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Case Report

Mucoepidermoid Carcinoma of the Breast Found during Treatment of Lymphoma

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Keywords
Mucoepidermoid carcinoma · Breast · Lymphoma

Abstract
A 71-year-old woman, previously treated for malignant lymphoma, was admitted to our hospital with a tumor in the right breast. The tumor size was 2.0 cm in diameter, and the borderline was unclear. The core needle biopsy material revealed an invasive adenocarcinoma with metaplastic change. Right mastectomy and sentinel lymph node biopsy was performed. Histologically, the tumor was composed of mucus-secreting, epidermoid, and intermediate cells. These findings confirmed the diagnosis as mucoepidermoid carcinoma (MEC) of the breast. MEC is more frequently observed in the salivary glands and occurs rarely in the breast, with an incidence of approximately 0.3% of all breast cancers. Because of the rarity of the disease, the clinicopathological features and clinical outcome have not been fully investigated. The relationship between MEC of the breast and lymphoma are unclear. Here we report a rare case of MEC of the breast.

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Introduction

Mucoepidermoid carcinoma (MEC) is the most common histological type of both major and minor salivary gland neoplasms. Approximately half of these tumors occur in the major salivary glands and the other half occur in the minor salivary glands. The ratio of men to women diagnosed with MEC is three to two [1]. MEC also arises in the pancreas [2], lacrimal gland [3], skin adnexa [4], bile duct [5], intestinal mucosa [6], and breast [7]. MEC in the breast represents an unusual variant of breast cancer that accounts for about 0.3% of breast carcinomas. Predicting prognosis of MEC is difficult as it shows a wide range of low to high grade.

A previous study in 1996 showed that MEC of the salivary glands exhibits t(11;19)(q21;p13) translocation [8]. Cytological features of MEC breast tumors are similar to MEC of the salivary glands and include mucus-secreting, epidermoid, and intermediate cells. Because of the rarity of the disease, only a limited number of case series have been published, and thus, the clinicopathological features and clinical outcome of MEC of the breast have not been fully investigated. Here we report a case of MEC of the breast diagnosed by pathological assessment of the lesion.

Case Presentation

A 71-year-old Japanese postmenopausal woman was referred to us for evaluation of a tumor in the right breast. She had suffered from malignant lymphoma (diffuse, medium to large B-cell lymphoma) treated with chemotherapy consisting of eight cycles of R-CHOP and radiotherapy (total 46 Gy) to the head for the previous 3 years. She had undergone hysterectomy for myoma of the uterus at the age of 41 years. In addition, she had a medical history of hypertension and hyperlipidemia. There was no remarkable family history.

Physical examination demonstrated an elastic hard lump on palpation located in the lower lateral quadrant of the right breast. The tumor size was 2.0 cm in diameter, and the borderline was unclear. No skin change or dimpling was seen. Nipple charge was not evident. No axillary lymph node swelling was found. All laboratory data were unremarkable, and there was no increase of tumor markers such as CEA and CA15-3.

Mammography of the right breast showed an unclear mass with accumulation of calcification (Fig. 1). Ultrasonography showed a hyperechoic lesion within a hypoechoic area, with rough surface (Fig. 2). Enhanced magnetic resonance imaging revealed a mass of high intensity in the right breast (Fig. 3).

Histopathological evaluation of the core needle biopsy material revealed an invasive adenocarcinoma with metaplastic change, but definitive histological diagnosis could not be determined. There was no proliferation of atypical lymphocytes.

The patient underwent right mastectomy and sentinel lymph node biopsy. The frozen section of the sentinel lymph node was found to be free of disease by intraoperative diagnosis.

Macroscopically, cut sections revealed a white, solid, and well-circumscribed tumor measuring approximately 17 × 15 mm (Fig. 4). Histopathologically, the tumor was composed of cancer cells forming papillary or tubular structures with an abundant mucus cytoplasm, which was positive for periodic acid-Schiff staining, and accompanied by psammoma bodies (Fig. 5, Fig. 6). Squamoid cancer cells proliferated in sheet-like patterns, but intracellular

bridges or keratinization were not seen (Fig. 7). Intermediate cells were also seen (Fig. 8). In the stroma, many inflammatory cells proliferated around the tumor.

Immunohistochemical findings showed that the tumor cells were positive for cytokeratin 7, cytokeratin 5/6, cytokeratin 14, epidermal growth factor receptor, p63, and MUC-1, and negative for gross cystic disease fluid protein-15, estrogen receptor, progesterone receptor, and human epidermal growth factor receptor-2. Ki-67 labeling index was 22%. The mitotic index was one mitosis per 10 high-magnification fields. No vascular or perineural invasions were observed. Histological examination determined MEC of the breast, intermediate histological grade.

Discussion

MEC was first reported by Foote et al. [7] as a malignant epithelial neoplasm arising in major and minor salivary glands. Salivary gland MEC is the most frequent type of salivary gland tumors and represents approximately 30% of malignant tumors of salivary glands. It is characterized by a mixture of mucous-secreting, epidermoid, and intermediate cells.

Foote et al. [7] proposed two distinct forms of MEC, the low-grade form and high-grade form. Recently, Goode et al. [9] proposed a grading system in which five histopathologic features are used to define low-, intermediate-, and high-grade tumors. The 5-year survival rates in low-, intermediate-, and high-grade tumors were 97, 90, and 54%, respectively. In high-grade tumors, high Ki-67 labeling index (>10%) correlated with decreased patient survival, increased recurrence, and metastasis.

MEC is characterized by a recurrent chromosomal translocation t(11;19)(q21;p13) [8]. This alteration results in a MECT1-MAML2 fusion. The fusion transcript fuses the binding of exon 1 of mucoepidermoid carcinoma translocated 1 (MECT1), a novel gene of unknown function, at 19p13 with exons 2–5 of a novel member of the Mastermind-like gene family (MAML2) at 11q21 [10]. This fusion transcript may be specific to MEC and associated with a distinct MEC subset that exhibits favorable clinicopathologic features and an indolent clinical course [11]. Preliminary studies of other carcinoma subtypes of the breast and thyroid are negative for this fusion gene [12]. Recently, Nakano et al. [13] reported that HER2 gene amplification and an increased EGFR gene copy number were detected in high-grade MEC irrespective of MAML2 fusion status. They suggested that HER2 or EGFR gene abnormality could play an important role in the development of the progression from MAML2 fusion-positive low-/intermediate-grade to high-grade in a subset of MEC [13]. In our case, MAML2 fusion was not detected using reverse transcriptase-polymerase chain reaction.

In 1979, Patchefsky et al. [14] for the first time reported two cases of MEC of the breast. MEC of the breast is an unusual variant of breast cancer and similar to its salivary counterpart. The histological features include varying proportions of mucus-secreting, epidermoid, and intermediate cells, as recognized by the World Health Organization [15]. MEC of the breast is rare, with an incidence of approximately 0.3% of all breast cancers. Because of the rarity of the disease, only a limited number of case series have been published and thus the clinicopathological features and clinical outcome of MEC of the breast have not been fully investigated.

Horie et al. [16] described the prognosis of 23 breast MEC cases in which 4 patients died of breast cancer, 2 died of other causes, 1 patient remained alive with recurrence, and 14 patients remained alive without recurrence. Patients with low-grade MEC were disease free in the follow-up period, whereas high-grade MECs usually showed aggressive behavior with

metastasis to axillary nodes and distant organs [17]. Immunohistochemically, MUC5AC is expressed in more than 50% of high-grade tumors and MUC1 expression correlates with shorter disease-free survival [18].

According to the past reports, no case of MEC of the breast with psammoma bodies has yet been described until the current study. Psammoma bodies are typically seen in papillary adenocarcinoma of thyroid and meningioma. In MEC, the presence of psammoma bodies are frequently observed in thyroid MEC rather than salivary or pulmonary MEC [19]. Maruta et al. [20] reported that psammoma bodies may be an indicator of lymph node metastasis in papillary adenocarcinoma of thyroid. The significance is unclear, but we cannot deny the possibility of a role of psammoma bodies in MEC.

Breast lymphoma is a rare tumor. None of the imaging features of breast lymphoma are pathognomonic [21]. Because the imaging features showed atypical findings as invasive breast carcinoma in this case, and our case had a medical history of malignant lymphoma, we considered breast lymphoma as the differential diagnosis. However, histopathologically there was no proliferation of atypical lymphocytes, and thus we did not diagnose breast lymphoma.

A previous study reported a case of MEC of the parotid grand in a child with acute lymphoblastic leukemia (ALL) treated with chemotherapy and irradiation [22]. In children previously treated for ALL, second cancers of the salivary glands are most often related to previous head and neck irradiation. MEC is the most common cancer of the major salivary glands occurring after irradiation [23]. On the other hand, Gibod et al. [22] reported that MEC occurred in a patient of ALL in childhood treated without irradiation, only by chemotherapy. In the current case, she was treated with multidrug chemotherapy and irradiation to the head. The relationship between MEC of the breast and lymphoma has not been described, but the possibility of a correlation between the two remains.

In conclusion, we report herein a case of MEC of the breast. Because MEC of the breast is a rare entity, there is no standard treatment and the prognostic features are not well established. Careful follow-up of this patient is required.

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Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

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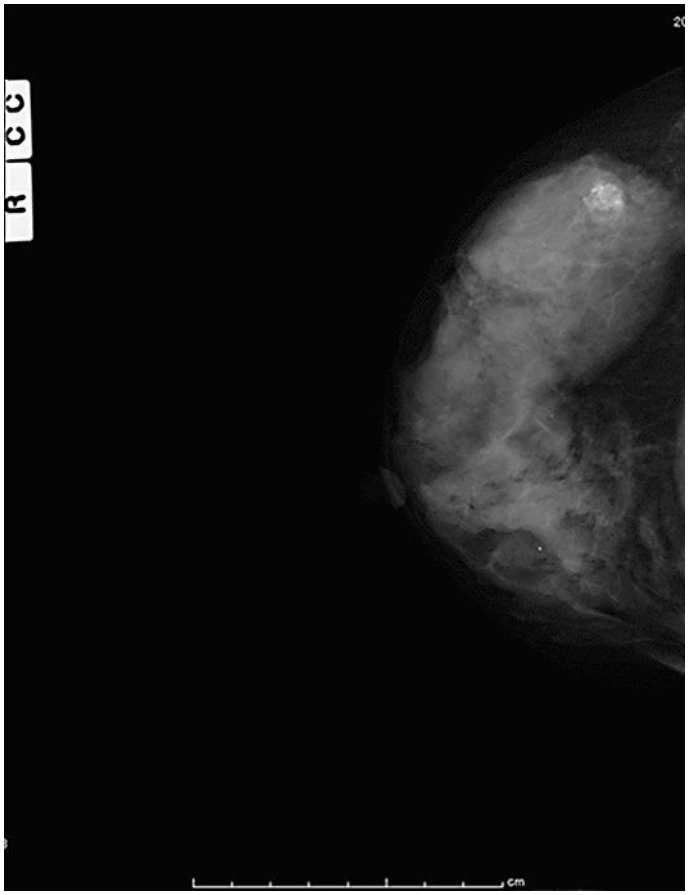

Fig. 1. Mammography showed unclear mass with accumulation of calcification.

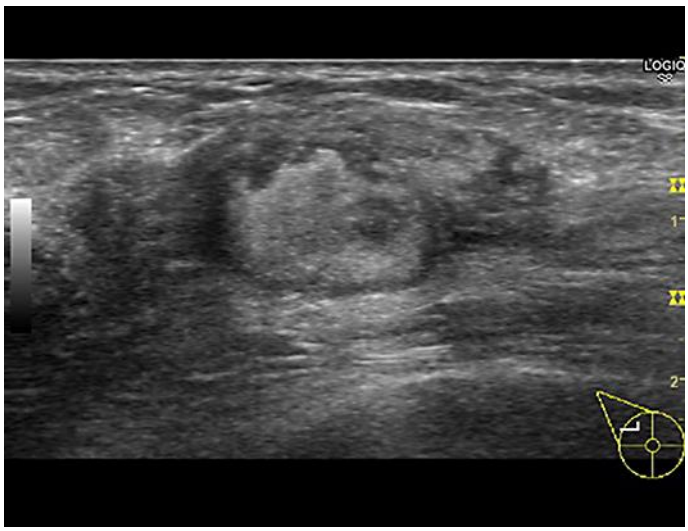

Fig. 2. Ultrasonography showed a hyperechoic lesion within a hypoechoic area, with rough surface.

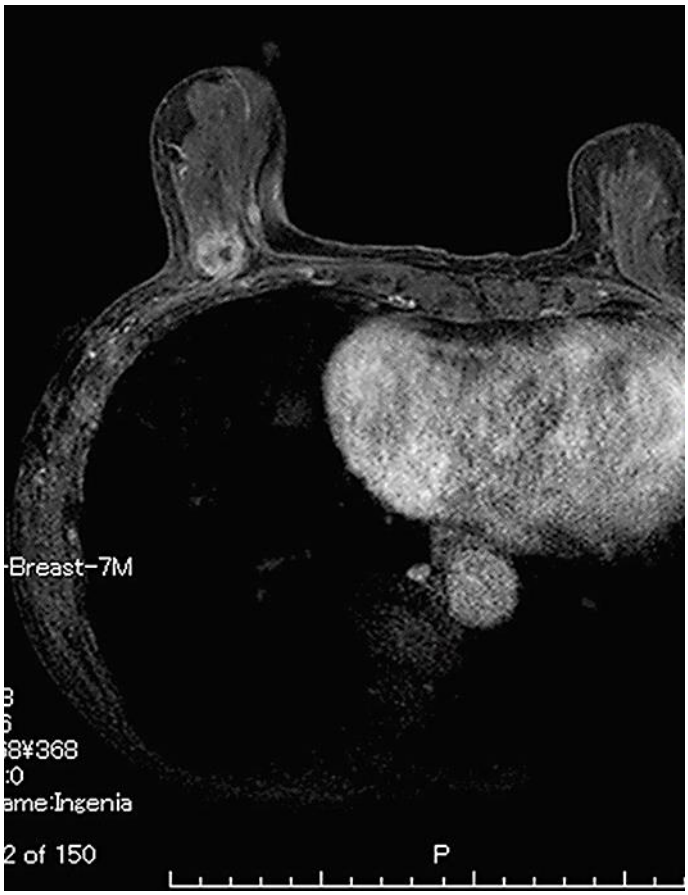

Fig. 3. Enhanced magnetic resonance imaging revealed a mass of high intensity in the right breast.

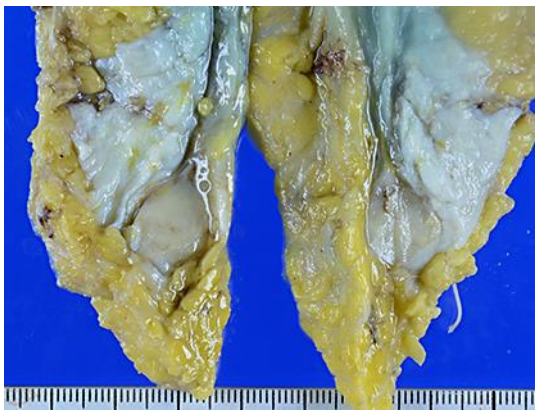

Fig. 4. Macroscopically, cut sections demonstrated white, solid, and well-circumscribed tumor.

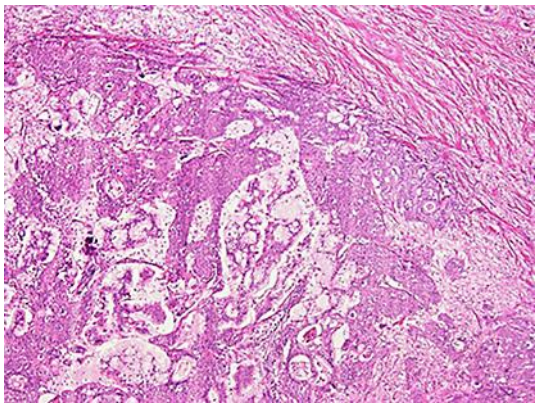

Fig. 5. Microscopically, the tumor showed predominantly solid pattern with focal mucin and psammoma body (×20).

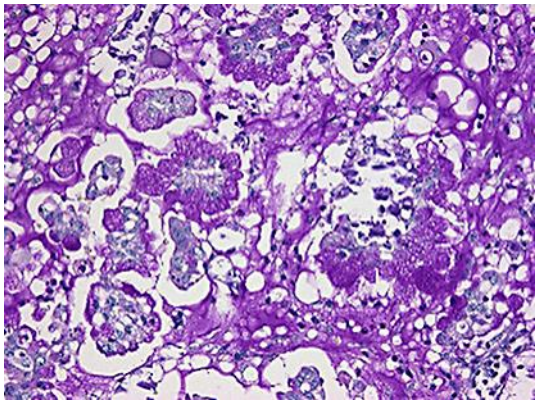

Fig. 6. The mucus-containing cancer cells formed papillary or tubular structures, which were positive for periodic acid-Schiff staining (×200).

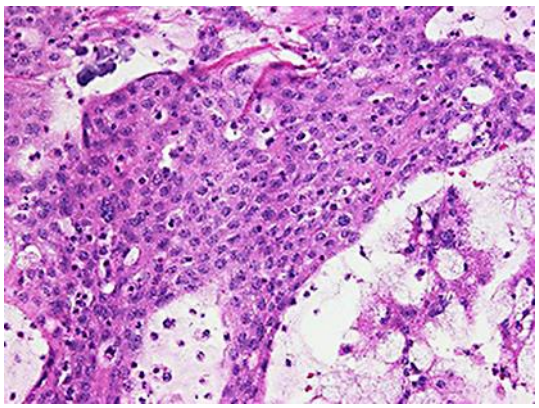

Fig. 7. Squamoid cancer cells proliferate in sheet-like patterns (×200).

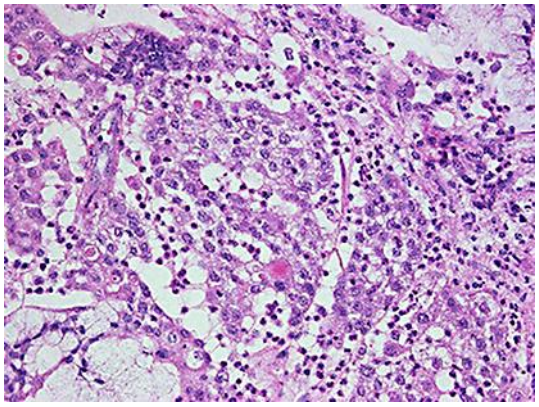

Fig. 8. Intermediate cells (×200).