Case Report

Clinicopathological and Therapeutic Challenge: A Case Report of a Malignant Peripheral Nerve Sheath Tumor

Abdullah Demirbaş[1], Dilek Bayramgürler[1], Semanur Çakır Serinbaş[1], Ahmet Tuğrul Eruyar[2], Esin Diremsizoğlu[1]
[1]Department of Dermatology, Kocaeli University Faculty of Medicine, Kocaeli, Türkiye
[2]Department of Pathology, Kocaeli University Faculty of Medicine, Kocaeli, Türkiye

Abstract

Malignant peripheral nerve sheath tumors (MPNSTs) are rare sarcomas associated with Schwann cells and neurofibromatosis type 1. The cutaneous subtype of MPNST is diagnosed primarily through histological findings, but immunohistochemistry is limited because of the overlap of markers with other soft tissue tumors. Treatment involves surgical excision followed by radiotherapy. Herein, we report a 37-year-old female patient who presented with a progressive, painless, cutaneous lesion in the left frontal region. Histopathological and immunohistochemical analyses revealed spindle cell neoplastic proliferation with strong S100 and SOX10 positivity, confirming the diagnosis of cutaneous malignant peripheral nerve sheath tumors (C-MPNST). The tumor was excised, and adjuvant radiotherapy at a dose of 64 Gy. Our findings provide valuable insights into the clinical and pathological characteristics, management strategies, and prognostic factors of C-MPNSTs.

Keywords: Malignant peripheral nerve sheath tumors, neurofibromatosis 1, schwann cells, cutaneous neoplasms, radiotherapy, adjuvant, immunohistochemistry

Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) are rare, aggressive soft tissue sarcomas originating from peripheral nerves or their sheaths. The cutaneous malignant peripheral nerve sheath tumors (C-MPNST), a subtype located in the dermis, is more likely to be surgically removed because of its superficial location and is associated with neurofibromatosis type 1 (NF-1). Two types of MPNST have been defined: Type 1, which is associated with NF-1, and type 2, which occurs sporadically. These tumors are particularly rare, with limited literature available on their clinical and pathological characteristics. Diagnosis primarily relies on histopathological examination, which typically reveals spindle cell neoplastic proliferation with varying cell densities and patterns, such as storiform or whorled arrangements. Immunohistochemical markers frequently used to support diagnosis include S100, SOX10, and CD34, although their expression can overlap with that of other soft tissue tumors, thereby complicating the diagnosis. Surgery remains the main treatment for localized MPNSTs, but achieving wide margins can be challenging due to the tumor's invasive nature and anatomical location. Adjuvant therapies, such as radiation and chemotherapy are often required.[1,2] Herein, we report a 37-year-old female patient with C-MPNST, which posed challenges in both clinical and pathological diagnosis. This case report aims to contribute valuable insights into the diagnosis and treatment challenges of this rare tumor, emphasizing the need for more extensive studies to improve patient outcomes.

Case Report

A 37-year-old female patient with no previous medical history was admitted to our clinic because of progressive increase in the size of a red, painless lump in the left frontal region over the past 3 months. This was her initial presentation, and she had not received any previous treatments. A dermatological

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Adress for correspondence: Esin Diremsizoğlu, MD, Department of Dermatology, Kocaeli University Faculty of Medicine, Kocaeli, Türkiye
Email: mdesinarslan@gmail.com
ORCID ID: 0000-0001-9824-481X

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examination revealed a 4x5 cm infiltrating tumoral lesion on the left frontal area (Figure 1a, b). To further evaluate the nature of the lesion, punch biopsy was performed. Histopathological examination revealed a spindle cell neoplastic proliferation throughout the dermis with varying densities (Figure 2a). The tumor had poorly defined margins and was composed of cells forming long fascicles in storiform or whorled patterns. High-magnification imaging revealed Schwann cells with large, hyperchromatic, tapered nuclei and fibroblasts arranged in thick bundles around the nerve tissue (Figure 2b). Nuclear pleomorphism varied from mild to severe, mitotic activity was brisk, and no tumoral necrosis was observed. The Ki-67 index was 14%. Immunohistochemistry revealed nuclear and cytoplasmic S100 protein expression and nuclear SOX10 positivity (Figure 2c, d). There were no expressions of HMB45 and Melan A. Based on histopathological findings, he was diagnosed with a C-MPNST. To identify the extent and boundaries of the tumor, the patient underwent maxillofacial magnetic resonance imaging (MRI) and positron emission tomography/computed tomography (PET/CT). Preauricular lymphadenopathy was detected, but no peripheral metastases or NF-1-related tumors were identified on PET/CT. The complete 4.5 cm lesion and the preauricular lymph node were surgically excised with a 2 cm margin. Following tumor excision, no tumor was observed at the lateral surgical margin; however, since it was adjacent to the basal surgical margin in one area, fascia excision was performed. No tumor was detected in the excised temporal fascia. Pathological examination of the preuricular lymph node revealed reactive lymphoid hyperplasia. The plastic surgeon used an anterolateral thigh perforator free flap to reconstruct the region. The left superficial temporal artery and concomitant vein were used as recipient vessels. Postoperative recovery was uneventful, and the patient was discharged on the fifth postoperative day. Due to the high risk of tumor recurrence, the patient underwent adjuvant radiotherapy (64 Gy/32 fx). She was followed up regularly with clinical examinations and imaging studies. Over the past 2.5 years, there has been no evidence of local recurrence or metastasis. The patient responded well to treatment, showed no signs of residual disease, and provided written informed consent for the publication of this case report. The multidisciplinary team continues to monitor the patient every six months clinically and with MRI to detect any potential recurrence at an early stage.

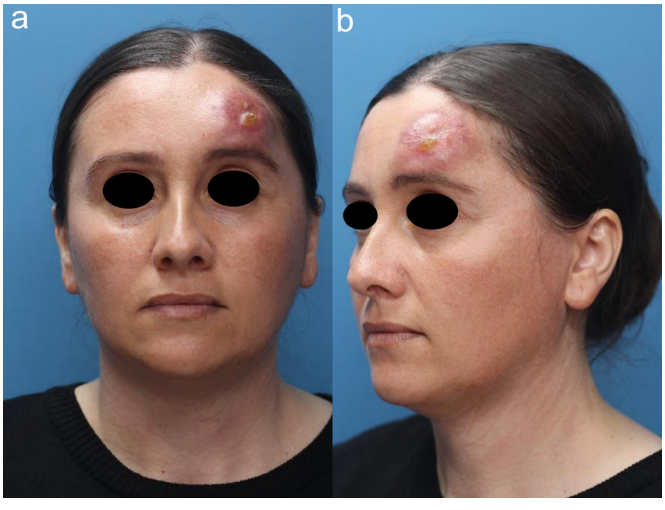

Figure 1. (a, b) Tumoral lesion in the left frontal area (anterior and lateral aspect)

Discussion

MPNST is a rare malignant sarcoma originating from Schwann cells or neural crest cells, but other tissue types may also be involved. Determining the nature of MPNST is important, with sporadic cases being common; approximately half of the cases are associated with NF-1, which is linked to a more unfavorable prognosis.[1,2] C-MPNST, a subtype located superficially in the dermis and subcutis, is less commonly linked to NF-1 compared with the classical type, yet both exhibit similar rates of recurrence and metastasis.[1] MPNST does not have a specific histochemical marker or imaging method, but relatively typical histological findings, such as spindle cell neoplastic proliferation with varying densities and patterns, are helpful in diagnosis. The role of immunohistochemistry in MPNST is limited by the diverse and inconsistent staining properties of frequently used markers such as S100 protein, CD34, Glial Fibrillary Acid Protein, and Epithelial Membrane Antigen.[1-3] Differential diagnoses include other spindle cell

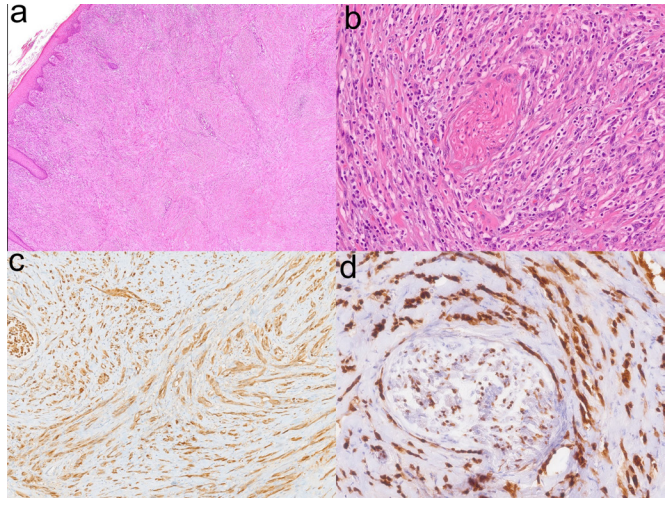

Figure 2. (a) Spindle cell tumoral infiltration consisted of alternating hypocellular and hypercellular areas with the formation of thick fascicles in the dermis hematoxylin and eosin (H&E, x40). (b) Atypical spindle tumor cells with marked pleomorphism form scattered bundles around the peripheral nerve (H&E, x100). (c) Cytoplasmic and nuclear S100 expression in tumor cells determined by immunohistochemistry (S100, x100). (d) Intense nuclear SOX10 expression in tumor cells determined by immunohistochemistry (SOX, x200)

neoplasms such as schwannomas, sarcomas, and malignant melanoma.[1]

In our case, although the NF-1 mutation could not be assessed, the absence of NF-1-related tumors and a negative family history suggested that this was a type 2 sporadic MPNST. Histopathological findings of spindle cell proliferation and immunohistochemical positivity for S100 and SOX10 were crucial for diagnosis. The absence of HMB45 and Melan-A indicated no melanocytic differentiation, which helps exclude melanoma and supports the diagnosis of MPNST by focusing on its neuroectodermal origin.

Factors that determine poor prognosis include large tumor volume, positive surgical margins, increased Ki-67 proliferation index, and head and neck location. PET/CT is recommended to detect possible metastases and differentiate MPNST from neurofibroma, which lacks such aggressive behavior. The main components of MPNST treatment are surgery and adjuvant radiotherapy.[3] Adjuvant radiation therapy should be administered to patients with tumors larger than 5 cm, high grade, or with positive margins. Chemotherapy is recommended for inexcusable tumors and metastatic MPNSTs.[4] In our patient, the tumor, which was localized on the head and measured 4.5 cm in size, had a high Ki-67 proliferation index. Therefore, adjuvant radiotherapy was included in the treatment plan. However, chemotherapy was not recommended due to the absence of metastasis.

Clinical studies targeting RAS and tyrosine kinase receptor pathways have not shown significant positive responses, indicating ongoing limitations in developing targeted therapies for MPNST.[5] The five-year survival rate for MPNST located in the head and neck can be as low as 20%.[3] Comparing our case with the literature, defining the roles of radiation therapy and chemotherapy in the management of C-MPNSTs remains controversial.[5] In accordance with the literature recommending radiation therapy over 60 Gy for MPNST, a dose of 64 Gy radiotherapy was applied to reduce local recurrence and improve long-term outcomes.[5] In the literature, local recurrence rates in MPNST are reported to be more frequent than metastasis, with the highest occurrence of local recurrence observed within the first 2 years after resection. Early detection of local recurrence is crucial for the success of surgical resection.[6] Although there is no consensus in the literature on the follow-up of MPNST, sarcoma guidelines recommend follow-up every 3 to 6 months for the first 2 years.[7] We have been monitoring the patient for every six months clinically and with MRI over the past 2.5 years without signs of recurrence.

Our case report provides insights into the management of C-MPNSTs. This report presents a rare presentation of C-MPNST in the absence of NF-1 and highlights the diagnostic complexities involved due to the tumor's rarity and the overlap of its histological features with other soft tissue neoplasms. We highlight the importance of detailed histopathological and immunohistochemical findings, particularly the roles of S100 and SOX10 markers. The multidisciplinary treatment approach, which included surgical excision and adjuvant radiotherapy, led to positive patient outcomes. Overall, this case highlights the need for further genetic and molecular research to explore additional mutations and develop effective targeted therapies for sporadic C-MPNSTs.

Footnote

Informed Consent: The patient responded well to treatment, showed no signs of residual disease, and provided written informed consent for the publication of this case report.

Authorship Contributions

Surgical and Medical Practices: A.D., D.B., S.Ç.S., A.T.E., E.D., Concept: A.D., D.B., S.Ç.S., A.T.E., E.D., Design: A.D., D.B., S.Ç.S., A.T.E., E.D., Data Collection or Processing: A.D., D.B., S.Ç.S., A.T.E., E.D., Analysis or Interpretation: A.D., D.B., S.Ç.S., A.T.E., E.D., Literature Search: A.D., D.B., S.Ç.S., A.T.E., E.D., Writing: A.D., D.B., S.Ç.S., A.T.E., E.D.

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