Archival paraffin embedded material of 11 MPC, as defined by the 2003 WHO classification, and 2 axillary lymph node metastasis, one with a cartilaginous matrix component and one without, were retrieved from the Pathology Department and reviewed. All tumors displaced a regular infiltrating duct carcinoma component and a variable amount of heterologous elements with a chondroid matrix.

Selected 4 μm thick formalin-fixed deparaffinized sections were stained examined by immunohistochemistry for the expression and localization of SOX9 (polyclonal, R&D), Versican (polyclonal, Novus Biological), Aggrecan (6-B-4, Abcam), p63 (4A4, Dako) and S100 (N/A, Dako).

Expression of Cartilage-specific Markers in Breast Carcinomas with Chondroid Differentiation
A. Contreras, MD/PhD, T. Krausz, MD, A. Montag, MD, M. Tretiakova, MD/PhD, R. Wilcox, MD, K. Gwin, MD/PhD
The University of Chicago Medical Center, Department of Pathology, Chicago, Illinois

Background

Metaplastic breast carcinoma with chondroid differentiation (MPC) is a rare variant of metaplastic breast carcinoma with mixed epithelial and myxochondroid mesenchymal elements. Previous studies indicated that MPC are of epithelial origin and are associated with a myoepithelial-like differentiation. Little is known about the precise matrix composition or if a true chondrogenic transition occurs. The differentiation of mesenchymal cells into chondrocytes involves a multistep pathway and can be traced by evaluating marker genes of chondrocytic development. The transcription factor SOX9 is expressed early in mesenchymal condensation and has, with the chondroitin sulfate proteoglycan Versican, an essential function in the subsequent differentiation of prechondrogenic precursor cells into chondrocytes. Differentiated chondrocytes express cartilage-specific markers such as the chondroitin sulfate proteoglycan Aggrecan.

Immunohistochemistry:
- SOX9 revealed strong nuclear expression in the heterologous chondroid tumor component, moderate nuclear expression in the regular ductal carcinoma component and in both lymph node metastasis.
- Strong cytoplasmatic staining for Versican was found in both tumor components
- All cases showed variable degrees of immunoreactivity for Aggrecan.
- The metaplastic tumor cells showed moderate to strong nuclear staining for p63
- Nuclear and cytoplasmic staining for S100 was observed in the tumor cells of the chondroid matrix
- None of the cartilage-specific markers were expressed in adjacent normal mammary tissue

Results

Conclusions

Expression of the transcription factor SOX9, which induces cartilaginous differentiation, and Versican, its co-factor for differentiation of prechondrogenic precursor cells into chondrocytes, supports true chondrocytic differentiation of the matrix. This is further stressed by the presence of Aggrecan, a typical gene product of differentiated chondrocytes, and immunoreactivity for S100, which is relatively constantly expressed in neoplastic chondrocytes.

The morphologic impression of a chondroid matrix component in MBC is supported by the IHC expression of cartilage specific matrix molecules (proteoglycans) and chondrocyte gene products. Our findings indicate that breast carcinoma cells of initially epithelial origin transdifferentiate into chondrocyte-like cells following the pathway of normal chondrocytic development.

Expression of cartilage specific matrix molecules remains preserved in axillary LN metastasis with and without cartilaginous matrix.

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