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YUSHO STILL UNSOLVED PROBLEM

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Introduction

In 1968 when the Kanemi rice oil had found to be polluted with some contaminants, 14627 people went health centers near their residential area and complained of ingestion of toxic oil. But only 913 people(6.2%) (2nd July 1969(1,3)) designated as toxicosis “Yusho victim “ according with Criteria for Diagnosis,Yusho(2) . In addition, at that time, there were people who were not given any information, though they had eaten the toxic oil. Long after the accident some people claimed that they had eaten the toxic oil. From 1993 to 2003, only 1 person out of 467 tested cases was admitted as a Yusho victim(3). Even in 2011, total 1966(4) people(including dead people) were designated as Yusho victims, though they had felt ill. Besides there are few studies about prenatal effects of Yusho descendants.

The toxicity of Kanemi rice oil had proved to be PCB in 1968 and PCDFs in 1975. ((5)Nagayama,Masuda,1977) PCDFs were detected in tissues of Yusho victims in 1977.In 2004 new criteria ((6)Furue,Uenotsuchi, 2005)for admitted Yusho were adopted (blood level of PCDFs and dl-PCBs(dioxin like PCBs) after 36 years or more, small number of people were acknowledged as admitted Yusho. But these criteria have a serious defect. In Japan there were no blood conservation of those days and this criteria have been applied only blood of these days (after 36 years or more). The authorities denied the influence towards children born after 1969, for blood concentrations of them were lower than their criteria.

We are now worried about the influences towards the next and third generations.

Since 1968 many studies on Yusho were published, but we had a lot of difficult questions on the results. The number of patients, who were admitted as official Yusho-patients, has been very small as mentioned above. The authorities may have neglected the symptom of large majority of victims, to say nothing of children born after 1969. We should examine minutely including not-admitted Yusho patients to clarify real Yusho syndromes and their influences over descendants.

Materials and Methods

We had organized a volunteer group of medical practitioners (internal medicinists, psychosomatic medicinst, psychiatrists, gynecologist, dermatologist) and dentists. The purpose of this organization is to clarify the clinical Yusho with medical examinations.

A part of this examination we use to clear the effects of PCBs and Dioxins over exact understanding of second and third generations.

One of these examinations was done 13 not-certified (3 familes) at a hospital in Nagoya city(on December 2015). We had decided clinical Yusho patients who had eaten toxic oil, and have shown difficulties characteristic of Yusho victims.

Subjective symptoms were asked with CMI. Women were examined their uterus and ovary by trans-abdominal ultra-sonograph, If medical records were accessible, we referred to them. For those who were born after the accident, we referred, if possible, their maternity record books. We have also taken 4 case histories of Yusho children who are now over fifties, and asked, if they have, the situation of their children and grandchildren.

Results and Discussions

Results: First we show three girls’ cases(caseA,caseB,caseC) and their descendants. These are members of three families which we examined at Nagoya City. They were relatives by marriage. They came from a village of a remote island of Kyusyu. At that time, they were not given any information, though they had eaten the toxic oil.

CaseA: She ate toxic oil when she was 12 or 13 years old, and at our medical check she was 60 years old. She was suffered from Hashimoto disease, angina pectoris, TIA suspected, hydrocele in thyroid.

She married with a man who had lived in the same village. He was also a Yusho victim who was admitted after 2012. She gave birth two children(case A-1,case A-2).

CaseA-1(the 1st child of caseA) was born in 1991. Her (case A) morning sickness was severe until the 5th months of pregnancy and her body weight was only 1kg increase. Birth weight was 2700g, 37weeks gestation. In his childhood he had often nasal hemorrhage. He had atopic dermatitis till now. He always

complained of severe itching. His symptom has become lighter now. He was nervous, inattentive and easily confused. He was 24 years old at our medical check. He was unmarried.

CaseA-2(the 2nd child of caseA) was born in 1993. He was born premature delivery, 1504 gr, 30 weeks gestation. His difficulties were febrile seizure, footdrop, and easily fall down, nasal hemorrhage. Seven teeth were absent. Lower second molars bilaterally were absent and canine tooth and upper and lower incisors were absent. A milk tooth still remained. He had no sexual interest since the end of teenage.

CaseB: CaseB is a younger sister of caseA. We had examined case B. She had eaten toxic oil in 10 years old. She had married healthy man and gave birth two children. We had not yet examined her children. But we can refer their maternal records. First child was born 1982, 2050 g, 39 gestational weeks, male. He was small for date baby. 2nd child was female born in 1984. Her body weight was 2670g, 37 gestational weeks.

CaseC:She was born in1950. She ate toxic oil in her 17 years old. She had married with healthy man. She gave birth 5 children (one spontaneous abortion). We did medical checks for 4 children. Now she has 4 grand- children. We had examined three of them.

Four children of CaseC(caseC-1female born in 1973,caseC-2 female, born in 1974 ,caseC-3,male,born in1975,caseC-4 male, born in 1975, caseC-5 female, born in1983.) One of her daughter((caseC-2) ground-child of caseC)had no upper molars. She (case 1-2) also had hyperostosis. Two of her children ((caseC-2-1and caseC-2-2,) ground-children of caseC) were male.

CaseC-2-1 19 years old,male. Diseases in childhood: frequent massive nasal hemorrhage, extended penis, obesity, rigid abdomen.

Physical examination: B.P 129/70 mmHg, He feels drowsy on arising in the morning. Pigmentation on neck and axilla. Brownish patch on left cruris. He has some trouble about his sexual behavior; impotence, stiffed penis, and premature ejaculation. Gingivitis upper and lower 3-3.

CaseC-2-2 16 years old, male. Diseases in childhood:frequent massive nasal hemorrhage,short and small penis, obesity, diabetes (since 13 years old treatment with drugs).

Physical examination:B.P116/68 mmHg,near sighted, slightly uninterested,irritable, capricious. diabetes (under medical treatment),small and short penis. gingivitis, dregs. teeth and alignment good.

They have some trouble of genital organ. One of her children((case C-2-3) ground-child of caseC)female)) has delayed eruption of 6th both under molars and right under incisor.

Case D (She had three children, and a grandchild)

She was born in 1949.She ate toxic rice oil 19 years old at the home where she lived as a live-in worker. Her master was a ship-master of fishermen. She prepared meals for all the members of family and employees, almost every day she used to cook tempura (deep-fried fishes and vegetables) and stir-fried vegetables. They all especially liked tempura. She married 23 years old with a 28years old fisherman who also ate toxic oil. In 2007 her blood dioxin concentration was measured, it showed still high, 98.28 pg/g lipid.

CaseD-1 :She had her first child when she was 24 years old(in 1973). The baby had complex anomalies : anal atresia, cleft palate, and cardiovascular anomaly. 4months after he died. His umbilical cord was remained, and the concentration was measured , it was 15.7 pg/g lipid.

CaseD-2 :She had a miscarriage when she was 25 years old(in 1974).

CaseD-3:She had a baby boy when she was 26 years old (1975). His 2nd molars were defective. He had abnormally dark skin. He had had chronic rhinitis since childhood. He had a disease of an autotoxication. He had no appetite. He was an introversive man. He is now forty years old, still unmarried.

CaseD-4: She had a baby girl when she was 28 years old (1977). Her daughter was not yet examined. She(caseD) has now a grandchild, 9 years old boy.

Discussions: We have reported three families (girl's cases (caseA,caseB,caseC) and their descendants). They are sisters (caseA,caseB) and relatives(caseC) by marriage. For our information we have reported caseD and her children.

We have focused their children and ground children.

We have noticed small for date babies, spontaneous abortion and premature birth (30 weeks gestation) long after the Kanemi food poisoning incident (Yusho).

Thukimori(7) et al reported spontaneous abortion and premature delivery caused by the toxic rice oil were observed, in statistically important cases, only after 10 years. But their study was limited to officially admitted Yusho. We found so high the appearance of abnormal eruptions of molars and or incisors in a family. One of them was Case A-2 who was born 30 weeks gestation premature delivery. Molar teeth come from dental lamina which is made 6 weeks viviparity. At birth dental lamina extend towards deep into the backward of chin, and make dental buds. Roots of teeth are made between late viviparity and early days after birth. So it is difficult to decide the origin (prenatal or premature delivery) of the molar

abnormality of Case A-2. Miettinen H.M(8) reported the most critical window of sensitivity for the development of the third molar of dioxin-sensitive line C rats was during the early morphogenesis, from tooth initiation to early bud stage, after which the sensitivity substantially decreased. In human case it is very difficult to decide such critical window of sensitivity. We should be attentive to the influence of dioxins to the fetus.

We had reported CaseD-2 who was born after his brother who had so many anomalies. He (CaseD-2) had second lower molar defects. This shows blood level of dioxins of his mother was less than that of her first and second pregnancy (spontaneous abortion). All other families (3families) we studied reported abnormal eruption of teeth. Of course we should make more study about this point.

Another findings were the anomalies of male genital organ. It is important to study the effects of dioxins to fetal genital organ. To assure ourselves of this we intend to further examinations.

Human body is consisted of many organs. It is not homogeneous liquid. PCBs and PCDFs have strong affinity to adipose tissue. When energy metabolism needs lipolysis, PCBs and PCDFs may dissolve into blood, and change their blood concentration. If she is pregnant the effects over the fetus is serious. And such a condition happens easily when a pregnant woman suffers from emesis. So even long after the accident it is possible to affect fetus. The influences over next generation may be possible.

There had been no official inquiry about the status of Yusho victims. In 2008 an official study of the Yusho victims' status was carried out for the first time by the Ministry of Health, Labor and Welfare of Japan. The inquiries asked about the health and well-being of Yusho victims. The questionnaires were mailed to Yusho victims.

This investigation was limited to officially admitted Yusho victims. 1,131 Yusho victims filled the questionnaire. In 2010 the results (Official Report of Health and Welfare Japan) of study were announced. Comparison of this results with those from comprehensive survey of living conditions of the people on health and welfare showed more than 1.5times predominance of diseases(4) such as manic-depressive psychosis, schizophrenia, hallucination, easily offended, anxiety neurosis, vertigo, acroesthesia of teeth, nasal hemorrhage, autonomic imbalance, orthostatic hypotension, and so on. These are newly recognized disorders. About 40% of Yusho victims complained the influences of toxic Kanemi rice oil on their children and 10% on their grand children.

In 2012 the government decided to admit as a (newly admitted) Yusho victim (at his or her request) with whom a (past admitted) Yusho was living at that time. But those who were born after 1969 from Yusho mothers were not admitted as official Yusho victims. The authorities would not admit the long term effects of the toxicity of Kanemi rice oil to the filial (next) generations.

The influence over next generation is important and a hard fact. We are going to study more cases.

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Reference

- 1) Announcement of Ministry of Health and Welfare, Japan 1969
- 2) Katuki S. Fukuoka Acta Med. (1969) 60, 403-7
- 3) Shimoda M, A Prayer for the Restoration (40 th memorial book of Kanemi (Yusho) accident) in Japanese, (2008) 104-105
- 4) Announcement of Ministry of Health, Labor and Welfare, Japan 2013
- 5) Nagayama J, Masuda Y, Kuratune M. Determination of polychlorinated dibenzofurans in tissues of patient with 'Yushio'. Food Cosmet. Toxicol. 1977; 15, 195-198
- 6) Furue M, Uenotsuchi. The process of determination of new diagnostic criteria for Yusho (in Japanese) Acta Med. 2005; 124-134
- 7) Thukimori K, Morokuma S, Ohtera Y. Obstetrical and Gynecological Abnormalities of Yusho Patients (in Japanese) Yusho Kenkyu #. 2010; 120-129
- 8) Miettinen H.M, Alaluusua S, Tuomisto J, Viluksela, M. Toxicology and Applied Pharmacology, 184, 57-66, 2002