

Fibroblastic reticular cell tumor of the breast: A case report and review of the literature

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Received March 10, 2015; Accepted November 18, 2015

DOI: 10.3892/etm.2015.2922

Abstract. Fibroblastic reticular cells (FBRCs) are basic mesenchymal cells that belong to the dendritic cell family. Primary extranodal FBRC tumor (FRCT) cases are rare, with only 19 cases reported in the literature thus far. However, none of these cases originated in the breast tissue. To the best of our knowledge, the present study reported the first FRCT case of the breast in a 57-year-old woman. The patient complained of a painless mass that was located in the right breast and was ~3.5x2.5 cm in size. The patient underwent modified radical mastectomy subsequent to the diagnosis of FRCT after analysis of the lumpectomy specimen. Pathological examination revealed that the tumor was mainly composed of oval and spindle cells, and was infiltrated with lymphocytes and plasma cells. The tumor cells were immunoreactive for vimentin and negative for CD21, CD35 and S-100 protein. Six axillary lymph nodes were found to have been involved. Following surgery, the patient received four cycles of mesna, doxorubicin, ifosfamide and dacarbazine regimen chemotherapy (70 mg adriamycin day 1; 2.0 g ifosfamide days 1-3; 0.4 g dacarbazine day 1-3), which cycled every 21 days. The patient was uneventfully followed-up for 20 months following chemotherapy. In conclusion, the present study reported what appeared to be the first case of primary breast FRCT. The diagnosis, treatment and prognosis details presented in this study will help improve the diagnosis of the disease.

Introduction

Antigen-presenting cells (or immune accessory cells) present antigens to the T and B-cells, and include various cell types, such as dendritic cells and macrophages. Dendritic cells are part

of the non-lymphocytic type and are also known as reticular cells. They are classified into four major groups based on their morphology and immunophenotype, as follows: Langerhans cells, interdigitating dendritic cells (IDCs), follicular dendritic cells (FDCs) and fibroblastic reticular cells (FBRCs) (1,2). FBRCs are commonly located in the capsule, hilar and mesenchymal areas of the lymph nodes, while other sites include the parafollicular zone of the spleen and tonsils (3). FBRCs are considered to form the reticular network, which may facilitate the migration of lymphocytes and the transport of cytokines and other modulatory factors (3). Primary extranodal FBRC tumors (FRCTs) rarely occur and, to the best of our knowledge, only 19 cases have been reported in the literature thus far (4-15). However, none of these FRCT cases were located in the breast tissue.

The present study is the first to report a case of primary FRCT of the breast in a 57-year-old woman. In addition, the clinical, cytological, histological and immunophenotypical features of this tumor were discussed in detail.

Case report

A 57-year-old woman presented at the Ninghai Maternity and Child Care Hospital (Ninghai, China) complaining of a pinching sensation in the right breast for ~2 weeks in December 2013. The patient had previously undergone drainage for the management of mastitis, which was diagnosed 30 years before, in the same breast. Upon physical examination, a firm, painless mass with a size of ~3.5x2.5 cm was observed in the right breast. Ultrasound examination showed a non-homogeneous and hypoechoic mass with a resistance index of ~67% and a size of ~3.3x2.6 cm (Fig. 1). Mammography scans revealed a high density node with a clear boundary (Fig. 2). Surgical resection of the mass was performed on December 25, 2013 and the preliminary pathological diagnosis was uncertain according to the analysis of a frozen section. Further immunohistochemical analysis rendered the diagnosis of FRCT, based on the unusual morphological expression and the immunophenotypical results, which indicated positive lymph nodes.

The resected tumor was fixed in 10% neutral formalin, dehydrated with a graded alcohol series, and then embedded in paraffin. Next, 3- μ m paraffin sections were stained with hematoxylin and eosin. Immunohistochemical studies were performed

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Key words: immunohistochemistry, fibroblastic reticular cells, breast

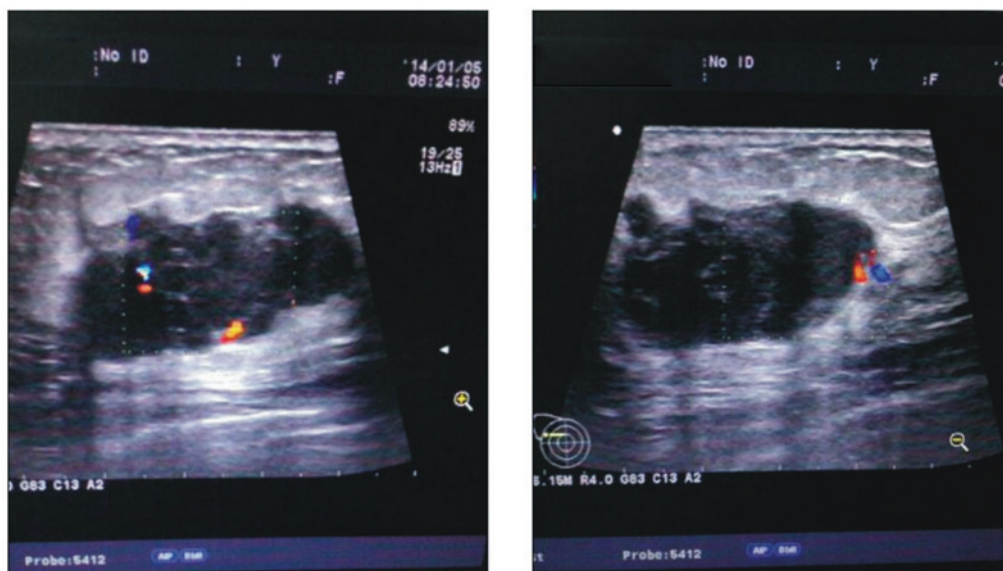


Figure 1. Ultrasound examination revealed a non-homogeneous, hypoechoic, 3.3x2.6-cm mass in the upper outer quadrant of the right breast.

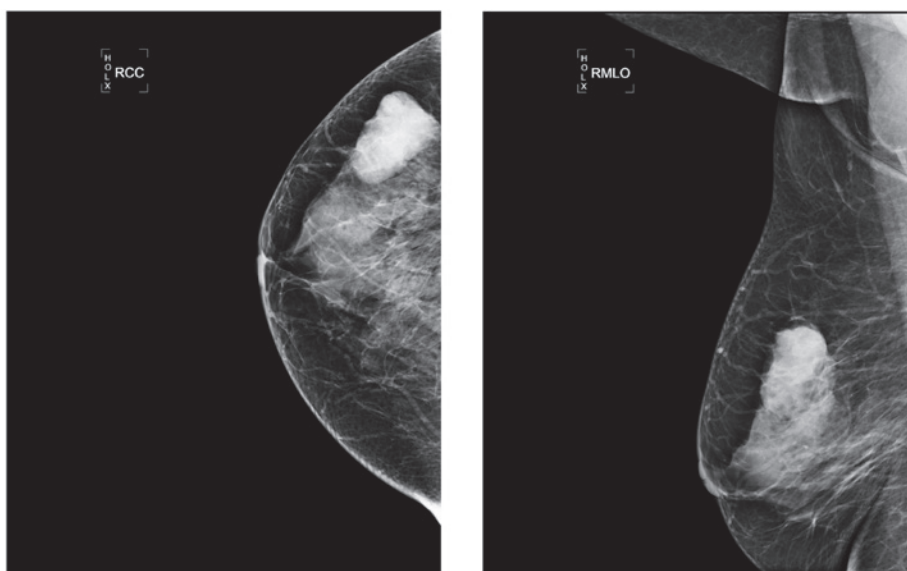


Figure 2. Mammography showed a high density node with a clear border in the upper outer quadrant of the right breast.

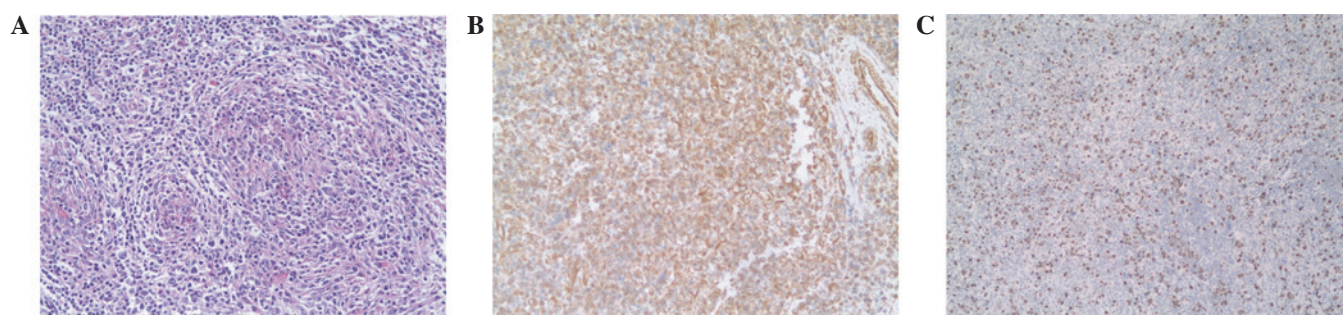


Figure 3. (A) Hematoxylin and eosin staining demonstrated oval and spindle cells with lymphocytes and plasma cells in the tumor (magnification, x20). Immunohistochemical analysis showed the tumor cells were (B) positive for vimentin (magnification, x20) and were (C) ~60% positive for Ki-67 (magnification, x10).

on the sections (Fig. 3) using the avidin-biotin peroxidase complex method, as previously demonstrated (16). The following

primary antibodies were used in the analyses: CD1a (clone 010; 1:50), CD68/KP1 (clone PG-M1; 1:200), desmin (clone D33;

1:50), HER2/neu (clone CB11; 1:50) and epidermal growth factor receptor (clone EP38Y; 1:30) that were purchased from Thermo Fisher Scientific, Inc. (Waltham, MA, USA); CD3 (clone PS1; 1:100), CD21 (clone 2G9; 1:20), CD30 (clone Ber. H2; 1:10), CD35 (clone E11; 1:100), vimentin (clone V9; 1:100), cytokeratin (clone AE1/AE; 1:100), keratin 7 (clone Ov-TL 12/30; 1:100), keratin 19 (clone RCK108; 1:50), epithelial membrane antigen (clone E29; 1:100), smooth muscle actin (clone 1A4; 1:100) and Ki-67 (clone GM001; 1:200) that were purchased from Dako (Glostrup, Denmark); CD23 (clone SP23; 1:80) was obtained from Novacastra (Leica Biosystems, Wetzlar, Germany); CD31 (1:300; clone JC70A), CD45 (1:300; clone 2B11 + PD7/26/16), S-100 protein (1:3,000; 790-2523), estrogen receptors (1:200; clone SP1) and progesterone receptors (1:500; clone SP2) that were purchased from Ventana Medical Systems, Inc. (Tucson, AZ, USA).

The surgical tumor specimen contained a white-grey cross section with clear boundaries and it measured ~3.5 cm in diameter. Tumor cells were mainly composed of oval and spindle cells, and were infiltrated with lymphocytes and plasma cells. The immunohistochemical analysis results showed that the tumor cells were only positive for vimentin, while Ki-67 was ~60% immunoreactive (Fig. 3). These results rendered the diagnosis of fibroblastic reticular cell tumor. Subsequently, a right modified radical mastectomy was performed on January 15, 2015 followed by the initiation of four cycles of mesna, doxorubicin, ifosfamide and dacarbazine regimen chemotherapy on February 11, 2014, which cycled every 21 days. The regimen was as follows: 70 mg adriamycin day 1 (Pfizer, Inc., New York City, NY, USA); 2.0 g ifosfamide days 1-3 (Baxter Healthcare Corporation, Deerfield, IL, USA); 0.4 g dacarbazine day 1-3 (Fresenius Kabi, Bad Homburg, Germany). Pathological report showed that six axillary lymph nodes had been involved, and the immunohistochemical results were similar to those of the primary mass. There was no evidence of disease detected at other sites.

Discussion

Dendritic cell tumors are extremely rare, and common types include FDC sarcoma (FDCS), IDC sarcoma (IDCS) and FRCT, according to the World Health Organization classification (17). FRCTs may be further subdivided into cytokeratin-negative and cytokeratin-positive based on their cytokeratin expression (18). Achieving an accurate diagnosis of dendritic cell sarcoma (DCS) is difficult, particularly in extra-nodal sites. In addition, these neoplasms must be differentiated from other more common tumors, including carcinomas and soft tissue sarcomas.

To the best of our knowledge, the current study presented the first case of FRCT originating from the breast. The first documented FRCT case was detected in the thoracic lymph nodes and was reported by Gould *et al* in 1990 (5) and, to date, only 19 cases of FRCT have been reported in the literature (1). The involved organs in previous cases included the lymph nodes, liver, lung, spleen, soft tissue and bone. However, the data on FRCT is limited due to its rare incidence, and no etiology associated with this disease has been confirmed. The patient of the present study experienced breast abscess and received drainage therapy ~30 years prior to the FRCT

diagnosis. Although the occurrence site of the abscess was almost identical as that of the FRCT, no association between the two conditions can be inferred due to the long time interval between their occurrence.

FDCS has the highest incidence when compared to other dendritic cell tumor types (1). Certain FDCS cases were found to express CD21 protein, which is a receptor for Epstein-Barr virus, and that may be a pathogenesis cause (19,20). IDCS may be originated from the hematopoietic or solid organ, and only 2 cases of IDCS originating from the breast have been reported (21,22). The malignant transformation and trans-differentiation of B cells may be a possible cause of IDCS formation (23).

For the accurate diagnosis of DCS, a combination of observations from macroscopic, immunohistochemical and electron microscopy examinations is required. Macroscopically, FRCT cells present as whorls, fascicles or a storiform pattern, and their shape may be a spindle, circle or ovoid. Lymphoplasmacytic infiltration and epithelioid cells were observed between tumor cells (4). FRCT cells have been demonstrated to have certain myofibroblastic-like features with immunoreactivity for vimentin, smooth muscle actin and desmin, whereas they were negative for CD21, CD35 and S-100 protein (9). Differentiating between FBRC subtypes that express cytokeratins and other epithelial markers from carcinoma is challenging (24,25). Electron microscopy can be used to observe evident signs of smooth muscle differentiation in tumor cells, however, these properties are not observed in all cases. The morphology of FDCs and IDCs is similar to that of FBRCs; however, FDCs are immunoreactive for CD21, CD35, Ki-FDRC1p and Ki-M4p (21,26), whereas IDCs are immunoreactive for S-100 protein and variably immunoreactive for CD1a and histiocytic markers (27). Furthermore, FDCs are found to have a fluffy cytoplasm bulge and marked desmosome upon electron microscopy observation, while IDCs cells have a slender cytoplasm bulge and no desmosome. Notably, Jones *et al* (7) demonstrated that a differentiation intermediate exists between FDCs and FBRCs, which suggests there may be an association between the FDCs and FBRCs (7).

The accepted strategies for the treatment of FRCTs remain controversial. Due to the small number of cases with various treatment modalities, no conclusion can be made from previous studies. Commonly, surgical resection is performed as a primary treatment modality for FDCs and FRCT. However, in IDCs, the surgery was not found to have an effect on the overall survival of patients (18). The role of adjuvant therapy, such as radiotherapy and chemotherapy, in these tumors remains uncertain. In early disease, adjuvant therapies are considered to have no beneficial effect on the prognosis of sarcomas (28). Localized FRCT cases have been treated with radiotherapy more frequently than chemotherapy (18). The current patient received modified radical mastectomy as the primary treatment, and a pathological report showed that six axillary lymph nodes had been involved. Subsequent to the surgery, the patient received chemotherapy. The patient was followed-up for 20 months following the chemotherapy and the recovery was uneventful.

In conclusion, the present study reported the first case of primary breast FBRC tumor. FBRC tumors are rarely observed and are easily misdiagnosed. The diagnosis, treatment and

prognosis details reported for the current patient will assist in improving the knowledge on the characteristics of this disease.

Acknowledgements

The authors would like to thank Dr Ping Gong from New York Presbyterian Hospital (New York City, NY, USA) and Professor Xiaoqiu Li from Fudan University Shanghai Cancer Center (Shanghai, China) for their precise advice on the diagnosis in the present study.

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