PECULIOR REMAINING OF SOME PCB CONGENERS IN THE PATIENTS WITH YUSHO FOR MORE THAN 30 YEARS

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Introduction

Rice oil polychlorinated biphenyl (PCB) poisoning called Yusho occurred in Fukuoka and Nagasaki Prefectures, Japan, in 1968□Patients have been suffering from various symptoms with keeping persistent PCB and polychlorinated dibenzofuran (PCDF) congeners in the body for more than 30 years. Yusho particular PCB pattern of relatively low concentration of 2,3',4,4',5-pentaCB (#118) and high concentration of 2,3,3',4,4',5-hexaCB (#156) is one of important signs for diagnosis of Yusho[1]. We analyzed the blood samples recently collected from Yusho patients and normal persons in Fukuoka for concentrations of PCB congeners and some chlorinated pesticides and statistically examined concentration profiles of these congeners in Yusho patients.

Materials and methods

PCB analysis of blood from Yusho patients Blood samples were collected from Yusho patients at annual health examination in Fukuoka from 2000 to 2002. Blood sample 3 g was added with internal standards of 6 ^{13}C-PCBs 5 ng and 1M-KOH/ethanol solution 3 ml and heated at 50ºC with occasional stirring for 3 hours. After cooling, the solution was extracted with hexane 5 ml twice. The hexane extract was washed with water, dried over anhydrous sodium sulfate and chromatographed on silica gel (1 g) column, eluting with hexane 30 ml. The hexane eluate was concentrated to 0.1 ml or less and injected to gas chromatograph/mass spectrometer (Shimazu GC-17A and QP-5000).

PCB analysis of blood from Fukuoka residents Blood samples were collected from normal Fukuoka residents in 1999. Blood 10 ml was extracted with acetone/hexane (2 : 1) and the extract was concentrated to dryness to determine the lipid weight. The lipid was dissolved in hexane/dichloromethane (1 : 1), added with internal standards of 12 ^{13}C-PCBs, and fractionated on a gel permeation column of Bio-Beads S-X3. The fraction for PCBs was analyzed for 48 PCB congeners by HRGC/HRMS (Hewlett Packard 5890J gas chromatograph-JEOL SX-102 mass spectrometer)

Results

Table 1 shows average and median concentrations of #118, 2,2',4,4',5,5'-hexaCB(#153), 2,2',3,4,4',5'-hexaCB(#138), 2,2',3,4,4',5',6-heptaCB(#183), #156, 2,2',3,4,4',5,5'-heptaCB (#180), 2,2',3,3',4,4',5-heptaCB(#170), total 24 PCB congeners for Yusho patients or total 48 PCB congeners for Fukuoka

controls, hexachlorobenzene (HCB) and dichloro-dichlorophenyl ethylene (DDE) in Yusho patients and Fukuoka residents. Concentration ratio, Yusho/control, of PCB#118 (1.8) is lower than the ratio of total PCBs (5.4), while the ratio of PCB#156 is high as 19.0

Table 1 Concentrations (ppb in whole blood) of 7 PCB congeners and total PCBs, HCB and DDE in Yusho patients and Fukuoka control and their ratio Yusho/Control at median

	Yusho A+B (n=28)			Control (n=151)			Ratio Yusho/Cont at Median
	Average	SD	Median	Average	SD	Median	
Age	67.8	9.86	69.6	36.6	11.83	35.1	2.0
PCB#118	0.062	0.032	0.051	0.038	0.035	0.028	1.8
PCB#153	0.689	0.380	0.551	0.167	0.156	0.123	4.5
PCB#138	0.800	1.471	0.410	0.081	0.069	0.060	6.8
PCB#182	0.117	0.063	0.099	0.041	0.035	0.029	3.4
PCB#156	0.310	0.242	0.246	0.018	0.014	0.013	19.0
PCB#180	0.491	0.269	0.381	0.126	0.100	0.087	4.4
PCB#170	0.327	0.221	0.260	0.039	0.030	0.028	9.3
Total PCBs	4.117	3.340	2.927	0.759	0.616	0.547	5.4
HCB	0.107	0.050	0.095	0.045	0.033	0.043	2.2
DDE	2.914	1.725	2.609	0.749	0.531	0.605	4.3

Figure 1 describes correlation profiles between age and concentrations of PCB#118, #153 and #156 in Yusho patients A (typical Yusho PCB congener type) and B (PCB congener type between A and control type) and Fukuoka residents. Concentrations of the three PCB congeners in Fukuoka controls are well correlated with age. Concentrations of PCB#156 in Yusho patients are higher than the regression line of the control persons, while concentrations of PCB#118 in Yusho patients are lower than the regression line of the controls. Figure 2 describes correlation profiles between age and concentrations of total PCBs, HCB and DDE in Yusho patients and controls. DDE profile is somewhat similar to PCBs in Yusho patients, in spite of that neither DDE nor DDT (chlorinated pesticide which is metabolized to DDE in the human body) had been ingested by Yusho patients with the PCB contaminated rice oil

Correlation coefficients between age and 7 PCB congeners in Yusho patients and control persons are shown in Table 2. High significantly positive correlations between age and 7 PCB congeners are observed in the control persons, while in Yusho patients, only some PCB congeners are significantly positively correlated with age. Most of the correlations between PCB congeners in Yusho patients and control persons are highly significant, but very low correlation coefficient is observed between PCB#118 and #156 in Yusho patients.

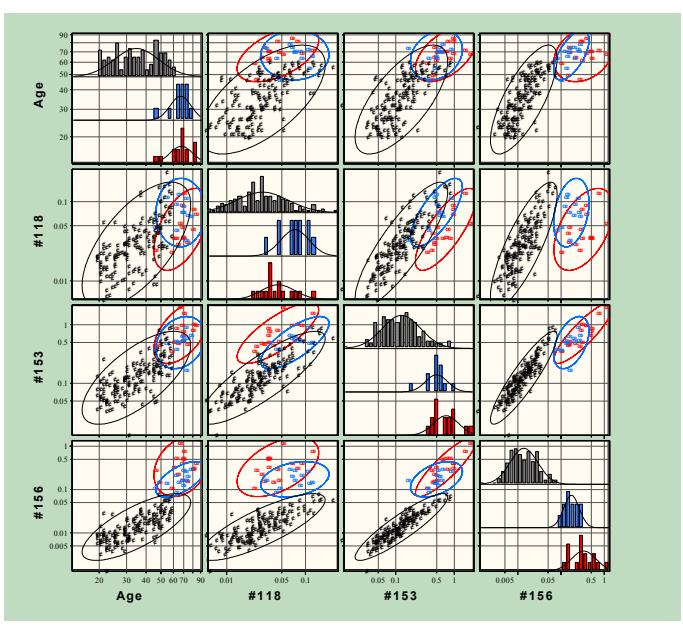

Figure 1 Ellipse of constant distance (95%) between age, PCB#118, PCB#153 and PCB#156 of Yusho A (●), Yusho B (○) and Fukuoka control (Δ). Histograms of Fukuoka control (n=151, upper), Yusho B (n=12, middle) and Yusho A (n=16, lower) in the diagonal squares

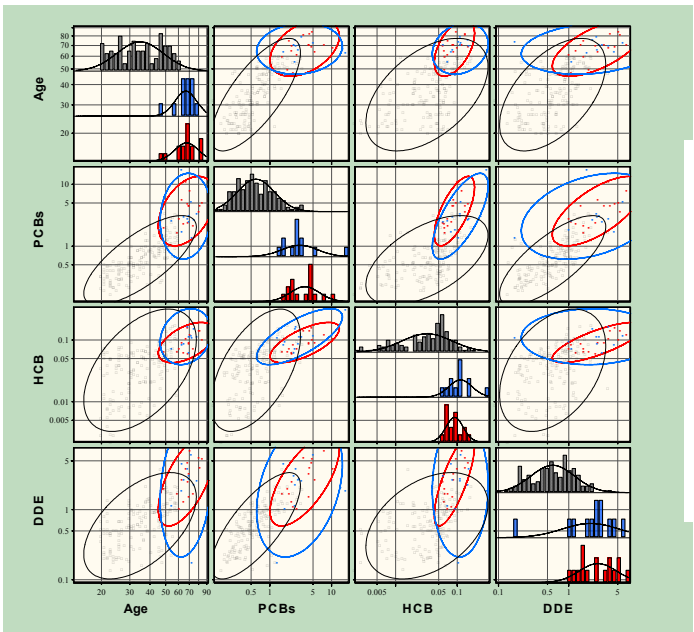

Figure 2 Ellipse of constant distance (95%) between age, total PCBs, HCB and DDE of Yusho A (●), Yusho B (○) and Fukuoka control (Δ). Histograms of Fukuoka control (n=151, upper), Yusho B (n=12, middle) and Yusho A (n=16, lower) in the diagonal squares.

Table 2 Correlation coefficients between age and 7 PCB congeners in Yusho patients

and control persons

	Age	#118	#153	#138	#182	#156	#180	#170
Correlation coefficients in Yusho patients (n = 28, p < 0.05: >0.374)								
Age	1.0000							
#118	0.2804	1.0000						
#153	0.3958	0.4280	1.0000					
#138	0.1758	0.3960	0.6826	1.0000				
#182	0.4565	0.6620	0.8772	0.6400	1.0000			
#156	0.3273	**0.0722**	0.7892	0.5783	0.6482	1.0000		
#180	0.3527	0.4008	0.8722	0.5938	0.9046	0.8473	1.0000	
#170	0.2423	0.2612	0.7879	0.8038	0.7643	0.8957	0.8889	1.0000
Correlation coefficients in Fukuoka control persons (n = 151, p < 0.001: >0.32)								
Age	1.0000							
#118	0.6395	1.0000						
#153	0.6933	0.8424	1.0000					
#138	0.6678	0.8944	0.9466	1.0000				
#182	0.6933	0.8303	0.9139	0.8792	1.0000			
#156	0.7450	0.8110	0.9016	0.8840	0.8655	1.0000		
#180	0.7537	0.8136	0.9297	0.8982	0.9237	0.9267	1.0000	
#170	0.7238	0.7968	0.9212	0.8835	0.9178	0.9336	0.9582	1.0000

Discussion

The PCB concentrations in the blood of Yusho patients were higher than those of Fukuoka controls and concentration ratios of Yusho/Control were various depending on PCB congeners, being 1.8 on PCB#118, 19.0 on PCB#156 and 5.4 on total PCBs. Correlation coefficients between age and concentrations of 7 PCB congeners, HCB and DDE in the blood of Fukuoka residents were significantly positive each other ($p < 0.001$), while in Yusho patients, the correlation coefficients were positive but various depending on the congeners, and correlation coefficient between PCB#118 and PCB#156 in the Yusho patients was remarkably low, indicating their peculiar accumulative properties in Yusho patients. Prominently high concentrations of PCB#156 in the rice oil had been produced by heating the Kanechlor (commercial brand of PCBs) at high temperatures for a long time and eventually remained in the Yusho patients. Relatively low concentrations of PCB#118 in the Yusho patients were probably made by strong enzyme induction of PCDFs and PCBs which are still remaining at high concentrations in the Yusho patients. Sandau et al[2] determined hydroxylated metabolite of PCB#118 in umbilical cord plasma samples from coastal populations in Quebec and suggested that hydroxylated PCBs are possibly altering thyroid hormone status. The concentration of PCB#118 had been markedly decreased after the ingestion of PCBs and would be metabolized to hydroxylated PCB, which might cause hormone disturbance in the Yusho patients

References

1. Masuda Y. (1996) in: YUSHO (Kuratsune, M, et al Ed), pp 47-80, Kyushu University Press,

2. Sandau CD, Ayotte P, Dewailly E, Duffe J and Norstrom, RJ, (2002) Environ Health Perspect 110, 411-7.