Abstract

Objectives: Ductal carcinoma in situ (DCIS) is a non-invasive lesion of an increasing clinical importance. Individual risk assessment is essential for an optimal treatment. Our objective was to identify clinical and molecular characteristics of a subgroup of DCIS with an unfavorable prognosis.

Methods: In a population study, we analyzed women with DCIS diagnosed within one mammography screening unit. In the experimental part of this work, we conducted a comparative analysis of five biological markers in normal tissue, DCIS and invasive breast cancer by means of gene expression analysis and analysis of loss of heterozygosity (LOH).

Results: We demonstrated a high proportion of pure (no invasive component) DCIS (14.41%) of all breast lesions described as malignant. In our sample, we saw a homogeneous distribution of risk factors without noting a clear pattern identifying high-risk subtypes. We noted significant differences in clinical management of tumors with similar characteristics, which demonstrates the present state of limited use of clinical predictors. In the laboratory experiment, we showed differences in loss of heterozygosity (LOH) between DCIS and invasive breast cancer for BRCA1 (8.69% vs. 44.74%) and BRCA2 (9.52% vs. 45.0%). In contrast, we did not find any differences for p53 (31.82% vs. 32.5%). In normal breast tissue, we did not observe any LOH. Gene expression analysis, which was conducted by real-time PCR proved no significant difference between DCIS and invasive breast cancer for VEGF (12.0% vs. 14,3%) and Bcl-2 (8,0% vs. 11,9%). Alterations of genes involved in angiogenesis and apoptosis are probably early events in carcinogenesis. On the contrary, alterations of genes involved in DNA repair seem to be a specific feature of invasive cancer, allowing us to differentiate a subgroup of DCIS with high-risk biological behaviour.