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Case Report

Peripheral Neural Sheath Breast Sarcoma: Case Report and Literature Review

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Soft tissue sarcoma · Neurofibrosarcoma · Breast neoplasms

Abstract
Primary sarcomas of the breast are heterogeneous neoplasms derived from the non-epithelial elements of the mammary gland. Malignant peripheral nerve sheath tumors comprise 5–10% of all malignant soft tissue sarcomas. Its heterogeneity and low incidence (1 in 100,000) limit the performance of prospective studies. Therefore, most published articles include individual reports and case series with a small number of patients, making it impossible to determine clear treatment standards in this scenario. A 36-year-old young woman with no personal history consulted the National Cancer Institute of Colombia with a 1-year progression of a rapidly growing mass in her left breast until reaching an approximate tumor size of 20 × 20 cm. Histopathological analysis with a tru-cut biopsy taken from the lesion revealed the presence of a breast sarcoma with positive staining for SOX-10 and S-100. A radical mastectomy as her first treatment included the resection of a costal arch and, therefore, the reconstruction of the chest wall with coverage of the defect with an extended latissimus dorsi flap followed by consolidation therapy with adjuvant radiotherapy (RT) and chemotherapy. Evidence regarding malignant peripheral nerve sheath sarcoma of the breast treatment corresponds to retrospective analyses and case reports with high heterogeneity and variability about strategies in surgical procedures and adjunctive therapy such as complementary chemotherapy and RT; therapeutic approach should always include a multidisciplinary team.

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Introduction

Breast sarcomas are malignant neoplasms of the mammary gland originating in the interlobular mesenchymal tissue of the breast. Malignant peripheral nerve sheath tumors (MPNSTs) have similarities with other primary breast sarcomas making diagnosis difficult, unsuspected and misdiagnosed without high clinical suspicion and inmunohistochemistry [1]. Evaluation includes a physical examination, breast images (mammography/ultrasound/nuclear magnetic resonance), extension studies (usually chest and abdominal tomography), and histological characterization associated with immunohistochemistry due to a wide variety of presentations [2, 3].

These tumors represent about 1% of all malignant neoplasms of the breast and less than 5% of all soft tissue sarcomas [4, 5]. They generally appear in women between 45 and 60 years of age, except for angiosarcomas, which can occur in younger women (around 40 years of age) [6]. In most patients, they appear as a solitary tumor mass, well-circumscribed, firm, not painful, and fast-growing. Two categories used for classification include primary, when it appears de novo, and secondary, related to specific medical treatments such as radiotherapy (RT) or axillary lymphadenectomy [7].

MPNSTs are a rare type of malignancy accounting only 5–10% of all malignant soft tissue sarcoma. Their incidence is 1:100,000 and they are mostly associated with von Recklinghausen's neurofibromatosis, and the most common sites of involvement are trunk (51%), extremities (45%), and head and neck (4%). MPNST of the breast is a very rare occurrence [1].

Surgical management of locoregional disease is surgery with wide negative margins, and there is no standard approach in complementary adjuvant treatment. In some cases, chemotherapy and RT treatment protocols are homologated to those used in soft tissue sarcomas in the extremities [8].

Clinical Case

A 36-year-old female patient consulted the National Cancer Institute of Colombia with a left breast mass lasting 1 year without additional symptoms suggestive of systemic compromise. Past medical history was relevant for an uncle with a malignant breast neoplasm of unknown etiology.

Physical examination revealed a large mass in her left breast, 20 × 20 cm diameter, which completely replaced deeper tissues and her skin on the external quadrants as an ulcerative lesion. The evaluation of the left axilla showed inflammatory-appearing adenopathy of 1 cm diameter. The contralateral breast and axilla (right) were clinically negative. Extension studies and tru-cut biopsy of the lesion were requested.

Chest computed tomography revealed a necrotic mass that occupied the entire left breast parenchyma with signs of infiltration to the skin and the pectoral muscle associated with pectoral and axillary ganglia on the same side with a secondary neoplastic appearance (Fig. 1a, b). The computed tomography of the abdomen and pelvis did not report distant metastatic involvement. Biopsy of the lesion by tru-cut showed evidence of a high-grade malignant spindle cell neoplasm with an osteochondral component, extensive necrosis, and cytokeratins negative staining considering a phyllodes tumor of the breast versus primary breast sarcoma as a differential diagnosis (Fig. 2a).

Patient referral to the national cancer institute was mandatory due to its experience in managing unusual pathologies. Discussion of the case included a sarcoma tumor board with experts from Ohio, USA, and a multidisciplinary team at the center composed of breast,

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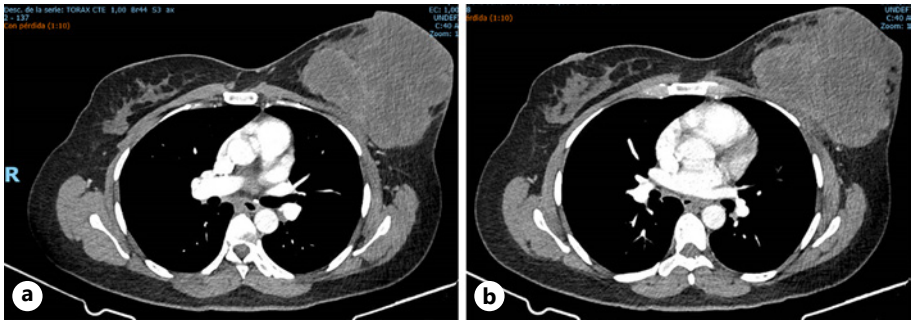

Fig. 1. a, **b** Chest CT with a 20 × 20 cm dependent necrotic mass of the left breast, left lower quadrant with signs of infiltration to the skin and the pectoral muscle associated with the presence of ipsilateral pectoral and axillary ganglia. CT, computed tomography.

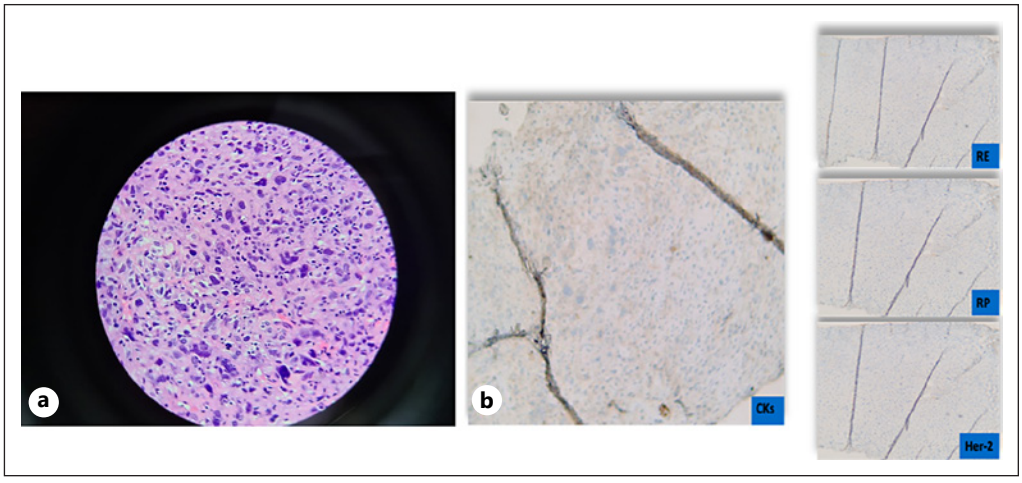

Fig. 2. Spindle cells with high-grade atypia and moderate mitotic (**a**) and Immunohistochemical staining negative for RE, PRs, HER-2, and CKs (**b**). PR, progesterone receptor; CK, cytokeratin; RE, estrogen receptors.

thoracic, and plastic surgeons. The decision to carry out an R0 resection included curative treatment and a high failure rate with a more conservative approach. Discussion and explanation of treatment options with the patients allow her to decide for an R0 resection and posterior chemoradiotherapy due to her fear of disease progression. The definitive report of the pathology of the surgical specimen showed wide negative margins on each side (>1 cm). Except for the deep border, whose margin width was 1.5 mm performing a 4th coastal arch resection, reconstruction of the chest wall with a titanium bar, and coverage of the defect with an extended V-Y latissimus dorsi musculocutaneous flap for anterior chest wall reconstruction. The extended study of the surgical specimen made it possible to complete the immunohistochemistry with positive stainings for SOX-10 and focal S-100 and negative staining for cytokeratin CAM 5.2, epithelial membrane antigen (EMA), smooth muscle actin, CD10, HMB-45, 34ßE12, and CD34. Final results allowed us to consider a high-grade spindle cell, epithelioid and pleomorphic sarcoma with chondromyxoid areas that favor a high-grade origin peripheral neural disease. However, we consider that it would also have benefited from performing additional markers such as GLUT-1 and Claudin-1 associated with malignant perineural differentiation (Fig. 2b).

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Due to the characteristics of the lesion, the initial tumor size, and the histological subtype, the administration of adjuvant RT was considered by employing an intensity-modulated RT technique with fractionation of 2 Gy up to a total dose of 60 Gy with subsequent adjuvant with MAI scheme (doxorubicin, ifosfamide, and mesna). Currently, the patient is receiving the second cycle of systemic therapy with good compliance, without dose-limiting toxicity and toxicity due to alopecia, grade 1 gastrointestinal symptoms after doxorubicin administration. At the moment, no hematological toxicity has been documented.

Discussion

Approximately 25% of patients with soft tissue sarcomas develop distant metastatic disease even after curative resection of the primary tumor. Metastasis-free survival at 5 years is registered in 43% for tumors that present a high histological grade, tumor size greater than 5 cm, those found in the depth of the fascia, and not reported data exists for MPNS breast sarcomas. For that reason, a multidisciplinary and individualized approach is essential [9]. In about 70% of cases, metastases occur to the lung [10].

Clinical Recognition and Diagnostic Approach

Initial evaluation for MPNS sarcomas of the breast includes the same imaging studies used in other women who present with symptoms of a breast nodule: mammography, breast ultrasonography, and contrasting breast magnetic resonance imaging, the latter being the standard because it allows assessing for the extent of the disease and planning surgical approaches [3].

The most common finding on mammography is a single, oval, hyperdense mass with indistinguishable or circumscribed margins with or without calcifications or spiculated lesions [2, 4, 11].

By ultrasound, most sarcomas of the breast are hypoechoic and without the presence of posterior acoustic shadowing [11]. Magnetic resonance imaging generally identifies oval, heterogeneous masses with irregular margins, which generate hypointense signals on T1 and hyperintense on T2 [11].

Pathology, Diagnosis, and Presentation

An accurate histopathological diagnosis is essential since the management of epithelial malignancy differs profoundly from that of breast sarcomas and because the histological subtypes of sarcomas can influence important clinical decisions requiring multidisciplinary and personalized management [10]. For correct histopathological characterization for MPNS breast sarcomas, differential diagnoses must be considered, such as (1) phyllodes tumor, excluded from breast sarcomas due to the presence of a benign epithelial component, (2) metaplastic breast carcinomas, which they represent a varied combination of a poorly differentiated adenocarcinoma, with sarcomatous mesenchymal components, (3) inflammatory carcinomas, (4) mammary lymphomas, among others [8].

Malignant peripheral neural sheath tumors morphologically resemble fibrosarcomas due to the presence of spindle cells in a matrix of myxoid areas associated with cells with wavy nuclear contours [8]. MPNS of the breast are sporadic o associated with neurofibromatosis, and in those that involve deeper tissues, their prognosis depends on its complete removal [12].

In this setting, fine needle aspiration biopsy has limited use since it does not help to establish either subtype or histological grade. The ideal biopsy in every breast lump is the tru-cut/core biopsy, and if for some reason, tru-cut/core biopsy is not available, surgical removal in terms of incisional biopsy can be considered and should be oriented in a way that allows biopsy scar to be removed entirely until definitive surgical treatment.

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Immunohistochemistry

The estimated lifetime risk of being diagnosed with a MPNS breast sarcoma is completely unknown [4]. MPNS sarcomas of the breast, such as the one found in the patient, are considered a highly aggressive histological subtype. Predominantly, they appear in the extremities from myelinated Schwann cells that surround the axons of neurons. They generally develop sporadically (50%) in young adults and older adults or in association with neurofibromatosis type 1 (NF1), in which an overactivation of the Ras gene and signaling pathway predominates.

As a histological subgroup of soft tissue, sarcomas have complex karyotypes characterized by genetic alterations of CDKN2A and the repressor complex 2 PRC2, containing SUZ12, or EED. The inactivation of PRC2 leads to the loss of the triple methylation of histone H3 to lysine 27, which generates a change in gene expression and determines in itself a poor prognostic marker for survival [9].

Typically, the PRC2 complex represses multiple genes in the cyclin-dependent kinase (CDK) pathway, including CDKN2A and the genes encoding cyclins D1 and E1, CCND1, and CCNE1. Tumor development is through the abolition of RB1 activity, the inactivation of TP53 and the loss of CKD inhibitors, and/or the amplification of cyclin E1 expression [9].

By immunohistochemistry, it should be taken into account that normal Schwann cells have positive staining for protein *S-100*, *SOX-10* (SYR [sex-determining region Y] – box 10), *CD-57*, *PGP 9.5* (protein gene product 9.5), *laminin*, *calretinin*, and *E-cadherin* and negative staining for *EMA*, *Glut-1*, *claudin-1*, actin, and various cytokeratins. In contrast, normal perineural cells are characteristically positive for *EMA*, *Glut-1*, *claudin-1* and negative for the *S-100* protein. It is also important to highlight that MPNSTs are positive only for the *S-100* protein in a focal pattern; if it is strong and diffuse, it should be suspected that the diagnosis is not a malignant tumor of the peripheral nerve sheath but possibly a cellular schwannoma or metastatic melanoma [13]. In our case, the focal pattern and strong positivity for the *S-100* and *SOX-10* staining are associated with characteristics of a malignant tumor of the peripheral nerve sheath of the epithelioid type with lobulated growth, epithelioid cells, eosinophilic cytoplasm, and myxoid extracellular matrix confirmed the diagnosis.

Staging Systems

There have been inconsistencies and some controversy in the reporting and classification of breast sarcomas. Many published series include patients with pathologies such as dermatofibrosarcomas protuberans, carcinosarcoma, and phyllodes tumors, which fall outside the strict definition of sarcoma.

The most commonly used system for breast sarcomas is the American Joint Committee on Cancer staging system [14]. Histological grade, tumor size, nodal involvement, and distant metastases contribute to this system. However, its most important limitation is the exclusion of specific histotypes, making it impossible to individualize the patient, and they are potentially less specific than nomograms [10]. Breast carcinoma staging system is not very helpful for breast sarcoma as nodal metastases are rare in soft tissue sarcomas [5, 14, 15]. Additionally, the definition of the thoracic wall must be taken into account for the classification of breast tumors, which includes the ribs, intercostal muscles, the serratus anterior muscle but not the pectoral muscle, so its compromise in the absence of invasion of the structures mentioned above does not constitute an invasion of the thoracic wall, and its characterization then relies on the tumor size. For this reason, breast sarcoma is considered and classified according to its location and using the AJCC staging system for thoracic location (also used for phyllodes tumor staging) [16]. As for MPNS breast sarcomas, no classification systems exist specifically for this subtype.

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Treatment

The Sarculator (www.sarculator.com) is an online technological tool used to stratify the risk of distant metastasis and overall survival (OS), obtaining an accurate prognosis and staging in patients with soft tissue sarcoma in whom adjuvant or neoadjuvant chemotherapy is proposed. However, in our case, we found a limitation to using it because the system was constructed only with patients with soft tissue sarcoma of the extremities [17].

Surgical Therapy

Complete surgical excision with negative margins is the primary goal, as is seen in soft tissue sarcomas. Complete surgical removal allows achieving adequate local control and the potential of curative treatment [12].

Total mastectomy is the gold standard for surgical therapy in breast sarcomas, and we believe that it will become the usual practice in MPNS sarcomas of the breast, especially in masses greater than 5 cm; axillary regional node dissection is not indicated since they are not usually affected (they are reactively enlarged) and the mode of dissemination, like other sarcomas, is primarily hematogenous [1, 18] except in osteosarcomas, alveolar sarcoma, Ewing's sarcoma, and rhabdomyosarcomas.

Chemotherapy

No prospective clinical trials are evaluating the benefit of adjuvant chemotherapy in MPNS sarcomas of the breast, unless the tumor is superficial, small and low grade [1]. For this reason, treatment recommendations on chemotherapy are generally derived from clinical trials of soft tissue sarcomas of the extremities and/or trunk [18] and have an impact on treating metastatic disease and downstaging unresectable primaries as neoadjuvant setting [1, 12]. The prognosis is poor, with data needed to calculate median survival or prognosis of MPNS sarcomas of the breast. However, the initial tumor size, site of origin, surgical resection with free edges, and increased mitotic activity could alarm for poor response.

Currently, chemotherapy regimens used relies on the evidence derived from the experience of the Italian sarcoma group of Gronchi et al. [19] on soft tissue sarcomas. They propose the management with adjuvant therapy with a regimen of 3 total doses of epirubicin associated with ifosfamide, with an absolute benefit on average of 20% for relapse-free survival and OS at 46 months of 0.89 and 0.64 (log-rank $p = 0.033$) compared with another type of regimen. Most described toxicities included neutropenia (86%), anemia (24%), and thrombocytopenia (21%) being the most common [19].

On the other hand, this same author demonstrated that neoadjuvant chemotherapy with a "conventional regimen" including anthracycline plus ifosfamide was superior to chemotherapy guided by histological subtype, demonstrating an advantage in OS and time to relapse in patients who received neoadjuvant therapy with high-risk characteristics [20]. Disease-free survival at 46 months is 62% (95% CI: 48–77) in the standard chemotherapy group and 38% (22–55) in the chemotherapy group according to histological type (log-rank $p = 0.004$, HR 2.00, 95% CI: 1.22–3.26; $p = 0.006$) [20].

Given the unclear response rate to chemotherapy, neoadjuvant therapy is recommended only for large or histologically classified high-grade tumors in which negative margins are considered complex [2, 21]. Like other sarcomas, recommended regimens generally include anthracyclines associated with ifosfamide and for MNPS sarcomas of the breast the optimum chemotherapy is yet to be discovered, some studies propose using imatinib with a response rate around 17% [22], and other trials have failed to produce and objective response with tipifarnib and sorafenib. Table 1 resumes case reports publish and treatment specifications.

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Table 1. Case reports on malignant peripheral nerve sheath sarcoma of the breast

Author	Age, yr	Sex	Sporadic/genetic	Tumor size, cm	Axillary involvement	Treatment	Distant metastases
Hauser et al. [28]	27	F	Sporadic	1.2	No	Wide local excision followed by RT (50 Gy over 5 weeks) followed by chemotherapy with doxorubicin, ifosfamide, and dacarbazine	Sarcomatous pleuritis (10 months after surgery)
Malas et al. [18]	71	F	NF1	6	No	Mastectomy with axillary clearance followed by RT	No
Berrada et al. [29]	26	F	Sporadic	8	No	Mastectomy with axillary clearance	Lung and bones (after 11 months)
Medina-Franco et al. [30]	4	F	NF1	2.5	No	Wide local excision plus RT	Not reported
Elsaify et al. [31]	18	F	Sporadic	4	No	Wide local excision plus RT	No
Thanapaisal et al. [32]	19	F	Sporadic	7	No	Simple mastectomy plus RT	Not reported
Dhingra et al. [33]	38	F	Sporadic	3	No	Lumpectomy	Not reported
Woo et al. [34]	56	F	Sporadic	29	No	Modified radical mastectomy and axillary dissection	No
Wnag et al. [35]	62	M	Sporadic	2.6	No	Simple mastectomy followed by RT	Not reported
Yi et al. [12]	59	F	Sporadic	2.5	No	Wide local excision followed by RT	No
AKhator et al. [36]	41	F	NF1	10	No	Modified radical mastectomy and axillary dissection	No, but local recurrence after 9 months
Chalkoo et al. [37]	60	F	Sporadic	26	No	Simple mastectomy with axillary clearance	No
Shuayb and Begum [1]	16	F	Sporadic	11	No	Wide local excision and chemotherapy	No
Miyazaki et al. [2]	52	F	Sporadic	10	No	Neoadjuvant chemotherapy (ifosfamide plus doxorubicin) Simple mastectomy with axillary clearance	No

Adapted from Shuayb and Begum [1]. Unusual primary breast cancer – MPNST: a case report and review of the literature.
F, female; info, information; M, male; NF1, neurofibromatosis 1; RT, radiation therapy.

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Radiotherapy

The benefit of adjuvant RT has not been established in the management of MNPS sarcomas of the breast [4]. Some literature suggests a positive effect in the prevention of local recurrence, without a significant impact on OS [5]. However, much of the information is contradictory and comes from retrospective studies evaluating the experience in a single institution [23, 24]. Given the heterogeneity in the selection of treatment and the high rate of local recurrence, there are no definitive conclusions in this regard, as well as no consensus about specific risk factors for local recurrence that support this therapy (tumor size >5 cm, high histological grade, positive margins not susceptible to enlargement?) [7, 9]. Most of the experience is extrapolated from controlled clinical trials (CCT) of sarcomas of the extremities. To date, there are no CCTs in these specific subjects.

Some institutions have evaluated their particular experience, for example, in a series from the M.D. Anderson Cancer Center, administration of adjuvant RT to 59 patients with sarcomas of the breast did not show a statistically significant benefit in local recurrence. However, the low number of patients is likely partly responsible for this result [25]. Finally, when administering adjuvant RT to patients MPNS sarcomas of the breast, the treatment must ensure an efficient target area of coverage with high doses, generally between 50 and 60 Gy, to guarantee better local control [26].

Differential Diagnosis

Tumors with unique histopathological characteristics, especially if their glandular component can be partially or replaced by nonglandular components that can differentiate into squamous cells, spindle cells, chondroid components, and other lines, are configuring different histological variants and in our case. Specifically, metaplastic carcinoma with mesenchymal differentiation is of importance (it has mixtures of cartilaginous, bone, muscle, or neuroglial tissue) in which the search for a carcinomatous component prevails to perform the differential diagnosis. In cases where this finding is not revealed, characterization by immunohistochemistry becomes relevant [27].

All variants of metaplastic carcinoma are negative for estrogen receptors, progesterone, and overexpression for HER-2/neu. They are positive by immunohistochemistry for high molecular weight cytokeratins including CK5/6, CK7 (approximately 30–60% positive), CD10 (94% positive in the presence of spindle cells), 34ßE12, p63 (86.7% sensitivity, and 99.4% specificity) [27].

Conclusions

For patients with MPNS sarcomas of the breast, surgery continues to be the standard management therapy and is the only therapeutic option that seeks a curative potential. Adjuvant chemotherapy for high-grade aggressive lesions is an alternative treatment without clear evidence to support this practice and should always be discussed in a multidisciplinary team, establishing risks and possible benefits according to the tumor profile and patient comorbidities. In our case, there are no reports in the literature on the median survival or prognosis of malignant tumors of the peripheral neural sheath of the breast.

Statement of Ethics

Ethical approval is no required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient, and she approved to publish medical information and photographs that never reveal her identity.

Conflict of Interest Statement

None author in this manuscript has direct or indirect financial interest, is currently employed by, or is consultant to or under contract to a proponent neither has ownership interest.

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Author Contributions

All authors contributed to the preparation of the manuscript and approved its publication. Professor Ricardo Elías Brugés helped review the content according to actual clinical evidence and made contributions correcting grammatical errors. Professor Fernando Contreras reviewed the content and advised on the manuscript structure and correcting grammatical errors. Doctor Martin Ignacio Zapata Laguado and Doctor Ximena Briceño helped write the manuscript and made valuable contributions regarding the information on surgical treatment. Doctor Yency Johana Forero structured the manuscript and translated its content.

Data Availability Statement

All data underlying the results are available as part of the article, and no additional sources of data are required. The information gathered in this manuscript is supported by the patient's medical record as for academic information it relies on bibliographical references.

References

1 Shuayb M, Begum R. Unusual primary breast cancer – malignant peripheral nerve sheath tumor: a case report and review of the literature. J Med Case Rep. 2017;11(1):161–7.
2 Miyazaki C, Shiozawa M, Koike R, Ogihara K, Sasaki Y, Shiba S, et al. Neoadjuvant chemotherapy for primary sarcoma of the breast: a case report. J Med Case Rep. 2019;13(1):1–6.
3 Pencavel TD, Hayes A. Breast sarcoma: a review of diagnosis and management. Int J Surg. 2009;7(1):20–3.
4 Hsu C, McCloskey SA, Peddi PF. Management of breast sarcoma. Surg Clin North Am. 2016;96(5):1047–58.
5 Al-Benna S, Poggemann K, Steinau HU, Steinstraesser L. Diagnosis and management of primary breast sarcoma. Breast Cancer Res Treat. 2010;122(3):619–26.
6 Voutsadakis IA, Zaman K, Leyvraz S, Hsu C, McCloskey SA, Peddi PF, et al. Management of breast sarcoma. Radiol Bras. 2016;20(5):1047–58.
7 Yin M, MacKley HB, Drabick JJ, Harvey HA. Primary female breast sarcoma: clinicopathological features, treatment and prognosis. Sci Rep. 2016;6:31497.
8 Idowu MO, Shah PA, Hackney MH, Grimes MM, Geyer CD, Arthur DW, et al., editor. Diagnosis and management of breast tumors. 1st ed. Vancuver: Springer; 2017. p. 261.
9 Kohlmeyer JL, Gordon DJ, Tanas MR, Monga V, Dodd RD, Quelle DE. CDKs in sarcoma: mediators of disease and emerging therapeutic targets. Int J Mol Sci. 2020;21(8):1–30.
10 Gamboa AC, Gronchi A, Cardona K. Soft-tissue sarcoma in adults: an update on the current state of histiotype-specific management in an era of personalized medicine. CA Cancer J Clin. 2020;70(3):200–29.
11 Matsumoto RAEK, Hsieh SJK, Chala LF, de Mello GGN, de Barros N. Sarcomas of the breast: findings on mammography, ultrasoundand magnetic resonance imaging. Radiol Bras. 2018;51(6):401–6.

12 Yi JM, Moon EJ, Oh SJ, Lee A, Suh YJ, Baek JN, et al. Malignant peripheral nerve sheath tumor of the breast in a patient without neurofibromatosis: a case report. J Breast Cancer. 2009;12(3):223–6.
13 Camacho-Partida IG, Ortiz-Hidalgo C. El diagnóstico histológico y la inmunohistoquímica de las neoplasias de la vaina del nervio periférico correspondencia patología revista latinoamericana. Patologia. 2017;55(4): 445–64. Available from: www.revistapatologia.com.
14 Tanaka K, Tsumura H. Eighth edition of the American Joint Committee on Cancer staging system for soft tissue sarcoma of the trunk and extremity: in search of a better staging system. Ann Transl Med. 2019;7(Suppl 1): S11.
15 Daigeler A, Kuhnen C, Moritz R, Stricker I, Goertz O, Tilkorn D, et al. Lymph node metastases in soft tissue sarcomas-a single center analysis of 1,597 patients. Langenbeck's Arch Surg. 2009;394(2):321–9.
16 MR. MFC. Staging soft tissue sarcomas of trunk and extremities [Internet]. 2021. [cited 2021 Jul 27]. Available from: www.pahtologyoutlines.com. www.pathologyoutlines.com/topic/softtissuesstagingtrunkextremities.html.
17 Callegaro D, Miceli R, Bonvalot S, Ferguson PC, Strauss DC, van Praag VVM, et al. Development and external validation of a dynamic prognostic nomogram for primary extremity soft tissue sarcoma survivors. EClinicalMedicine. 2019;17:100215.
18 Malas S, Krawitz HE, Sur RK, Uijs RR, Nayler SJ, Victor Levin C. Von recklinghausen's disease associated with a primary malignant schwannoma of the breast. J Surg Oncol. 1995;59(4):273–5.
19 Gronchi A, Ferrari S, Quagliuolo V, Broto JM, Lopez-Pousa A, Grignani G, et al. Sarcoma full-dose neoadjuvant anthracycline + ifosfamide chemotherapy is associated with a relapse free survival (RFS) and overall survival (OS) benefit in localized high-risk adult soft tissue sarcomas (STS) of the extremities and trunk wall: Interim analysis of a prospective randomized trial. Ann Oncol. 2016;27(Suppl 6):vi587.
20 Gronchi A, Ferrari S, Quagliuolo V, Broto JM, Pousa AL, Grignani G, et al. Histotype-tailored neoadjuvant chemotherapy versus standard chemotherapy in patients with high-risk soft-tissue sarcomas (ISG-STS 1001): an international, open-label, randomised, controlled, phase 3, multicentre trial. Lancet Oncol. 2017;18(6): 812–22.
21 Gronchi A, Palmerini E, Quagliuolo V, Broto JM, Lopez Pousa A, Grignani G, et al. Neoadjuvant chemotherapy in high-risk soft tissue sarcomas: final results of a randomized trial from Italian (ISG), Spanish (GEIS), French (FSG), and Polish (PSG) Sarcoma Groups. J Clin Oncol. 2020;38(19):2178–86.
22 Robertson KA, Nalepa G, Yang F, Bowers DC, Ho CY, Hutchins GD, et al. Imatinib mesylate for plexiform neurofibromas in patients with neurofibromatosis type 1: a phase 2 trial. Lancet Oncol. 2012;13(12):1218–24.
23 Holm M, Aggerholm-Pedersen N, Mele M, Jørgensen P, Baerentzen S, Safwat A. Primary breast sarcoma: a retrospective study over 35 years from a single institution. Acta Oncol. 2016;55(5):584–90.
24 May DS, Stroup NE. The incidence of sarcomas of the breast among women in the United States, 1973–1986. Plast Reconstr Surg. 1991;87(1):193–4.
25 Barrow BJ, Janjan NA, Gutman H, Benjamin RS, Allen P, Romsdahl MM, et al. Role of radiotherapy in sarcoma of the breast: a retrospective review of the M.D. Anderson experience. Radiother Oncol. 1999;52(2):173–8.
26 Cozzolino M, Oliviero C, D'Andrea B, Guglielmi G, Califano G, Caivano R, et al. The role of adjuvant radiotherapy for a case of primary breast sarcoma: a plan comparison between three modern techniques and a review of the literature. Case Rep Med. 2018;2018:4137943.
27 McMullen ER, Zoumberos NA, Kleer CG. Metaplastic breast carcinoma: update on histopathology and molecular alterations. Arch Pathol Lab Med. 2019;143(12):1492–6.
28 Hauser H, Beham A, Steindorfer P, Schmidt F, Smola MG. Malignant schwannoma of the breast. Langenbeck's Arch Surg. 1995;380:350–3.
29 Berrada R, Chahtane A, Lakhdar A, Elhanchi Z, Ferhati D, Baidada A, et al. Malignant schwannoma of the breast. A case report. J Gynecol Obs Biol Reprod. 1998;27(4):441–4.
30 Medina-Franco H, Gamboa-Dominguez A, de La Medina AR. Malignant peripheral nerve sheath tumor of the breast. Breast J. 2003;(9):330–2.
31 Elsaify W, Elsaify M, Melek R. De novo malignant peripheral nerve sheath tumor of the breast: case report number one. Eur Surg. 2007;39:192–5.
32 Thanapaisal C, Koonmee S, Siritunyaporn S. Malignant peripheral nerve sheath tumor of breast in patient without Von Recklinghausen's neurofibromatosis: a case report. J Med Assoc Thai. 2006;3:377–9.
33 Dhingra K.K, Mandal S, Roy S, Khurana N. Malignant peripheral nerve sheath tumor of the breast: case report. World J Surg Onc. 2007;5(1).
34 Woo OH, Yong HS, Lee JB, Kim A, Koo BH, Kang EY. A giant malignant peripheral nerve sheath tumour of the breast: CT and pathological findings. Br J Radiol. 2007;80:44–7.
35 Wang H, Ge J, Chen L, Xie P, Chen F, Chen Y. Melanocytic malignant peripheral nerve sheath tumor of the male breast. Breast Care. 2009;4:260–2.
36 Akhator A, Oside CP, Inikori A, Nwanchokor FN. Malignant peripheral nerve sheath tumour: a rare tumour of the breast. Online J Health Allied Scs. 2010;9(1).
37 Chalkoo M, Ahangar S, Laharwal AR, Patloo AM, Mohd A, Dar SA. Primary malignant peripheral nerve sheath tumor of the breast—a case report. Surg Sci. 2011;2(3):137–9.