Case Report

Extramammary Myofibroblastoma in the Axilla of a Male Patient: A Case Report and Literature Review

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Mammary type myofibroblastoma in an extramammary location is an extremely rare benign lesion. The site involved is usually along the embryonic milk line with the inguinal/groin region as a common location. Here we report a case of such lesion in an old man who presented with a painless mass in the right axilla. Histologically the lesion was comprised of loosely distributed bland spindle cells in a pseudoangiomatous background. No cellular atypia or mitosis was identified. Immunohistochemistry showed the spindle cells were immunoreactive to CD34, ER, and Bcl-2, but negative for desmin, cytokeratin, S-100, CD99, PR, CD21, and CD23. Ki-67 proliferative index for the spindle cells are very low. A diagnosis of extramammary myofibroblastoma was rendered after multiple extramural expert consultations. The uniqueness of this case includes: 1) pseudo-angiomatous and loose stroma background with on obvious interspersed collagen bundles; 2) negative for desmin, which is usually positive for this type of tumor; and 3) positive for Bcl-2, which has never been reported. Comparison of this entity with spindle cell lipoma at genetic level and a literature review were also conducted.
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Key Words: *myofibroblastoma, extramammary, spindle cell, desmin, estrogen receptor (ER), Bcl-2*

INTRODUCTION

Mammary myofibroblastoma (MMFB) is a rare benign neoplasm arising in breast tissue.[1] Extramammary myofibroblastoma (EMMFB) is an even rarer counterpart of MMFB. The most common site of this tumor is the inguinal/groin area, with an apparent predilection for the embryonic milk-line that stretches from the axilla to the medial groin.[2-4] One case of peri-auricular location has also been reported.[5] Similar to MMFB, EMMFB also commonly arises in elderly male patients or in a less extent, in postmenopausal women, with an age range of 35 to 67 years (median 53 years).[2-5]

Different from MMFB, which arises from mesenchymal component of the breast, EMMFB usually occurs subcutaneously, manifesting as a slowly growing, painless, well circumscribed mass with a size of 1-4 cm, although size as large as 10 cm has been also reported.[2-5] EMMFB, like MMFB, is mainly composed of spindle cells with myofibroblastic differentiation, surrounded by collagen-rich stroma and variable amount of adipose tissue and mast cells. Immunophenotypically, the spindle cells are positive for CD34, and desmin, in accordance with their mammary origin and myofibroblastic differentiation.[1-5]

Recently, cytogenetic analysis revealed that EMMFB harbored rearrangements or losses of chromosomes 13q or 16q that involved RB, FKHR, and FOXO1 genes. These genetic changes are typically seen in spindle cell lipoma.[6] Consequently, a link between these two entities has been speculated and EMMFB being a variant of spindle cell lipoma is under serious consideration.

CASE REPORT

Patient History

The patient was a 79 years old male who came to hospital complaining a painless growing right axillary lump. Clinicians' primary impression was lymphadenopathy and an excisional biopsy was performed to rule out lymphoma.

Specimen and Morphology

Pathology lab received a 5.5x4.5x3 cm well circumscribed specimen with a red/tan homogenous cut surface. No lymph node architecture was found. Microscopically, this was a vascular rich lesion with bland appearing spindle cells dispersed in a background of loose stroma. No nuclear atypia or mitosis was identified. The vessels were thicken-walled and prominent in number, showing an angiomatous feature (**Figure 1A/1B**). Focal mature adipose tissue was also present (not shown).

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Immunohistochemistry

The spindle cells were positive for CD34, ER (**Figure 1C/1D**), vimentin, and Bcl-2 (**Figure 2A/2B**), but negative for desmin and CD117 (**Figure 2C/2D**), pan-CK, S-100, CD99, CD21, and CD23. Ki-67 proliferation index is very low for the spindle cells (< 1%).

Final Diagnosis

The case was finally diagnosed as EMMFB after expert consultations in multiple institutions. The patient was recovered after one week and had no complaint since then.

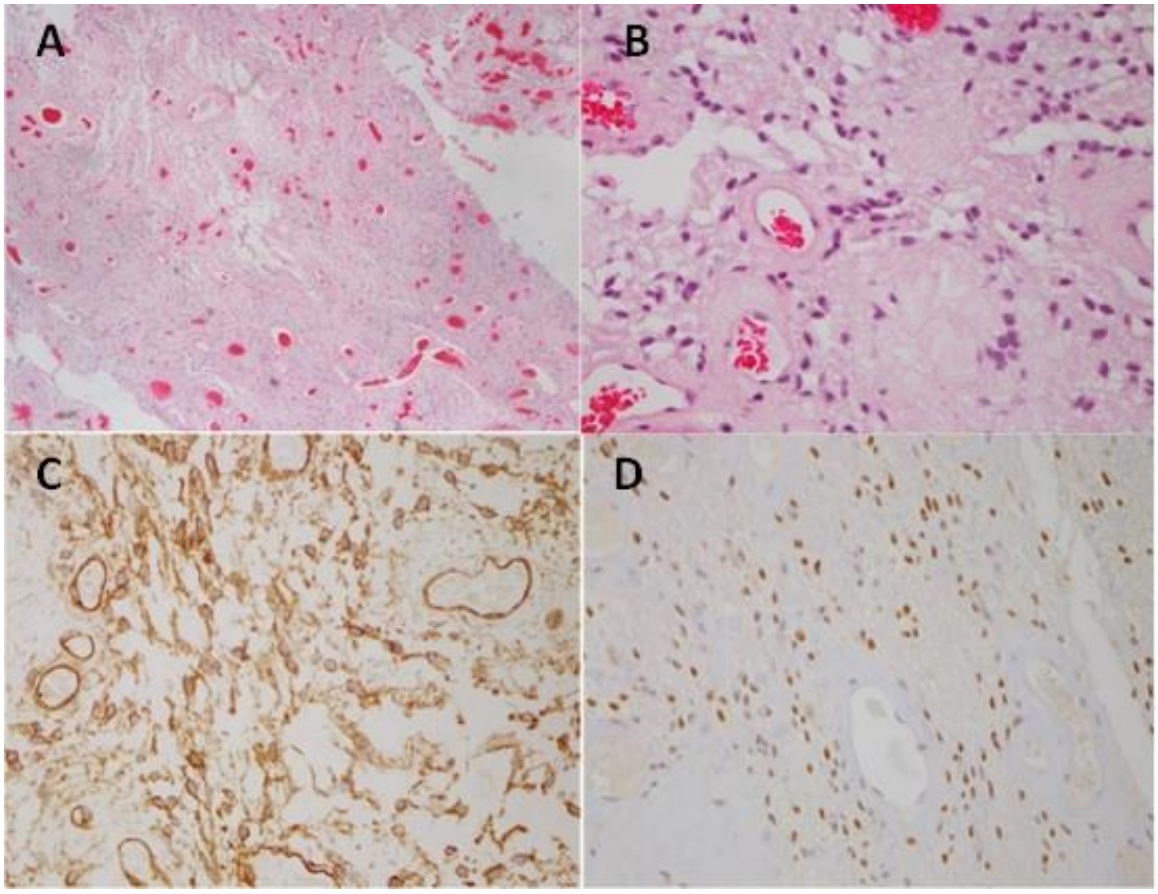

Figure 1. Histology and immunophenotype in a case of EMMFB. **A.** H&E staining at 40x. The tumor is vascular rich and with a loos stroma. No collagen bundles seen. **B.** H&E staining at 400x. The tumor cells are of bland appearing spindle cells. No atypia or mitosis seen. **C.** Immunostaining for CD34. Tumor cells are positive. **D.** Immunostaining for ER. Tumor cells are positive (nuclear staining).

DISCUSSION

Here we report a case of EMMFB, a very rare entity commonly occurring subcutaneously along the embryonic milk line. There are only about 20 of similar cases that have been reported in literature.[2-5]

EMMFB was first described by Wargotz et al in 1987 when they were reporting a case series on myofibroblastoma of the breast.[1] In 2001 McMenamin and Fletcher published a case series of 9 EMMFB located in the inguinal area, vaginal wall, buttock, abdominal wall, and mid back.[2] From then on, several single case reports on this entity trickled into literature, including a rare location of head and neck region.[5] All reported cases were elderly male predominant and mostly located along the embryonic milk line. All lesions were painless, well circumscribed, and of subcutaneous site, with a size ranging from 2-13 cm.[2-6] Grossly, all lesions were unencapsulated, whitish/pinkish color with a whorling or nodular appearance. Microscopically, the lesional mass consists of fascicles of bland appearing spindle cells embedded in a loose or myxoid collagenous stroma, mixed with variable mature adipose tissue and abundant mast cells.[2-6] Generally there was no cellular atypia or increase in mitosis, although in rare cases slightly atypical, multinucleated, or epithelioid cells had been identified.[2] Immunophenotypically, the spindle cells were commonly positive for CD34, desmin, and occasionally smooth muscle actin.[2-6] Prognosis-wise, complete excision is a cure for the patients. No recurrence has been reported.[2]

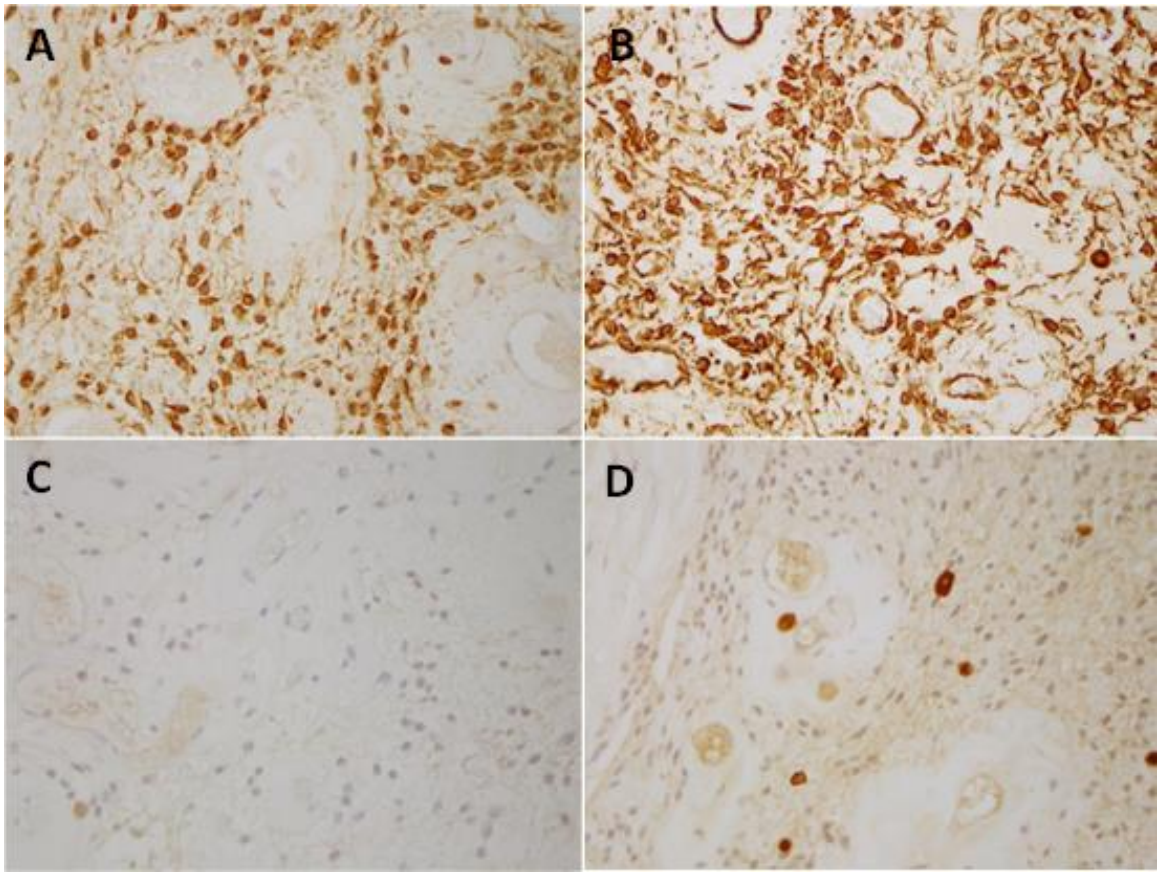

Figure 2. Immunophenotype of a case of EMMFB. The tumor cells are positive for Bcl-2 (**A**) and vimentin (**B**), but negative for desmin (**C**) and CD117 (**D**). The positive cells in D are mast cells, which are commonly seen in EMMFB.

Our case presented some unique features not described in the reported cases, which made it difficult to reach a consensus diagnosis. First, our lesion was rich in thick-walled vessels, mimicking an endothelial proliferation-related disease such as angiofibroma or follicular dendritic cell sarcoma. Secondly, there was scarce of collagen-rich stroma that were commonly described in published cases, instead, there were plenty of spindle cells scattered in a loose connective tissue meshwork. Thirdly, our tumor was negative for desmin, but positive for ER and Bcl-2. This combination was not seen in all other reported cases. The cause behind these variations possibly lies in the pathogenesis of MMFB/EMMFB and their close link with spindle cell lipoma (SCL).

Cytogenetic studies on several cases of MMFB and one case of EMMFB revealed that both these lesions contained losses of RB13q14, FKHR13q14, or 16q, which are commonly seen in SCL.[3,4,7] Indeed, SCL and MMFB/EMMFB share many clinical and morphological features, such as predilection for elderly males, well circumscribed mass lesion, tumor with admixture of fascicle-forming bland spindle cells, interspersing bands of collagen, scattered mast cells, and mature adipose tissue.[4-8] Therefore, postulation about common origin of MMFB/EMMFB and SCL has been entertained for some time. The variations in immunophenotype and morphology, such as positivity for desmin, ER, Bcl-2, amount of adipose tissue, the extent of vascular proliferation, density of stroma, etc., could be explained by the extent of differentiation of the common ancestor cells for these disease entities.

Differential diagnosis of MMFB/EMMFB includes garden variety of benign and malignant spindle cell tumors, such as cellular angiofibroma (spindle cells are CD34-)[9], angiomyofibroblastoma, peripheral nerve sheath tumor (S-100+), nodular fasciitis, solitary fibrous tumor/hemangiopericytoma (desmin-, CD99+, STAT6+)[10,11] and dermatofibrosarcoma protuberans (desmin-), etc. Clinical history, microscopic morphology, and immunohistochemistry profile would be helpful to differentiate one from the other.

In conclusion, we report a case of EMMFB with unique morphology and immunophenotype that are deviating from what has been described in literature regarding this entity. Potential common origin of MMFB/EMMFB and SCL, and different direction/stage of differentiation, could be the key to understand the variation among this group of diseases.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

REFERENCES

1. Wargotz ES, Weiss SW, Norris HJ. Myofibroblastoma of the breast. Sixteen cases of a distinctive benign mesenchymal tumor. Am J Surg Pathol. 1987;11:493–502.
2. McMenamin ME, Fletcher CD. Mammary-type myofibroblastoma of soft tissue: a tumor closely related to spindle cell lipoma. Am J Surg Pathol. 2001;25:1022–1029.
3. Maggiani F, Debiec-Rychter M, Verbeeck G. Extramammary myofibroblastoma is genetically related to spindle cell lipoma. Virchows Arch. 2006;449:244–247.
4. Pauwels P, Sciot R, Croiset F. Myofibroblastoma of the breast: genetic link with spindle cell lipoma. J Pathol. 2000;191:282–285.
5. Hox,V, Poorten, VV, Delaere, PR, Hermans, R, Rychter, M, Sciot, R. Extramammary myofibroblastoma in the head and neck region. Head and Neck. Sep. 2009 1240-1244.
6. Chin D, Sciot, R, Polito P. Lesions of 13q may occure independently of 16q in spindle cell/pleomorphic lipomas. Histopathology 1997;31:222-225.
7. Fletcher CD, Martin-Bates E. Spindle cell lipoma: a clinicopathological study with some original observations. Histopathology. 1987;11:803–817.
8. Dahlen A, Debiec-Rychter M, Pedeutour F. Clustering of deletions on chromosome 13 in benign and low-malignant lipomatous tumors. Int J Cancer. 2003;103:616–623.
9. Flucke U, van Krieken JH, Mentzel T. Cellular angiofibroma: analysis of 25 cases emphasizing its relationship to spindle cell lipoma and mammary-type myofibroblastoma. Mod Pathol. 2011;24:82–89.
10. Fritchie KJ, Carver P, Sun Y. Solitary fibrous tumor: is there a molecular relationship with cellular angiofibroma, spindle cell lipoma, and mammary-type myofibroblastoma? Am J Clin Pathol. 2012;137:963–970.
11. Guillou L, Gebhard S, Coindre JM. Lipomatous hemangiopericytoma: a fat-containing variant of solitary fibrous tumor? Clinicopathologic, immunohistochemical, and ultrastructural analysis of a series in favor of a unifying concept. Hum Pathol. 2000;31:1108–1115.