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PAPER

Breast cancer in systemic lupus erythematosus (SLE): receptor status and treatment

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Objective: There is a decreased risk of breast cancer in systemic lupus erythematosus (SLE) versus the general population; little is known regarding the receptor status of breast cancers in SLE, or treatment. **Methods:** Breast cancer cases occurring after SLE diagnosis were ascertained through linkage with tumor registries. We determined breast cancer positivity for estrogen receptors (ER), progesterone receptors (PR), and/or Human Epidermal Growth Factor Receptor 2 (HER2), as well as cancer treatment. **Results:** We obtained information on ER, PR, and/or HER2 status for 63 SLE patients with breast cancer. Fifty-three had information on ER and/or PR status; 36 of these (69%) were ER positive. Thirty-six of the 63 had information on HER2 status; of these, 26 had complete information on all three receptors. Twenty-one of these 26 (81%) were HER2 negative; seven of 26(27%) were triple negative. All but one patient underwent surgery; 11.5% received both non-tamoxifen chemotherapy and radiotherapy, 16.4% radiotherapy without non-tamoxifen chemotherapy, and 14.7% received non-tamoxifen chemotherapy without radiotherapy. **Conclusion:** ER positivity was similar to historical general population figures, with a trend toward a higher proportion of triple-negative breast cancers in SLE (possibly reflecting the relatively young age of our SLE patients). *Lupus* (2018) **27,** 120–123.

Key words: Breast cancer; systemic lupus erythematosus; receptor; estrogen; progesterone

Introduction

Compared to the general population, patients with systemic lupus erythematosus (SLE) have a slightly increased risk of cancers overall; however, they appear to have a decreased incidence of hormone-sensitive cancers—such as breast, endometrial and possibly ovarian cancer.[1]

The majority of breast cancers (70%–80%) are invasive ductal carcinoma,[2] and approximately 70% of those are estrogen receptor positive. Our objective was to provide a brief analysis of receptor status of the breast cancers that developed in an SLE cohort.

As a secondary objective, we assessed breast cancer treatment therapies (surgery, chemotherapy, and radiotherapy), since it has been reported that radiation treatment for SLE patients may be avoided because of fear of possible adverse reactions.[3]

Methods

For this study, we analyzed data from 10 SLE cohorts who had participated in our multi-centre

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study of cancer in SLE. These centres included Montreal, Toronto, Baltimore, New York, Chicago, San Francisco, Los Angeles, Mexico City (Mexico), Lund (Sweden) and Seoul (Korea).

Cancer cases were ascertained through linkage with regional tumor registries. The California cancer registry was able to provide some information on whether the breast cancer was positive for estrogen receptors (ER), progesterone receptors (PR), and/or Human Epidermal Growth Factor Receptor 2 (HER2). For the remainder of the centres, the breast cancer receptor information was ascertained from pathology reports.

Cancer cases were included only if they had occurred after SLE diagnosis. We reported demographic characteristics (age and SLE duration at time of cancer diagnosis, race/ethnicity), histology, receptor status, and treatment (chemotherapy other than tamoxifen, radiotherapy, and surgery) for the breast cancer cases in this SLE cohort.

Results

Among the 10 centres involved in these analyses, from 1989 to 2014, 131 SLE patients had breast cancer, and of these 63 breast cancer cases had information on ER, PR, and/or HER2 status recorded from the cancer registry or a pathology report. The missing information was due either to missing entries in the California cancer registry or inability to locate pathology reports, which occurred primarily when the patient's cancer treatment took place at a centre other than where her lupus care took place.

Among the 63 patients with breast cancer receptor information, the median age at cancer diagnosis was 43 years (interquartile range 14.75), and the median SLE duration at the time of cancer diagnosis was 13 years (range 0–45). Most ($N=43$) of these cases originated from the United States (US), with eight from Canada, seven from Mexico, four from Sweden and one from Korea. All were female.

Out of these 63 SLE cancer patients, four had limited information on histology (i.e. indicated as 'poorly differentiated'). The most common breast cancer histological type in the remaining 59 was ductal adenocarcinoma ($N=43$, 72.9%) followed by lobular adenocarcinoma ($N=9$, 15.3%), mixed ductal and lobular carcinoma ($N=4$, 6.8%), and one case each of comedo carcinoma, mucinous/adenocarcinoma, and medullary breast cancer.

Information on staging was obtained for 51 of these breast cancers. Four were in situ (three ductal and one lobular), 34 were localized, 11 regional and two metastatic.

Regarding the 63 breast cancers, 53 had information on ER and/or PR status, while 36 of the 63 had information on HER2 status. The missing information was related to incomplete records in the California cancer registry, since the collection of ER and PR information was required only from 1990 onward (and even after 1990 the data were inconsistently reported). Overall, 16 of 52 cases with information on ER were ER negative (31%) and 20 of 53 cases were PR negative (38%). In addition, 31 of 52 (60%) were positive for both ER and PR and 14 of 52 (27%) were negative for both.

Details regarding the 26 patients with complete information on all three receptors including HER2 are presented in Table 1. As indicated, five of 26 (19%) breast cancers were HER2 positive. In this sample of 26, seven (27%) breast cancer cases were triple negative (the 95% confidence interval (CI) for this proportion is 14%, 46%).

Regarding treatment of breast cancer in our SLE cohort, we identified 61 patients with information on non-tamoxifen chemotherapy and radiotherapy. All but one (98%) underwent surgery, seven

Table 1 Information regarding the 63 breast cancer cases in the systemic lupus erythematosus (SLE) sample with some information recorded regarding estrogen receptors (ER), progesterone receptors (PR) and Human Epidermal Growth Factor Receptor 2 (HER2)

Receptor information[a]	N *(%)*
ER + PR+ ($N=31$)	
HER2[b]	16 (25)
HER2–	12 (19)
HER2+	3 (5)
ER + PR– ($N=5$)	
HER2[b]	2 (3)
HER2-	2 (3)
HER2+	1 (2)
ER–PR– ($N=15$)	
HER2[b]	7 (11)
HER2–	7 (11)
HER2+	1 (2)
Other ($N=12$)	
ER– PR + HER2[b]	1 (2)
ER– PR + HER2+	1 (2)
ER[b] PR– HER2[b]	1 (2)
ER[b] PR[b] HER2–	7 (11)
ER[b] PR[b] HER2+	3 (5)
Total ($N=63$)	

[a]Incomplete information regarding receptor type is indicated by[b]; receptor positive is indicated by +, receptor negative is indicated by –.

Table 2 Breast cancer cases in the systemic lupus erythematosus (SLE) sample, highlighting the available information on receptor status and chemotherapy (chemo)/radiation (radio) therapy

Receptor information[a]	*Chemo*	*Radio*	*Total*
ER + PR+	**5**	**6**	**19**
HER2[b]	2	4	11
HER2–	3	2	8
ER + PR–	**2**	**3**	**4**
HER2[b]	0	0	1
HER2–	1	2	2
HER2+	1	1	1
ER–PR–	**6**	**3**	**9**
HER2[b]	2	2	5
HER2–	3	1	3
HER2+	1	0	1
Other	**3**	**3**	**11**
ER– PR + HER2[b]	1	0	1
ER[b] PR[b] HER2–	1	3	8
ER[b] PR[b] HER2+	1	0	2
Unknown receptors	**0**	**2**	**18**
Total ($N = 61$)[c]			

[a]ER: estrogen receptor; PR: progesterone receptor; HER2: Human Epidermal Growth Factor Receptor 2. Incomplete information regarding receptor type is indicated by[b]; receptor positive is indicated by +, receptor negative is indicated by –.
[c]Two of the 63 cases had no available information.

(11.5%) received both non-tamoxifen chemotherapy and radiotherapy, 10 (16.4%) radiotherapy without non-tamoxifen chemotherapy, nine (14.7%) received non-tamoxifen chemotherapy without radiotherapy, while 35 (57.3%) patients received neither (although these patients may have been on tamoxifen). California was the only jurisdiction where we had information about tamoxifen, in 29 patients; of these, four received tamoxifen. Table 2 highlights the available information on receptor status and chemotherapy/radiation therapy for the breast cancer cases for these 61 cases in our SLE sample.

Discussion

There are considerable data that women with SLE have a decreased risk of breast cancer versus the general population. In a meta-analysis, the standardized incidence ratio for breast cancer in SLE, versus the general population, was 0.76 (95% CI: 0.69, 0.85), that is, almost a 25% reduction in breast cancers in women with SLE, versus the general population.[4]

In the general population, up to 80% of breast cancers are ductal carcinomas,[2] which was similar to the SLE patients we studied.

About 30% of breast cancer cases in the general population are ER negative, while triple-negative breast cancer accounts for approximately 15% of breast cancer cases.[4] A previous study using Veteran Affairs data suggested a decreased incidence of ER-negative breast cancer in females with SLE,[5] though only in seniors. Based on that, our hypothesis was that the decreased risk of breast cancer in SLE might be mostly explained by a decrease in ER-negative cases. However, we did not note a difference in the total number of ER positivity in our SLE breast cancer cases versus general population rates. There are several potential reasons why our data did not show the same findings as the Veteran Affairs data. One possibility is that their sample did not require clinical confirmation of SLE, but rather based the diagnoses on administrative coding. Other reasons could be that we relied on pathology reports, which were not available on all patients.

We did see a higher proportion of triple-negative breast cancers in the SLE cases versus the general population, in whom about 12% of breast cancers are triple negative. This may reflect the relatively young age of our SLE sample (triple-negative breast cancer tends to occur in younger patients, e.g. before the age of 50), compared to other *breast cancer*s. In the SLE patients who had a triple-negative cancer, the mean age was 47.5 years, which, as expected, was younger than the average across all the 63 cases (56.8 years).

Previously, concern has been raised about administering radiotherapy in SLE, given reports of adverse reactions to this therapy in patients with systemic autoimmune rheumatic disease.[6–8] However, this avoidance may be unwarranted as a literature review did not demonstrate unusual radiotherapy toxicity in lupus patients.[3] A report based on general population data from Canadian provincial cancer agencies suggested that 61.6% of breast cancer patients started radiotherapy within two years of diagnosis in 2009,[9] and US data from 1975–2007 suggest about 48% of breast cancer cases received radiotherapy in this period (both for early and late stages). However, only 27.9% of the 63 patients in our SLE cohort underwent radiotherapy. An earlier study found that 65% of SLE patients with cancer could have received curative or symptomatic radiotherapy but only 10% actually received it.[2] Non-tamoxifen chemotherapy was used in 26.2% of the breast cancer cases in our SLE cohort, which appears also to be lower compared to that used in the general North American population of breast cancers (approximately 40%).[10] We cannot exclude the possibility that

there may be valid clinical reasons for the individual choices of therapy for breast cancer cases. Another explanation for differences in breast cancer therapy in SLE versus the general population might be differences in age or stage at presentation. However, in an earlier analysis, the majority of the breast cancers in SLE patients (75%) were localized compared to the general population Surveillance, Epidemiology, and End Results Program (SEER) data (61%),[11] and indeed (where information on stage was available) most of the cases in our sample were regional or localized. Still, a limitation of our study is that we did not describe and compare use of chemotherapy and radiotherapy by cancer stage and receptor status.

In conclusion, the prevalence of ER positivity in our SLE breast cancer cases was similar to that in the general population, but we saw a higher proportion of triple-negative breast cancers in the SLE cases versus the general population, which may reflect the relatively young age of our SLE patients.

Declaration of conflicting interests

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