

Not Otherwise Specified-Type Sarcoma of Breast with CD10 Expression: Case Report

Bermal Hasbay¹ , Filiz Aka Bolat¹ , Hülya Aslan² , Hüseyin Özgür Aytaç³ 

¹Department of Pathology, Başkent University School of Medicine, Adana Dr. Turgut Noyan Hospital, Adana, Turkey

²Department of Radiology, Başkent University School of Medicine, Adana Dr. Turgut Noyan Hospital, Adana, Turkey

³Department of General Surgery, Başkent University School of Medicine, Adana Dr. Turgut Noyan Hospital, Adana, Turkey

ABSTRACT

Primary breast sarcomas are very rare and account less than 1% of invasive breast carcinomas. Primary sarcomas of breast are leiomyosarcoma, angiosarcoma, liposarcoma, fibrosarcoma, rhabdomyosarcoma, malignant peripheral nerve sheath tumor and pleomorphic sarcoma. Recently, a new CD10 positive group of sarcoma was identified. These tumors cannot be classified as a soft tissue sarcoma and show diffuse strong positive staining pattern with CD10 (NSCD10). Herein we report clinical and morphological characteristics of two cases diagnosed with not otherwise specified-type sarcoma with CD10 expression by histologically and immunohistochemical findings with the literature. NSCD10 shows similarity with leiomyosarcoma and sarcomatoid-type metaplastic carcinoma histomorphologically among specific sarcomas of breast. CD10 expression should be taken into consideration in the presence of not diagnosed and not specified tumors and CD10 should be added to the immunohistochemical panel.

Keywords: Breast, sarcoma, CD10 positive sarcoma

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Introduction

Primary breast sarcomas are very rare and account less than 1% of invasive breast carcinomas (1). Primary sarcomas of breast are a heterogeneous group of tumors including angiosarcoma, liposarcoma, leiomyosarcoma and pleomorphic sarcoma as the most common types (2). Primary breast sarcomas differ from the primary breast carcinomas with behavior pattern such as the soft tissue sarcomas of the other parts of body. They show distant metastatic spread pattern rather than nodal involvement.

They present as painless, mobile, circumscribed and hard masses. They are more frequently seen among women between the ages of 45-55 years (2).

In the diagnosis of primary breast sarcoma, there are two important features. Distant metastasis from another site should be eliminated and spindle cell metaplastic carcinoma (MC) and also malignant phylloides tumors (MPT) are important in the differential diagnosis.

The treatment modality of the primary breast sarcoma is surgery. Recently, wide local excision providing tumor free borders is sufficient for the treatment. Axillary lymph node dissection is unnecessary. It is recommended if there is a palpable lymph node is present.

CD10 (CALLA) neutral endopeptidase is a surface cell receptor and is expressed by lymphoid precursor cells and myoepithelial cells of breast (3-4)

Recently published studies suggest that CD10 could be a good indicator of stem cells in breast carcinoma, particularly precursors of metaplastic carcinomas (5). CD10 is positive in phylloides tumors that showing aggressive pattern in breast (3). Recently, a not otherwise specified-type sarcoma with CD10 expression is identified (1, 6-8). In this case report we aimed to discuss two cases diagnosed with not otherwise specified-type sarcoma with CD10 expression at our department with the literature data.

Case Presentations

Case 1

A 70-year-old female was admitted to the oncology department with a history of surgically excised lesion with a diagnosis of leiomyosarcoma one year ago. Her tumor was an ulcerated, hemorrhagic and discharging lesion. The paraffin blocs were referred to our department to re-evaluation.

Histological examination of outer center preparations; A tumoral lesion with hyperchromatic nuclei, apparent nucleoli and large eosinophilic cytoplasm in diffuse infiltrative pattern was seen under the stratified squamous epithelium and stroma of the breast. The tumor was also containing spindle shaped bundles with apparent nucleoli in some areas (Figure 1).

Perineural invasion was positive with in the tumor. In immunohistochemically evaluation, the tumor was strongly positively stained by smooth muscle actin (SMA), Calponin (Clone CALP, Code M3556, Dako, Denmark) and CD10 (Figure 2, Clone 56C6, Neomarkers, USA) however CD68 (MS-397-PCS, Thermo Scientific, USA) was focal positively stained.

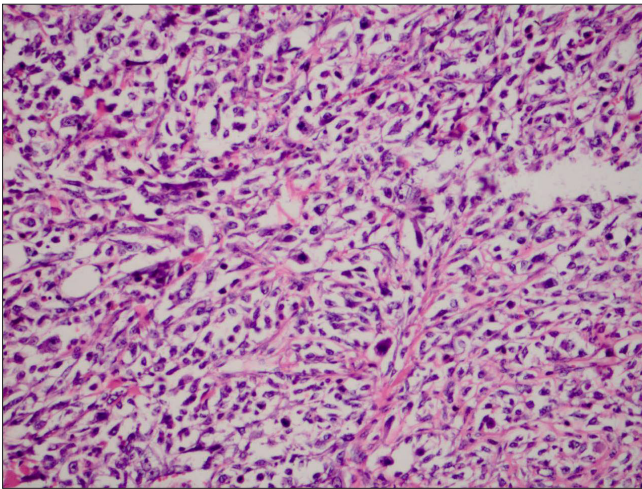


Figure 1. Tumor showed hyperchromatic nuclei, apparent nucleoli and large eosinophilic cytoplasm in diffuse infiltrative pattern (HE x200)

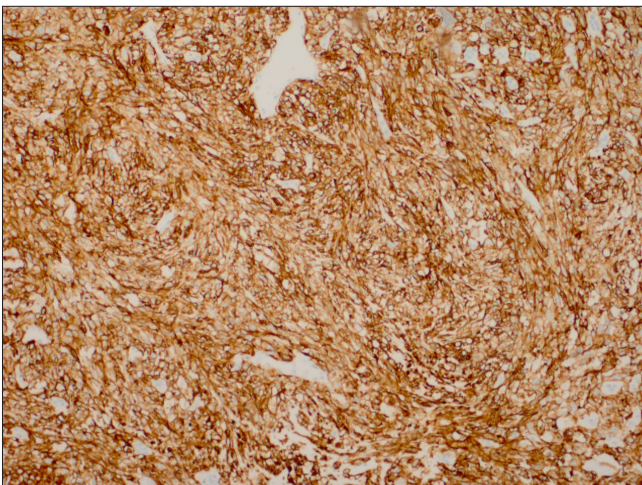


Figure 2. Immunohistochemically CD10-positive in tumor cells (x200)

Pan-cytokeratin (Clone AE1/AE3, Genemed, Germany), Desmin (Clone D33, Dako, Denmark), H-Caldesmon (Clone h-CD, Code IR054, Dako, Denmark), S-100 protein (Code ZO311, Dako, Denmark), p63, HMB45, CD34 (Clone QBEnd-10, Dako, Denmark), ER (Clone EP1, Code M3643, Dako, Denmark), PR (Clone Y85, 60-0056-7, Genemed, Germany), Cerb-2 (Code A0485, Dako, Denmark) were negative. The case was diagnosed with not otherwise specified-type sarcoma with CD10 expression with these morphological and immunohistochemical findings. Then the patient was followed-up at another center.

Case 2

A 38-year-old female was admitted to the department of general surgery at our hospital with a history of rapidly growing mass in the upper outer quadrant of right breast within the two months. The patient gave birth eight months ago. The mass has been first identified three months ago. At that time the longest diameter of the lesion was 6 mm at ultrasonography reports. At the second control the mass was within 35 mm diameter sonographically. The patient went to core-needle biopsy and the tumor was reported as a malignant tumor.

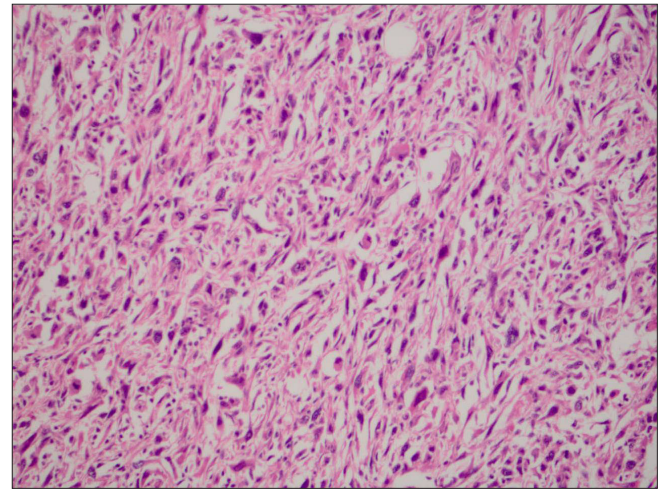


Figure 3. Tumor showed hyperchromatic-pleomorphic nuclei, apparent nucleoli and eosinophilic cytoplasm within the tumor fascicles (HE x200)

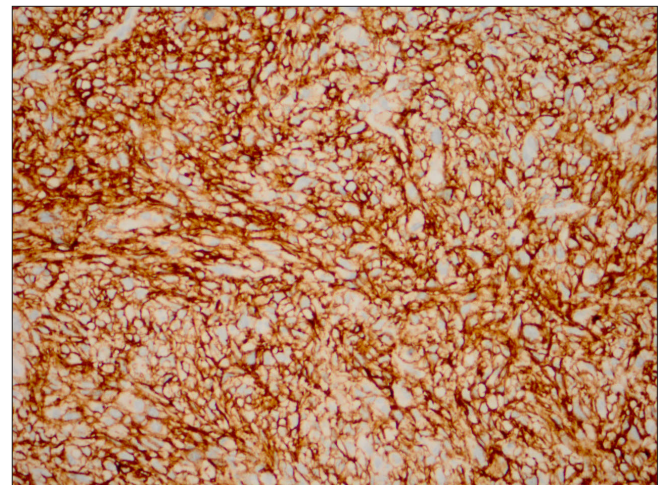


Figure 4. Immunohistochemically CD10-positive in tumor cells (x200)

The paraffin blocs were referred to our department for re-evaluation. These blocs showed a tumoral lesion composed of fasciculated spindle cells with hyperchromatic, pleomorphic nuclei, apparent nucleoli and eosinophilic cytoplasm in the breast stroma.

Immunohistochemically the tumor was positive for SMA (Clone 1A4, Code M0851, Dako, Denmark). Pan-cytokeratin, H-Caldesmon, S-100 protein, Bcl-2 (Clone 124, Code IR614, Dako USA), CD34, ER, PR and Cerb-B2 were negative.

The patient was diagnosed with malignant spindle cell tumor with the morphologic and immunohistochemical findings. Metaplastic carcinoma, breast sarcomas and malignant phyllodes tumor were considered within the differential diagnosis.

Magnetic Resonance Imaging (MRI) of the breast showed a subcutaneously located malignant lesion within a 5x6 cm diameters in the upper outer quadrant of the right breast. The tumor showed restricted diffusion. There were axillary lymph nodes with asymmetric cortical thickening.

The patient went mastectomy. Macroscopic evaluation showed a hard and solid mass measured at 6x5.5x4.5 cm diameters in the upper outer quadrant of the mastectomy specimen. The mastectomy specimen was weighted at 495 gr with 22x14 cm diameters.

The histologic evaluation of the tumor showed hyperchromatic- pleomorphic nuclei, apparent nucleoli and eosinophilic cytoplasm within the tumor fascicles and necrotic areas (Figure 3). 10 High-power fields presented 19-20 mitotic activity.

Immunohistochemically, CD10 (Figure 4), SMA and Calponin was positive, whereas pan-cytokeratin, CK5/6, HMWCK (Clone 34bE12, Genemed, Germany), P63 (Clone DAK, Code IR662, Dako, Denmark), Desmin, H-Caldesmon, bcl-2, CD34, ER, PR and cerb-b2 were negative with in the tumor.

The case was diagnosed with not otherwise specified-type sarcoma with CD10 expression with these morphological and immunohistochemical findings. The patient received chemotherapy and radiotherapy. The patient was alive and healthy at 18th month following surgery. Patients gave orally informed consent.

Discussion and Conclusion

Primary breast sarcomas are very rare and the most common types are angiosarcoma and liposarcoma (1, 2). Fibrosarcoma, leiomyosarcoma, malignant peripheral nerve sheath tumor, rhabdomyosarcoma and osteosarcoma can be seen less frequently (2, 9).

Recently, not otherwise specified undifferentiated breast sarcoma (NOS) characterized by myoepithelial markers was identified among some of the CD10 expressing cases (1, 6-8). Patients are commonly presented with painless hard masses. They are common among 45-55 years.

Radiologically breast sarcomas can be seen as irregular or oval shaped masses at both mammography and MRI. Breast sarcomas are originating from the interlobular mesenchymal elements supporting the breast stroma.

For instance, angiosarcoma is originated from endovascular cells; however, clarifying the origins of bone and cartilage containing tumors

is hard. This is because the breast does not contain these tissues (8). Recently published studies showed that sarcomas are originating from the primitive cells with the totipotential differentiation capacity. Some studies suggested that CD10 is a good marker to monitor the stem cells in breast carcinoma particularly precursors of metaplastic carcinomas (5).

Metaplastic carcinomas that originating from the stem cells show two types of differentiation from epithelium and myoepithelium. However, NOSCD10 sarcomas are believed to be differentiated to mesenchyme and myoepithelium (5, 8). Because the immunophenotype of NOS type sarcoma with CD10 expression suggests that these neoplasms represent a mammary sarcoma variant with myoepithelial features (8).

If a spindle cell malignant lesion is identified in a breast, MC and/or MPT should be first come to mind in the differential diagnosis rather than a sarcoma. Undifferentiated mammary sarcoma or not otherwise specified sarcoma with CD10 expression is an exceedingly rare and diagnosis is made after exclusion of all other malignant cell tumors (for example: Metaplastic carcinoma, malignant phylloides tumors, spindle cell sarcoma, leiomyosarcoma, fibrosarcoma) in the breast (6).

Axillary lymph node dissection should be added in the treatment of particularly the MC due to the tendency of MC to lymphatic dissemination. Thus, NOS CD10 positive sarcomas and other breast sarcomas should be differentiated from MC (1).

Studies showed that axillary lymph node dissection is unnecessary in the treatment of breast sarcomas (9). Invasive breast carcinomas and/or in-situ carcinoma areas should be searched with multiple samplings to show the presence of spindle cell lesion that is made of pure spindle cells or mixed with epithelial components (squamous or glandular) or not. A large cytokeratin panel should be performed in tumors containing pure spindle cells.

Malignant phyllodes tumors should be differentiated from breast sarcomas. The presence of benign epithelial component or leaf like structure supports the diagnosis of phyllodes tumors. A lot of sampling should be needed. However, patient history should be questioned carefully because apparent stromal growth occurs in high grade or recurrent phyllodes tumors.

Particularly, MPT's can show the positivity of CD10, SMA and Vimentin. For this reason, differential diagnosis should be made with CD34 and BCL-2 positivity with immunohistochemical staining (1, 3, 10). In our cases CD34 and BCL-2 were negative and epithelial component cannot be seen in multiple samples.

Not otherwise specified-type sarcoma with CD10 expression shows similarity with leiomyosarcoma and sarcomatoid type metaplastic carcinoma histomorphologically among specific sarcomas of breast.

Immunohistochemically, CD10 was negative in leiomyosarcoma or it can show positivity in focal areas and at least one of SMA as well as also desmin or h-Caldesmon is positive. However, CD10 is strongly positive, desmin and h-Caldesmon is negative in 'not otherwise specified-type' sarcoma (1, 8). In both of our cases, CD10 was positive, while desmin and h-Caldesmon were negative.

In metaplastic carcinomas, multiple sampling as well as a large cytokeratin immunohistochemical panel should be performed. In both of our cases, p63, CK7, CK5/6 and HMWCK are negative.

The primary treatment of breast sarcomas is surgery. The role of radiotherapy and chemotherapy is not clear in the treatment strategies (9). The treatment protocol of the CD10 positive sarcomas will be clarified in the future with the increased number of defined cases. Thus, it should be kept in mind in the differential diagnosis.

The molecular studies to clarify the origins of NSCD10 tumors should be performed together due to the closed relationship between MC, PT and NSCD10.

Although, NOSCD10 sarcomas are proposed to be originating from the primitive stem cells and showing mesenchymal and myoepithelial differentiation, histopathogenesis is still unclear.

As a result, not otherwise specified-type sarcoma with CD10 expression should be taken into consideration in the presence of not diagnosed and not specified tumors and CD10 should be added to the immunohistochemical panel.

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