Metaplastic carcinoma with extensive dendritic cell differentiation: a previously unrecognised type of triple-negative breast cancer

We report on the case of a 48-year-old lady presenting a nodule, 24 mm in diameter, in the right breast. A core biopsy showed an undifferentiated tumour made of large cells in syncitial arrangement, featuring vesicular irregularly shaped nuclei with prominent nucleoli, and a high mitotic activity. A huge number of inflammatory cells, particularly lymphocytes and plasma cells, were intermingled with the neoplastic cells (Figure 1A). Immunohistochemistry carried out by applying antibodies raised against cytokeratin (CK) MNF-116, CK7, p63, S100-protein, CD31, desmin, CD21, and CD35 showed a strong and diffuse immunoreactivity for CD21 (Figure 1B) and CD35. Based on the above morphological and immunophenotypical findings, a diagnosis of dendritic cell sarcoma was rendered. The patient received simple mastectomy without adjuvant systemic therapy. The nodule showed the same histologic features as the core biopsy. Immunostaining for CKs, CD21, and CD35 was carried out in one of the five blocks obtained from the tumour, the results being consistent with dendritic cell sarcoma. Seven months after mastectomy, an enlarged ipsilateral axillary lymph node was noted, and a complete lymph node dissection was carried out. In one of the 18 lymph nodes, a metastatic tumour was found, composed of cells morphologically indistinguishable from those of the breast neoplasia. At variance with the breast tumour, however, the neoplastic cells in the lymph node were strongly immunoreactive for CK7 and unreactive for the dendritic cell markers CD21 and CD35. An extensive morphological and immunohistochemical revision of all the breast tumour samples yielded to pinpoint two foci of neoplastic cells strongly positive for CK7. Noteworthy, one of these foci was composed of large cells packed in cords, immunoreactive for CK7 only (Figure 1C), whereas the other focus showed a few cells immunoreactive for either CK7 or the dendritic cell marker CD21 (Figure 1D). Clusterin resulted strongly positive in the dendritic cell component also. Estrogen receptor, progesterone receptor and Her-2/neu were negative in both primary tumour and metastasis.

These findings raised two hypotheses: a collision tumour (dendritic cell sarcoma and poorly differentiated duct carcinoma) or a metaplastic carcinoma showing differentiation towards dendritic cell sarcoma. Given the morphological and immunohistochemical findings, we strongly favoured the second hypothesis. The patient was treated with four cycles of adjuvant chemotherapy by using the scheme FEC90 (5-fluorouracil, epirubicin, and cyclophosphamide). She is alive and well 8 months after the lymph node relapse.

Few cases of *bona fide* follicular dendritic cell sarcoma of the breast have been described in the literature to date ([1] online, [1–3]). Metaplastic carcinoma of the breast is an entity

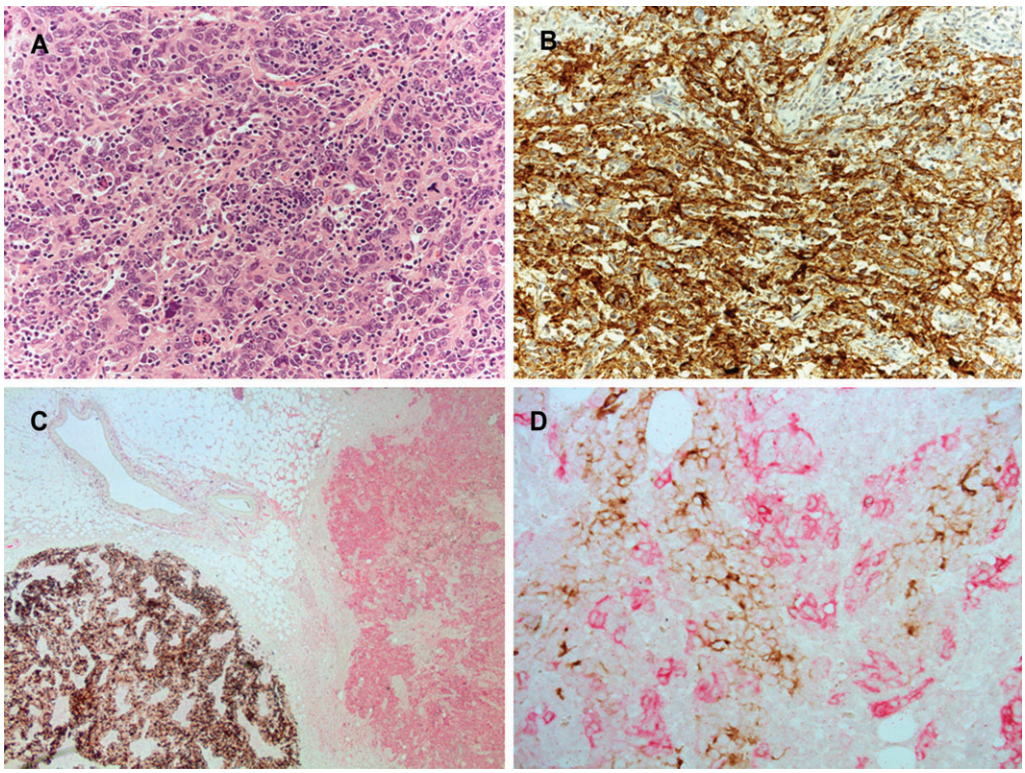

Figure 1. Large neoplastic cells in syncitial arrangement with intermingled inflammatory component (A); immunohistochemical positivity for CD21 in neoplastic cells (B); double immunostaining for CK7 (brown) and CD21 (red) highlights the two foci of carcinoma in the mammary tumour. One of the foci expresses only the epithelial marker CK7 (C), while the other is composed of cells showing either epithelial or dendritic differentiation (D).

encompassing many different histopathologic features, and its classification includes two main subtypes: the purely epithelial carcinoma, with the morphological variants of squamous carcinoma, adenosquamous carcinoma, and adenocarcinoma with spindle cell metaplasia, and the mixed epithelial and mesenchymal tumours, i.e. carcinoma with chondroid, osseous, and rhabdomyosarcomatous differentiation, as well as carcinosarcoma [4]. Anectodic cases of breast carcinomas showing unusual heterologous components, such as melanocytic and neuroglial, have also been reported, raising the question whether a multipotential cell could play a role in this multilineage differentiation [5]. A correct distinction between metaplastic carcinoma and dendritic cell sarcoma is far from being a merely nosologic issue: mammary metaplastic carcinoma is usually associated with a poor prognosis, and is almost invariably triple negative, deserving therefore to be treated by intensive chemotherapy, independent of the lymph node status ([2] online), while dendritic cell sarcoma is considered an intermediate grade malignancy ([3] online) that may be cured by surgery only, especially if it does not involve regional lymph nodes [2].

In summary, the first case of a metaplastic carcinoma of the breast showing extensive dendritic cell differentiation, herein reported, expands the histopathologic spectrum of metaplastic carcinoma and underlines the clinical usefulness of recognising even small foci of epithelial differentiation in otherwise *bona fide* mammary dendritic cell sarcoma.

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disclosure

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