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Case Report

Malignant Peripheral Nerve Sheath Tumor with Rhabdomyoblastic Differentiation: Diagnostic Challenges and Literature Review

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Abstract: Malignant Peripheral Nerve Sheath Tumor (MPNST) is a rare sarcoma originating from Schwann cells or pluripotent cells of the neural crest. It accounts for 5–10% of soft tissue sarcomas, with a prevalence of 1:100,000 in the general population. Its etiology may be sporadic, associated with neurofibromatosis type 1 (NF1), or related to prior radiation exposure. Diagnosis is complex and relies on imaging studies complemented by histopathological and immunohistochemical analysis. The ideal treatment is complete surgical resection, while chemotherapy and radiotherapy are reserved for unresectable tumors. Prognosis is generally poor, with a five-year survival rate between 50–60%. We report the case of a 53-year-old female patient who presented with pain, swelling in the left thigh, and an inguinal nodule initially misdiagnosed as an inguinal hernia. A biopsy revealed a spindle cell neoplasm, and the patient was referred for further evaluation. Magnetic resonance imaging revealed an abdominal mass of 361.6 cm^3, with peritoneal metastases and pulmonary nodules. Initial immunohistochemical analysis suggested rhabdomyosarcoma, but a subsequent biopsy confirmed the diagnosis of MPNST with rhabdomyoblastic differentiation. The treatment was changed to chemotherapy with doxorubicin and ifosfamide, but the patient showed unfavorable progression and was transitioned to palliative care.

Keywords: Sarcoma; Peripheral Nerve Sheath Tumor; Radiation-Induced Neoplasms.

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1. Introduction

1.1. Definition and Epidemiology

Malignant Peripheral Nerve Sheath Tumor (MPNST) is a rare type of soft tissue sarcoma, originating from Schwann cells or pluripotent cells of the neural crest [1]. It accounts for 5–10% of all soft tissue sarcomas [2,3], with a prevalence of 1:100,000 in the general population and affects men and women equally [4]. This disease typically arises between the ages of 30 and 50 but may occur earlier depending on risk factors [5]. According to the WHO, this neoplasm can be classified into subtypes, including epithelioid, glandular, and Triton tumor.

1.2. Etiology and Risk Factors

Regarding the etiology of MPNST, there appears to be an association between the disease and certain risk factors, such as neurofibromatosis type 1 (NF1), prior exposure to

ionizing radiation (including radiotherapy), and advanced age, considering that the disease takes several years to develop [5]. Cases not associated with these conditions are generally considered sporadic [6]. In a retrospective study, 50% of patients with MPNST had NF1, and 10% had a history of prior radiation exposure [4]. Similarly, a literature review reported that 10–13% of MPNST cases had a previous history of therapeutic irradiation [7], and in such cases, a systematic review indicated a latency period of 13±8 years between radiation exposure and MPNST diagnosis [8]. In NF1-associated MPNST, there is evidence suggesting that this malignancy arises from the progression of precancerous lesions, such as plexiform neurofibroma (PN) and atypical neurofibromatous neoplasms of uncertain biological potential (ANNUBP). However, this process is slow, justifying the recognition of "advanced age" as a risk factor [5].

1.3. Clinical Manifestations

Clinically, MPNST presents pain, paresthesia, and muscle weakness, making it difficult to differentiate from other neuropathic conditions. It most frequently occurs in the proximal portions of the limbs, trunk, head, and neck [4,9–12]. It may initially appear as a small, painless mass that evolves with rapid growth, neuropathic pain, and associated weight loss [1]. As the tumor grows and the disease progresses, complications such as brain metastases, Brown-Séquard syndrome, and cauda equina syndrome have been reported [1].

1.4. Diagnosis

Regarding the diagnosis of this type of tumor, there are no highly accurate criteria, as similarities with other soft tissue sarcomas make differentiation difficult [5]. As summarized in the 2022 guideline of the National Comprehensive Cancer Network (NCCN), this diagnosis can be conventionally established using imaging and pathological studies or complemented by genetic and molecular analysis to improve accuracy and disease staging. In terms of imaging, the NCCN recommends both magnetic resonance imaging (MRI) and positron emission tomography (PET scan).

On MRI, MPNST appears hypointense on T1-weighted images (T1WI) and hyperintense on T2-weighted images (T2WI). A specificity of 100% can be achieved with this method if perilesional edema, necrosis/cystic degeneration, and irregular margins are present simultaneously [13]. The NCCN guideline also recommends PET scan for diagnosing this neoplasm, as it may be more sensitive than MRI for this purpose. This exam can also reveal real-time evidence of metastases.

Core needle biopsy is strongly recommended for diagnosing MPNST, due to its generally high accuracy and low risk of lesion dissemination along the needle path [5]. However, it is important to be aware of the potential risks, such as nerve injury and worsening pain [14,15]. Alongside the biopsy, fine needle aspiration is advised, along with immunohistochemical testing using the H3K27me3 marker [16]. Nonetheless, the decision to biopsy may be debated if upfront resection is feasible, as there is a risk of false-negative results—biopsies may not capture representative malignant cells, especially since MPNST cells tend to be intermixed with benign or precursor lesions [17].

In the context of pathological analysis, there is no specific marker panel defined for MPNST, making it difficult to distinguish it from other soft tissue sarcomas. Thus, the diagnosis is primarily one of exclusion [5]. Macroscopically, the tumor presents as a solid, white mass often connected to a nerve root [30]. Microscopically, its features are not specific and cannot be used alone for diagnosis; however, they are useful for ruling out other neoplasms [31].

1.5. Treatment

Given the high aggressiveness of this neoplasm, the therapeutic arsenal is relatively limited. Complete surgical resection with clear margins remains the only effective treat-

ment, resulting in higher five-year survival rates and lower recurrence rates [18]. Chemotherapy may be an option for patients with unresectable lesions. In this context, doxorubicin is considered the first-line treatment. As for its use as an adjuvant to surgery, several studies have shown no significant increase in survival or reduction in recurrence rates [19].

Radiotherapy has shown excellent local control in the management of MPNST [20,21] and is frequently recommended in cases of high-grade lesions or tumors larger than 5 cm [22]. As an adjuvant to surgery, radiation alone does not improve survival but may render previously unresectable tumors operable [23]. Similarly, brachytherapy may also offer benefits [24]. Targeted therapy may become an option for patients with unresectable or metastatic disease. As outlined in [5], several regimens have been tested, but none are currently well-established or clearly superior, although some drugs show promise [32,33].

1.6. Prognosis

Despite recent advances in the treatment of MPNST, its prognosis remains poor. The median survival is approximately six years [25], and the five-year survival rate remains around 50–60% [4,25–28]. Additionally, there is no consensus on prognostic or outcome prediction systems for this disease [5]. However, it is noteworthy that the sarcoma grading system developed by the French Federation of Cancer Centers Sarcoma Group shows a strong correlation with survival outcomes when the disease is classified as “high grade” [34,35]. Independent factors associated with poor prognosis include the presence of NF1 mutation [25,26,29]; age over 60 years [25]; tumor size greater than 5 cm [4,25]; and R2 resection (compared to R0 or R1) [5].

2. Case Report

2.1. Clinical History

A 53-year-old female patient presented to the oncology outpatient clinic of a tertiary hospital on September 22, 2023, referred due to biopsy findings. She reported pain, warmth, and swelling in the anterior aspect of the left thigh, along with a nodule in the left inguinal region. During the consultation, the patient explained that the inguinal nodule had appeared four months prior and was initially diagnosed as an inguinal hernia. She underwent surgical correction for this presumed hernia at the end of August. However, during the surgery, the surgical team did not find a hernia sac but instead encountered a mass of unknown origin at the lesion site. A biopsy was performed, which revealed a "spindle cell neoplasm"—the reason for the referral.

Physical examination confirmed the patient’s complaints and revealed a dehiscent surgical wound in the left inguinal region, draining bloody-serous fluid. Regarding her medical history, although there was no family history of cancer, she had a previous diagnosis of cervical cancer in 2013, treated with surgery and radiotherapy. Given the need for neoplasm staging, immunohistochemical analysis of the biopsy specimen, evaluation for possible deep vein thrombosis (DVT), and marked inflammation in the inguinal region, the decision was made to admit the patient to the hospital.

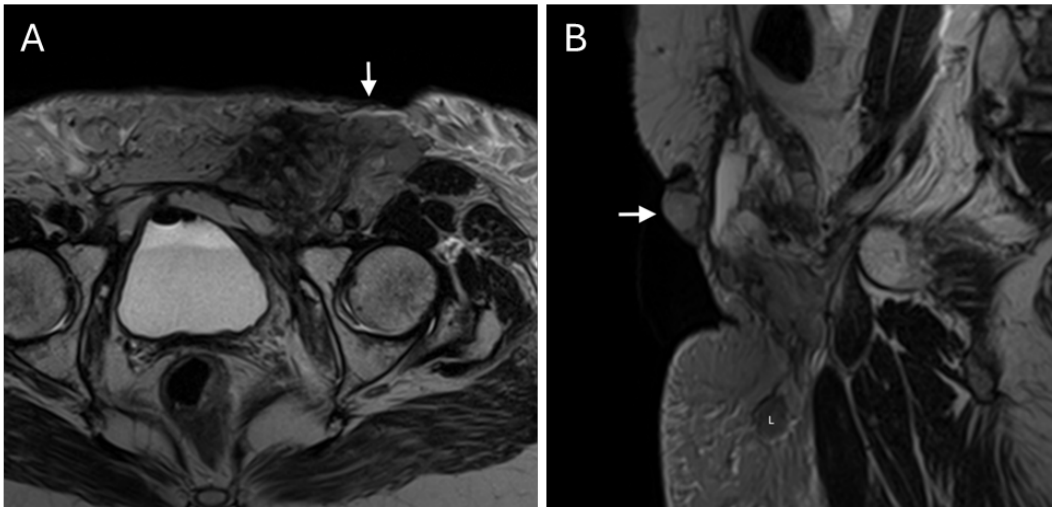
2.2. Imaging Investigation

During hospitalization, an extensive complementary investigation was conducted. Among the imaging exams performed, two are particularly noteworthy: pelvic magnetic resonance imaging (MRI) and thoracic computed tomography (CT), with findings shown in Figures 1 and 2 and described below. MRI (Figures 1A and 1B) revealed a thrombus in the left external femoral vein and an abdominal wall mass measuring 361.6 cm^3, with lobulated contours, hypointense on T1, hyperintense on T2, restricted diffusion, and enhancement after contrast administration. These findings were consistent with a neoplastic lesion involving the skin, subcutaneous tissue, underlying muscle planes, the belly of the left rectus abdominis muscle, and the adductor muscles of the thigh, also compressing the

common femoral vein. Several nodules with similar radiological characteristics were identified, including one in the right rectus abdominis muscle (measuring 1.4 cm^3, likely a secondary neoplastic lesion) and others implanted in the peritoneum, the largest measuring 13 cm^3.

The chest CT revealed scattered pulmonary nodules with lobulated contours and soft tissue density, suggestive of secondary neoplastic lesions. At this point, immunohistochemical (IHC) analysis was also requested. On September 24, 2023, the patient was discharged with instructions to retrieve the IHC results once available and to schedule a follow-up oncology consultation for therapeutic planning.

Figure 1. Magnetic resonance images from September 23, 2023, T2-weighted, axial (A) and sagittal (B) planes, showing a mass in the abdominal wall of the left iliac fossa involving muscle planes and subcutaneous fat tissue up to the skin surface (white arrow in A and B). Left inguinal lymphadenopathy can also be observed ("L" in B).



3.3. Histopathological Analysis and Initial Immunohistochemistry

At the patient's follow-up visit to the outpatient clinic, the previously requested examination revealed a "malignant neoplasm with a spindle cell pattern and rhabdoid component," classified as high-grade (grade 3 according to the Fédération Nationale des Centres de Lutte Contre le Cancer — FNCLCC), with a mitotic index of up to 23/mm^2 and areas of tumor necrosis. Based on these findings, the main working diagnosis was spindle cell/sclerosing rhabdomyosarcoma. Regarding immunohistochemical markers, there was positivity for desmin (clone DE-R-11), myogenin (clone F5D), MyoD1 (clone EP212), and INI-1 (clone MRQ-27); and negativity for pancytokeratin, C-KIT, DOG1, CD34, S100, actin, TLE1, MUC4, and SATB2. Based on this information, a therapeutic plan was outlined consisting of 15 sessions of radiotherapy, with a dose of 2.5 Gy per session.

Complementary laboratory tests were requested, including a complete blood count, coagulation profile, and fasting blood glucose, as well as imaging exams (panoramic radiograph and Cone Beam computed tomography of the maxilla) (Figure 2).

3.4. Second Immunohistochemical Analysis

Given the low prevalence of the diagnosis suggested by the initial histopathological study, the medical team requested a second immunohistochemical analysis of the previously collected tissue sample from another pathology service, aiming to confirm the diagnosis due to the rarity of the case and the potential implications for treatment planning. In this new analysis, the diagnosis was clarified as "Malignant Peripheral Nerve Sheath Tumor (MPNST) with rhabdomyoblastic differentiation," high-grade (grade 3 according to FNCLCC).

Regarding the histological markers, there was positivity for desmin (clone D33), myogenin (clone FD5), MyoD1 (clone 5.8A), and CDK4 (clone EP180); and negativity for S-100 protein (polyclonal), actin, cytokeratins, CD34, MDM2, and notably H3.3 K27me (clone K27-C36B11), whose loss of expression supports the MPNST diagnosis. The differences between the findings of the first and second analyses are shown in Table 1.

3.5. Treatment and Outcome

At this point, the treatment regimen was modified to reflect the new diagnosis, with the implementation of a chemotherapy protocol using doxorubicin and ifosfamide. However, only a single cycle of this medication was administered, as the patient's condition deteriorated rapidly. Following a shared decision with her family, care was transitioned to a palliative approach only.

Figure 2. Non-contrast computed tomography scan dated January 8, 2024, axial view, showing lesion growth with increased skin involvement and intermixed gaseous and calcified foci.

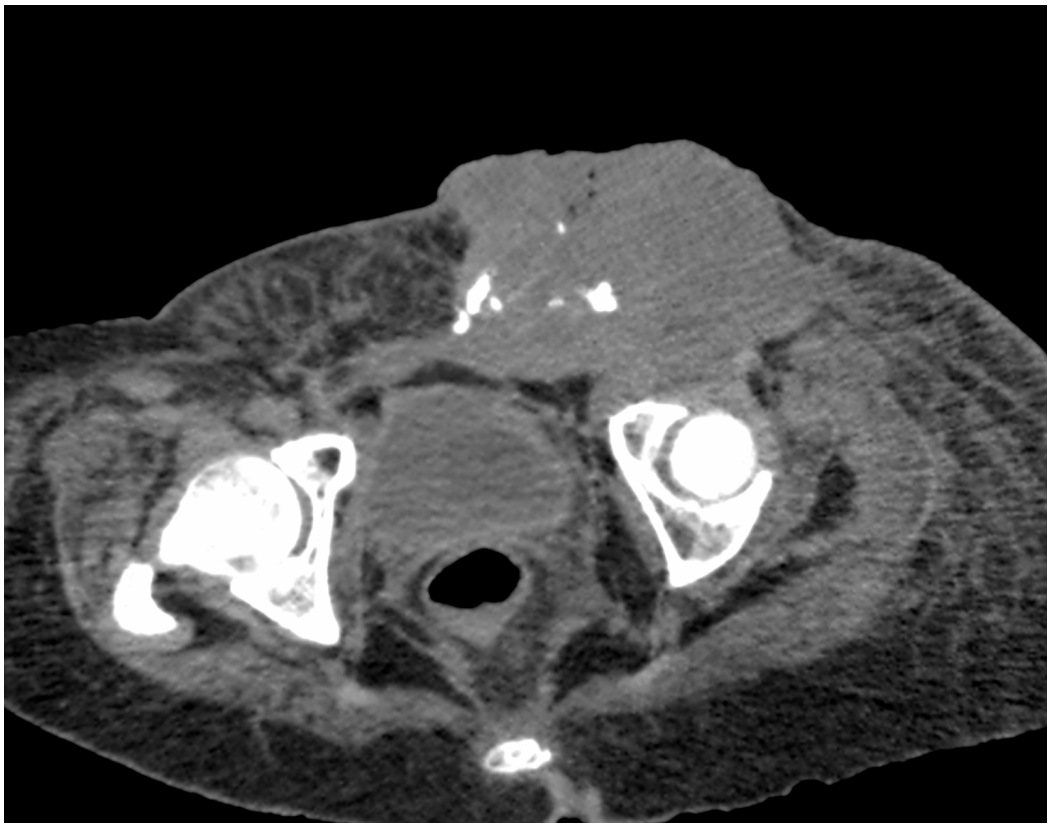


Table 1. Key differences between the immunohistochemical markers tested in both analyses and their respective results. Notably, the loss of H3.3 K27me expression observed in the second analysis supports the diagnosis of MPNST. The positivity for desmin, myogenin, and MyoD1, along with the negativity for cytokeratins and S-100 protein, would suggest rhabdomyosarcoma in the absence of H3.3 K27me loss.

Marker	First IHC Analysis	Second IHC Analysis
Desmin	Positive (clone DE-R-11)	Positive (clone D33)
Myogenin	Positive (clone F5D)	Positive (clone FD5)
MyoD1	Positive (clone EP212)	Positive (clone 5.8A)
INI-1	Positive (clone MRQ-27)	Not tested
CDK4	Not tested	Positive (clone EP180)

S-100 protein	Negative (polyclonal)	Negative (polyclonal)
Actin	Negative	Negative
Cytokeratins	Negative	Negative
CD34	Negative	Negative
C-KIT	Negative	Not tested
DOG1	Negative	Not tested
TLE1	Negative	Not tested
MUC4	Negative	Not tested
SATB2	Negative	Not tested
MDM2	Not tested	Negative
H3.3 K27me	Not tested	Negative

3. Discussion and Conclusion

The case presented supports findings described in the literature on Malignant Peripheral Nerve Sheath Tumor (MPNST) with rhabdomyoblastic differentiation—a rare and aggressive neoplasm. The patient had a history of prior radiotherapy, a known risk factor for the development of this tumor [5]. This observation aligns with studies indicating an average latency of 13 ± 8 years between radiation exposure and the diagnosis of MPNST [8], reinforcing the hypothesis of a causal relationship between these events.

The patient's clinical course also followed patterns reported in the literature, with nonspecific initial manifestations such as neuropathic pain and mass growth in a typical location (trunk and proximal thigh) [4,9–12]. This highlights the diagnostic difficulty of this type of tumor, as early symptoms may be mistaken for benign conditions. Diagnostic confusion was evident in this case, as the lesion was initially interpreted as an inguinal hernia, delaying oncologic investigation.

The definitive diagnosis of MPNST with rhabdomyoblastic differentiation was established only after detailed immunohistochemical analyses. The expression of markers such as desmin, myogenin, and MyoD1 confirmed rhabdomyoblastic differentiation—a rare but documented feature in the literature [16]. Loss of H3K27me3 protein expression corroborated the diagnosis, underscoring the importance of immunohistochemistry in differentiating soft tissue sarcomas.

Staging revealed advanced disease, with metastases to the peritoneum and lungs—a pattern consistent with prior reports of MPNST dissemination [1,4,6]. Studies indicate that the presence of metastases at diagnosis is associated with poorer prognosis, significantly reducing overall survival [25]. This, along with the high histologic grade of the tumor (grade 3 according to FNCLCC classification), suggested a guarded prognosis for the patient [34,35].

The initial treatment with radiotherapy was based on the preliminary diagnosis of rhabdomyosarcoma. However, following confirmation of MPNST, the approach was adjusted to chemotherapy with doxorubicin and ifosfamide, a regimen recommended for high-grade sarcomas [19]. Despite adopting this strategy, the patient's condition deteriorated, prompting a shift in treatment focus to palliative care.

This case illustrates the complexity of managing MPNST, highlighting both diagnostic and therapeutic challenges. The lack of standardized treatment guidelines for this neoplasm also presents a clinical obstacle, making individualized therapeutic approaches essential. In this context, complete surgical resection remains the primary curative option, though it is not always feasible in advanced-stage disease. Additionally, the case underscores the limitations faced during diagnosis and treatment, such as the unavailability of molecular studies and restricted access to therapeutic options, which may have negatively impacted patient management [18].

From a prognostic perspective, the most relevant factors influencing survival include tumor size greater than 5 cm, age over 60 years, NF1 mutation, and incomplete resection (R2) [25,26,29]. In the present case, the presence of several of these adverse factors emphasized the severity of the condition and the low likelihood of treatment success. This reinforces the importance of early diagnosis and aggressive therapeutic interventions in MPNST management. Furthermore, the role of multidisciplinary teams is essential in the care of rare sarcomas, enabling a comprehensive case assessment, greater diagnostic precision, and more appropriate therapeutic decisions. Future studies are crucial to developing new treatment strategies, including targeted therapies and immunotherapies, that may offer improved outcomes for patients with such a highly unfavorable prognosis.

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Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Silva ET, Oliveira RT, Leles CR. Fatores associados ao edentulismo funcional em idosos brasileiros. Comun Ciênc Saúde. 2016;27(2):129-138.
2. Baehring JM, Betensky RA, Batchelor TT. Malignant peripheral nerve sheath tumor: The clinical spectrum and outcome of treatment. Neurology. 2003 Sep 9;61(5):696–698. doi:10.1212/01.wnl.0000078813.05925.2c. PMID: 12963767.
3. Cai Z, Tang X, Liang H, Yang R, Yan T, Guo W. Prognosis and risk factors for malignant peripheral nerve sheath tumor: a systematic review and meta-analysis. World J Surg Oncol. 2020 Sep 30;18(1):257. doi: 10.1186/s12957-020-02036-x. PMID: 32998743; PMCID: PMC7528472.
4. Vauthey JN, Woodruff JM, Brennan MF. Extremity malignant peripheral nerve sheath tumors (neurogenic sarcomas): a 10-year experience. Ann Surg Oncol. 1995 Mar;2(2):126-31. doi: 10.1007/BF02303627. PMID: 7728565.
5. Stucky CC, Johnson KN, Gray RJ, Pockaj BA, Ocal IT, Rose PS, Wasif N. Malignant peripheral nerve sheath tumors (MPNST): the Mayo Clinic experience. Ann Surg Oncol. 2012 Mar;19(3):878-85. doi: 10.1245/s10434-011-1978-7. Epub 2011 Aug 23. PMID: 21861229.
6. Yao C, Zhou H, Dong Y, Alhaskawi A, Hasan Abdullah Ezzi S, Wang Z, Lai J, Goutham Kota V, Hasan Abdulla Hasan Abdulla M, Lu H. Malignant Peripheral Nerve Sheath Tumors: Latest Concepts in Disease Pathogenesis and Clinical Management. Cancers (Basel). 2023 Feb 8;15(4):1077. doi: 10.3390/cancers15041077. PMID: 36831419; PMCID: PMC9954030.
7. Ducatman BS, Scheithauer BW, Piepgras DG, Reiman HM, Ilstrup DM. Malignant peripheral nerve sheath tumors. A clinicopathologic study of 120 cases. Cancer. 1986 May 15;57(10):2006-21. doi: 10.1002/1097-0142(19860515)57:10<2006::aid-cncr2820571022>3.0.co;2-6. PMID: 3082508.
8. Farid M, Demicco EG, Garcia R, Ahn L, Merola PR, Cioffi A, Maki RG. Malignant peripheral nerve sheath tumors. Oncologist. 2014 Feb;19(2):193-201. doi: 10.1634/theoncologist.2013-0328. Epub 2014 Jan 27. PMID: 24470531; PMCID: PMC3926794.
9. Yamanaka R, Hayano A. Radiation-Induced Malignant Peripheral Nerve Sheath Tumors: A Systematic Review. World Neurosurg. 2017 Sep;105:961-970.e8. doi: 10.1016/j.wneu.2017.06.010. Epub 2017 Jun 8. PMID: 28602926.
10. Mowery A, Clayburgh D. Malignant peripheral nerve sheath tumors: Analysis of the national cancer database. Oral Oncol. 2019 Nov;98:13-19. doi: 10.1016/j.oraloncology.2019.09.010. Epub 2019 Sep 13. PMID: 31525622.
11. Yan P, Huang R, Hu P, Liu F, Zhu X, Hu P, Yin H, Zhang J, Meng T, Huang Z. Nomograms for predicting the overall and cause-specific survival in patients with malignant peripheral nerve sheath tumor: a population-based study. J Neurooncol. 2019 Jul;143(3):495-503. doi: 10.1007/s11060-019-03181-4. Epub 2019 May 14. PMID: 31089923.
12. Le Guellec S, Decouvelaere AV, Filleron T, Valo I, Charon-Barra C, Robin YM, Terrier P, Chevreau C, Coindre JM. Malignant Peripheral Nerve Sheath Tumor Is a Challenging Diagnosis: A Systematic Pathology Review, Immunohistochemistry, and Molecular Analysis in 160 Patients From the French Sarcoma Group Database. Am J Surg Pathol. 2016 Jul;40(7):896-908. doi: 10.1097/PAS.0000000000000655. PMID: 27158754.
13. Zhou HY, Jiang S, Ma FX, Lu H. Peripheral nerve tumors of the hand: Clinical features, diagnosis, and treatment. World J Clin Cases. 2020 Nov 6;8(21):5086-5098. doi: 10.12998/wjcc.v8.i21.5086. PMID: 33269245; PMCID: PMC7674743.
14. Broski SM, Johnson GB, Howe BM, Nathan MA, Wenger DE, Spinner RJ, Amrami KK. Evaluation of (18)F-FDG PET and MRI in differentiating benign and malignant peripheral nerve sheath tumors. Skeletal Radiol. 2016 Aug;45(8):1097-105. doi: 10.1007/s00256-016-2394-7. Epub 2016 Apr 26. PMID: 27115884.

15. Graham DS, Russell TA, Eckardt MA, Motamedi K, Seeger LL, Singh AS, Bernthal NM, Kalbasi A, Dry SM, Nelson SD, Elashoff D, Levine BD, Eilber FC. Oncologic Accuracy of Image-guided Percutaneous Core-Needle Biopsy of Peripheral Nerve Sheath Tumors at a High-volume Sarcoma Center. Am J Clin Oncol. 2019 Oct;42(10):739-743. doi: 10.1097/COC.0000000000000591. PMID: 31436746.
16. Pianta M, Chock E, Schlicht S, McCombe D. Accuracy and complications of CT-guided core needle biopsy of peripheral nerve sheath tumours. Skeletal Radiol. 2015 Sep;44(9):1341-9. doi: 10.1007/s00256-015-2185-6. Epub 2015 Jun 16. PMID: 26078215.
17. Mito JK, Qian X, Doyle LA, Hornick JL, Jo VY. Role of Histone H3K27 Trimethylation Loss as a Marker for Malignant Peripheral Nerve Sheath Tumor in Fine-Needle Aspiration and Small Biopsy Specimens. Am J Clin Pathol. 2017 Aug 1;148(2):179-189. doi: 10.1093/ajcp/aqx060. PMID: 28898989.
18. Prudner BC, Ball T, Rathore R, Hirbe AC. Diagnosis and management of malignant peripheral nerve sheath tumors: Current practice and future perspectives. Neurooncol Adv. 2019 Nov 14;2(Suppl 1):i40-i49. doi: 10.1093/noajnl/vdz047. PMID: 32642731; PMCID: PMC7317062.
19. Dunn GP, Spiliopoulos K, Plotkin SR, Hornicek FJ, Harmon DC, Delaney TF, Williams Z. Role of resection of malignant peripheral nerve sheath tumors in patients with neurofibromatosis type 1. J Neurosurg. 2013 Jan;118(1):142-8. doi: 10.3171/2012.9.JNS101610. Epub 2012 Oct 26. PMID: 23101443.
20. Zehou O, Fabre E, Zelek L, Sbidian E, Ortonne N, Banu E, Wolkenstein P, Valeyrie-Allanore L. Chemotherapy for the treatment of malignant peripheral nerve sheath tumors in neurofibromatosis 1: a 10-year institutional review. Orphanet J Rare Dis. 2013 Aug 23;8:127. doi: 10.1186/1750-1172-8-127. PMID: 23972085; PMCID: PMC3766199.
21. Sloan L, Terezakis SA, Blakeley JO, Slobogean B, Kleinberg LR. Long-term outcomes of radiation therapy (RT) in the management of malignant peripheral nerve sheath tumors (MPNST) in patients with neurofibromatosis type 1 (NF1). Int J Radiat Oncol Biol Phys [Internet]. 2018;102(3):e474–e475. Available from: http://dx.doi.org/10.1016/j.ijrobp.2018.07.1357
22. Kahn J, Gillespie A, Tsokos M, Ondos J, Dombi E, Camphausen K, Widemann BC, Kaushal A. Radiation therapy in management of sporadic and neurofibromatosis type 1-associated malignant peripheral nerve sheath tumors. Front Oncol. 2014 Nov 17;4:324. doi: 10.3389/fonc.2014.00324. PMID: 25452937; PMCID: PMC4233912.
23. Ferner RE, Gutmann DH. International consensus statement on malignant peripheral nerve sheath tumors in neurofibromatosis. Cancer Res. 2002 Mar 1;62(5):1573-7. PMID: 11894862.
24. Wang D, Zhang Q, Eisenberg BL, Kane JM, Li XA, Lucas D, Petersen IA, DeLaney TF, Freeman CR, Finkelstein SE, Hitchcock YJ, Bedi M, Singh AK, Dundas G, Kirsch DG. Significant Reduction of Late Toxicities in Patients With Extremity Sarcoma Treated With Image-Guided Radiation Therapy to a Reduced Target Volume: Results of Radiation Therapy Oncology Group RTOG-0630 Trial. J Clin Oncol. 2015 Jul 10;33(20):2231-8. doi: 10.1200/JCO.2014.58.5828. Epub 2015 Feb 9. PMID: 25667281; PMCID: PMC4486342.
25. Wong WW, Hirose T, Scheithauer BW, Schild SE, Gunderson LL. Malignant peripheral nerve sheath tumor: analysis of treatment outcome. Int J Radiat Oncol Biol Phys. 1998 Sep 1;42(2):351-60. doi: 10.1016/s0360-3016(98)00223-5. PMID: 9788415.
26. Martin E, Coert JH, Flucke UE, Slooff WM, Ho VKY, van der Graaf WT, van Dalen T, van de Sande MAJ, van Houdt WJ, Grünhagen DJ, Verhoef C. A nationwide cohort study on treatment and survival in patients with malignant peripheral nerve sheath tumours. Eur J Cancer. 2020 Jan;124:77-87. doi: 10.1016/j.ejca.2019.10.014. Epub 2019 Nov 21. PMID: 31760312.
27. Miao R, Wang H, Jacobson A, Lietz AP, Choy E, Raskin KA, Schwab JH, Deshpande V, Nielsen GP, DeLaney TF, Cote GM, Hornicek FJ, Chen YE. Radiation-induced and neurofibromatosis-associated malignant peripheral nerve sheath tumors (MPNST) have worse outcomes than sporadic MPNST. Radiother Oncol. 2019 Aug;137:61-70. doi: 10.1016/j.radonc.2019.03.015. Epub 2019 May 9. PMID: 31078939.
28. Valentin T, Le Cesne A, Ray-Coquard I, Italiano A, Decanter G, Bompas E, Isambert N, Thariat J, Linassier C, Bertucci F, Bay JO, Bellesoeur A, Penel N, Le Guellec S, Filleron T, Chevreau C. Management and prognosis of malignant peripheral nerve sheath tumors: The experience of the French Sarcoma Group (GSF-GETO). Eur J Cancer. 2016 Mar;56:77-84. doi: 10.1016/j.ejca.2015.12.015. Epub 2016 Jan 26. PMID: 26824706.
29. Watson KL, Al Sannaa GA, Kivlin CM, Ingram DR, Landers SM, Roland CL, Cormier JN, Hunt KK, Feig BW, Ashleigh Guadagnolo B, Bishop AJ, Wang WL, Slopis JM, McCutcheon IE, Lazar AJ, Torres KE. Patterns of recurrence and survival in sporadic, neurofibromatosis Type 1-associated, and radiation-associated malignant peripheral nerve sheath tumors. J Neurosurg. 2017 Jan;126(1):319-329. doi: 10.3171/2015.12.JNS152443. Epub 2016 Apr 1. PMID: 27035165; PMCID: PMC5045773.
30. Porter DE, Prasad V, Foster L, Dall GF, Birch R, Grimer RJ. Survival in Malignant Peripheral Nerve Sheath Tumours: A Comparison between Sporadic and Neurofibromatosis Type 1-Associated Tumours. Sarcoma. 2009;2009:756395. doi: 10.1155/2009/756395. Epub 2009 Apr 7. PMID: 19360115; PMCID: PMC2666272.
31. Thway K, Fisher C. Malignant peripheral nerve sheath tumor: pathology and genetics. Ann Diagn Pathol. 2014 Apr;18(2):109-16. doi: 10.1016/j.anndiagpath.2013.10.007. Epub 2013 Nov 23. PMID: 24418643.
32. Coindre JM, Terrier P, Guillou L, Le Doussal V, Collin F, Ranchère D, Sastre X, Vilain MO, Bonichon F, N'Guyen Bui B. Predictive value of grade for metastasis development in the main histologic types of adult soft tissue sarcomas: a study of 1240 patients from the French Federation of Cancer Centers Sarcoma Group. Cancer. 2001 May 15;91(10):1914-26. doi: 10.1002/1097-0142(20010515)91:10<1914::aid-cncr1214>3.0.co;2-3. PMID: 11346874.

33. De Raedt T, Walton Z, Yecies JL, Li D, Chen Y, Malone CF, Maertens O, Jeong SM, Bronson RT, Lebleu V, Kalluri R, Normant E, Haigis MC, Manning BD, Wong KK, Macleod KF, Cichowski K. Exploiting cancer cell vulnerabilities to develop a combination therapy for ras-driven tumors. Cancer Cell. 2011 Sep 13;20(3):400-13. doi: 10.1016/j.ccr.2011.08.014. PMID: 21907929; PMCID: PMC3233475.
34. Jessen WJ, Miller SJ, Jousma E, Wu J, Rizvi TA, Brundage ME, Eaves D, Widemann B, Kim MO, Dombi E, Sabo J, Hardiman Dudley A, Niwa-Kawakita M, Page GP, Giovannini M, Aronow BJ, Cripe TP, Ratner N. MEK inhibition exhibits efficacy in human and mouse neurofibromatosis tumors. J Clin Invest. 2013 Jan;123(1):340-7. doi: 10.1172/JCI60578. Epub 2012 Dec 10. PMID: 23221341; PMCID: PMC3533264.
35. Wakeman KM, Zhang QS, Bandhlish A, Cranmer LD, Ricciotti RW, Mantilla JG. Fédération Nationale Des Centres de Lutte Contre Le Cancer (FNCLCC) Grading, Margin Status and Tumor Location Associate With Survival Outcomes in Malignant Peripheral Nerve Sheath Tumors. Am J Clin Oncol. 2022 Jan 1;45(1):28-35. doi: 10.1097/COC.0000000000000877. PMID: 34962906.
36. Lucas CG, Vasudevan HN, Chen WC, Magill ST, Braunstein SE, Jacques L, Dahiya S, Rodriguez FJ, Horvai AE, Perry A, Pekmezci M, Raleigh DR. Histopathologic findings in malignant peripheral nerve sheath tumor predict response to radiotherapy and overall survival. Neurooncol Adv. 2020 Oct 1;2(1):vdaa131. doi: 10.1093/noajnl/vdaa131. PMID: 33880447; PMCID: PMC8044670.