Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Pattern of oestrogen, progesterone and Her2neu receptors expression in a heterogeneous carcinoma of the breast in a lactating woman

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Summary

Oestrogen-progesterone-Her2neu receptor status was studied in various loci/foci of heterogeneous carcinoma of the breast and its metastatic secretory component in the lymph node in a lactating woman. All the carcinoma variants were negative for the trio markers except tumour components evolved to secretory or lactating carcinoma, which showed focal positivity. Findings showed that oestrogenic receptors, progesterone receptors and Her2neu negative primitive carcinoma in a heterogenous breast cancer may evolve into oestrogen receptor, progesterone receptor and Her2neu positive secretory/lactating carcinoma alongside other receptor negative carcinoma variants. Focal marker positivity/negativity underlined the fact that a diagnostic/prognostic marker status report may account for the tumour area included in the section/sample only. Study of the immune marker expression/status in various loci may help identification of the components, morphogenesis and dynamics of heterogeneous carcinoma of the breast.

BACKGROUND

Oestrogen-progesterone-Her2neu receptor expression was studied in various loci/foci of a known heterogeneous carcinoma of the breast after septic disruption of lactiferous ducts in a lactating woman and its metastatic lactating component in a lymph node.¹

CASE PRESENTATION

Metastatic secretory papillary-columnar, cuboidal and polygonal clear cell components were negative for Her2neu receptors²⁻³ except single focus of polygonal clear cell type (<5% of tumour area) showing Her2neu positivity (figure 1A–C). All the other carcinoma loci in the breast

Figure 1 (A) Her2neu receptor status of columnar secretory and (B, C) cuboid and polygonal secretory carcinoma.

Figure 2 Patch of false positive Her2neu staining at the margin of the section.

Figure 3 Progesterone receptor negative status of primitive lactiferal ectodermal cell (PLEC) carcinoma locus (A), scattered positivity in PLEC transient to early secretory carcinoma (B) and progesterone receptor negative status of myoepithelioid granulomatous carcinoma (C, D).

section were negative for Her2neu (figure 2). A patch of false positivity appeared in one corner of the section. A report from a sister institute of medical education (on blinded diagnosis) concluded the primary and the meta-static lesion as negative for the Her2neu receptor marker.

Progesterone receptor staining was negative in the tumour loci comprising of polygonal cells with large nuclei, high nuclear cytoplasmic ratio and thick (low glycogen) cytoplasm characteristic of primitive lactiferal ectodermal cell (PLEC) carcinoma (figure 3A). Loci comprising of

Figure 4 Progesterone receptor status of cuboid-polygonal secretory (A) and columnar papillary lactating carcinoma (B).

Figure 5 Oestrogenic receptor status of secretory/lactating carcinoma.

similar cells with comparatively thin cytoplasm (higher glycol content) showed occasional scattered cells showing progesterone receptor marker positivity (figure 3B). Loci of myoepithelioid granulomatous carcinoma (MGC), including the myoepithelioid giant cells, displayed progesterone receptor negativity (figure 3C,D). The clear, cuboid and columnar cell areas of the secretory (lactating) carcinoma

component in the primary and metastatic tumour showed strong focal positivity (about 50% of total area of secretory carcinoma) for the progesterone receptors (figure 4A,B). A marker expert from the sister institution reported 50% focal positivity of the tumour for the progesterone receptor marker.

Figure 6 Oestrogenic receptor status of the primitive lactiferal ectodermal cell carcinoma (A,B), early secretory carcinoma (C), myoepithelioid granulomatous carcinoma (D) and adjoining loci of bipolar differentiation with respect to oestrogenic receptor (E,F).

Figure 7 Summary results of oestrogen-progesterone-Her2neu receptor status in different loci/foci of heterogeneous carcinoma of the breast.

Metastatic secretory carcinoma in the lymph node showed focal, varied intensity, oestrogenic receptor marker positivity in 80% of the tumour area (figure 5). In the breast, tumour loci of PLEC carcinoma were oestrogenic receptor negative (figure 6A,B). Areas of PLEC transient to early secretory (thin cytoplasm) stained faintly positive

(figure 6C). Loci of MGC with giant cells were oestrogenic receptor negative (figure 6D) and seen in direct vicinity to the foci of bipolar differentiation of PLEC carcinoma into oestrogen-receptor positive (apical/secretory variant) cells intermingled with negative (primitive myoepithelioid variants) cells (figure 6E,F). Loci of very small cell carcinoma

(reflective of primitive epiderm type and neurocrine metaplastic elements) and 20–30% of secretory (including columnar) carcinoma were oestrogenic receptor marker negative. The rest of the secretory carcinoma was positive. An expert reported 80% focal positivity of the tumour for the oestrogenic receptor marker. An attempt is made to summarise, locus wise, oestrogen-progesterone-Her2neu receptor status results in the presently heterogeneous carcinoma of the breast (figure 7).

DISCUSSION

In this study, the lactating/secretory component of heterogeneous carcinoma of the breast, showing 5% focal positivity for Her2neu, 50% focal positivity for progesterone receptors and >50% focal positivity for oestrogenic receptors, indicated either partial loss of receptors due to mutation or evolution, and progressive morphogenesis of oestrogenic receptor/progesterone receptor positive secretory carcinoma from its oestrogenic receptor/progesterone receptor negative counterpart. However, in the former case, receptor negative cells would be scattered throughout marker-positive secretory carcinoma, which is not the situation in the present case. Well-defined marker-positive foci along with negative foci of comparable sizes in the secretory carcinoma, scattered cell progesterone positivity and faint oestrogenic marker positivity in the loci (reflecting transition of PLEC to early secretory carcinoma) substantiated the evidence of morphogenesis of oestrogen-progesterone-Her2neu receptor variable-positive secretory carcinoma from oestrogen-progesterone-Her2neu receptor negative PLEC carcinoma of the breast. Oestrogenic and progesterone receptors appeared to evolve in secretory carcinoma simultaneously, but with the former on a focally diffuse and gradually developing weak to strong pattern, while the latter strongly positive from inception but involving the cells on a one by one basis. Her2neu-oestrogen-progesterone receptor negative MGC, adjoining to the locus of PLEC carcinoma showing bipolar differentiation with respect to oestrogenic-marker positivity/negativity of cells, evidenced morphogenesis of MGC from the PLEC carcinoma. Oestrogen-progesterone-Her2neu receptor negativity of the PLEC and very small cell carcinoma components was affirmative of their primitive nature and relevant to primitive (single layer phase) epiderm/primitive ectoderm cell character.^{4,5} These observations on immune-marker application in various loci are complementary to those made on H&E stained sections and may be helpful in identification of the components, morphogenesis and dynamics of heterogeneous carcinoma of the breast.

Another interesting observation was that per cent positivity of all the three markers—oestrogen receptor, progesterone receptor and Her2neu—grossly increased as the secretory carcinoma in the breast evolved to high-grade metastatic in the lymph node. This observation in a heterogeneous carcinoma of the breast neither agrees with the hypothesis that oestrogen/progesterone receptor positivity essentially decreases with carcinoma becoming high grade or metastatic nor to the oestrogen/progesterone receptor inverse correlation with Her2neu expression.⁶ The findings in this present case are affirmative of the view that expres-

sion of oestrogen, progesterone and Her2neu receptors in the breast carcinoma is heterogeneous;⁷ hence, explanatory of oestrogen, progesterone and Her2neu variability in terms of receptor status in an evolving lactating/secretory carcinoma. Heterogeneous focal pattern of marker positivity/negativity in the breast carcinoma underlines the fact that a carcinoma even if homogeneous under H&E stain may be heterogeneous with respect to immune-marker status; hence, a report on diagnostic/prognostic marker status may account for the tumour area included in the section/sample only.⁸

Learning points

- ▶ Oestrogen receptor, progesterone receptor and Her2neu negative primitive carcinoma in a heterogeneous breast cancer may evolve into oestrogen receptor, progesterone receptor and Her2neu positive secretory/lactating carcinoma alongside other receptor negative carcinoma variants.
- ▶ Oestrogen receptors may appear first followed by progesterone receptors and Her2neu and the per cent positivity of all three receptors may show increasing trend with the carcinoma evolving to high grade/metastatic.
- ▶ Heterogeneous focal pattern of marker positivity/negativity in breast carcinoma underlines the fact that a carcinoma, even if homogeneous under H&E stain, may be heterogeneous with respect to immune marker status; hence, a report on diagnostic/prognostic marker status may account for the tumour area included in the section/sample only.
- ▶ Study of the immune marker status in various loci may help identify the components, morphogenesis and dynamics of heterogeneous carcinoma of the breast.

Competing interests None.

Patient consent Obtained.

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