

Lipid-rich carcinoma of the breast that is strongly positive for estrogen receptor: a case report and literature review

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Abstract: Lipid-rich carcinoma (LRC) of the breast is a rare breast cancer variant that accounts for <1% of all breast malignancies. It has been reported that LRCs are negative for estrogen receptor. Here, we report a case of LRC of the breast that was strongly positive for estrogen receptor and treated with endocrine adjuvant therapy. A 52-year-old postmenopausal female noticed a lump in her right breast by self-examination and presented to our hospital. Physical examination revealed an elastic 30 mm ×20 mm hard mass in the upper medial part of her right breast. The findings obtained using ultrasonography, mammography, and contrast-enhanced magnetic resonance imaging suggested breast cancer. Core needle biopsy resulted in the diagnosis of invasive carcinoma. The patient underwent mastectomy and sentinel lymph node biopsy. Histopathologically, the tumor cells were abundant in foamy cytoplasm. Because the presence of marked cytoplasmic lipid droplets was confirmed by Sudan IV staining and electron microscopic examination of the tumor and the lipid droplets were negative for periodic acid–Schiff staining, the tumor was diagnosed as an LRC. Immunohistochemically, estrogen and progesterone receptors of the tumor were strongly positive, human epidermal growth factor receptor type 2 was negative, and the ratio of Ki-67-positive cells was ~30%. After surgery, the patient underwent combination chemotherapy with anthracycline, cyclophosphamide, and 5-fluorouracil, followed by docetaxel. Thereafter, the patient was treated with letrozole and has remained well for 24 months with no signs of recurrence.

Keywords: breast cancer, estrogen receptor, endocrine therapy

Introduction

Lipid-rich carcinoma (LRC) of the breast is a rare form of breast cancer that accounts for <1% of all breast malignancies according to the World Health Organization's classification of breast tumors¹ and is considered to be aggressive with a poor prognosis.² Although LRC is thought to be negative for estrogen receptors (ERs),^{2,3} we recently experienced a case of breast LRC that was strongly positive for ERs. To the best of our knowledge, our case is the second report of ER-positive LRC, which was treated with endocrine therapy. Here, we report a case of LRC strongly positive for ER and review the literature. Written informed consent was obtained from the patient to use her data for publication. Approval was obtained from the ethics committee of Shinshu University, School of Medicine.

Case report

A 52-year-old postmenopausal female noticed a painless lump in her right breast on self-examination and presented to our hospital. The patient had no past or family history



of serious disease and received no past hormonal therapy. Physical examination revealed a firm lump in the upper medial quadrant of the right breast. The tumor was 30 mm ×20 mm in size. No nipple discharge or swelling of the axillary lymph node was observed. Blood examination results, including tumor markers, were within normal limits. Mammography showed an irregularly shaped mass with a microlobulated border. Ultrasonography showed a hypoechoic 25.8 mm ×22.9 mm mass with an irregular and indistinct border (Figure 1). Contrast-enhanced magnetic resonance imaging revealed an irregularly shaped mass with strong enhancement in the early phase. No intraductal spread of the tumor was detected (Figure 2). Core needle biopsy of the tumor led to a diagnosis of invasive carcinoma. ¹⁸F-Fluorodeoxyglucose positron emission tomography revealed no sign of distant metastasis. The patient was diagnosed as stage IIA breast cancer and underwent mastectomy and sentinel lymph node biopsy. Histopathologically, the tumor cells were abundant in foamy cytoplasm (Figure 3A and B). Sudan IV staining (Figure 3C) and electron microscopic examination of the tumor (Figure 3D) demonstrated the presence of marked cytoplasmic lipid droplets, which were negative for periodic acid–Schiff (PAS) staining (Figure 3E). Furthermore, gross cystic disease fluid protein-15 (GCDFP-15) staining (Figure 3F) was negative in the cytoplasm of the tumor cells. On the other hand, cytokeratin (CK) 5/6 staining was weakly positive (Figure 3G), while p53 staining was positive (Figure 3H). Based on these findings, the tumor was diagnosed as LRC. Immunohistochemically, ERs and progesterone receptors (PgRs) of the tumor were strongly positive (Figure 4A and B), human epidermal growth factor receptor type 2 (HER2)

was negative (Figure 4C), and the ratio of Ki-67-positive cells was ~30% (Figure 4D). No lymph node metastasis was detected in the axilla. Taking into consideration the high ratio of Ki-67-positive cells and aggressiveness of LRC, the patient received standard adjuvant chemotherapy of anthracycline, cyclophosphamide, and 5-fluorouracil, followed by docetaxel. Thereafter, the patient received letrozole and has remained well for 24 months with no signs of recurrence.

Discussion

LRC is histopathologically characterized by cells with numerous optically free vacuoles of various sizes in the cytoplasm that are positive for Sudan IV staining.¹ Although it is important to differentiate LRC from other vacuolated or clear cell tumors, such as glycogen-rich and apocrine carcinomas, these tumors are appropriately differentiated by special staining or immunohistochemical staining. For example, glycogen-rich and apocrine carcinomas are positive for PAS, whereas LRC is negative. With regard to GCDFP-15 staining, apocrine carcinoma is positive and LRC is negative.^{1,4,5} In our case, the tumor cells were negative for PAS and GCDFP-15. Furthermore, an electron microscopic examination revealed the presence of cytoplasmic lipid droplets that were positive for Sudan IV staining, which met the criteria of LRC.

The clinical characteristics of LRC are not well known because only ~70 cases have been reported in the English literature to date. However, Shi et al² analyzed the clinicopathological data of 49 LRCs among 3,206 patients with breast cancer and reported lymph nodes metastases in 38 (78%) and that the 2- and 5-year survival rates of patients with LRC were 64.6% and 33.2%, respectively. Thus, LRC

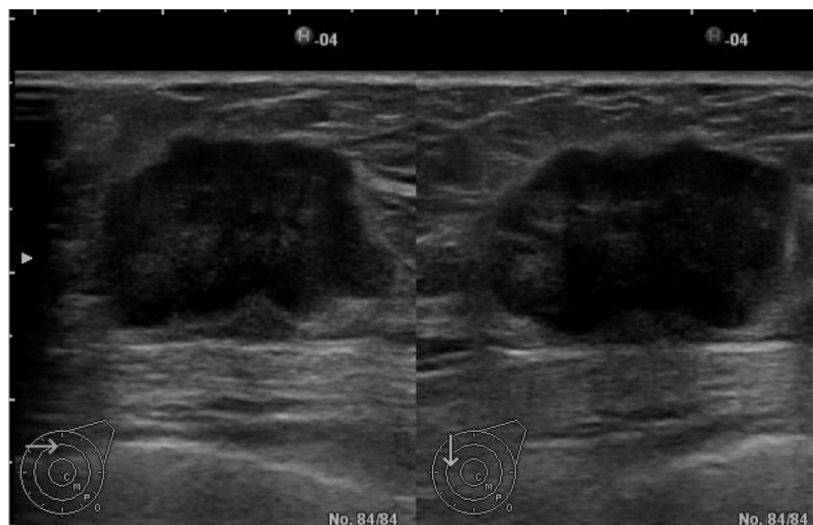


Figure 1 Ultrasonographic findings of the right breast.

Note: An irregularly shaped hypoechoic 25.8 mm ×22.9 mm mass with an indistinct border was detected.

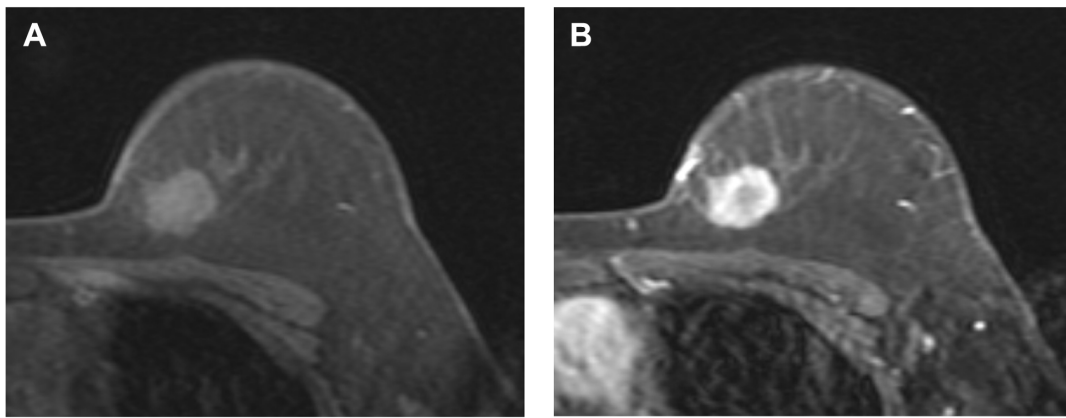


Figure 2 Contrast-enhanced magnetic resonance imaging findings of the right breast.

Notes: Contrast-enhanced magnetic resonance imaging revealed an irregularly shaped mass with strong enhancement in the early phase. **(A)** Before the injection of contrast agent. **(B)** One minute after the injection of contrast agent.

is generally considered to be an aggressive phenotype of breast cancer.

Because of the rarity of LRC, the association between the subtype and clinical features of LRC has not been extensively studied. LRC cases reported in the English literature are summarized in Table 1.^{2,3,6,7-14} Guan et al³ investigated the clinicopathological features of 17 patients with LRC and reported that none were ER positive, whereas one (5.9%)

was PgR positive; however, all patients were HER2 positive. Shi et al² studied 49 cases of LRC and reported that none were ER positive, five (10.2%) were PgR positive, and 35 (71.4%) were HER2 positive. The ratios of HER2-positive cancer in both studies were higher than the general average of 20%–30%.^{6,15} In addition, >30% of Ki-67-positive tumor cells were detected in 27 (55.1%) cases in the study by Shi et al.² Moreover, LRC was ER negative in 12 of the

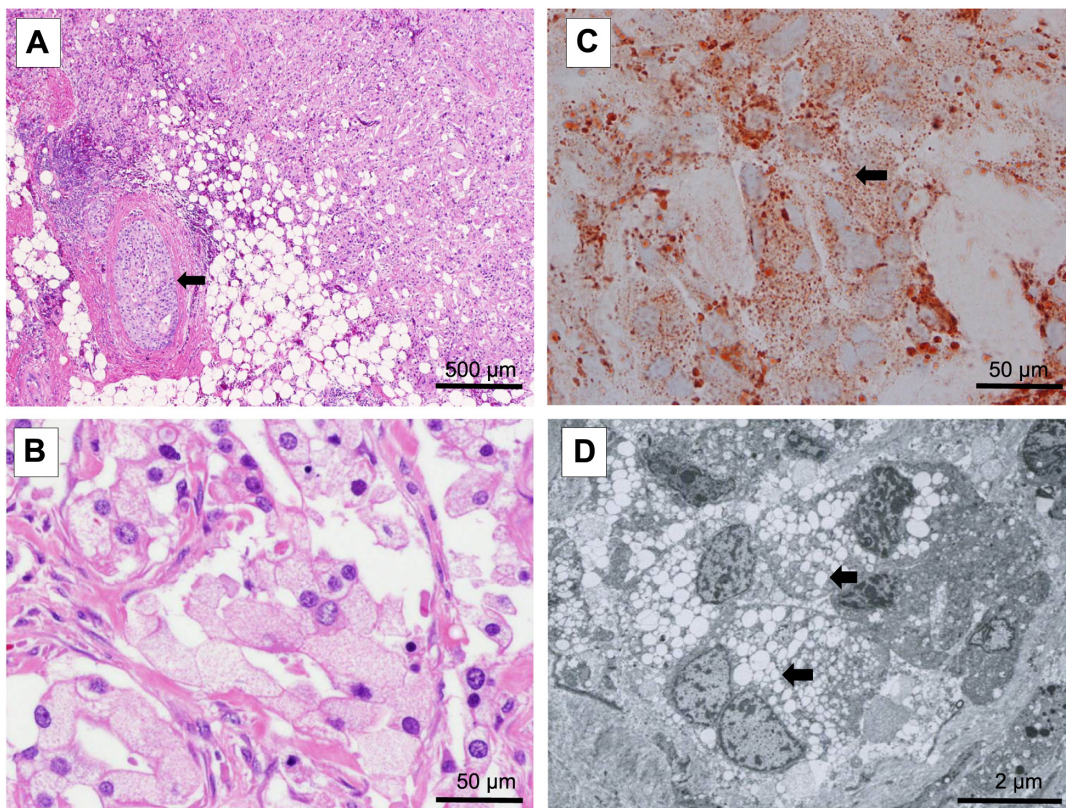


Figure 3 (Continued)

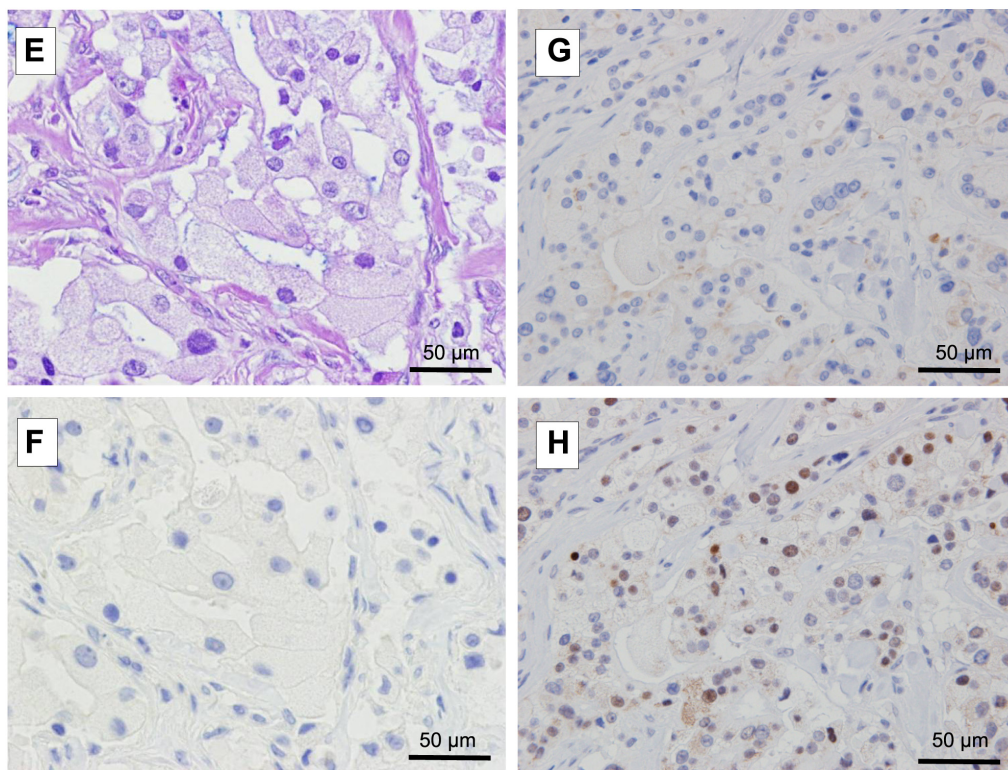


Figure 3 Histopathological findings of the lipid-rich carcinoma.

Notes: Tumor cells with abundant foamy cytoplasm and in situ neoplasm were present (arrow). Hematoxylin and eosin staining (**A**: $\times 40$; **B**: $\times 400$). Sudan IV staining (**C**: $\times 400$) and electron microscopic examination (**D**: $\times 400$) confirmed the presence of cytoplasmic lipid droplets (arrows) that were negative for PAS staining (**E**: $\times 400$). GCDFP-15 staining (**F**: $\times 400$) was negative for the cytoplasm of the tumor cells. Cytokeratin (CK) 5/6 (**G**: $\times 400$) was weakly positive, and p53 was positive in the tumor cells (**H**: $\times 400$).

Abbreviations: PAS, periodic acid–Schiff; GCDFP-15, gross cystic disease fluid protein-15.

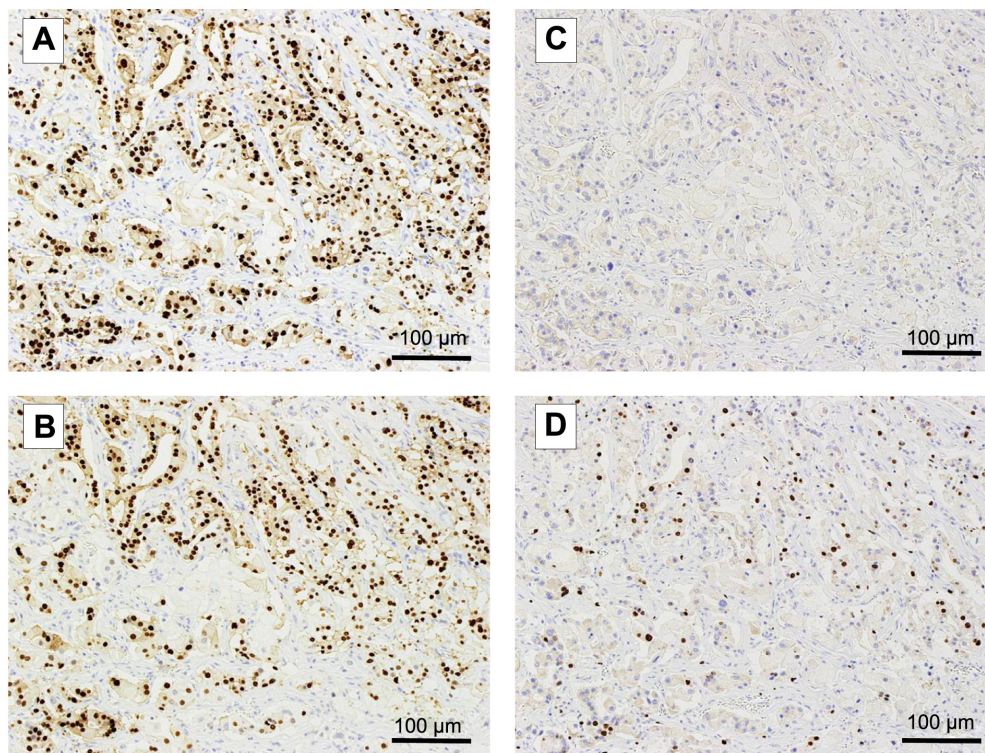


Figure 4 Immunohistochemical findings of the lipid-rich carcinoma.

Notes: More than 90% of the tumor cells were positive for estrogen receptors (**A**: $\times 200$), ~70% were positive for progesterone receptors (**B**: $\times 200$), all were negative for human epidermal growth factor receptor type 2 (**C**: $\times 200$), and the positive rate of Ki-67 was ~30% (**D**: $\times 200$).

Table 1 Lipid-rich carcinoma of the breast reported in the English literature

Authors	No of patients	Age, years	Surgery	TNM stage	Lymph node metastasis	ER	PgR	HER2	Adjuvant therapy	Prognosis
Shi et al ²	49	22–72 (mean, 45)	M, Ax: 43 (87.7%)	I: 4 (8.2%)	+ : 38 (77.5%)	+ : 0 (0%)	+ : 5 (10.2%)	+ : 35 (71.4%)	CT: 49 (100%)	Median survival 35.0 months (24.6–45.4)
			M: 1 (2.1%)	II: 9 (18.4%)	- : 11 (22.5%)	- : 49 (100%)	- : 44 (89.8%)	- : 14 (28.6%)		
			BCS, Ax: 5 (10.2%)	III: 35 (71.4%)						
			ND	ND: 1 (2.0%)	+ : 17 (100%)	+ : 0 (0%)	+ : 1 (5.9%)	+ : 17 (100%)	CT: 17 (100%)	Median survival 16 months (11–28)
Guan et al ³	17	37–69 (mean, 58)	ND	I: 1 (5.9%)	+ : 17 (100%)	+ : 0 (0%)	+ : 16 (94.1%)	+ : 0 (0%)		
				II: 15 (88.2%)	- : 0 (0%)	- : 17 (100%)	- : 16 (94.1%)	- : 0 (0%)		
				III: 1 (5.9%)	+ : 3 (60%)	+ : 0 (0%)	+ : 0 (0%)	+ : 0 (0%)	ND	Median survival 16 months (1–30)
Wrba et al ⁷	5	62–81 (mean, 70)	M, Ax: 4 (80%)	I: 1 (20%)		+ : 0 (0%)	+ : 0 (0%)	+ : 0 (0%)		
			BCS: 1 (20%)	I: 3 (60%)	- : 1 (20%)	- : 5 (100%)	- : 5 (100%)	- : 5 (100%)		
				III: 1 (20%)						
Cong et al ⁴	2	55–56 (mean, 55.5)	M, Ax: 2 (100%)	II: 2 (100%)	ND: 1 (20%)	+ : 1 (50%)	+ : 0 (0%)	+ : 0 (0%)	CT: 2 (100%)	Median survival 19 months (12–25)
					+ : 2 (100%)	- : 1 (50%)	- : 2 (100%)	- : 2 (100%)	ET: 2 (100%)	
					- : 0 (0%)					
Umekita et al ⁸	1	78	M, Ax	III	+	-	-	ND	ND	ND
Varga et al ⁹	1	56	BCS, Ax	I	-	-	-	ND	Irradiation, CT	7 months, alive
Russo et al ¹⁰	1	73	M, Ax	II	-	-	-	-	ND	ND
Kimura et al ¹¹	1	57	M, Ax	I	-	-	-	-	ND	20 years, alive
Nagata et al ¹²	1	68	BCS, Ax	0	-	-	-	ND	Irradiation	8 years, alive
Machalekova et al ⁵	1	56	M, Ax	II	+	-	-	+	CT	2 months, alive
Kurusu et al ¹³	1	ND	BCS, SLNB	0	-	+	+	-	None	ND
Oba et al	1	52	M, SLNB	II	-	+	+	-	ET	24 months, alive

Abbreviations: TNM, tumor–node–metastasis; ER, estrogen receptor; PgR, progesterone receptor; HER2, human epidermal growth factor receptor type 2; ND, not described; M, mastectomy; Ax, axillary dissection; BCS, breast-conserving surgery; SLNB, sentinel lymph node biopsy; CT, chemotherapy; ET, endocrine therapy.

14 case reports.^{5,8–14} Thus, all LRCs except for two cases^{13,14} have been reported to be ER negative, and there has been a tendency for LRC to be HER2 positive and contain highly proliferative cells. Hence, the aggressiveness of LRC may be attributed to these biological features. However, the significance of Ki-67 levels in LRC has been not elucidated. Shi et al² reported that Ki-67 status was not associated with overall survival among 49 patients with LRC. However, more clinical data are required to elucidate the significance of Ki-67 in the prognosis of LRC.

Treatment of LRC is typically performed on the basis of standard treatment protocols for breast cancer. However, considering the aggressiveness of LRC, systemic therapy should be an important part of the treatment regimen and appropriate systemic therapies according to the subtype and stage of each tumor should be administered. Shi et al² performed an in vitro chemosensitivity assay and found that lipid-rich tumors were sensitive to paclitaxel, carboplatin, and cisplatin. Thus, chemotherapy including paclitaxel or platinum agents may have the potential to improve the prognosis of recurrent LRC. On the other hand, because all LRCs except for two previously reported cases^{13,14} have been ER negative, the effect of endocrine therapy on LRC has not been established. In the present case, endocrine therapy is expected to be effective because the tumor was strongly ER positive.

Conclusion

The present case is the second report of LRC that was positive for ER expression and treated with endocrine therapy. Although LRC is generally considered to be negative for ERs, our case suggests that a small percentage of LRCs are ER positive.

Acknowledgment

Written informed consent was obtained from the patient to use her data for publication.

Disclosure

The authors report no conflicts of interest in this work.

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