High Concentrations of Organochlorines in a Patient with Kidney Cancer and Anorexia-cachexia Syndrome

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Abstract: ***Purpose:*** To determine persitent organic pollutants in adipose tissue in a patient with kidney cancer.

Methods: Adipose tissue was sampled from the abdominal wall during autopsy of a 75-year old man who had died from a kidney cancer. The concentrations of polychlorinated biphenyls (PCBs), *p,p´*-dichlorodiphenyltrichloroethane (DDE), hexachlorobenzene (HCB), chlordanes and tetrabromodiphenyl ether (TeBDE) were determined on lipid basis. For comparison results from 29 male population based subjects aged 70-80 years were used.

Results: All concentrations except for TeBDE were very high in the patient; sum of PCBs 18 808 ng/g fat (median for controls 997), DDE 14 183 (median for controls 751), HCB 424 (median for controls 46), and sum of chlordanes 2 389 (median for controls 62). The patient lost weight from 80 kg to 48 kg when he died, which may have contributed wholly or partly to the very high concentrations of organochlorines.

Conclusion: Changes in weight must be recorded in cancer patients and the concentrations of persistent organic pollutants should be normalized to weight. The concentrations in this patient were 10- to almost 40-times higher than in the controls. Such very high concentrations may give clinical symptoms in the final stage of a wasting cancer patient.

Key Words: Kidney cancer, organochlorines, tetrabromodiphenylether.

INTRODUCTION

Kidney cancer amounted in 2004 to 2.1 % of all new cancer cases in Sweden [1]. The risk factors for kidney cancer are not well established although cigarette use, drugs such as diuretics and phenacetin, occupations with exposure to polycyclic aromatic hydrocarbons, cadmium and petroleum products have been suggested to increase the risk [2-4].

Based on a case history on pesticide exposure we judged it to be of interest to determine the concentrations in adipose tissue of some organohalogenated compounds: polychlorinated biphenyls (PCBs), *p,p´*-dichlorodiphenyltrichloroethane (DDE), hexachlorobenzene, chlordanes and tetrabromodiphenyl ether (TeBDE) in a patient with kidney cancer. These compounds were chosen since they are included in our studies on the association between persistent organic pollutants and certain malignant diseases [5-8]. Thus, the tissue sample from this patient could be analyzed in the same series as samples from a study on non-Hodgkin's lymphoma at the same time.

PCBs were introduced commercially in 1929 in e.g., capacitors and transformators due to their flame resistance [9]. It was not until mid 1960´s that PCBs were identified to be persistent environmental pollutants. In 1972 usage of PCBs in sealants, plastics and paints was banned in Sweden, in 1978 the import of PCBs in closed systems was stopped (capacitors and transformers) and in 1995 also all use of PCBs in old equipment was prohibited. The concentrations in the environment have declined since these restrictions were inaugurated [10]. DDE is the main persistent metabolite of *p,p´*-trichlorodiphenyltrichloroethane (DDT). DDT has been used as an insecticide on a broad scale since the Second World War. The ecological consequences of large-scale DDT usage were not identified until the publication of Rachel Carson's book *Silent Spring* [11]. The use of DDT was prohibited in Sweden in 1975. However, it is still used for control of malaria mosquistos in certain other countries. Thus, global pollution by DDT is still a concern. Hexachlorobenzene (HCB) has been used as a fungicide and can also be found as a by-product from incineration processes and the chlorine industry. It is a widely distributed persistent organic pollutant. Chlordanes are insecticides used to combat e.g., termites. This group of insecticides has not been used in Sweden since 1969.

Brominated flame-retardants such as TeBDE are chemicals that have been identified in the environment more recently. They are chemically related to PCBs but contain bromine instead of chlorine and have been shown to be persistent in the environment as the earlier described chlorinated organic persistent pollutants. TeBDE has been used as a

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flame retardant since early 1970's in e.g., electronic equipment, paints, textiles, and plastics. It was identified in human tissue in the late 1990´s [8,12]. The concentration was increasing in Swedish mother's milk with an estimated doubling time of 5 years [10].

METHODS

Case History

A 75-year-old man was diagnosed in June 1996 with a clinically suspected prostate cancer. This was based on a fine needle biopsy from the left prostate lobe. Already at that time the patient had bone metastases and prostate specific antigen (PSA) level was slightly elevated. The patient was treated with hormones, but the disease progressed, however. The patient died in March 1998. Autopsy revealed the primary cancer to be located in the left kidney with metastases in liver, bone, and retroperitoneum. The retroperitoneal tumor on the right side was descending to the right groin, and was growing near the prostate.

The patient was a non-smoker since 1951. He had no history of intake of phenacetin or diuretics. The Swedish Railways had employed him during 1945-81 as a lineman. During that period he had occasionally been exposed to different organic solvents and asbestos. From early 1950's until early 1970's the patient had taken part in the yearly spraying operations against weeds with phenoxyacetic acids and amitrol. The phenoxy herbicides used were a combination of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and 2,4-dichlorophenoxyacetic acid (2,4-D) with the trade name Hormoslyr®. The patient was a driver of a railroad truck used for spraying for about one week each summer. No personal protection was worn during this process and his clothes were wet and smelled of the phenoxy herbicides. The patient described that he could feel the taste in his mouth while eating. His boiler suit was brought home after one week spraying and was washed at home.

His exposure to herbicides was discussed with his physician (H.W.) by the relatives. After informed consent from the relatives adipose tissue from the abdominal wall was taken during autopsy for analysis of organohalogenated compounds.

Determination of Concentrations of Organochlorines

Fat was extracted, cleaned and analyzed by high-resolution gas chromatography and low-resolution mass spectrometer (HRGC-MS). All results are expressed in ng/g adipose tissue. The method has been described in detail elsewhere [13].

RESULTS

In total 34 congeners of PCBs were analyzed for. The sum of PCBs was 18 808, Table **1**. This is to be compared with the median sum of PCBs of 997 ng/g lipid (range 428-2 047) in 29 male comparison group aged 70-80 years in our at the same time on-going study on NHL [14]. Also the concentration of HCB was increased to 424 ng/g lipid, as well of DDE to 14 183 ng/g lipid. Four different chlordanes were analyzed. The sum of chlordanes was 2 389 ng/g lipid in the

Table 1. Concentrations of Certain Persistent Organic Pollutants in a Patient with Kidney Cancer and Comparison with 29 Men Aged 70-80 Years in the Swedish Population. The Concentrations are Expressed in ng/g Lipid

	Patient	29 men aged 70-80 years		
		Mean	Median	Range
Sum PCB	18 808	1 090	997	428-2 047
-PCB#28	8	4.4	2.8	1.5-29
-PCB#52	4	1.3	0.9	0.2-5.7
-PCB#47	2	0.4	0.4	0.1-1.0
-PCB#74	243	15	12	6.2-49
-PCB#66	13	2.4	1.9	0.9-9.8
-PCB#101	11	2.4	1.7	0.8-11
-PCB#99	357	19	15	6.6-36
-PCB#110	n.d.	0.7	0.6	0.1-1.4
-PCB#118	727	37	35	12-79
-PCB#114	5	1.8	1.6	0.4-3.9
-PCB#105	411	6.9	5.4	2.3-18
-PCB#153	4 049	275	249	103-576
-PCB#138	3 194	209	189	1.8-398

(Table 1. Contd….)

	Patient	29 men aged 70-80 years		
		Mean	**Median**	**Range**
-PCB#128/167	143	11	10	4.4-18
-PCB#156	686	28	28	10-50
-PCB#157	102	4.4	4.2	1.2-7.0
-PCB#182/187	883	54	58	21-91
-PCB#183	293	22	21	7.6-49
-PCB#174	182	13	12	5.1-23
-PCB#177	130	9.0	8.4	2.7-22
-PCB#172/192	165	11	12	3.2-23
-PCB#180	2 886	179	179	75-359
-PCB#193	159	8.7	9.5	0.5-18
-PCB#170/190	1 336	85	87	30-175
-PCB#189	56	3.5	3.4	1.1-5.8
-PCB#202	201	5.9	5.9	0.8-14
-PCB#201	487	17	17	2.8-28
-PCB#196/203	628	21	21	4-41
-PCB#195	133	5.7	5.2	1.0-20
-PCB#194	725	21	20	9.8-39
-PCB#208	149	3.0	3.0	0.5-6.4
-PCB#207	58	1.4	1.5	0.3-5.8
-PCB#206	206	4.7	4.5	0.5-9.9
-PCB#209	176	6.1	5.7	2.1-17.7
DDE	14 183	950	751	167-3 725
HCB	424	47	46	14-90
Sum chlordanes	2 389	83	62	23-198
-Oxychlordane	14	26	19	7-62
-MC 6	346	8	7	2-19
-Trans-nonachlor	1 688	44	33	12-113
-Cis-nonachlor	341	5	4	1-16
TeBDE	2	2	0.7	0.4-13

patient to be compared with median sum of 62 ng/g lipid (range 23-198) in the 29 controls. Only for TeBDE a similar concentration as in the controls was found in the adipose tissue from this patient.

DISCUSSION

A very high concentration of all studied organochlorines was found except for TeBDE . The detected concentrations of PCBs, HCB, DDE and chlordanes are much higher than would be expected. Of interest in this context is the wasting of body weight that the patient experienced during his disease. When the patient was diagnosed with a malignant disease his body weight was 80 kg and his weight had been stable for about ten years before that time. When he died 21 months later he had lost weight to 48 kg. Thus, the measured concentrations may largely be due to weight loss.

The patient did not report any pesticide exposure during his leisure time. In his occupation he had for several years used phenoxy herbicides and amitrol. A carcinogenic potential of both phenoxyacetic acids [15] and amitrol [16] has been reported. 2,4,5-T was prohibited in Sweden in 1975 due to its contamination with 2,3,7,8-tetrachloro-*p*-dioxin (TCDD). In 1997 TCDD was classified by IARC as a human carcinogen [17,18]. Certainly this patient was exposed to TCDD since he had sprayed with a mixture of 2,4-D and 2,4,5-T. It would have been desirable to include analysis of dioxins and dibenzofurans from his adipose tissue. However, this was not the topic of the current NHL study in which this person's specimen was included.

Pesticide exposure has in some studies yielded increased risk for kidney cancer [19,20] whereas this was not shown in another investigation [21]. Chlorophenols are chemically related to phenoxy herbicides. They have been widely used as impregnating agents until the ban in Sweden in 1977. Two cohort studies of chlorophenol exposed workers showed increased risk for kidney cancer [22,23]. A cluster of three cases with kidney cancer among electric power utility workers exposed to PCB has been published [24].

Due to the loss of weight in this patient it is not possible to judge if the concentrations of organochlorines were higher than among the controls in 1996 when he was diagnosed with cancer. However, an association with other chlorinated persistent chemicals cannot be excluded from information concerning the work situation of the patient. These results show that it is necessary to assess information on the weight at the time of collection of tissue specimens for analysis of persistent organic pollutants. Moreover, changes in the weight and total body fat content over the last 5 to 10 years should be recorded. In addition it is important to report the concentrations of persistent organic pollutants normalized to lipid weight. Persistent chlorinated organic compounds are stored in the body fat and concentrations should thus be compared on lipid basis. Measurements based on wet weight or whole blood can be misleading indicated from the case described above. These data show that the concentrations of toxic pollutants may be very high in a cancer patient at the final stage of the disease. The now presented concentrations are so high that toxic symptoms with e.g., impairment of the immune system, may develop in the patient, an aspect so far not considered in the clinical management of cancer patients. Of course no conclusion on an association between persistent organic pollutants and kidney cancer can be drawn from this cases report.

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