Low frequency of E-cadherin alterations in familial breast cancer

ABSTRACT

The screening of 19 familial breast cancer patients, who displayed loss of heterozygosity (LOH) at the E-cadherin locus, revealed no pathogenic germline alterations. However, a somatic mutation (49-2AC) was detected in one of the tumors, which displayed ductal and lobular histology. A study also screened for mutations in other families with breast, gastric, and colon cancers to determine if this change is likely to increase the risk of

INTRODUCTION

Many people with breast cancer have E-cadherin alterations, a type of antigen that is present in high levels in breast tumours. The presence of E-cadherin alterations in breast cancer is thought to be due to the effect of E-cadherin on the immune system. It is estimated that about 2.5 million women in the UK suffer from E-cadherin alterations, which can lead to the development of cancer. It is also thought that around 1.5% of breast cancers are caused by E-cadherin alterations. The presence of E-cadherin alterations in breast tumours has been associated with an increased risk of developing breast cancer, as well as other diseases.

E-cadherin is expressed in the breast gland, and Defining the topic: The presence of E-cadherin (CDH1) on the cell surface in most epithelial tissues is rapidly increasing evidence that this product plays a part in epitomizing epithelialic tumourigenesis. Germline mutations in E–cadraledolus have been described in families with early-onset diffuse gastric cancer and loss of function of this gene has been implicated in the pathogenesis of early stage colorectal cancer, while its expression is reduced in 50% of invasive ductal carcinoma, but genes expressed within both A study of a family with diffuse gastric cancer revealed the presence of an E-cadherin germline mutation that cosegregates with this disease. This missense mutation in exon 12 (Ala592Thr) was also found in the mother of the index patient, who had ductal breast cancer. To investigate whether this altered the predisposing factor to breast Cancer, we examined 1328 patients with sporadic or familial breast carcinoma and 497 control individuals. Materials and technique The screening process included the detection of 19 probands with familial breast cancer that displayed LOH at chromosome 16q, as well as 12 patients from 10 families with breast, gastric, and colorectal cancers. Additionally, nine tumours from the 19 breast Cancer cases were screened for somatic mutations, while the frequencies of the 1774GA variant (Ala592Thr) were determined in DNA extracted from 358 unconnected probrethren, 214 unrelated earlybreast cancer, BRCA1 and B D16S7/p79-2-23 and APRT/HUAP15 were used to identify LOH, similar to a previous study on allelic loss at 16q in familial tumours. To screen for possible mutations in the E-cadherin gene, we used single-stranded conformation polymorphism (SSCP) and denaturing high-performance liquid chromotography (DPPLC) to screen 16 exons. The primers were similar to those described by Berx et al and Salahshor a. (manuscript submitted) but with some modifications. Only samples that displayed aberrant bands on the SSPC gel or an altered DHPLC pattern were sequenced. What are the results? In 12 patients from families with known breast, gastric or colon cancer, we found no pathogenic mutations in them and instead searched for germline alterations in 19 individuals with familial breast cancer who showed LOH at the E-cadherin locus in their tumours. We also tested nine other cases of somatic carcinoma (Fig. 2), and one case of such a change (49-2AC) in one of these cases. A germline

missense mutation in exon 12 (Ala592Thr) of E-cadherin was detected by us in a previous study of two non-BRCA1/Bastato-carrier women with familial diffuse gastric cancer. Although the penetrance was not complete, it was present in the mother's ductal breast cancer at 65 years old. In family 205 (Fig. 1b, II:2), one of the women showed the Ala592-Thr variant. Her two sisters, who had no unusually exhibited this type of breast The screening of all 126 BRCA1 or BRAC2 carriers from various families resulted in the discovery of the mutation in one patient with a BRAF1 germline mutation (delC2594) in family 4056. A sample from her sister was also present, and she shared the Ala592Thr variant (Fig. 1d). As both tumours were of ductal type, they were not likely to have predispose to breast cancer because neither of these had been caused by another germ line BRC1 mutation. The debate revolves around the topic of education. There have been only 17 cases of E-cadherin germline mutations in diffuse gastric cancer families, while the frequency of such mutation (often fewer than 5–7 years) in breast cancer reported by other groups is relatively low. In contrast, 10 families that included breast, gastrin or colon cancer patients showed no pathogenic alteration; however, these mutation(s) were found to be less common in women with a higher percentage of germplasm than those with aninherited predisposition to breast Cancer. Despite being found in two different groups, the frequency of Ala592Thr alteration in those groups did not align with their risk factors for breast cancer. However, other studies have suggested that germline E-cadherin mutations may have an impact on breast tumor phenotype. In summary, the results of this study and earlier data indicate that a germline E-cadherin mutation is not primarily responsible for breast cancer, but these findings suggest that germlines and somatic mutations in this gene may impact tumour phenotypic divergence and prognosis, as well as other genetic changes or epigenetic changes. Introduction The presence of E-cadherin (CDH1) on the cell surface in most epithelial tissues is rapidly increasing evidence that this mammalian E–cadurhérin gene product plays a role in tumourigenesis, with loss of function having been found to cause increased proliferation and invasion of many malignant epithelium tumours, mutations in E Despite evidence suggesting that E-cadherin mutation may contribute to the development of hereditary gastric cancer, there is no conclusive research on whether this is true. To further investigate the possible role of E-3 cancer in breast cancer prevention, we examined all 16 exons of human epidermal medullary hormone (ECH) in 31 breast carcinoma patients (out of 10 families) who had not been diagnosed with BRCA1 or BRAF2 and had no family history. Twelve of these patients had LOH at 16q in their tumour that had either genetic Our study examined 1328 patients with sporadic or familial breast cancer and 497 individuals who were control subjects. In one case, we found an E-cadherin germline mutation that cosegregated with the previous study. This mutation was also present in the mother of the index patient, who had ductal breast Cancer, and also in another study where we observed a missense mutation in exon 12 (Ala592Thr) which may be linked to breast carcinoma.

CONCLUSION

Despite previous reports indicating that a germline mutation in E-cadherin is not primarily responsible for breast cancer, this study has also found that other genetic changes or epigenetic events may impact the metastatic behaviour of cancer cells, leading to improved phenotypic divergence and prognosis. Simplified expressions. Denaturing high-performance liquid chromatography, LOH, polymerase chain reaction, and SSCP are the terms used to describe this process.