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Case Report

Epithelioid Malignant Peripheral Nerve Sheath Tumor of the Breast with Breast Cancer in the Contralateral Breast: A Case Report

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Keywords
Malignant peripheral nerve sheath tumor · Breast · Epithelioid type

Abstract
Introduction: Malignant peripheral nerve sheath tumors (MPNSTs) are common in the peripheral nerves of the head, neck, and limbs, with few reports of their occurrence in the breasts, and the epithelioid type is rare. Here, we aimed to report a case of an epithelioid MPNST of the breast. ***Case Presentation:*** A 76-year-old woman presented with bilateral breast masses. Pathological findings showed a 60-mm invasive ductal carcinoma (T3N0M0 stage IIB) on the right breast and an epithelioid MPNST on the left breast. After surgical resection, the patient was treated with endocrine therapy alone for right breast cancer, and no recurrence was observed 4 years after surgery. ***Conclusion:*** Reports of MPNSTs in the breasts are rare. The pathological analysis showed atypia of spindle cells, positive staining for vimentin, S100, SOX10, and epithelial-like cells, and positive staining for cytokeratin AE1/AE3. H3K27me3 is reportedly absent in typical MPNSTs; however, it is expressed in epithelioid types. It sometimes occurs in patients with a germline mutation in *SMARCB1/INI1*, where INI1 is absent in tumor cells. In this case, the tumor cells expressed H3K27me3 and also maintained INI1.

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Introduction

Of the 12,608 cases of malignant soft tissue tumors registered in the National Soft Tissue Tumor Registry in Japan between 2006 and 2015, 567 were malignant peripheral nerve sheath tumors (MPNSTs) that are common in the peripheral nerves of the head, neck, and limbs, with few reports of their occurrence in the breast. In addition, a rare subtype of this tumor is epithelioid MPNST. This is a case of a right breast invasive ductal carcinoma complicated by a left breast epithelioid MPNST.

Case Presentation

A 76-year-old woman was admitted to our hospital with enlarged bilateral breast masses that she had been aware of in the past year. Her mother was diagnosed with stomach cancer. She had no family history of neurofibromatosis or breast, ovarian, pancreatic, or prostate cancer. She had no café-au-lait spots on the body, Lisch nodules, or cutaneous neurofibromas. The right and left breast masses measured 40 and 80 mm, respectively. Both were elastic, hard, and had reddish skin. Blood tests revealed no abnormalities. Mammography revealed a round, indistinct margin, high-density mass on the right breast (BI-RADS 4C) and an irregular shape, indistinct margin, high-density mass on the left breast (BI-RADS 4C) (Fig. 1a, b).

Breast ultrasound showed a 41-mm intracystic mass in the right breast (BI-RADS 4C, Fig. 2a) and a 68-mm, irregular shape, circumscribed margin, and hypoechoic mass in the left breast (BI-RADS 5, Fig. 2b). Breast contrast magnetic resonance image showed a cystic mass in the right breast with early dense staining in the surrounding area (BI-RADS 4C, Fig. 3a), a left breast lobulated mass with rim enhancement, and the tumor compressing the mammary gland (BI-RADS 5, Fig. 3b) Preoperative biopsy of the right breast showed invasive ductal carcinoma (ER: Allred score TS8 = PS5+IS3, J-score = 3b; PgR: Allred score TS8 = PS5+IS3, J-score = 3b, HER2 1+, Ki67: 7%). A preoperative needle biopsy of the left breast revealed a mesenchymal tumor. Both tumors were treated surgically. Similarly, right total mastectomy, sentinel lymph node biopsy, and left total mastectomy were performed. Histopathological findings showed that the right breast mass was an invasive ductal carcinoma (pT3N0M0 stage II B, solid type, 50 × 42 × 60 mm). The left breast mass was 75 × 70 × 60 mm and macroscopically yellowish-white, elastic, and hard tumor with some lobes, with scattered dot-like hemorrhages and no necrosis (Fig. 4). Histological examination revealed spindle cells with spindle-shaped nuclei and nuclear atypia, with numerous mitotic figures and the mild invasion of the mammary gland tissue at the periphery (Fig. 5a). In addition, cells with cuboidal epithelial morphology and enlarged nuclei with a wide eosinophilic cytoplasm were observed (Fig. 5b).

Immunohistochemical examination showed that proliferating cells were positive for vimentin, S100, and SOX10, suggesting a nerve tumor. Cells with epithelial morphology were partially positive for cytokeratin (AE1/AE3) staining. H3K27me3 expression was also maintained (Fig. 5c) These results prompted the diagnosis of epithelioid MPNST, a subtype of MPNST (pT2, stage IIIA, tumor differentiation score 3, mitotic count score 1, tumor necrosis score 1, and histological malignancy grade 2). Oral anastrozole was administered as postoperative endocrine therapy for right breast cancer. No adjuvant therapy was administered for the epithelioid MPNST in the left breast. It has been 3 years since the surgery, and there has been no recurrence of the right breast cancer or epithelioid MPNST of the left breast.

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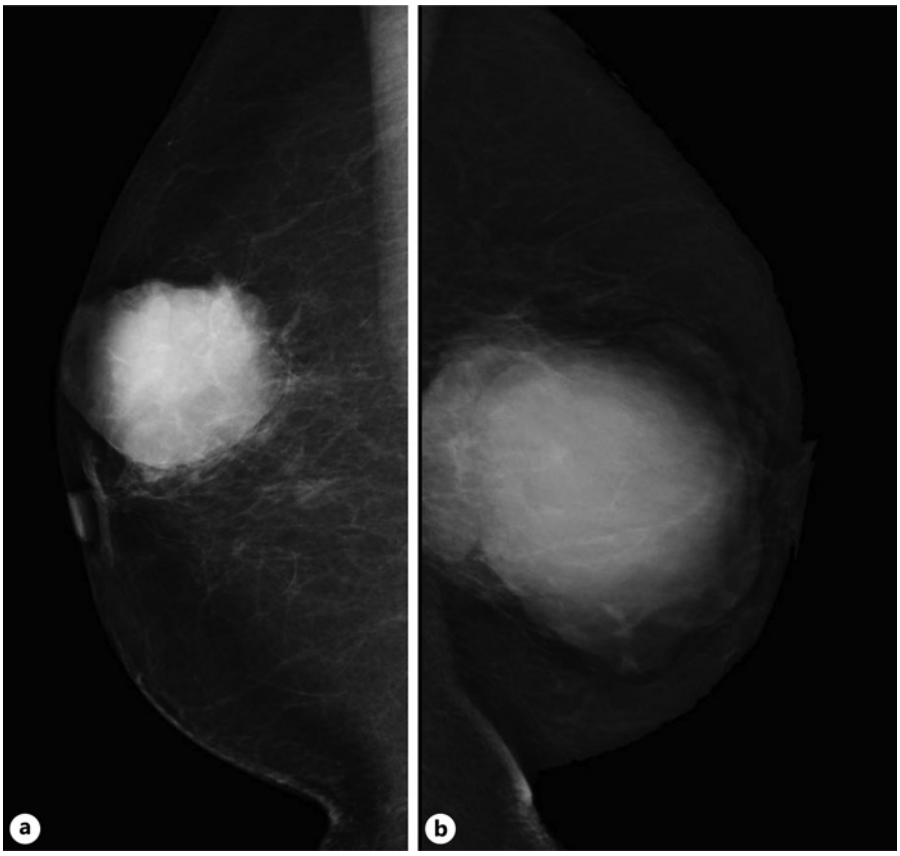

Fig. 1. Mammography. **a** Right MLO: round, high-density mass with an unclear border. **b** Left MLO: lobulated, high-density mass with an unclear border.

Discussion

MPNSTs are a type of malignant soft tissue tumor that affects 5 per million people per year. They originate from Schwann cells, and approximately half of these cases are patients with type I neurofibromatosis (NF1) [1]. There were 567 cases of MPNSTs registered in the National Soft Tissue Tumor Registry in Japan between 2006 and 2015 [2]. Epithelioid MPNSTs constituted less than 5% of these cases, and 18 cases, including our case, have been reported [3–18]. These are summarized in Table 1. Half of the patients with typical MPNSTs have NF1, whereas epithelioid types are less associated with NF1. It usually occurs superficially, such as on the body surface, facilitating its early detection compared with that of typical types. Of the 18 cases summarized in the table, 4 were patients with NF1. Ten cases occurred on the surface of the body. Vickie et al. [19] reported that of 63 cases of epithelioid MPNSTs, one was NF1, and the tumor sites were the dermis in 5 cases, subcutaneous tissue in 38 cases, muscle layer in 15 cases, and deep organs in 5 cases. Pathological findings of typical MPNSTs showed proliferation of atypical spindle cells, and immunohistochemical staining indicated partial positivity for S100 protein and cytokeratin negativity, whereas epithelioid MPNSTs were characterized by diffuse strong positivity for S100 protein [20] and cytokeratin positivity [21]. H3K27me3 is reportedly absent in typical MPNSTs and expressed in epithelioid types [22]. H3K27me3 was also found to be expressed in this case. In addition, Carter et al. [17] reported an epithelioid MPNST in a patient with neuroblastoma-like schwannoma with a

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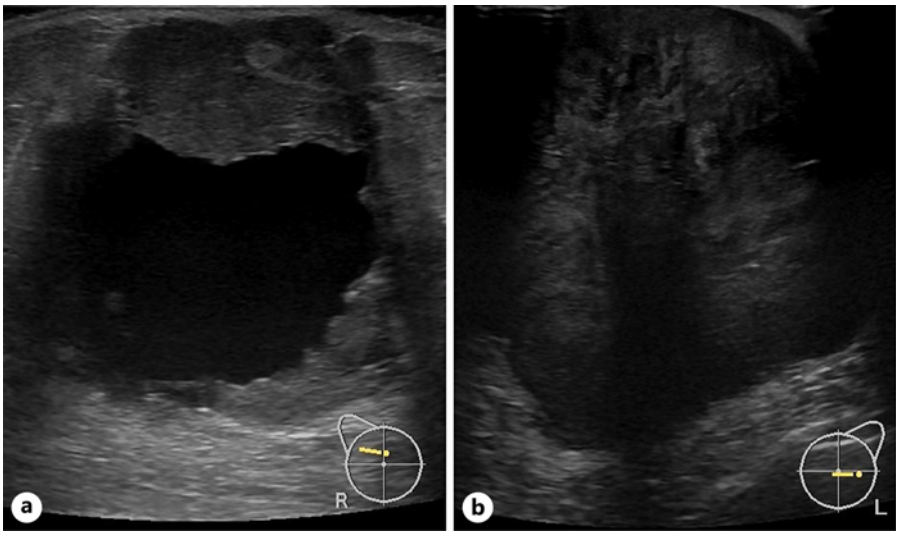

Fig. 2. Breast ultrasound. **a** A 41-mm intracystic mass of the right breast. **b** A 68-mm lobulated, clearly bordered, low-echoic mass of the left breast.

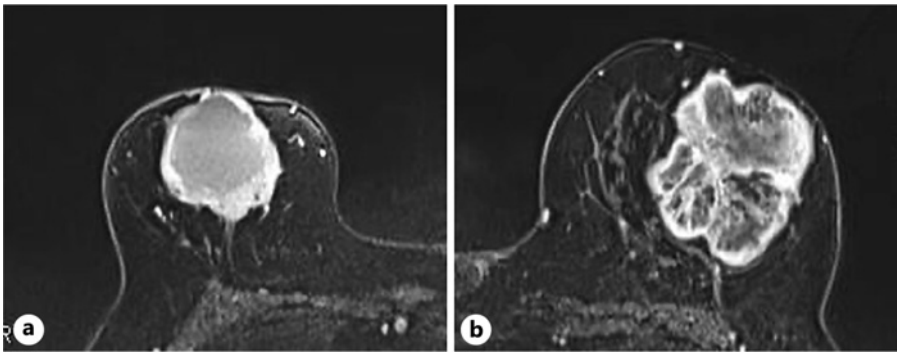

Fig. 3. Breast contrast MRI. **a** Right breast. Mass with cystic components and early staining of the surrounding solid area. **b** Left breast. Lobulated mass with contrast enhancement at the edges. Poor contrast effect inside. It compresses the mammary gland.

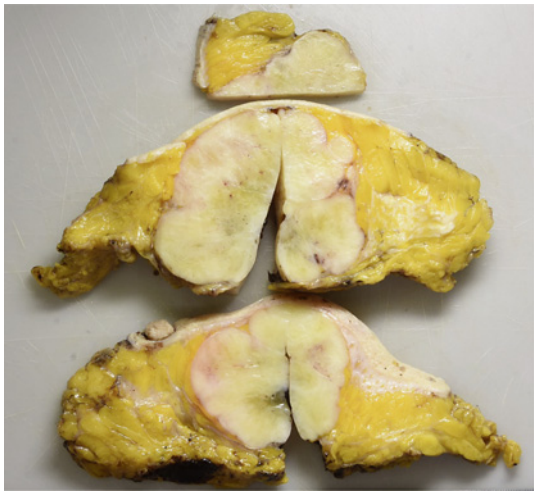

Fig. 4. Left breast epithelioid MPNST.

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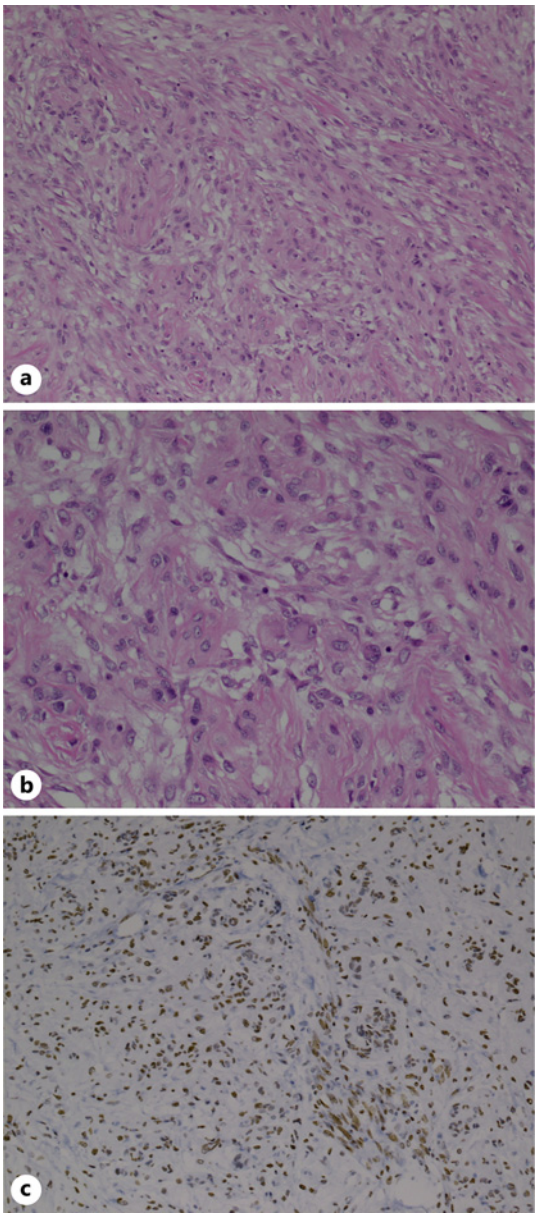

Fig. 5. Left breast epithelioid MPNST. **a** H&E staining. ×100. Dense proliferation of spindle cells with spindle nuclei with nuclear atypia and mitotic figures. **b** H&E staining. ×200. Cuboidal cells with wide cytoplasm and swollen nuclei. **c** H3K27me3 (+). ×100.

germline mutation in *SMARCB1/INI1*, and INI1 was absent in the tumor cells. In this case, INI1 was maintained in the tumor cells, and of the 18 cases summarized in the table, INI1 was absent in five out of eight (62%) involving INI1 evaluation. A similar result was reported by Vickie et al. [19], who demonstrated that INI1 was absent in 67% of epithelioid MPNSTs.

Imaging findings showed that the tumor was primarily enhanced at the periphery on contrast-enhanced MRI, with patchy contrast effects within the tumor and a nonenhanced area in the center. The tumor compressed the mammary gland and appeared different from breast cancer. The primary treatment is surgical resection. Poor prognostic factors include NF1, occurrence other than the limbs, size, high degree of dysplasia, positive resection margins, and local recurrence. Postoperative radiation therapy is effective in preventing local recurrence [2]. In this case, after surgical resection, the patient was treated with endocrine therapy alone for the right breast cancer, and no recurrence was observed 4 years after

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Table 1. Epithelioid malignant peripheral nerve sheath tumors

Author	Year	Age	Sex	Location	Size, cm	NF1	SMARCB1/INI-I	Treatment	Outcome
Lee	1997 [6]	63	F	Vulva	6 × 4 × 1.5	No	NA	Resection	Alive
Ikebe	2010 [5]	82	F	Axilla	10 × 10	No	NA	Resection	Alive
Minagawa	2011 [8]	62	M	Foot	7 × 4.3	No	NA	Resection+chemotherapy*1	Alive
Carter	2012 [17]	31	F	Leg	6.7	No	Absent	Resection	NA
Atsumi	2014 [3]	60	M	Transverse colon	14.5 × 6.6	Yes	NA	Transverse colon resection	Dead
Kusumoto	2015 [14]	70	M	Axilla	21 × 17 × 8	No	NA	Resection	Dead
Gupta	2017 [9]	40	M	Flank	9.7 × 7.5	Yes	NA	None	Dead
Du	2019 [12]	71	F	Lower back	20 × 13 × 8	Yes	NA	Resection+radiotherapy	Alive
Patra	2019 [16]	65	M	Rectum	5.5 × 3.5 × 3.5 cm	No	Retained	Resection	Alive
Patra	2019 [16]	47	F	Rectum	5 cm	No	Retained	Polypectomy, radiotherapy	Dead
Matsumoto	2020 [4]	49	F	Rectum	30 × 25 × 25	Yes	NA	Posterior pelvic exenteration	Dead
Zhang	2020 [7]	16	F	Lung	4 × 4 × 3	No	NA	Lobectomy	Dead
Heatley	2020 [18]	25	F	Thigh	2.1 × 1.1 × 1.1	No	Absent	Resection	Alive
Guzin	2021 [10]	56	F	Vagina	3 × 2 × 2.5	No	NA	Resection	Alive
Biglow	2021 [15]	47	F	Finger	0.8 × 0.5 × 0.8	No	Absent	Resection	Alive
Treeck	2022 [13]	20	F	Liver	11 cm	No	Absent	NA	NA
Qi	2023 [11]	3	M	Lumbar 5, sacral 1	4.2 × 3 × 2.1 cm	No	Absent	Resection+chemotherapy*2+radiotherapy	Alive
Our case	2025	76	F	Breast	7.5 × 7 × 6	No	Retained	Mastectomy	Alive
							NA	*1 doxorubicin+ifosfamide+mesna	
								*2 vincristine+cyclophosphamide+doxorubicin/ ifosfamide+etoposide	

NA, not available.

surgery. There have been only five reports of MPNST occurring in the breast, including cases with NF1 [23–27]. There have been no reports of breast MPNST with contralateral breast cancer, as in this case.

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Statement of Ethics

Ethical approval is not required for this study per national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000545496).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

R.F., T.Y., H.I., T.W., and A.M. treated the patients and acquired the clinical data. R.F. wrote the manuscript. T.Y. and A.M. supervised this study.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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