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Abundance and distribution of polychlorinated biphenyls (PCBs) in breast tissue

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ABSTRACT

Many environmental chemicals accumulate in human tissues and may contribute to cancer risk. Polychlorinated biphenyls (PCBs) are associated with adverse health effects, but relationships between PCB exposure and breast cancer are unclear. In this study, we sought to determine whether bioaccumulation of PCBs differs within regions of the human breast and whether PCB levels are associated with clinical and pathological characteristics in breast cancer patients. Tissue sections ($n=245$) were collected from breast quadrants from 51 women with a diagnosis ranging from disease-free to metastatic breast cancer. Ninety-seven PCB congeners were assayed by high resolution gas chromatography. ANOVA was used to examine PCB distribution within the breast and relationships with clinical/pathological variables. Pearson product-moment correlations assessed relationships between age at mastectomy and PCB levels. PCBs were abundant in breast tissues with a median concentration of 293.4 ng/g lipid (range 15.4–1636.3 ng/g). PCB levels in breast tissue were significantly different ($p<0.001$) among functional groupings of congeners defined by structure-activity properties: Group I (28.2 ng/g), Group II (96.6 ng/g), Group III (166.0 ng/g). Total PCB concentration was highly correlated with age at mastectomy, but the distribution of PCBs did not differ by breast quadrant. PCB levels were not associated with patient status or tumor characteristics. In conclusion, PCB congeners with carcinogenic potential were present at high levels in the human breast, but were not associated with clinical or pathological characteristics in breast cancer patients.

1. Introduction

Breast cancer is the most common cancer among women worldwide, with an estimated 1.677 million new cases (25% of all cancers) diagnosed, and 6.3 million women alive with disease, in 2012 (Ferlay et al., 2015). Since 2008, the incidence of breast cancer has increased internationally by more than 20% and mortality has increased by 14%, making breast cancer the leading cause of cancer death among women (Forman and Bray, 2013). Established risk factors such as age, family history of breast cancer, and genetics account for a relatively small proportion of breast cancer cases and causative factors remain ambiguous and poorly understood. Given the number of women impacted by breast cancer, nearly 8 million women throughout the world, and the long-term consequences of breast cancer in terms of morbidity, mortality, and health care costs, there is considerable interest in understanding relationships between nontraditional risk factors, such as environmental chemicals, and breast cancer. Although research on environmental chemicals and their potential contribution to an increased risk of disease is still in the early stages of development, a variety of environmental pollutants have shown evidence of an association with breast cancer (Weyandt et al., 2008).

Polychlorinated biphenyls (PCBs) consist of a family of 209 congeners of halogenated hydrocarbons that were first used commercially in 1929. A unique combination of properties, including low electrical conductance, thermal stability, and low reactivity promoted the widespread use of PCBs in industrial and commercial products such as lubricants, liquid sealants, flame retardants, and electrical insulators (Manzetti et al., 2014). Through improper disposal, leakage from industrial products, and chemical spills, PCBs have become ubiquitous world-wide environmental contaminants. Despite passage of the Toxic Substances Control Act of 1976, which curtailed production and distribution of PCBs in open applications, PCBs remain persistent in the environment

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(Beyer and Biziuk, 2009).

The International Agency for Research on Cancer classified PCBs as a group 1 carcinogen in 2013. Similar to other environmental chemicals, PCBs are lipophilic and bioaccumulate in human adipose tissues (Müllerová and Kopecký, 2007). PCBs and their metabolites also have estrogenic properties, which mimic the effects of endogenous hormones. Because a large percentage of cancers in women, including breast cancer, are hormonally regulated, researchers have begun to question whether there is a causal link between PCBs and various forms of cancer (Freeman and

Table 1
Clinical and pathological characteristics of patients.

Patient	Diagnosis[a]	Age[b]	ER/HER2 status[c]	AJCC stage[d]	Grade[e]	Tumor size[f]	LN status[g]	Current status[h]
1	Prophylactic	31						NED
2	Prophylactic	33						NED
3	Invasive	34	+/+	IIA	2	T2	+	NED
4	Invasive	37	−/+	IIA	3	T2	−	NED
5	In situ	38		NA				NED
6	In situ	39		0				NED
7	Invasive	39	−/−	IIIC	3	T3	+	DOD
8	Invasive	41	+/NP	IIA	1	T2	−	NED
9	Invasive	42	+/−	IIB	1	T2	+	NED
10	Invasive	43	−/+	IIIB	3	NP	+	DOD
11	Invasive	43	NA	NA	NA	NA	NA	NED
12	Invasive	45	+/−	IIIA	1	T2	+	NED
13	Invasive	47	NA	NA	NA	NA	NA	NED
14	Invasive	47	−/+	IIA	3	T2	−	NED
15	Invasive	45	NP	I	3	T1	−	NED
16	Invasive	49	+/+	IIA	2	T2	−	LTF
17	Invasive	50	−/+	IIA	2	T2	−	NED
18	Invasive	50	+/−	I	1	T1	−	NED
19	Invasive	51	+/NP	I	1	T1	−	LTF
20	Invasive	52	+/−	I	3	T1	−	NED
21	Invasive	51	+/−	I	1	T1	−	NED
22	Invasive	55	+/−	IIIA	2	T3	+	NED
23	Invasive	56	+/−	IIB	2	T2	+	NED
24	Invasive	57	+/−	IIA	1	T2	+	NED
25	Invasive	57	+/−	IIA	1	T2	−	NED
26	Invasive	57	−/−	I	3	T1	−	NED
27	Invasive	59	+/−	I	1	T1	−	NED
28	Invasive	59	−/+	IIA	3	T3	−	DOD
29	Invasive	60	+/−	I	1	T1	−	NED
30	Invasive	60	+/−	IV	2	T2	−	AWD
31	Invasive	63	+/−	I	1	T1	−	NED
32	Invasive	63	+/−	I	1	T1	−	NED
33	Invasive	60	−/+	IIA	NP	T1	+	NED
34	In situ	63		0				NED
35	Invasive	63	+/−	I	1	T1	−	DOC
36	Invasive	64	−/+	I	3	T1	−	NED
37	Invasive	65	+/+	IIA	1	T1	−	NED
38	Invasive	68	+/+	IV	2	T2	+	DOD
39	In situ	68		0				DOC
40	Prophylactic	67						NED
41	Invasive	73	+/−	I	2	T1	−	NED
42	Invasive	79	−/−	IIA	3	T2	−	NED
43	Invasive	57	−/+	IV	3	T3	+	AWD
44	Atypical	23						NED
45	Prophylactic	46						NED
46	In situ	42		0				NED
47	Invasive	45	+/−	I	1	T1	−	NED
48	Invasive	50	+/−	I	1	T1	−	NED
49	In situ	52		0				NED
50	In situ	52		0				NED
51	Invasive	55	−/+	IIA	3	T1	+	NED

Note:Patient 5 diagnosed with in situ carcinoma in left breast; right (prophylactic) breast was analyzed for PCBs. Patient 11 diagnosed with stage IIIA invasive carcinoma in right breast; left (prophylactic) breast was analyzed for PCBs. Patient 13 diagnosed with stage IIA invasive carcinoma in right breast; left (prophylactic) breast was analyzed for PCBs. PCB levels were determined in both breasts for patients 44–51: patient 44, atypical hyperplasia both breasts; patient 45, double prophylactic mastectomy; patient 46, carcinoma in situ left breast, prophylactic mastectomy right breast; patient 47, stage I invasive carcinoma right breast, prophylactic mastectomy left breast; patient 48, stage I invasive carcinoma right breast, carcinoma in situ left breast; patient 49, carcinoma in situ left breast, prophylactic mastectomy right breast; patient 50, carcinoma in situ right breast, prophylactic mastectomy left breast; patient 51, stage IIA invasive carcinoma left breast, prophylactic mastectomy right breast.

[a] Atypical, atypical hyperplasia; In situ, ductal carcinoma or lobular carcinoma in situ; Invasive, invasive ductal or invasive lobular carcinoma; Prophylactic, voluntary prophylactic mastectomy.

[b] Age at mastectomy.

[c] Estrogen receptor (ER)/human epidermal growth factor receptor 2 (HER2) status; NA, not applicable; NP, not performed.

[d] American Joint Committee on Cancer staging system.

[e] 1, well differentiated; 2, moderately differentiated; 3, poorly differentiated.

[f] T1, $\leq$2.0 cm in greatest dimension; T2, $>$2.0 cm but $\leq$5.0 cm; T3, $>$5.0 cm.

[g] Axillary lymph node status.

[h] AWD, alive with disease; DOC, deceased from other causes; DOD, deceased from disease; LTF, lost to follow-up; NED, no evidence of disease.