A CASE REPORT OF SECOND AND THIRD GENERATIONS OF A YUSHO FAMILY

R.Takeda[1],

[1] Clinic Rei Takeda, Shibuya, Tokyo, Japan,151-0071, reiclios@blue.ocn.ne.jp, Osaka, Univ. Dept. Health Promotion Science Graduate School of Medicine,565-0871,TokyoUniv.Dept.IT Healthcare Social Cooperation Program, Graduate School of PharmceuticalScience,113-0033

Introduction

50years have passed since the first report on newspaper " The cause of strange disease spread over western Japan was rice oil made by Kanemi warehouse".

14627people went health center near their residential area and complaint of ingestion of toxic oil. But only 913 people designated as toxicosis "Yusho victim" according with Criteria for Yusho [1].

Kanemi rice oil was contaminated with PCBs and PCDFs leaked from defects of the deodorizing tube [2] during the refining process.

In Nagasaki prefecture, which has the highest number of islands in Japan, so much toxic oil had shipped[3].

So many people who had not known their eating toxic oil, though they had experienced symptoms characteristic of Yusho victims. Long after the accident they noticed they had eaten toxic oil in those days, because so many people living in their village were in poor health. They claimed, but almost all people were denied to become certified Yusho because blood concentration "PCDFs ,PCQ and type of PCB" did not confirm standard values and patterns [4].

In 1969 authorities had created "Criteria for 'certified Yusho' and Temporary Treatment Guidelines", this criteria had changed in 1972,1976,1981,2004 [4],In 2004 new criteria were decided (blood level of PCDFs and dioxin like PCBs) after 37 years or more. [4] In Japan there was no blood conservation of Yusho victims in 1968.

2012 family members were admitted as certified Yusho who lived together in 1968 with past certified Yusho[5].In 2013 there were 212 of newly certified Yusho.

In this Criteria children born after 1969 were not admitted as Yusho. Children born after 1969were left unattended. Blood level of dioxins and PCBs were lower than the criteria which were decided upon unreliable source. "Children born after 1969 are not affected by the toxicated oil" (Yusho study group's official opinion).

We had studied Yusho victims who were inhabitants of remote island Nagasaki, Kyusyu district. They are supposed to take toxic oil. Children born after the accident should be carefully examined including the knowledge of growing process taking from their parents and grandparents**.**

Materials and Methods

We have organized a volunteer group of medical practitioners for Yusho people to clarify Yusho (including

uncertified Yusho).These group consists of dentists, internal medicinists, psychosomatic medicinist, psychiatrists, gynecologist, dermatologist.

December 2018 we had investigated 2 Yusho family including 2nd and 3rd generations with Panoramic Radiograph, Electro Cardiograph, Ultra Sound examination for thyroid organ and cervical blood vessels(right and left IMT(intima media thickness)and plaque formation in right and left carotid sinus.

In this report we concentrate on 2nd and 3rd generations, because these generations are not admitted as certified Yusho, and there are few studies of these people.

We examined 11 members including not certified Yusho(2nd generation (4 people)and 3rd generations(3 prople)) at a hospital in Nagoya,Aichi. Their native places are a remote island of Nagasaki,Kyusyu Naru Island.

Prior to this examination we have asked past history and done daily medical check from each Dr.'s speciality in December 2015. Connecting these two examinations we will discuss actual situations of 2nd and 3rd generations as a whole.

Results and Discussion

We found here following findings in this Yusho 2nd and 3rd generations.2nd generations（4people from25y.o to 45y.o） and 3rd generations (3people 9y.o.to 22y.o.).

Results.

1: Panoramic Radiographs: Congenital defects of permanent tooth were found 3/4 of 2nd generations, and 1/3of 3rd generations.

2: ECG: Incomplete RBBB(Right Branch Bundle Block) 2/4 of 2nd generations.

3: Ultra-sonographs of thyroid: Cysts in thyroid gland 4/4 of 2nd generations, and 2/3 of 3rd generations.

IMT(Intima Media Thickness): all normal

Plaque in Carotid sinus: no plaque formation in carotid sinus

4: Anamnesis: Thrombasthenia or frequent nasal bleeding in childhood all 2nd and 3rd generations.

Depression 2/4 of 2nd generations

Discussions

1. Congenital defects of permanent tooth or teeth

   We found defects here, 3 cases of 2nd generation, and 1 case of 3rd generation.

   The frequency of such defects among general population in Japan was not so high.

   These incidents in 2nd generations may be caused by pollution of PCB and dioxin through placenta or breast-feeding, but the case in 3rd generation might not be explained by such simple reasons.

2. ECG ,IMT and plaque formation

We have found 2 cases of incomplete RBBB in 2nd generations, and no case in 3rd generations.

We had already studied 40 Yusho victims (1st generations) in Naru island ,Nagasaki, Kyusyo district. We now studied the descendants of these islanders. We had reported above results[3]; There were 9 CRBBB or Incomplete RBBB cases. 3 cases out of 9 RBBB had experienced heart failure. The frequency of CRBBB among general population in Japan was at most 5 % or below. In this study group (2nd and 3rd generations) the frequency was so high although total number was so small but the result should not be overlooked.

We had also observed IMT and plaque of carotid sinus, they were almost normal, and no narrowing of blood vessels or no plaque formation. In these cases narrowing of blood vessel or ischemia may not the origin of such a slight abnormality. Let's think about the origin of CRBBB and in-complete RBBB. In these people the origin of CRBBB or in-complete RBBB may be attributed to conduction delay because of no narrowing blood vessels. Murai[6] who had reported the existence of such symptoms (sensory neuropathy symptoms and reduction of sensory nerve conduction velocity) were seen in Yusho victims. Sensory neuropathy syndrome such as numbness, pain and hypoesthesia in PCB poisoning were reported. These subjective or objective symptoms were included in Yusho Criteria decided in 1970[7].

Neural conduction delay may be attributable to mitochondrial dysfunction. Studies on liver biopsy from a Yusho patient revealed no particular changes based on microscopic findings, but definite changes were recognized by electron microscopy[8,9,10] .Liver of experimental animals (Guinea pigs and rats) showed different reaction 2 months(Guinea pigs) 1month(rats) after a single oral PCB administration[11].Liver mitochondria of Guinea pigs changed various sizes and irregular crista but that of rats showed no change in electron microscope. Hashiguchi[12] reported oral findings in animal-experiment (beagle dogs)with PCB poisoning. He had shown degenerated nerve terminal like structure which contained swollen degenerated mitochondria and amorphous materials was observed near the distorted Merkel cell. But there were no definitive abnormalities in nervous system of other animals (monkeys and mice) which were administered PCBs. Difference in the species may have contributed to these discrepancies.

Many experimental studies on Yusho (PCBs poisoning) used rats in those days, so the fact that PCBs act on cell organs especially mitochondria might not be paid attention. Recently it has shown PCB damage brain and liver mitochondria in rats.[13]

We should think about PCB and dioxin poisoning from a different point of view, that is, mitochondrial damages to all over human body.

3. Thyroid cysts were found all people 2nd and 3rdgenerations, but no malignancy suspected. The follow-up of

their courses of life is important.

4. Thrombasthenia or frequent nasal bleeding in childhood all 2nd and 3rd generations. These were frequent symptom of 1st generations who suffered Yusho disease in their childhood. These phenomena could not be explained as a simple Menderian inheritance for the frequency was so high in this group.

   If we suppose these as a direct poisoning of mitochondria in bone marrow in childhood, we could explain the phenomena.

Prospect for future study

If we treat Yusho disease as a mitochondrial dysfunction, the situation of Yusho study (including cure method) may develop a new turn.

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