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Case Report

Mammary leiomyomatous-type myofibroblastoma with symplastic atypia

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ABSTRACT

An unusual case of leiomyomatous-type mammary myofibroblastoma (MFB) with symplastic nuclear atypia is described in this report. The tumor occurred in a 67-year-old woman as a palpable 1 cm nodule. Histologically, the lesion was composed of myoid-appearing spindle cell fascicles with immunohistochemical positivity for CD34, Bcl-2, smooth muscle actin, desmin, h-caldesmon, calponin, estrogen receptor, p16, and cyclin-D1. Many tumor cells exhibited nuclear atypia resembling closely that of atypical (bizarre, symplastic) leiomyoma of the uterus. Mitotic activity was very low and MIB-1 index was 3%. Leiomyomatous MFB with atypia mimics malignant lesions which has to be considered in differential diagnosis.

KEY WORDS: Atypical leiomyoma, breast, immunohistochemistry, myofibroblastoma, uterus

INTRODUCTION

Mammary myofibroblastoma (MFB), described first by Wargotz *et al.* in 1987 [1], is a benign tumor occurring in both males and females [2,3]. In typical case, the lesion is a well-circumscribed nodule containing bland appearing myofibroblastic fascicles with focal hyalinization and with CD34-positive myofibroblastic immunophenotype [2,3]. The diagnosis in such typical cases is not difficult. However, non-typical histologic variants that mimic other lesions were recognized. These uncommon variants include cellular, infiltrating, collagenized/fibrous, lipomatous, myxoid, epithelioid, deciduoid-like, and leiomyomatous MFB [2-6]. Recently, we have seen a case of leiomyomatous MFB that showed an unusual symplastic atypia resembling strongly atypical leiomyoma of mullerian-type.

CASE REPORT

A 67-year-old obese woman with arterial hypertension, hepatal steatosis, and hypothyreosis presented with a palpable nodule in the left breast. Core cut biopsy showed stromal lesion with nuclear atypism, and therefore, a complete excision of the nodule was performed.

Grossly, the 3 cm × 3 cm × 2.5 cm excision specimen contained a 9 mm fibroadenoma-like nodule. Histologically, the nodule was well circumscribed and unencapsulated, and it was composed of ill-defined fascicles of spindle cells lying in hyalinized stroma [Figure 1a]. The spindle cells exhibited elongated nuclei and myoid-appearing eosinophilic cytoplasm [Figure 1b]. Rare nuclei were cigar-shaped. In approximately 80% of the lesion, the nuclei were not uniform, showing pleomorphism which resembled strongly that of uterine leiomyoma with bizarre nuclei [Figure 1c] [7,8]. These nuclei were of various size and shape, usually hyperchromatic, and some of them contained small nucleoli or intranuclear pseudoinclusions. They lacked significant mitotic activity; mitotic rate of the lesion was 1/50 hpf. The vasculature of the tumor included non-prominent capillaries and abnormal appearing vessels which were usually non-muscular. Around some vessels, foamy histiocytes were seen in the hyalinized stroma. Some mast cells were scattered through the tumor diffusely. Necrosis was not found.

Immunohistochemically, the tumor showed diffuse expression of alpha-smooth muscle actin, desmin, h-caldesmon, calponin, CD34, Bcl-2, and estrogen receptor (ER) [Figure 2a-g]. Cyclin-D1 and p16 were positive in 30% and 80% of the cells,

respectively [Figure 2h and i]. CD117 positivity was limited to numerous mast cells [Figure 2j]. MIB-1 index was 3% [Figure 2k]. The tumor was negative for myo-D1, myogenin, alpha-sarcomeric actin, pancytokeratin, cytokeratins CK5/6, CK34-BE12, CK7, CK20, epithelial membrane antigen (EMA), progesterone receptor, p63, p53, and S100 protein. The diagnosis of leiomyomatous MFB with atypical nuclear features was rendered and a follow-up was recommended. The patient is without recurrence 5 months after the excision.

DISCUSSION

Our case showed features of mammary MFB with leiomyomatous differentiation, such as expansive growth with well-circumscribed margin, fascicles of myoid-appearing cells with very low mitotic rate, stromal hyalinization, and immunohistochemical expression of CD34, calponin, Bcl-2, ER, and smooth muscle markers actin, desmin, and h-caldesmon [4]. In addition, numerous cells of the tumor had atypical bizarre nuclei without mitotic activity and, therefore, the morphology (along with positivity for ER and myoid markers) resembled strongly atypical leiomyoma of the uterus [7,8]. This histological picture

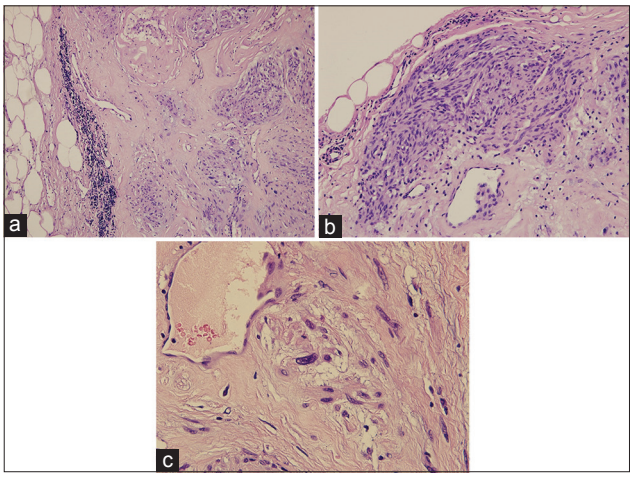

Figure 1: Histological features. (a) Low power shows short spindle cell fascicles and hyalinized stroma. Fibrous capsule of the tumor contains some lymphocytes (left), (b) cell fascicle composed of myofibroblastic cells with elongated nuclei, (c) an area with symplastic nuclear atypia (H and E, magnifications ×100, ×200, and ×400, respectively)

appears to be rare in leiomyomatous MFB. Fukunaga described two cases of mammary MFB, which contained small areas with the features of atypical leiomyoma of mullerian-type [5,6]. To the best of our knowledge, another case of leiomyomatous MFB with symplastic atypism was not described. However, some degree of nuclear atypism or scattered bizarre nuclei were reported in several cases of MFB of non-leiomyomatous type, including conventional, cellular, myxoid, deciduoid, and epithelioid MFB [3]. In these cases, it was supposed that atypism is degenerative in nature and it was liken to atypism in ancient schwannoma or symplastic/atypical uterine leiomyoma [3]. However, the recent molecular genetic study of uterine atypical leiomyomas by Zhang *et al.* found that nuclear atypism in these tumors represents a morphological correlate of genetic alterations, of which some are shared by both atypical leiomyoma and leiomyosarcoma [9]. In our case, the tumor cells show smooth muscle differentiation and ER positivity like smooth muscle tumors of mullerian-type, and therefore, we speculate that evolution of the atypism may be analogic with that of atypical leiomyoma of the uterus, i.e., the atypism is not degenerative but it reflects genetic alterations.

Differential diagnosis in our case included in the first place malignant spindle cell tumors such as leiomyosarcoma, rhabdomyosarcoma, metaplastic carcinoma, myofibroblastic sarcoma, and mammary stromal sarcoma [10-16]. Leiomyosarcoma and myofibroblastic sarcoma show in contrast with MFB infiltrative margin and mitotic/proliferative activity [10,13]. Rhabdomyosarcoma contains pleomorphic nuclei similar to those of our case. However, this tumor is an infiltrative lesion with mitoses and higher MIB-1 index. In addition, it is positive for skeletal muscle markers myogenin and myo-D1 [11]. Metaplastic carcinoma is an infiltrative tumor with mitotic and proliferative activity, and its epithelial phenotype is usually detectable by expression of at least some of epithelial markers (pancytokeratin, CK34-BE12, CK5/6, p63, and EMA) [12]. Stromal sarcoma of the breast [15,16] exhibits morphology and phenotype similar to the stromal component of malignant phyllodes tumor, with significant mitotic count, and infiltrative nature of the lesion. So-called periductal stromal tumor [16] is a low-grade appearing stromal sarcoma with a component of well-differentiated mammary ducts that were not found in our case. In addition, the present tumor had to be differentiated from intraparenchymal mammary

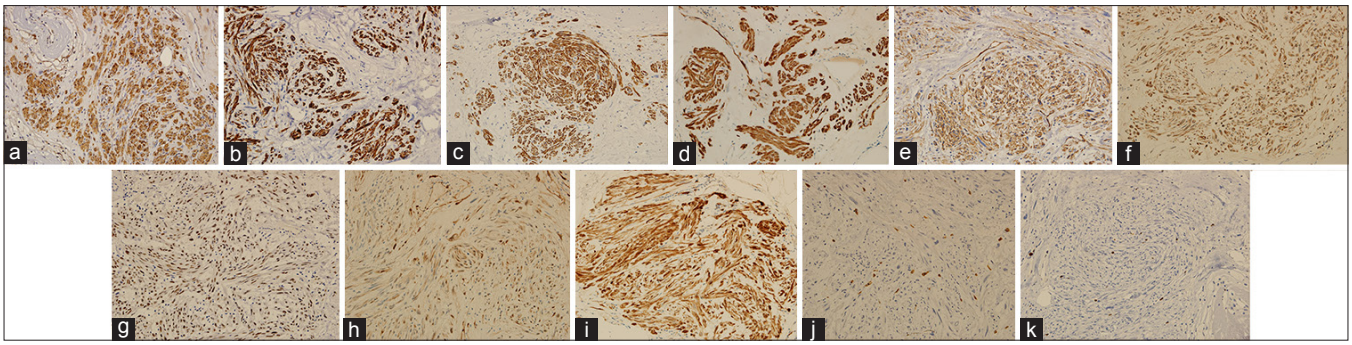

Figure 2: Immunohistochemical features. (a) Alpha-smooth muscle actin, (b) desmin, (c) h-caldesmon, (d) calponin, (e) CD34, (f) Bcl-2, (g) estrogen receptor, (h) cyclin D1 positivity in one third of the cells, (i) p16, (j) CD117, (k) MIB1 positivity in rare cells (magnifications x200)

leiomyoma [17] which represents an extremely rare lesion. In comparison with MFB, leiomyoma displays more compact and long fascicles and more numerous cigar-shaped nuclei [4,10]. Moreover, it lacks strong CD34 positivity seen in our case [18].

Mammary MFB is a benign tumor which is cured with complete surgical excision. However, a knowledge of the lesion with atypical nuclei is limited, and we think that in analogy with atypical leiomyoma of mullerian-type recommendation of follow-up is appropriate in our case.

CONCLUSION

We have described an unusual case of mammary MFB of leiomyomatous-type, which showed atypical features similar to atypical leiomyoma of mullerian-type. The pathologist should become aware of this unusual morphology of MFB to avoid misdiagnosis of sarcoma or metaplastic carcinoma of the breast.

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