complex and rare malignancies.

Key Words: *Malignant Peripheral nerve sheath tumour(MPNST); Submandibular Gland; Radiotherapy; Hypoglossal Nerve.*

INTRODUCTION:

Malignant peripheral nerve sheath tumors (MPNSTs) are a type of peripheral nerve sheath tumor that can develop spontaneously or from preexisting conditions such as neurofibromas or schwannomas. Approximately 50% of MPNST cases occur in individuals with Neurofibromatosis type I (NF1), often arising from preexisting neurofibromas. MPNSTs account for about 3-5% of all soft-tissue sarcomas and typically affect young to middle-aged adults, aged 20 to 50 years, without gender preference. [1]

These tumors often exhibit aggressive behavior, causing radiating pain along the nerve supply. In NF1-associated cases, patients are usually younger and present with larger tumors at diagnosis compared to those with sporadic MPNSTs. This younger age at presentation and larger tumor size are factors contributing to poorer survival rates in NF1-associated MPNSTs. Additionally, the presence of benign neurofibromas in NF1 patients complicates the differentiation between malignant and benign lesions, potentially delaying diagnosis and treatment. [2]

Given the rarity and aggressive nature of MPNSTs, early and accurate diagnosis, along with a comprehensive treatment approach, is crucial for improving patient outcomes. This case highlights the importance of considering MPNSTs in patients with symptoms of nerve involvement, particularly those with a history of NF1.

CASE REPORT :

History and Clinical Presentation:

A 55-year-old woman presented with swelling in the right mandibular region, accompanied by pain radiating to the right ear and frequent headaches that had worsened over the past 7 months. She had been managed conservatively until. Contrast-enhanced CT scan of the neck revealed a lobulated soft tissue mass, measuring 3.3 x 3.0 cm, located in the right submandibular region adjacent to the submandibular gland, with no signs of cervical lymphadenopathy (Fig 1.A ,Fig1.B). Fine needle aspiration cytology (FNAC) of the swelling suggested an undifferentiated carcinoma. However, a slide review indicated the possibility of a salivary gland tumor with cystic changes, inconclusive for malignancy.

Subsequently, a PET scan was performed, revealing increased FDG uptake in the heterogeneously enhancing mass lesion in the right submandibular region, inseparable from the right submandibular salivary gland, measuring 3.9 x 2.7 cm, with an SUV max of 5.4. The mass was found abut the right mylohyoid and hyoglossus muscles. (Fig 1.C)

Based on these findings, the patient was scheduled for a right-sided modified radical neck dissection with excision of the tumor.

Postoperative histopathological examination (HPE) revealed a spindle cell tumor surrounded by a pseudocapsule. The tumor exhibited high cellularity with moderate nuclear pleomorphism. Resected nerve endings showed no tumor infiltration, with no evidence of lymphovascular invasion (LVI). A malignant nerve sheath tumor of the right hypoglossal nerve FNCLCC grade 2 [3]was confirmed. Subsequently, an initial slide review was conducted to crosscheck the diagnosis of Malignant Peripheral Nerve Sheath Tumor (MPNST).

A postoperative MRI showed no signs of recurrence or residual tumor in the region of the right hypoglossal nerve. (Fig 1.D)

A postoperative HPE block review with immuno-histochemistry (IHC) was performed. IHC results showed positive for S100(EP32) and focal positive for SMA(1A4). (FIG 1.E, FIG 1.F , FIG 1.G)

As part of the treatment plan, the patient commenced adjuvant radiation therapy targeting the tumor bed with margins, with a total dose of 60 Gy administered in 30 fractions

TREATMENT:

Using Modern LINAC, as per RTOG guidlines, prior proper immobilisation, the tumour bed and Level IB, were planned for 60Gy in 30 fractions at high risk and Level II and III (Ipsilateral) were planned for 54 Gy in 30 fractions using conventional dose fractionation . OARs were contoured for Head and Neck. Fig 2.A, demonstrates the CTV(Pink) and PTV(Red) of the treatment.

Patient completed treatment in the 5 week time period without any gaps in treatment, and there wasn't any toxicities reported during the treatment other than Grade 1 Mucosities which was treated symptomatically.

DISCUSION

Malignant Peripheral Nerve Sheath Tumors (MPNSTs) are aggressive spindle cell tumors that originate from peripheral nerves, extra-neural soft tissues, neurofibromas, or neurilemmomas. Formerly known by various terms such as neurosarcomas, neurogenic sarcomas, neurofibrosarcomas, and malignant schwannomas, the World Health Organization now classifies them as "Malignant Peripheral Nerve Sheath Tumors" to reflect their aggressive nature.

MPNSTs are relatively rare and present significant diagnostic challenges, especially when they occur in hereditary conditions like Neurofibromatosis Type 1 (NF1) or Neurofibromatosis Type 2 (NF2), which are seen in about 50% of cases. Accurate diagnosis relies on specific criteria and the identification of malignant characteristics through immunohistochemical or cytogenetic markers.[4]

Typically, MPNSTs present between the ages of 30 and 55, primarily manifesting as pain and numbness in the proximal limbs. They can also occasionally occur on the trunk and, rarely, on nerves in the head and neck. Diagnosis involves radiological evaluation with contrast-enhanced MRI, which is confirmed through a histopathological report identifying Malignant Peripheral Nerve Sheath Tumors. In NF1 patients, fluorodeoxyglucose-positron emission tomography (FDG-PET) helps distinguish benign neurofibromas from MPNSTs.[5]

In immunohistochemistry, S-100 is a vital marker for identifying Schwann-associated tumors. For NF1 patients, the Ki67-labeling index is crucial; Ki67 levels above 10% may indicate MPNST, helping to differentiate them from typical and atypical neurofibromas[6]

Treatment modalities for MPNSTs include surgery, radiation therapy, and chemotherapy, with ongoing trials exploring the potential role of immunotherapy.

Surgery has a limited but crucial role in managing Malignant Peripheral Nerve Sheath Tumors (MPNSTs), with the primary goal of achieving complete resection and negative margins. Despite the high recurrence rate (22-69%) and significant post-operative morbidity linked to aggressive surgical approaches, the benefits often outweigh the drawbacks. It is noteworthy that MPNSTs associated with Neurofibromatosis Type 1 (NF1) typically develop from preexisting neurofibromas.[7]

Chemotherapy plays a minimal role in the treatment of MPNSTs, mainly used for metastatic or unresectable tumors. It is primarily helpful in down staging the tumor to make surgery more feasible. Doxorubicin is commonly used as a first-line treatment, with combination regimens like doxorubicin–ifosfamide showing promising responses in MPNST cases.[8] Radiation therapy is often recommended for high-grade lesions or tumors larger than 5 cm, providing excellent long-term local control outcomes.

Radiation therapy may also be utilized to shrink tumors, making subsequent surgical interventions more feasible. Brachytherapy and intraoperative electron radiation therapy are additional modalities incorporated into MPNST therapy, typically requiring a cumulative radiation dose of ≥60 Gy for effective local disease control.[9]

Phase II trials of targeted therapies for MPNSTs, including agents like Erlotinib, Sorafenib, Imatinib, Dasatinib, Bevacizumab, Sirolimus, among others, are currently underway. However, none of these trials have shown sufficient response rates to justify their cost-effectiveness. Further research is necessary to assess their efficacy in treating MPNSTs.

FIGURES :

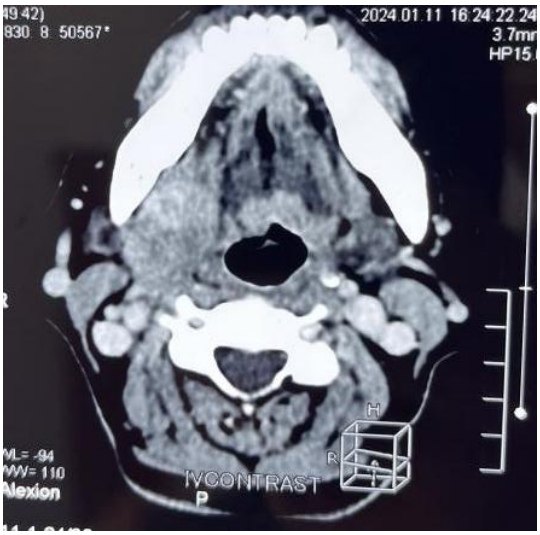

FIGURE 1A: Axial Section of CECT NECK , showing hetergenous enhancement in the Right submandibular region.

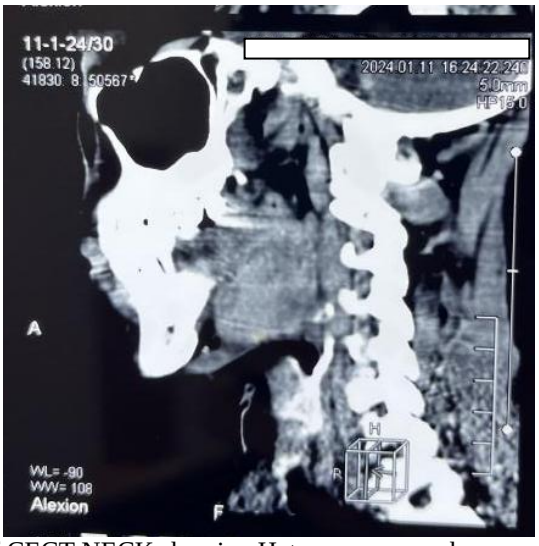

FIGURE 1B: Sagital Section of CECT NECK showing Heterogeneous enhancement in the submandibular region confined to the region.

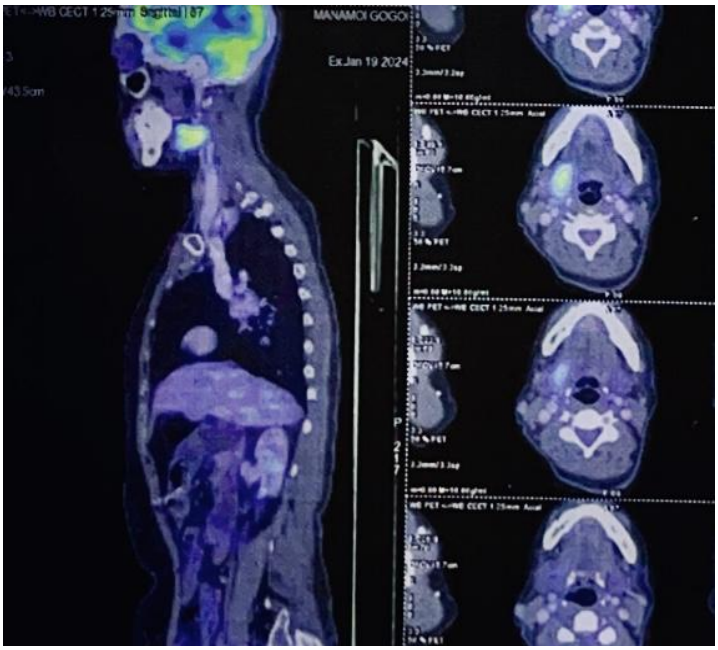

FIGURE 1.C: Whole Body PET-CT showing FDG uptake in the Right Subamndibular region

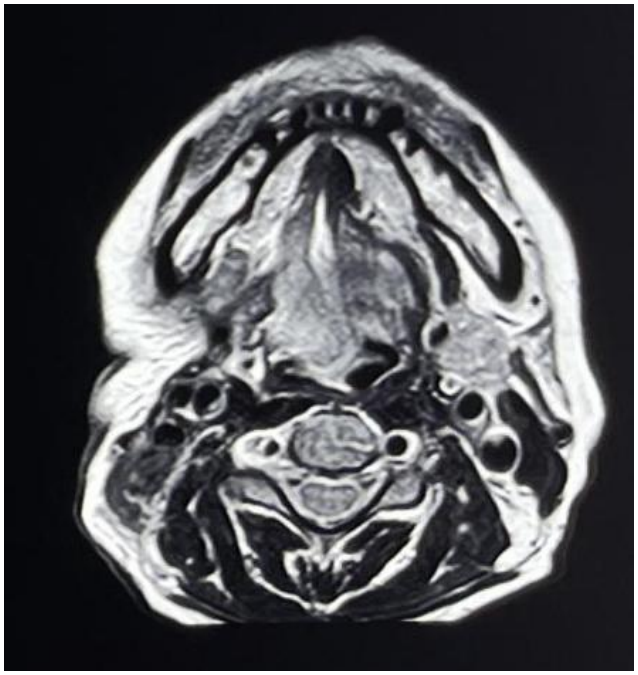

FIGURE 1.D: MRI T2 sections showing post opertive changes

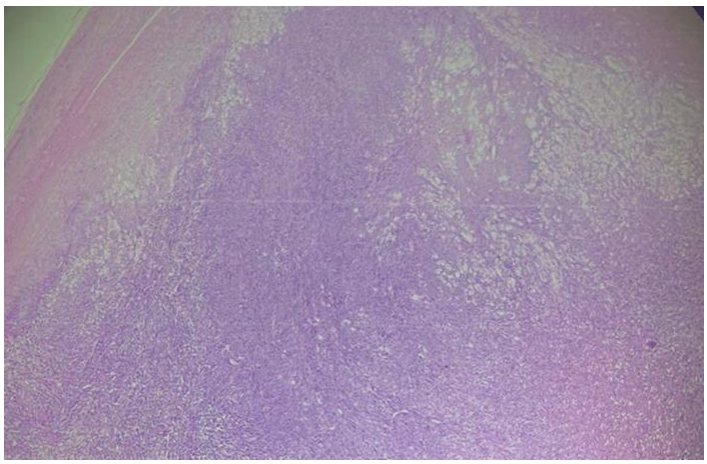

FIGURE 1.E: Postoperative Block review at LPF, showing fibrocolllagenous pseudocapsule

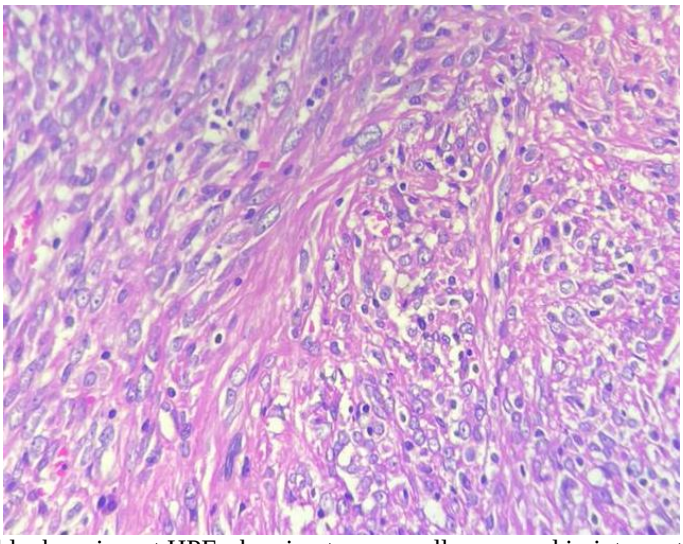

FIGURE 1.F: Postoperative block review at HPF, showing tumour cells arranged in intersecting bundles and fascicles set in a collagenous stroma, having oval to elongated hyperchromatic nuclei

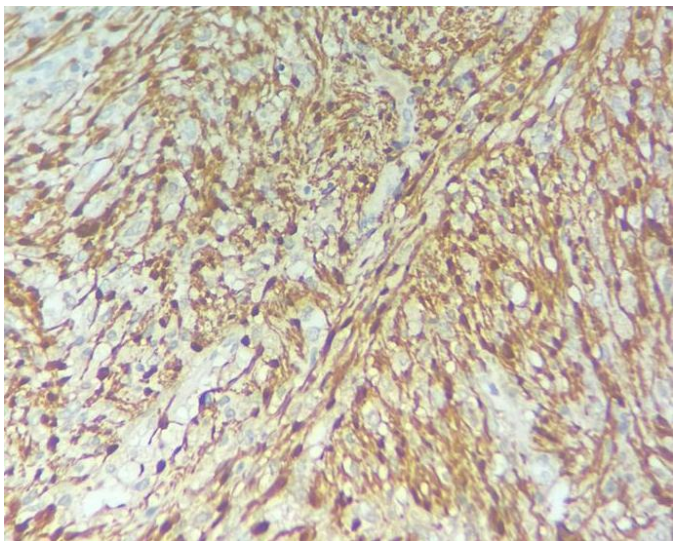

FIGURE 1.G: S-100 (EP32) positivity and focal positive for SMA(1A4) seen on HPE block reviewed with IHC

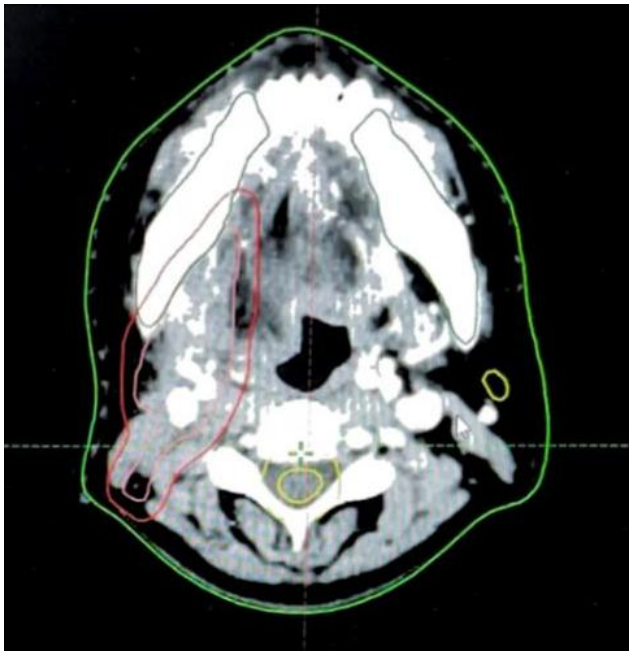

FIGURE 2.A: Treatment plan post CT- Simulation: PTV (RED) and CTV (PINK)

CONCLUSION:

Recent advancements in understanding and treating Malignant Peripheral Nerve Sheath Tumors (MPNSTs) represent significant progress in the medical field. Research has delved into risk factors like Neurofibromatosis type 1 (NF1) and radiation exposure associated with MPNST development. Moreover, the identification of precancerous lesions such as Plexiform Neurofibromas (PN) and Atypical Neurofibromatous Neoplasms of Uncertain Biologic Potential (ANNUBPs) has shed light on the genetic and molecular mechanisms driving MPNST pathogenesis.

In terms of diagnosis and treatment, there's been notable exploration of novel molecular biomarkers and the development of combined therapy protocols for MPNSTs. These advancements hold promise for improving diagnostic accuracy and tailoring treatment strategies to individual patients. By integrating these cutting-edge findings into clinical practice, healthcare professionals can better navigate the complexities of MPNSTs, ultimately leading to improved patient care and outcomes.

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