

CLINICAL ASPECTS OF YUSHO

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Abstract

Yusho is a type of food poisoning from rice bran oil contaminated with polychlorinated biphenyls (PCBs) and various dioxins such as polychlorinated dibenzofurans (PCDFs). The victims of Yusho suffered from dermatological manifestations (acneform eruptions, comedones, etc.) in association with systemic, ophthalmological, and mucosal symptoms. We recently started to measure the blood levels of dioxins in the annual medical check-up of Yusho patients. In this presentation, we reviewed the clinical and epidemiological findings elucidated over the past 36 years by the Study Group for Yusho with special reference to cutaneous and orthopedic manifestation. The development of therapeutic interventions is warranted in the near future.

Introduction

A mass poisoning involving at least 1,860 individuals occurred in Kyushu, western Japan, in 1968. The incident is called Yusho oil disease because it was caused by the ingestion of rice bran oil that was contaminated with Kanechlor-400, a commercial brand of Japanese polychlorinated biphenyls (PCBs). It was later found that the rice bran oil had been contaminated not only with PCBs but also with polychlorinated dibenzofurans (PCDFs), polychlorinated quaterphenyls (PCQs), and other related compounds. Yusho is thus recognized as poisoning by a mixture of PCBs, dioxins and related compounds. For more than 35 years the patients with Yusho have suffered from various symptoms such as general malaise, headache, acneform eruption, dark-brownish nail pigmentation, increased discharge from the eyes with swelling of the eyelids, pigmentation of oral mucosa, peripheral neuropathy, irregular menstruation in women, and growth retardation in infants and children.

Materials and Methods

In order to analyze the relationship between the concentrations of dioxins/PCBs and the subjective/objective complaints of patients with Yusho. We recently started to measure the blood levels of dioxins in the annual medical check-up of Yusho patients. In addition, we reviewed the clinical and epidemiological findings elucidated over the past 36 years by the Study Group for Yusho.

Results and Discussion

Although the blood levels of dioxins and dioxin-related compounds were very low, Todaka et al. recently developed a new method of determining the concentration of dioxins (PCDFs, PCDDs and coplanar PCBs) in a blood sample of just 5 g with satisfactory accuracy and reproducibility [1]. This technical advancement has allowed us to include the measurement of blood levels of dioxins in the annual medical check-up from 2001. As shown in Table 1, from 2001 to 2003 the mean blood levels of total dioxins (pg-TEQ/g lipid) and 2,3,4,7,8-PeCDF (pg/g lipid) in patients with Yusho was 3.4–4.8 and 11.6–16.8 times higher than the mean levels in normal controls, respectively. It is known that dioxins and PCBs remain in the tissue for a long time. It is indeed of note that, even 39 years after the incident, high concentrations of dioxins still remain in the blood of patients with Yusho. After the evaluation of validity, sensitivity and reproducibility of the blood levels of dioxins, we added the blood levels of 2,3,4,7,8-penta-CDF in the new diagnostic criteria in Sep. 29th, 2004.

In sharp contrast to the characteristic clinical features, the majority of laboratory findings remained within normal limits [2]. Notable elevation of serum lipid levels, particularly those of serum triglycerides, was evident [2]. The correlation between PCB exposure and elevation of serum triglyceride levels has been a great concern since the Yusho incident. A study on workers occupationally exposed to PCBs reported a correlation between blood PCBs and serum triglyceride concentrations [3].

One of the major symptoms of massive poisoning by dioxins is joint swelling and pain. This orthopedic symptom severely and continuously annoys some patients, which may result in degenerative destruction of joints. Osteoporosis may be a major concern in a part of victims. Such orthopedic problems should be addressed vigorously.

As for therapeutic approach, the Yusho Study Group is now conducting two clinical studies. One is carried out by oral administration of four different Chinese herbal drugs against four major symptoms such as general malaise, cough & sputum, muscle pain and paresthesia, comedones and acneform eruptions. The other study has just started using oral administration of cholestimide, an

anti-hyperlipidemia agent, aiming to reduce blood concentration of residual dioxins. Cholestyramine had been already used for the same purpose in Yusho patients with some beneficial effects. The outcome of Chinese herbal drugs could be partly presented in this talk.

Table 1

Blood concentrations of dioxins and dioxin-related congeners in patients with Yusho and normal controls

	Yusho patients at annual check-up			Normal controls (n = 52)
	2001 (n = 78)	2002 (n = 279)	2003 (n = 269)	
Blood concentration of total dioxins and dioxin-related congeners (pg-TEQ/g lipid)				
Maximum	1049.7	1126.1	1176.6	85.4
Minimum	13.9	7	5.5	8.5
Mean	179.3	136.4	125.0	37.0
SD	180.5	148.9	141.2	17.6
Blood concentration of 2,3,4,7,8-PeCDF (pg/g lipid)				
Maximum	1770.6	1889.7	1953.5	41.7
Minimum	6.6	301	2.6	3.5
Mean	256.1	192.0	176.2	15.2
SD	315.3	252.0	240.2	8.9

PeCDF: pentachlorodibenzofuran; SD: standard deviation; TEQ: toxic equivalent quantity.

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References

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