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Does Radiotherapy Have Consequences on Plasma Concentration of Toxic Pollutants?

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Polychlorinated biphenyl's (PCBs) and chlorinated pesticides [especially 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE), the major metabolite of 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (DDT)] are persistent compounds, accumulating in adipose tissues because of their solubility in lipids and their inefficient metabolism. In this regard, body weight loss occurring after chemotherapy or radiotherapy could be followed by an increase in blood concentration of potentially toxic pollutants (Chevrier et al. 2000). Confirmation that humans are exposed to chemicals that interfere with the hormonal system (endocrine disrupters) has prompted many epidemiological studies but an association between chemical residues and disease remains elusive. Many publications tend to establish a correlation between organochlorine pesticides in blood or tissues and male reproductive disorders (Aliva et al. 2001), precocious puberty (Krstevska-Konstantinova et al. 2001) or breast cancer (Dewailly et al. 1994; Hoyer et al. 2000), even if the possible etiological role in breast cancer development remains unclear (Zheng et al. 2000; Laden et al. 2001). Retrospective studies usually deserve blame because it is very difficult to set down the cancer development to the plasma concentration of the chemical compound. Indeed, the increased plasma concentration of pollutants could be subsequent to the cancer detection and treatment. The aim of this study was to evaluate the consequences of radiotherapy on plasma concentration of DDT, DDE, hexachlorobenzene (HCB) and PCBs n° 28, 52, 101, 118, 138, 153 and 180 in a group of sixty five cancer patients submitted to radiotherapy. A control group consisting of 55 subjects of similar mean age was also formed in order to compare plasma concentrations.

MATERIALS AND METHODS

The cases group (Table 1) was constituted of 65 patients suffering from different cancers who were undergoing radiotherapy treatment before or after surgery. Blood samples were collected just before the 1st radiation process and in the middle of the last week of treatment. Mean treatment duration was 4 weeks (SD = 1.22 weeks). Body weight was registered at the time of both blood samplings. A control group of 55 healthy individuals of the same age who were tested for plasma concentrations of the same compounds was formed in order to compare

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the results (Table 1). For each case or control individual, blood sample was immediately centrifuged and serum was kept frozen at -18°C until assay.

Table 1. Characteristics of the subjects (n=65) and controls (n=55)

	Subjects	Controls
Age (y)	62.7 ± 12.9	57.49 ± 12.6
BMI (kg/m²)		22.90 ± 6.8
Prior to radiotherapy	22.6 ± 5.2	
At the end of treatment	22.0 ± 5.8	

Values are means ± SD

All people gave their informed consent for participating in the study.

The identification and quantification of chlorinated hydrocarbons (DDE, DDT, HCB) and PCBs (congeners n°s 28, 52, 101, 118, 138, 153 and 190) in serum were done using a gas chromatographic analyser coupled to a Tandem mass spectrometer detector. Briefly, sample preparation included a liquid-liquid extraction (petroleum ether: diethylether, 98:2) followed by a solid-phase extraction (Bond Elut Certify, Varian). The eluate was evaporated to dryness, reconstituted in n-hexane and then injected into the gas chromatograph (Saturn 2000, Varian). The column was a HP-5 Trace from Agilent (30 m x 0.25 mm internal diameter). Ionisation by electronic impact occurred at 70eV. All solvents were pesticide-grade quality. Reference standards of all compounds were obtained from Cambridge Isotope Laboratories (Andover, MA, USA) or Dr Ehrenstorfer (Ausburg, Germany). The calibration curve was constructed from 0 to 30 ppb and linearity applied for this concentration range. Endosulfan-d4 (0.5 ppb) was used as internal standard. Limits of quantification were defined as ten times the standard deviation (SD) of the results from the lowest quality-control serum pool over the course of the analyses (n=15). These limits were approximately 0.5 ppb for organochlorines and 2 ppb for PCBs.

Samples were analysed in a blind procedure together with controls consisting of samples spiked with 2 or 5 ppb of each compound tested. Results were corrected for total lipid content calculated by the recommended method (Patterson et al. 1991) after total cholesterol, free cholesterol, phospholipids and triglycerides measurements were conducted using standard enzymatic procedure on a MEGA chemistry analyser.

In paired samples (before and after radiotherapy), the blood levels of chlorinated adjusted for total lipids were compared using Student's *t*-test after normalization of the data's distribution. The same test was used to compare cancer subjects with control group. Spearman's correlation coefficient was used to assess the relationship between body weight loss during radiotherapy and changes in pollutant concentration. All results were considered to be significant at the 5 % critical level ($p<0.05$).

RESULTS AND DISCUSSION

The results for all detected compounds are presented in Table 2.
The most frequent organochlorine residue was pp'DDE. HCB was also detected with a high frequency. The PCBs n° 28, 153 and 138 were more often present than not. Only PCB n°52 was never detected in these two groups.

Body weight loss was not important during radiotherapy, and no significant changes were found between the beginning and the end of the treatment. However, the plasma organochlorine concentration was significantly higher in this population than in controls (Table 3).

Table 2. Plasma organochlorines and PCBs prevalence and concentrations in cancer subjects before (Pre) and after (Post) radiotherapy, and in control subjects. Values are means ± SD.

Compounds	Cancer subjects : Pre (n = 65)		Cancer subjects : Post (n = 65)	
	Prevalence (%)	Concentration (µg/g lipid)	Prevalence (%)	Concentration (µg/g lipid)
pp'DDE	92.3	3.05 ± 1.02	92.8	3.03 ± 1.00
pp'DDT	10.4	1.24 ± 0.20	10.4	1.23 ± 0.18
HCB	24.6	1.40 ± 0.09	25.0	1.49 ± 0.11
PCB 28	34.8	0.84 ± 0.12	34.8	0.87 ± 0.13
PCB 52	0	-	0	-
PCB 101	10.8	0.32 ± 0.07	10.4	0.31 ± 0.08
PCB 118	12.9	0.94 ± 0.11	12.9	1.02 ± 0.08
PCB 138	27.6	0.62 ± 0.05	27.6	0.67 ± 0.08
PCB 153	30.2	0.46 ± 0.06	31.0	0.43 ± 0.10
PCB 180	14.5	0.39 ± 0.07	14.5	0.39 ± 0.12

Compounds	Control subjects (n = 55)	
	Prevalence (%)	Concentration (µg/g lipid)
pp'DDE	90.4	1.74 ± 0.85
pp'DDT	1.0	1.00 ± 0.06
HCB	17.0	0.94 ± 0.10
PCB 28	30.0	0.51 ± 0.07
PCB 52	0	-
PCB 101	6.0	0.17 ± 0.07
PCB 118	7.0	0.78 ± 0.12
PCB 138	19.0	0.31 ± 0.18
PCB 153	22.8	0.32 ± 0.09
PCB 180	6.0	0.31 ± 0.08

Table 3. Correlation's between changes in body weight and plasma concentrations in cancer patients and comparison between plasma concentrations in cancer patients (Pre and Post) and control subjects. NS: non-significant.

Compounds	Correlation's (r^2) with body weight loss	Comparison (p) with control subjects	
		Pre	Post
pp'DDE	NS	0.0008	0.0008
pp'DDT	NS	NS	NS
HCB	NS	0.0032	0.0036
PCB 28	NS	0.0245	0.0270
PCB 101	NS	0.0030	0.0030
PCB 118	NS	0.0016	0.0020
PCB 138	NS	0.0024	0.0026
PCB 153	NS	0.0027	0.0032
PCB 180	NS	0.0003	0.0003

Bioaccumulation of HCB, DDT, DDE and PCBs in human tissues is known to be correlated with age but this positive correlation is not sufficient to explain the significant difference between cases and controls in this study, since the mean ages are comparable between both groups. Additional follow-up studies are necessary to explain why the level of pollutants in the cancer group is higher than in the control subjects. Possible reasons are a significant body weight loss due to surgery, chemotherapy or to the cancer process (Wolff et al.1995; Chevrier et al. 2000; Wolff et al.2000). A retrospective examination of all patients' history could permit to evaluate the current presence of such xenobiotics in plasma but also its possible impact on human health. However, it can be concluded from the presented data that radiotherapy associated body weight loss is not significant enough to increase the plasma concentration of these chemical compounds.

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