



Fibromatosis-like metaplastic carcinoma of the breast: Two case reports

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Abstract

BACKGROUND

Fibromatosis-like metaplastic carcinoma is classified as a rare type of metaplastic carcinoma of the breast by the 2012 WHO pathological and genetic classification criteria for breast tumors, which takes hyperplastic spindle cells as the main component and is often misdiagnosed as benign stromal proliferative lesions or benign mesenchymal tumors of the breast because of its mild morphology. Here, we collected the clinical data of 2 cases of fibromatosis-like metaplastic carcinoma of the breast and performed pathomorphological observation and immunohistochemical staining of the surgically resected specimens. According to the clinical features, imaging features, immunophenotype, diagnosis and differential diagnosis of 2 cases of fibromatosis-like metaplastic carcinoma of the breast, it was further differentiated.

CASE SUMMARY

Case 1: A 56-year-old postmenopausal female was admitted due to "right breast mass for over 1 year and local ulceration for over 1 mo". Physical examination showed a mass with a diameter of 4.5 cm × 5.5 cm palpable at 2.5 cm from the nipple at 1 o'clock in the right breast. The skin on the surface of the mass ruptured about 3 cm, with a small amount of exudation and bleeding, less clear boundary, hard texture, fair activity, without obvious tenderness. No obvious abnormality was palpable in the left breast. No enlarged lymph nodes were palpable in the bilateral axillae and bilateral supraclavicular region. After removing the mass

tissue, it was promptly sent to the pathology department for examination. Case 2: Female, 52-years-old, premenopausal, admitted due to "right breast mass for more than 3 mo". Physical examination showed a 4.0 cm × 4.0 cm diameter mass palpable at 2.0 cm of the nipple in the lower outer 7 o'clock direction of the right breast, with less clear boundary, hard texture, fair activity, no significant tenderness, no palpable significant abnormalities in the left breast, and no palpable enlarged lymph nodes in the bilateral axillae and bilateral supraclavicular region. The mass was resected and sent for pathological examination. Postoperative pathological examination revealed fibromatosis-like metaplastic carcinoma of the breast in both patient 1 and patient 2. No systemic therapy and local radiotherapy were performed after surgery, and no tumor recurrence or metastasis was observed.

CONCLUSION

Fibromatosis-like metaplastic carcinoma of the breast is a rare subtype of metaplastic carcinoma that is often misdiagnosed, and the diagnosis relies on medical history collection, complete sampling, and full use of immunohistochemical assessment. The risk of lymph node and distant metastasis is low, and the current treatment is based on complete surgical resection. The efficacy of systemic radiotherapy and chemotherapy is not clear.

Key Words: Breast cancer; Fibromatosis-like metaplastic carcinoma; Metaplastic carcinoma; Spindle cell lesion; Pathology

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Core Tip: Fibromatosis-like metaplastic carcinoma is a rare type of metaplastic carcinoma of the breast with proliferating spindle cells as the main component, which is often misdiagnosed as low-grade mesenchymal tumors or proliferative lesions because of its mild morphology. Two cases of fibromatosis-like metaplastic carcinoma of the breast were reported and the literatures were reviewed. The pathological features were observed to ensure the correct diagnosis.

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INTRODUCTION

Metaplastic carcinoma of the breast (MBC) is a rare but aggressive form of breast cancer that accounts for less than 0.5% of all breast cancers. It has been recognized as a distinct pathological entity by the World Health Organization. Morphologically, it is characterized by differentiation of the neoplastic epithelium into squamous cells and/or mesenchymal elements (squamous cells, spindle cells, cartilage or bone, *etc.*)[1,2]. Fibromatosis-like metaplastic carcinoma (FLMCA), a subtype of MBC, is a very rare metaplastic carcinoma[3]. FLMCA is a locally aggressive tumor with low likelihood of lymph node and distant metastasis, but tends to recur after resection[4]. Therefore, understanding the histological features of FLMCA may be important for the treatment of FLMCA.

FLMCA is a low-grade tumor formed by spindle cells with mild or absent nuclear atypia. The tumor is dominated by spindle cells, which may be mixed with a small proportion of ductal or lobular carcinoma components of the breast[5,6]. Gobbi *et al*[7] found that low-grade spindle cells accounted for more than 95% of the total tumor area, and epithelial cells or low-grade carcinomas accounted for less than 5% of cases in 30 breast swelling samples. One of the main features of FLMCA is low-grade spindle cell proliferation, which is mainly characterized by infiltrative, focal mild atypia, and focal epithelioid differentiation[8]. Accurate diagnosis of FLMCA is very difficult due to morphological overlap with other low-grade spindle cell lesions and is often misdiagnosed as benign stromal proliferative lesions or benign mesenchymal tumors of the breast because of its mild morphology[9]. Understanding different morphologic, immunohistochemical, and molecular features is therefore important for diagnosis. In this study, we report on 2 cases of FLMCA that provide insights regarding the histological aspects.

CASE PRESENTATION

Chief complaints

Case 1: A 56-year-old postmenopausal female patient was admitted due to "right breast mass for more than 1 year and local ulceration for over 1 mo".

Case 2: Patient 2 was a 52-year-old premenopausal woman who was admitted to our hospital due to a right breast mass for more than 3 mo.

History of present illness

Case 1: The patient was found to have a mass in the right breast for more than 1 year. The tumor gradually increased in size, with hard texture, poor activity, no tenderness and nipple discharge, and no treatment was performed. One month ago, local ulceration of the right breast was found, and a mass with a diameter of 4.5 cm × 5.5 cm was palpable 2.5 cm from the nipple at 1 o'clock in the right breast. The skin on the surface of the mass ruptured about 3 cm, with a small amount of exudation and bleeding, less clear borders, hard texture, fair activity, and no significant tenderness. There was no remission in recent days, and the patient visited our hospital for further treatment.

Case 2: The patient found a mass in the right breast for more than 3 mo, which was located at 7 o'clock outside and below the right breast, and a mass with a diameter of 4.0 cm × 4.0 cm could be palpated 2.0 cm from the nipple, with less clear boundary, hard texture, fair activity, and no obvious tenderness. No treatment was performed during this period. The patient came to our hospital today for diagnosis and treatment.

History of past illness

Case 1: The patient had good physical fitness, denied the medical history of "hypertension and diabetes" and infectious diseases history such as "hepatitis and tuberculosis". There was no history of surgery, trauma, blood transfusion, poisoning, food or drug allergy, and the vaccination history was unknown.

Case 2: The patient denied any history of hepatitis, tuberculosis, malaria, hypertension, heart disease, diabetes, cerebrovascular disease, mental illness, surgery, trauma, blood transfusion, food or drug allergy, and had received the hepatitis B vaccination.

Personal and family history

Case 1: The patient was born in her native country, and had not been to other places for a long time; had no history of exposure to schistosomiasis infected water; no history of exposure to poisons, with regular daily life, no bad habits, and no history of major mental trauma. All family members were healthy and denied any genetic history of family diseases.

Case 2: The patient was born in her native country, and had not been to other places for a long time; had no history of exposure to schistosomiasis-infected water; no history of exposure to poisons, with regular daily life, no bad habits, and no history of major mental trauma. All family members were healthy and denied any genetic history of family diseases.

Physical examination

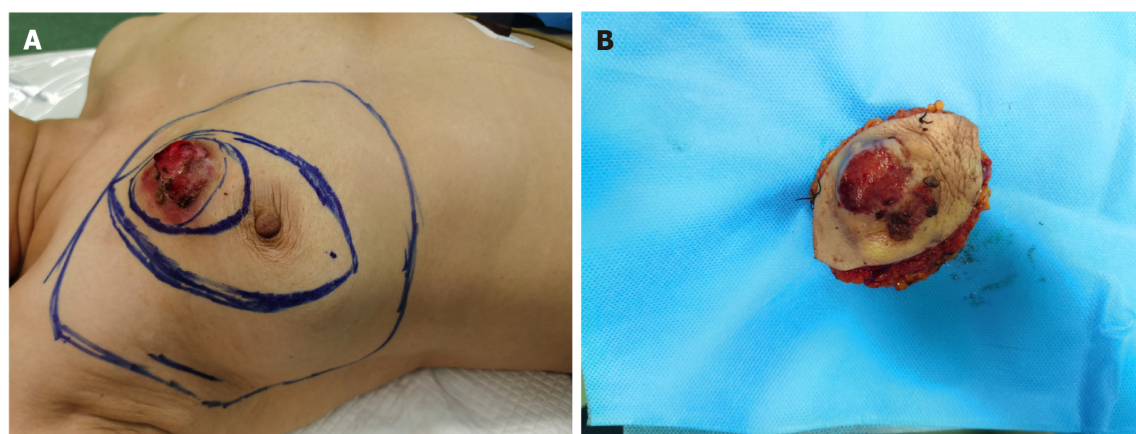
Case 1: A mass with a diameter of 4.5 cm × 5.5 cm was palpable 2.5 cm from the nipple at 1 o'clock in the right breast, and the skin on the surface of the mass had ruptured about 3 cm, with a small amount of exudation and bleeding, less clear borders, hard texture, fair activity, no significant tenderness, no significant abnormalities palpable in the left breast, and no palpable enlarged lymph nodes in the bilateral axillae and bilateral supraclavicular regions (Figure 1A and B).

Case 2: Physical examination showed a 4.0 cm × 4.0 cm diameter mass palpable at 2.0 cm of the nipple in the lower outer 7 o'clock direction of the right breast, with less clear boundary, hard texture, fair activity, no significant tenderness, no palpable significant abnormalities in the left breast, and no palpable enlarged lymph nodes in the bilateral axillae and bilateral supraclavicular region.

Laboratory examinations

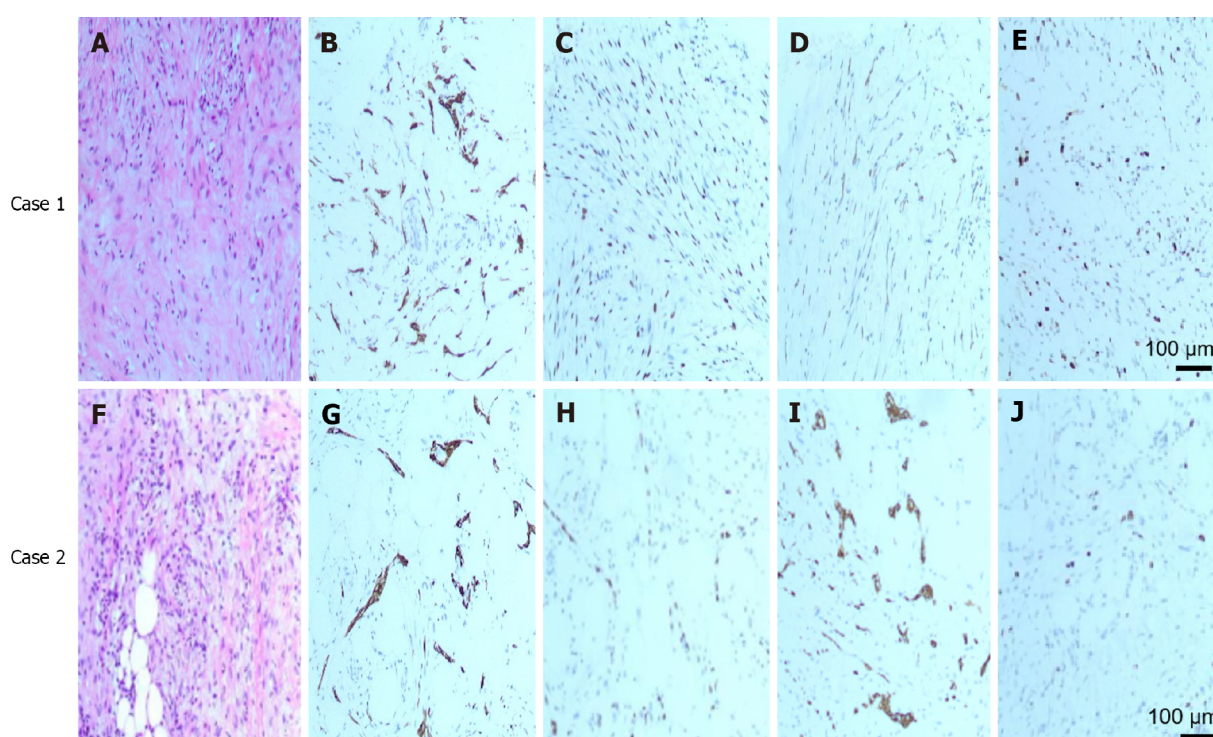
Case 1: The tumor puncture tissue was sent for pathological examination to consider sclerosing adenopathy, and the mass was sent for pathological examination after complete resection. Immunohistochemical examination revealed that the tumor was composed of spindle cells with mild morphology and mild atypia of the tumor cells. Envision was used to detect CKPan, P63 and CK5/6 positive in tumor cells, and the Ki-67 positive index was about 15% (Figure 2A and E). Diagnosis of fibromatosis-like MBC was confirmed.

Case 2: Tumor puncture was performed, and pathology showed puncture tissue, followed by



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Figure 1 Right breast mass image of Case 1. A: A mass measuring 4.5 cm × 5.5 cm in diameter was palpable in the right breast 2.5 cm from the nipple at 1 o'clock; B: Postoperative specimen of right breast mass.



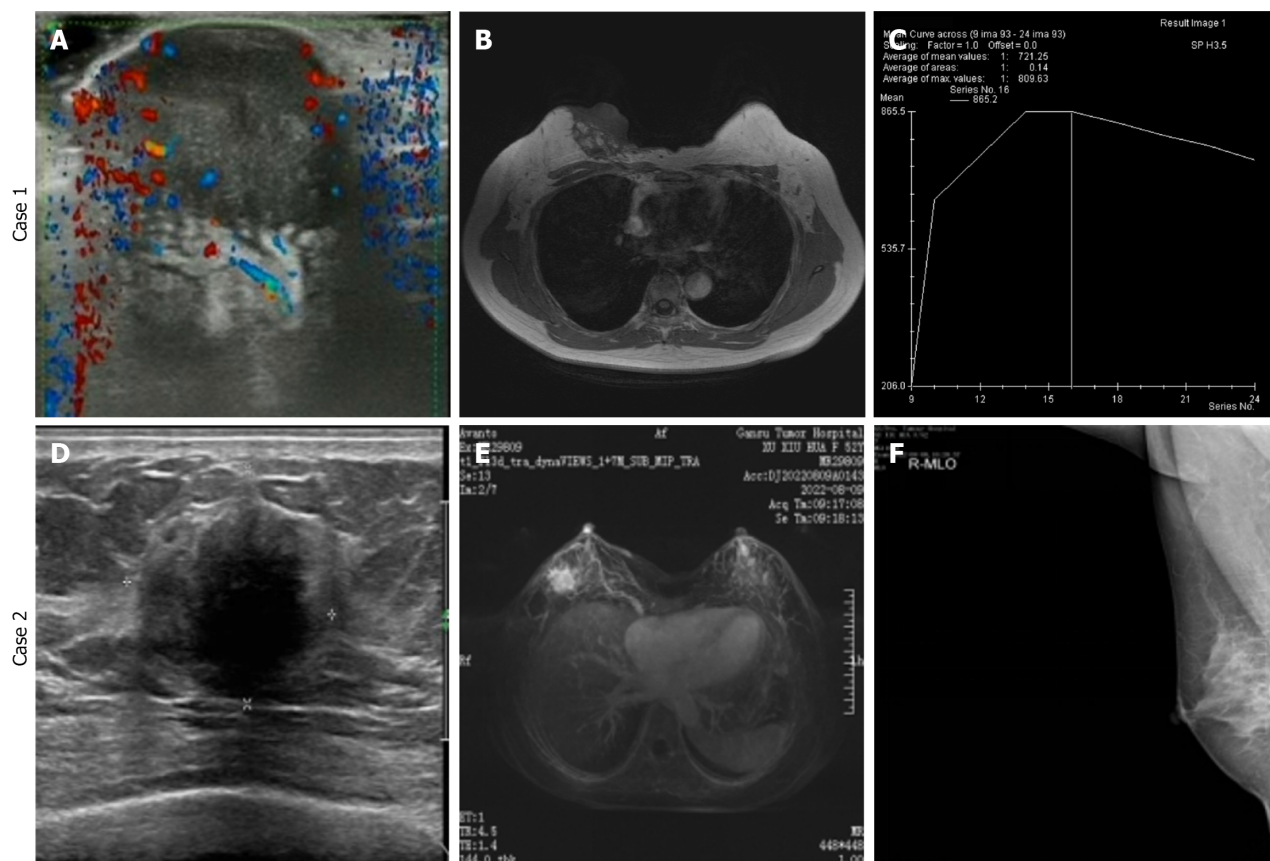
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Figure 2 Puncture pathology and immunohistochemistry of right breast mass. A: HE staining showed that the tumor was composed of spindle cells with mild morphology and mild atypia of the tumor cells; B: Tumor cells were positive for CKPan by Envision assay; C: Envision test showed that tumor cells were positive for p63; D: Envision test showed tumor cells positive for CK5/6; E: Envision test showed approximately 15% Ki-67 for tumor cells. F: HE stained tumor was composed of spindle cells with mild morphology and mild atypia of tumor cells; G: Tumor cells were positive for CKPan by Envision assay; H: Tumor cells were positive for p63 by Envision assay; I: Tumor cells were partially positive for CK5/6 by Envision assay; J: Ki-67 hotspot area of tumor cells detected by Envision method was about + 25%. Original magnification: × 400; Scale bars: 100 μm.

pathological examination, considering fibromatosis-like MBC. The tumor was composed of spindle cells with mild morphology, and the tumor cells were mildly atypical. Envision assay showed that CKPan, P63 and CK5/6 were positive in tumor cells, and the Ki-67 positive index was about 20% (Figure 2F and J).

Imaging examinations

Case 1: After admission, ultrasound and magnetic resonance imaging (MRI) were performed, which revealed breast imaging reporting and data system (BI-RADS) grade V (Figure 3A and C). Computed tomography showed a right breast mass and was considered a malignancy. Breast tumor markers were



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Figure 3 Imaging data of right breast mass. A: Ultrasonography showed breast imaging reporting and data system (BI-RADS) grade V; B and C: magnetic resonance imaging (MRI) showed breast BI-RADS grade V. D: Ultrasound showed breast BI-RADS grade V; E: MRI showed breast BI-RADS grade V; F: Molybdenum target examination showed breast cancer BI-RADS grade IVb.

unremarkable.

Case 2: After admission, breast ultrasound and MRI were performed, and revealed breast cancer BI-RADS grade IVc (Figure 3C and D), and molybdenum target examination revealed breast cancer BI-RADS grade IVb (Figure 3E), both of which suggested the possibility of malignant tumors in the right breast.

FINAL DIAGNOSIS

Cases 1 and 2: FLMCa of the right breast.

TREATMENT

Case 1: The patient was given a simple mastectomy of the right breast + axillary sentinel lymph node biopsy after complete resection of the right breast mass.

Case 2: Complete resection of the right breast mass was followed by simple mastectomy of the right breast + axillary sentinel lymph node biopsy.

OUTCOME AND FOLLOW-UP

Case 1

Postoperative pathology showed FLMCa of the right breast (3 cm × 4.5 cm) with ulceration of the skin surface. Pathological examination showed that the tumor was composed of spindle cells with mild morphology, and in immunohistochemical staining, the tumor cells were ER (-), PR (-), HER-2 (0), Ki-

67 (+ 10%), CK5/6 (+), P63 (+), calponin (+), B-Catenin (+), S-100 (local +), CK8/18 (+), CD34 (vascular +), BCL-2 (-), SMA (+), Desmin (-), Caldesmon (-), and CD10 (+) (Figure 4A and E).

No systemic therapy and local radiotherapy were performed after surgery, and no tumor recurrence or metastasis was observed 11 mo after follow-up.

Case 2

Postoperative pathology revealed a right breast mass size (2.0 cm × 1.7 cm), FLMCa of the right breast, cancer tissue invading the surrounding adipose tissue, and atypical hyperplasia of the ductal epithelium around the cancer. Under the original incision, hyperplasia of mammary glands, sclerosing adenopathy, common hyperplasia of ductal epithelium, massive angiectasia, congestion, foreign body granuloma and fat necrosis formation were observed, without clear residual tissue. Pathological examination revealed that the tumor was composed of spindle cells with mild morphology and mild atypia of the tumor cells. Immunohistochemistry showed tumor cells ER (-), PR (-), HER-2 (0), Ki-67 (+ 20%), E-cadherin (-), P120 (plasma +), CKpan (+), CK5/6 (+), P63 (+), SMA (+), CKH (partial +), P40 (partial +), calponin (-), AR (-), GATA-3 (-), SOX-10 (-), B-Catenin (partial plasma +), CK8/18 (-), CK7 (-), CD31 (vascular endothelium +), CD34 (vascular endothelium +), S-100 (local +) (Figure 4F and J). No systemic therapy and local radiotherapy were performed after surgery, and no tumor recurrence or metastasis was observed 15 mo after surgery.

DISCUSSION

FLMCa of the breast, a very rare variant of breast tumors, is a newly described metaplastic tumor in the 2012 WHO classification of breast tumors (4th edition). Low-grade fibromatosis-like spindle cell carcinoma is a very rare breast cancer, accounting for < 0.5% of all breast cancers[10,11]. It is a low grade tumor formed by spindle cells with mild or absent nuclear atypia embedded in collagenized stroma, and only < 5% of tumor cells exhibit epithelial traits[12,13]. Because its biological behavior is superior to that of spindle cell metaplastic carcinoma in general, this cancer type was added to the new WHO classification[14]. Because of its mild morphology, FLMCa is frequently misdiagnosed as benign stromal proliferative lesions or benign mesenchymal tumors, and usually requires conservative treatment because of its favorable clinical outcome[15]. Accurate diagnosis is therefore a challenging task, particularly in core biopsies.

Histopathologically, FLMCa is a spindle cell metaplastic carcinoma with mild morphology characterized histologically by spindle cells with mild morphology arranged in wavy, fascicular, and woven patterns. Also, the cellular stroma was collagenized to varying degrees, resembling fibromatosis of soft tissue, and showed finger-like infiltration into the surrounding mammary stroma, as studied by Kinkor *et al*[16]. Immunohistologically, tumor cells consistently express p63 and CK, but sometimes CK is focally expressed and rarely confined to obese spindle and epithelioid cells. Other antibodies ER, PgR and HER2 are generally negative, resembling normalised metaplastic carcinoma. As in our case, Rekhi *et al*[17], Nozoe *et al*[18], Rito *et al*[19] and others also found by immunohistochemical examination that FLMCa did not express estrogen receptors, progesterone receptors, and HER2 receptors, but mainly vimentin and basal cytokeratin. In addition, immunohistochemical expression of AE1/3 and CAM5.2 was also observed, and positive expression of epithelial and mesenchymal markers in these cells may be considered indicative of the "epithelial-mesenchymal" transformation observed in these tumors.

In the differential diagnosis, the diagnoses considered were nodular fasciitis, inflammatory myofibroblastic tumor, pseudoangiomatous stromal hyperplasia (PASH), myoblastoma, low-grade fibrosarcoma, and of course fibromatosis, which are very difficult to differentiate[20]. However, the development of immunohistochemistry has led to a better understanding of this histological type and allows for a better differential diagnosis. In our pathological examination, due to the lack of significant lymphoplasmacytic infiltration and myxoid background, we excluded nodular fasciitis and inflammatory myofibroblastic tumors[21,22]. Furthermore, PASH is less likely to be diagnosed because there is no slit-like space lined by fibroblasts[23]. Finally, there is a lack of fascicular arrangement and single row fibroblasts, which help to exclude fibrosarcomas and pleomorphic sarcomas[9].

CONCLUSION

In conclusion, due to the small number of previously reported cases, morphological features often do not reflect the nature of the lesion, and its lack of understanding is often misdiagnosed as proliferative breast lesions or low-grade soft tissue tumors, which may make the diagnosis and surgical treatment challenging. Given the small amount of published data, each reported clinical case may be important to improve the understanding of the argument. We therefore describe in detail the clinical, diagnostic, histopathological and therapeutic information observed in patients and compare it with information obtained from literature reviews. It was found that immunohistochemical analysis may be helpful in the

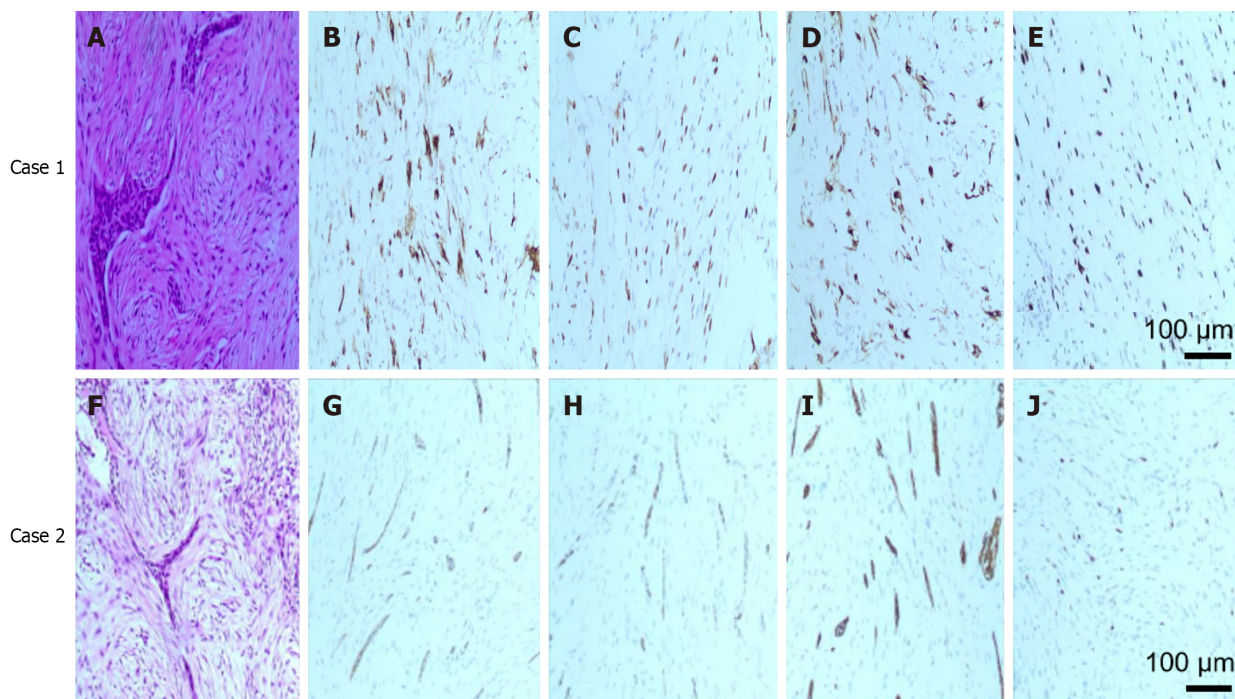


Figure 4 Postoperative pathology and immunohistochemistry of right breast cancer. A: HE staining showed that the tumor was composed of spindle cells with mild morphology and mild atypia of the tumor cells; B: Envision test showed tumor cells positive for CKPan; C: Envision test showed tumor cells positive for p63; D: Envision test showed tumor cells positive for CK5/6; E: Envision test showed approximately 20% Ki-67 for tumor cells. F: HE staining showed that the tumor was composed of spindle cells with mild morphology, and the tumor cells were mildly atypical; G: Tumor cells were positive for CKPan by Envision assay; H: Tumor cells were positive for p63 by Envision assay; I: Tumor cells were positive for CK5/6 by Envision assay; J: Ki-67 in tumor cells detected by Envision assay was about 20%. Original magnification: $\times 400$; Scale bars: 100 μm .

diagnosis. Because local recurrence rates are high and can only be detected by resection, understanding the role of surgical margins in reducing or eliminating local recurrence is particularly important to assign appropriate strategies for assessing early detection of local recurrence or distant metastasis.

FOOTNOTES

Author contributions: Bao WY conducted data management; Bao WY and Zhou JH wrote the manuscript; Luo Y and Lu Y conducted a review and editing; All authors have read and approved the final manuscript.

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