Metaplastic Carcinoma Of The Breast With CD117 Positive Staining. Case Report And Review Of Immunostaining

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Citation

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Abstract

Metaplastic carcinomas of the breast are rare and are reported to comprise less than 1% of all invasive breast tumors. The range of age at diagnosis as well as clinical symptoms does not differ from that of conventional invasive ductal breast cancer. The tumor can be composed of a variety of different cells making it difficult to correctly diagnose this type of growth due to the unknown origin of the cancer. Metaplastic carcinomas can be classified into purely epithelial or mixed epithelial and mesenchymal carcinomas. Features of an adenocarcinoma or squamous cell carcinoma can be seen along with mesenchymal components ranging from chondroid or osseus metaplasia to chondro- or osteosarcoma. (1) In this report we follow a case of metaplastic carcinoma with a immunohistochemistry study that shows positivity for CD117 and the potential consideration for effective treatment in such positivity with a current review of the literature.

REPORT OF CASE

A 52-year-old female presented to the family medicine clinic with a history of weight loss. The patient complained of a breast lump which had been present for 7 months in conjunction with nipple discharge. Local examination showed a 10 X 8 cm lump. The skin above the lump was peau d'orange, the area was ulcerated and inflamed with a blood stained discharge, along with a palpable lymph node at the right axilla. The left breast showed no signs of abnormality. There was no family history of breast cancer. Ultrasound revealed a 6.7 X 4.1 cm cross section diameter, heterogeneous, cystic and calcified mass in the right breast. Left breast by ultrasound was normal.

PATHOLOGICAL FINDINGS

The mastectomy specimen contained a 14 X 10 X 9 cm mass extended to the maxillary tail and adheres to the upper lateral quadrant with a 9X8cm ulcerating skin surface. Nipple and areola appeared normal. Cut section from the case showed a deeply necrotic myxoid soft heterogeneous mass containing questionable fatty areas with a cystic center. The mass extended closely to the smooth posterior resection margin surrounded by fibrotic tissue. Dissection of the axillary tail revealed 13 small lymph nodes.

Multiple sections of the mass (Figure 1) demonstrated vaguely defined high grade fibrosarcoma-like proliferation formed by intersection bundles, whorls and peculiar perivascular formations. Different microscopic forms were seen such as crisscross, herring bone, fascicular, storiform, neuronal and emangiopericitoma pattern.

The forms were composed of compact, crowded or loose cells presenting an eosinophillic abundant cytoplasm. The cells had an oval to spindle pleomorphic, hyperchromatic nuclei containing visible small nucleoli. Frequent mitotic figures and scattered mast cells were present.

Also rare scattered foci of malignant squamous cells were noted. White areas surrounding the tumor showed breast tissue with fibrocystic changes. All lymph nodes were free of tumor.

Immunohistochemistry (Figure 2) showed that tumor cells were reactive for CD 117, epithelial membrane antigen (EMA), Vimentin, Chemotrypsin and partially positive for Pan Cytokeratin. The cells were negative for estrogen receptors, progesterone receptors, Her-2 and CD34.

The diagnosis was invasive metaplastic carcinoma with a high grade spindle cell type. No lymphovascular invasion was present. The nipple, areola, resection margins and right axillary lymph nodes were free of tumor.

Figure 1

Figure 1: Metaplastic Carcinoma of Breast, Hematoxylin-Eosin Stain (H&E). A. (H&E) X10, B. (H&E) X20, C. (H&E) X40, D. Crisscross Pattern X20, E. Herring Bone Pattern X10, F. Hypo- and Hyper Cellular Areas X10, G. Fascicular Pattern X10, H. Mitotic Figures X40, I. Storiform Pattern X10, J. Neuronal Pattern X10, K. Hemangiopericitoma Pattern X40, L. Scattered Mast Cells X20.

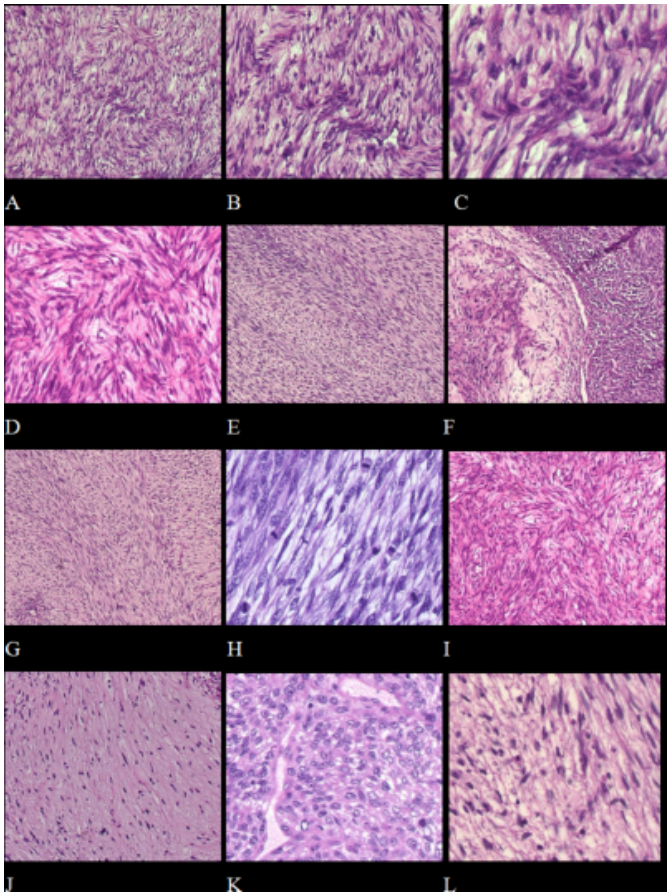
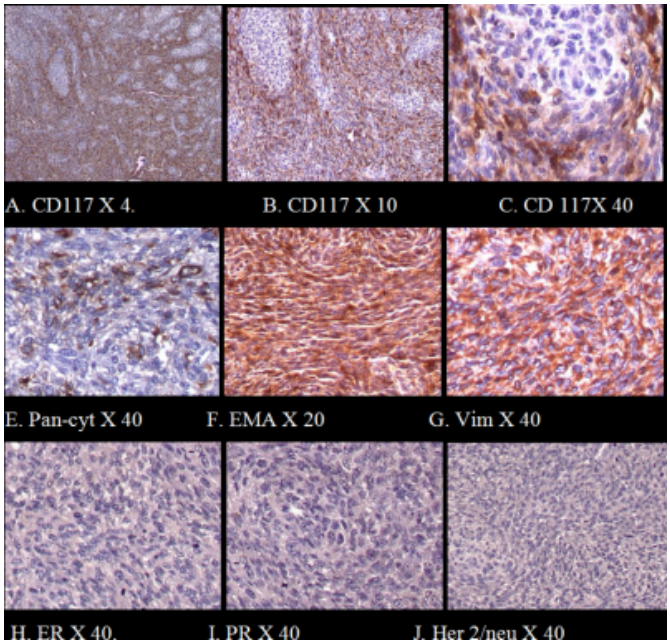


Figure 2

Figure 2: Immunostaining of CD117 (A, B, C), E. Pan Cytokeratin (Pan-cyt), F. Epithelial Membrane Antigen (EMA), G. Vimentin (VIM), H. Estrogen (ER), I. Progesterone (PR), J. Her 2/Neu.



DISCUSSION

Metaplastic carcinoma (carcinosarcoma, sarcomatoid carcinoma, malignant mixed tumor) is a biphasic tumor comprising of malignant epithelial and heterologous mesenchymal elements that produce a cartilaginous or osseous matrix (2-4).

Metaplastic malignancies pose a differential diagnostic problem for the pathologist because of the varied nomenclature and the need to distinguish a sarcoma from a carcinoma with sarcomatous features.

Hence, Oberman proposed the term metaplastic carcinoma to account for all mixed carcinomas of the breast (5-13).

Immunostaining in metablastic carcinoma is helpful in determining the marker expression of both epithelial and mysenchemal component, giving an idea about the prognosis and asset in determining the therapeutic plan.

The heterogeneous nature of tumor cells is corroborated by histopathologic staining for mesenchymal cells (vimentin), epithelial cells (cytokeratin), and myoepithelial cells (S-100 protein, actin, and high molecular weight cytokeratin). The cell of origin may be the myoepithelial cell in some cases, particularly spindle cell carcinomas, given the biphasic

expression of the tumor. (7, 9, 10, 14).

CD117, also called KIT or C-kit receptor, is a cytokine receptor expressed on the surface of hematopoietic stem cells as well as other cell types. Mutations in this gene are associated with gastrointestinal stromal tumors (GISTs), mast cell disease, acute myelogenous leukemia (CML), and piebaldism. Multiple transcript variants encoding different isoforms have been found for this gene (15-17). Imatinib, a mesylate salt, is currently used in CML, GISTs, and certain brain tumors, including high grade glioblastoma. It was also shown to be effective in treating systemic mastocytosis, including those who had the D816V mutation in c-Kit (18). On the other hand, patients with c-kit positive breast cancers revealed no benefit from high-dose chemotherapy(19). We propose in this report that immunostaining has a very important diagnostic value for metablastic breast carcinoma and for those who are positive for CD117; these individuals may benefit from treatment with Imatinib.

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