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Her-2/neu and *topoisomerase IIa*expression in primary and metastatic breast cancer

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Keywords

Breast cancer, *HER-2*, *topoisomerase II-a*, primary metastases

Context

The *HER-2/neu* oncogene and, more recently, the *topoisomerase II-a* gene have been implicated in the prediction of response to chemotherapy in breast cancer. *HER-2* amplification is also a prerequisite for therapy with trastuzumab (HerceptinR). Determination of *HER-2* and *topoisomerase II-a* gene amplification is usually done in primary tumour samples. However, therapy strategies used to target metastases may show reduced efficacy, as metastatic cancers may be biologically different to primary tumours.

Significant findings

The authors analysed *HER-2* and *topoisomerase II-a* gene amplification in 46 breast primary tumours and its metastases, using immunohistochemistry (IHC) and DNA *in situ* hybridisation techniques. *HER-2* amplification was seen in 28% (13 patients) of primary tumours and was always associated with amplification in its metastases; no metastases with *HER-2* amplification were seen without amplification in the primary tumour. The gene status of *topoisomerase II-a* (amplification/deletion/unaltered) remained unchanged in 10 of the 13 *HER-2* positive tumours; in three cases, the predominant cell population in metastatic tissue was present only as a subpopulation in the primary tumour. The authors conclude that amplification of *HER-2* in the primary tumour reflects its status in the metastases, and that only minor discrepancies exist, between primary and metastatic tissue, regarding *topoisomerase II-a* gene status.

Comments

Some facts must be taken in consideration when interpreting the results of this study. Firstly, the actual number of analysed patients, both in primary and metastatic sites, is very small (13 patients). Secondly, in some of the cases the metastases were local or regional, while in other cases the metastases were distant. It should not be assumed that both types of metastases are biologically equivalent. Notwithstanding, the results are consistent with other (all small) published studies, and appear to indicate that possible discrepancies in *HER-2* and *topoisomerase II-a* gene expression, between primary and metastatic tumours, are not a major cause of treatment failure in metastatic breast cancer. This conclusion, however, needs to be confirmed in larger studies. Accordingly, a series of 107 patients have been analysed, and the results found less than 10% of discordant cases between primary tumour and its distant metastases (Gancberg *et al*., unpublished data). Data from the present and similar articles also suggest that *HER-2* amplification probably occurs very early in the genetic cascade, at least before dissemination occurs.

Methods

FISH, chromomeric *in situ* hybridisation (CISH), IHC

Additional information

References

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