Recurrent dermatofibrosarcoma protuberans of the breast with rapid growth during pregnancy: a case report

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Case Report

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Abstract

Background:

Dermatofibrosarcoma protuberans (DFSP) is a rare soft-tissue sarcoma, with the characteristics of slow growth. Herein, we reported a unique rare case of recurrent DFSP on the breast, which rapid growth during pregnancy.

Case presentation:

The patient was a 35-year-old woman with recurrent tumor in left breast that as a large tumor due to rapid growth during pregnancy. Physical examination revealed the three adjacent lumps which were firm, fixed with a relatively well-defined border, and measured approximately 10×9 cm, 4×4 cm and 3×3 cm. The histopathological diagnosis was DFSP.

Conclusions:

We present a unique rare case of recurrent DFSP on the breast, which has rapid growing behavior during pregnancy.

Introduction

Dermatofibrosarcoma protuberans (DFSP) is a rare soft-tissue sarcoma which makes up only 1% of all soft-tissue sarcomas [1]. DFSP is a slow-growing, low- to intermediate- grade in malignant soft-tissue tumor with high local recurrence rate but low risk of metastasis [2]. DFSP derived from dermal fibroblasts with subsequent infiltration the subcutaneous tissues, and characterized by infiltrative growth of CD34+ spindle cells. However, the diffuse positive expression of CD34 is considered a diagnostic characteristic but not specific in DFSP [3]. The characteristic molecular genetic features of DFSP are a supernumerary ring chromosome derived from chromosomes 17 and 22 or a reciprocal chromosomal translocation t (17;22) (q22; q13), resulting in the genetic fusion of collagen type 1-alpha 1 (COL1A1) and platelet-derived growth factor beta (PDGFB) [2, 4]. DFSP is predominantly localized on the trunk (40-50%), followed by proximal extremities (40%), head and neck (10-15%), and then genitals (1%) [5]. Infrequently documented cases have been reported on the breast. We herein present a rare DFSP case on a female left breast that recurred as a large tumor due to rapid growth during pregnancy.

Case presentation

A 35-year-old Chinese woman accidentally found a 3 cm painless left breast lump before 10 years and underwent surgically removed. The original histological diagnosis was not known. No treatment was performed after surgery. No changes in this lesion were obviously noticed by the female, until the woman became pregnant 9 years later. The lesion began to growing rapidly in the second trimester of pregnancy.
Physical examination revealed the three adjacent lumps were about 10×9 cm, 4×4 cm and 3×3 cm. The lumps were firm, fixed with a relatively well-defined border, and blue-purple hyperpigmentation on the surface of skin (Figure 1). Ultrasound shows a hypoechoic mass with homogeneous internal echoes. After the end of pregnancy, magnetic resonance imaging (MRI) revealed fusion of multiple lesions, and the lesions were closely related to the adjacent skin (Figure 2). A biopsy was performed, and the histologic analysis found the tumor composed of mild spindle cells, and suggested a spindle cell tumor. Spindle cell tumors are rare in the breast, and challenging to diagnose. Then, the woman underwent surgical excision of the tumor with 1-cm normal-appearing tissue margins.

Histopathology examination revealed relatively bland and uniform spindle cells in the dermis and subcutaneous tissues, with cell abundance and without significant atypia (Figure 3A and 3D). The spindle cells are arranged in a storiform pattern (Figure 3C). They infiltrated the subcutaneous adipose tissue in a honeycomb pattern (Figure 3B).

Immunohistochemical staining revealed the tumor cells to be diffusely positive for CD34 and Vimentin (Figure 3E and 3F), and focally for CD99, and negative for Desmin, Caldesmon, ER (Figure 3G), PR (Figure 3H), EMA, STAT6, Bcl-2, CD117, DOG-1 and nuclear Beta-catenin. The Ki67 proliferation index was approximately 15% (Figure 3I). Fluorescence in situ hybridization (FISH) analysis was showed a fusion pattern of COL1A1 and PDGFB (Figure 4).

After the diagnosis was clear, further extension of the resection or treatment with imatinib or radiation were recommended, but the patient refused. At the 16 months follow-up, no recurrence was found.

Discussion

DFSP cases in the breast are very rare. Spindle cell tumors are difficult to diagnosed in the breast, and are often misdiagnose, because the diversity of morphologic and immunohistochemical features [6]. An accurate diagnosis is essential in the breast. Typical features of DFSP are uniformly monomorphic CD34+spindle cells with elongated nuclei and thin cytoplasm, showing little atypia and mitotic activity, and arranging in a storiform or spoke-wheel pattern. DFSP infiltrate subcutaneous adipose tissue along the septate presents with a characteristic “honeycomb” or “lace” pattern [3, 7]. Differential diagnosis of DFSP in the breast, such as phyllodes tumor of the breast, nodular fasciitis, classic-type myofibroblastoma, solitary fibrous tumor, and desmoid-type fibromatosis [6, 8]. FISH analysis showed a fusion pattern of COL1A1 and PDGFB which also supported the diagnosis of DFSP in our case.

According to our search of the literature on DFSP during pregnancy, no prior DFSP during pregnancy on breast cases have been reported. In this case, local recurrence occurred and the tumor has rapid growing behavior during pregnancy. A literature review of DFSP in pregnancy was reported that accelerated growth which about fourteen cases have been occurred in pregnancy [9].

DFSP showed rapidly growth during pregnancy, suggesting that female hormones may be associated with this biological alteration of DFSP. Currently, there were few literatures on this topic. Kibbi et al.
conducted a literature review of pregnant DFSP, a total of nine patients were analyzed for ER and PR expression, and none of them were ER positive and three were PR positive [9]. Whether female hormones play potential role was still need to further confirm which required detect in larger samples in pregnancy. However, DFSP in pregnancy are rare cases, studies were performed on nonpregnant patients including males. Until now, two studies have evaluated ER and PR expression in DFSP patients by immunohistochemistry, however, the positive rate results were inconsistent [10, 11]. One of the two studies have observed that loss of ER and PR expression in three recurrent DFSP compared to when they were in primary [10]. This suggested that loss of receptor expression might be associated with disease recurrence. The cause and reliability are unclear, while more research is needed to confirm role of female hormones in the biological characteristics of DFSP, particularly during pregnancy.

The pathogenesis of DFSP is not yet fully understood. The characteristic molecular genetic features of DFSP are a supernumerary ring chromosome derived from chromosomes 17 and 22 or a reciprocal chromosomal translocation t (17;22) (q22; q13), resulting in the genetic fusion of COL1A1 and PDGFB [2, 4]. PDGFB activates Ras mitogen-activated protein kinases (RAS-MARK) and Phosphatidylinositol 3-kinase-akt-rapamycin mammalian target of rapamycin (PI3K-AKT-mTOR) pathway leading to uncontrolled cell growth [12, 13]. Imatinib is an inhibitor of PDGFB-R, blocking signaling and interfering with phosphorylation of the receptor tyrosine kinase [14], and is used to the treatment of unresectable, recurrent, and/or metastatic DFSP in adult patients [15].

Although it is known that many of tumors can be successfully removed with a single stage and a margin of 1 cm, and larger tumors generally require wider margins [16]. Wide local excision (WLE) of DFSP is suggested that the adequate surgical resection margins is 2-3 cm [17, 18]. Positive or close margins are described as predicting factors for local recurrence [17]. Current recommendations are to follow-up with physical examination every 6 months for 5 years, and then annually for another 5 years as late recurrences have been reported [19].

**Conclusion**

Accelerated growth in DFSP has been reported only in a dozen cases during pregnancy, to our knowledge, we present a unique case of accelerated growth at the breast. The patient's surgical margins are insufficient and regular follow-up is required.

**Abbreviations**

DFSP: dermatofibrosarcoma protuberans; COL1A1: collagen type 1-alpha 1; PDGFB: platelet-derived growth factor beta; MRI: magnetic resonance imaging; FISH: fluorescence in-situ hybridization; PDGFB-R: platelet-derived growth factor beta receptor; RAS-MARK: Ras mitogen-activated protein kinases; PI3K-AKT-mTOR: Phosphatidylinositol 3-kinase-akt-rapamycin mammalian target of rapamycin; WLE: wide local excision
Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Data Availability

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

Competing interests

The authors declared that they have no competing interests.

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Author Contributions

MH drafted the manuscript. MJ and RZ analyzed the patient data and carried out image acquisition. MZ made suggestions about the manuscript. DZ participated in the design of the study and FISH testing and analysis. All authors read and approved the final manuscript.

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References


**Figures**

**Figure 1**

Photograph of the left breast showing the three adjacent lumps fixed with a relatively well-defined border.
**Figure 2**

Breast MRI. Fusion of multiple lesions in the left breast with closely related to the adjacent skin. (A) Coronal positions (B) Sagittal positions.
Figure 3

(A) densely arranged spindle cells (H&E stain, 40x); (B) spindle cells infiltrated the subcutaneous adipose tissue (H&E stain, 40x); (C) spindle cells are arranged in a storiform pattern (H&E stain, 100x); (D) uniform spindle cells with cell abundance (H&E stain, 400x); (E) CD34 staining showed positive (400x); (F) Vimentin staining showed positive (400x); (G) ER staining showed negative (400x); (H) PR staining showed negative (400x); (I) Ki67 staining showing proliferation index (400x).
Figure 4

FISH analysis revealing positive for COL1A1-PDGFβ fusion. The arrows represent the yellow fluorescence of the fusion.