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Null Results in Brief

No Link between Breast Cancer and Meningioma: Results from a Large Monoinstitutional Retrospective Analysis

Carmen Criscitiello[1,2], Davide Disalvatore[3], Michele Santangelo[4], Nicole Rotmensz[3], Barbara Bazolli[3], Patrick Maisonneuve[3], Aron Goldhirsch[1], and Giuseppe Curigliano[1,2]

Abstract

Background: The etiology of meningioma is largely unknown, although breast cancer has been suggested to play a role.

Methods: A monoinstitutional, retrospective analysis was performed at European Institute of Oncology on 12,330 patients with breast cancer. The cumulative incidence of meningioma was estimated using the Kaplan–Meier method and the log-rank test was used to assess differences between groups.

Results: In total, 33 patients with meningioma were identified from a study population of 12,330, with a 10-year cumulative incidence of meningioma of 0.37%. We did not find a significantly increased risk of meningioma among patients with breast cancer or an association between the hormonal receptor status and the risk of meningioma ($P = 0.65$).

Conclusions: Our results do not support a role of breast cancer or endocrine treatments in meningioma development.

Impact: This analysis adds new information on a debated topic. *Cancer Epidemiol Biomarkers Prev; 23(1); 215–7. ©2013 AACR.*

Introduction

Meningiomas are typically benign tumors arising from the meningothelial cells of the arachnoid membrane covering the brain and spinal cord. The etiology of meningiomas is largely unknown. There is evidence to suggest that breast cancer may play a role in the development of meningiomas, including the observation that these tumors occur more commonly in women (1, 2). Further evidence for a possible role for hormones in brain tumor etiology includes the presence of progesterone (PgR), estrogen (ER), and androgen receptors in some meningiomas, suggesting a link between breast cancer and meningiomas. Immunohistochemical studies have shown that about 70% of meningiomas express PgR and about 30% express ER, thus corroborating the hypothesis that meningioma is a hormone-sensitive tumor (3, 4). Our study was carried out to explore the possible association between breast cancer, endocrine therapy, and the risk of developing meningioma in a large monoinstitutional population of patients with breast cancer. We focused on endocrine-responsive tumors to find a potential link between these tumors and endocrine therapy.

Materials and Methods

Data from 12,330 women with early-stage breast cancer who underwent surgery at the European Institute of Oncology (IEO) in Milan between 1994 and 2011 were retrieved from two institutional databases: the Breast Cancer database, which contains information on patients with breast cancer operated at IEO, and the Tumor Registry. Patients who received neoadjuvant treatment, patients with a previous history of cancer, or patients with metastatic breast cancer at diagnosis were excluded from the analysis. Breast cancer–related data on age, menopausal status, surgery, histopathology (Ki-67 expression, ER/PgR expression, and HER2 status) and systemic treatment were analyzed. Usually, patients were followed up with physical examination every 6 months, annual mammography, breast ultrasound, and blood tests every 6 to 12 months, and additional evaluations when clinically indicated. Whenever possible, the health status of women who did not come back for scheduled follow-up visits for more than 1 year was obtained by phone contact. Institutional Review Board approved this retrospective analysis. The primary endpoint was the cumulative incidence of meningioma (cum-inc ME), calculated from breast surgery to meningioma diagnosis. The cum-inc ME was estimated using the Kaplan–Meier method. The log-rank test was used to assess differences between groups. All analyses were carried out with the SAS software 9.3 (SAS Institute).

Authors' Affiliations: [1]Breast Cancer Program, [2]Division of Early Drug Development, [3]Division of Epidemiology and Biostatistics, European Institute of Oncology, Milan; and [4]Department of Advanced Biomedical Sciences, Operative Unit of General Surgery and Transplants, University Naples Federico II, Napoli, Italy

Corresponding Author: Carmen Criscitiello, Division of Early Drug Development, Istituto Europeo di Oncologia, Via Ripamonti 435, 20141, Milano, Italy. Phone: 39-0294-3742-689; Fax: 39-0294-379-224; E-mail: carmen.criscitiello@ieo.it

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Table 1. Association between patients' characteristics and meningioma

Variable	All (% column)	Number of meningioma (% row)	10-year cumulative incidence (95% CI)	*P*
Number	12,330 (100)	33 (0.3)	0.37 (0.26–0.55)	
Age at surgery				0.24
<35	514 (4.2)	0 (0.0)	0.00 (0.00–0.00)	
35–50	5,005 (40.6)	13 (0.3)	0.38 (0.21–0.70)	
51–65	4,728 (38.3)	12 (0.3)	0.29 (0.16–0.53)	
>65	2,083 (16.9)	8 (0.4)	0.73 (0.32–1.65)	
ER				0.18
ER = 0	1,722 (14.0)	7 (0.4)	0.59 (0.23–1.49)	
ER > 0	10,608 (86.0)	26 (0.2)	0.34 (0.22–0.51)	
PgR				0.60
PgR = 0	3,015 (24.5)	7 (0.2)	0.25 (0.11–0.55)	
PgR > 0	9,315 (75.5)	26 (0.3)	0.42 (0.27–0.64)	
ER/PgR				0.65
Not expressed (Both 0)	1,655 (13.4)	5 (0.3)	0.28 (0.11–0.75)	
Expressed (ER > 0 or PgR > 0)	10,675 (86.6)	28 (0.3)	0.38 (0.25–0.58)	
HER2				0.08
Not expressed	9,557 (77.5)	21 (0.2)	0.36 (0.23–0.56)	
Intense and complete	1,655 (13.4)	8 (0.5)	0.51 (0.24–1.08)	
Ki-67				0.32
<14%	3,416 (27.7)	11 (0.3)	0.44 (0.24–0.83)	
≥14%	8,902 (72.2)	21 (0.2)	0.33 (0.20–0.54)	
Subtype 2013				
LUM A PgR > 20%	2,405 (19.5)	8 (0.3)	0.56 (0.27–1.12)	0.08
LUM B Ki-67 ≥ 14% or PgR ≤ 20%	7,183 (58.3)	15 (0.2)	0.33 (0.19–0.57)	
LUM B HER2 POS	1,086 (8.8)	4 (0.4)	0.38 (0.12–1.19)	
HER2+	630 (5.1)	4 (0.6)	0.71 (0.27–1.88)	
TN	1,024 (8.3)	0 (0.0)	0.00 (0.00–0.00)	
Menopausal status				0.08
Premenopausal	5,769 (46.8)	11 (0.2)	0.28 (0.14–0.55)	
Postmenopausal	6,561 (53.2)	22 (0.3)	0.46 (0.29–0.72)	
Hormone therapy performed				0.53
No	2,061 (16.7)	7 (0.3)	0.35 (0.16–0.79)	
Yes	9,947 (80.7)	26 (0.3)	0.38 (0.25–0.59)	
Hormone therapy				0.054
Tamoxifen	7,037 (75.2)	17 (0.2)	0.31 (0.18–0.52)	
Aromatase inhibitor	2,315 (24.8)	7 (0.3)	0.74 (0.32–1.72)	
Chemotherapy				0.98
No	7,099 (57.6)	18 (0.3)	0.35 (0.21–0.57)	
Yes	4,932 (40.0)	15 (0.3)	0.41 (0.23–0.73)	
CT/HT				0.66
Nil	509 (4.1)	3 (0.6)	0.75 (0.24–2.31)	
ET	6,520 (52.9)	15 (0.2)	0.32 (0.19–0.55)	
CT	1,521 (12.3)	4 (0.3)	0.22 (0.07–0.69)	
ET-CT	3,384 (27.4)	11 (0.3)	0.47 (0.24–0.90)	

Abbreviations: ET, endocrine therapy; CT, chemotherapy; HT, hormone therapy; TN, triple-negative.

Results

From January 1994 to December 2011, we identified a total of 12,330 consecutive patients with early-stage breast cancer. At a median follow-up of 7 years, 33 patients with meningioma were identified from a study population of 12,330. Table 1 describes selected demographic, clinical, and pathologic characteristics of the study population at the time of breast cancer surgery, systemic treatments

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administered, number of meningiomas, and 10-year cum-inc ME. Considering the entire population, the 10-year cum-inc ME was 0.37% [95% confidence interval (CI), 0.26%–0.55%]. No association was found between ER/PgR and the risk of meningioma. No association was found if we matched analysis coupling ER and PgR ($P = 0.65$) or considering them separately (ER, $P = 0.18$ and PgR, $P = 0.60$). Patients who received aromatase inhibitors had a trend of higher risk to develop meningioma compared with patients who received tamoxifen, with a borderline statistical significance ($P = 0.054$). No other significant association was observed in the analyzed variables.

Discussion

This large, retrospective study evaluated more than 12,000 patients with breast cancer with an average follow-up period of 7 years, and identified a total of 33 individuals with an incident case of meningioma. There was no significant association between meningioma development and breast cancer. Use of aromatase inhibitors conferred a trend of increased risk of meningioma in patients with breast cancer, although no statistical significance was observed. The link between breast cancer and meningioma has been reported in literature, with discordant results. What is behind this association is quite unclear, most likely being a hormonal etiology. Hormone receptors are involved in both tumor types. In meningiomas, PgR is more prevalent and more biologically active than ER. To ascertain a link between hormonal exposure and development of meningioma, we focused on endocrine-responsive breast cancer and on patients receiving endocrine therapy. In our cohort, the 10-year cum-inc ME was 0.37% (95% CI, 0.26–0.55), similar to that reported by Rao and colleagues (1). Our study has several limitations. Despite the large cohort, a major limitation of this study is the small number of meningioma cases recorded with exposure to endocrine therapy. However, it has to be acknowledged that the screening for meningioma is not routinely conducted in patients with breast cancer. Also, the endocrine therapy given to ER-positive patients may have influenced the development of meningioma during this period. Another limitation is related to the retrospective analysis. An important strength is that the records of potential cases were manually reviewed and the case status was validated by a data-monitoring system with a confirmation rate of 100%. In summary, this study, in contrast with previous cohort studies, found no association between development of meningioma and breast cancer.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: C. Criscitiello, D. Disalvatore, M. Santangelo, N. Rotmensz, P. Maisonneuve, G. Curigliano
Development of methodology: C. Criscitiello, D. Disalvatore, M. Santangelo, G. Curigliano
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): C. Criscitiello, D. Disalvatore, N. Rotmensz, G. Curigliano
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): C. Criscitiello, D. Disalvatore, M. Santangelo, N. Rotmensz, A. Goldhirsch, G. Curigliano
Writing, review, and/or revision of the manuscript: C. Criscitiello, D. Disalvatore, M. Santangelo, P. Maisonneuve, A. Goldhirsch, G. Curigliano
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): C. Criscitiello, D. Disalvatore, N. Rotmensz, B. Bazolli
Study supervision: C. Criscitiello, M. Santangelo, G. Curigliano

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