Acta Medica Okayama

Volume 18, *Issue* 1 1964 *Article* 5

FEBRUARY 1964

Leukemia autopsies in Japan

Satimaru Seno, *Okayama University*
Hisashi Monden, *Okayama University*
Takashi Shibata, *Okayama University*
Shuji Seki, *Okayama University*
Hikaru Asakura, *Okayama University*
Hisao Hamada, *Okayama University*
Kenichi Matsuoka, *Okayama University*
Yuki Toyama, *Okayama University*
Takashi Katano, *Okayama University*
Kenji Hayashi, *Okayama University*
Ayako Nakatsuka, *Okayama University*

Leukemia autopsies in Japan*

Satimaru Seno, Hisashi Monden, Takashi Shibata, Shuji Seki, Hikaru Asakura, Hisao Hamada, Kenichi Matsuoka, Yuki Toyama, Takashi Katano, Kenji Hayashi, and Ayako Nakatsuka

Abstract

For the purpose to know whether the annual increase of leukemia incidence in Japan is due to some leukemogenic factors or due to the increased detection rate, the authors made some statistical survey of autopsy cases in which the diagnosis is reliable and not any type of leukemias escape the detection. The results showed that acute leukemias, which are found mostly in younger age, is actually increasing. In addition, it has been deduced that among the suspected factors the increase in ionizing radiation will be one of the most probable factors for the increase in leukemia incidence

*PMID: 14201062 [PubMed - indexed for MEDLINE]

Acta Med. Okayama 18, 45—52 (1964)

LEUKEMIA AUTOPSIES IN JAPAN

Satimaru SENO, Hisashi MONDEN, Takashi SHIBATA,
Shuji SEKI, Hikaru ASAKURA, Hisao HAMADA,
Kenichi MATSUOKA, Yuki TOYAMA, Takashi KATANO,
Kenji HAYASHI and Ayako NAKATSUKA

Department of Pathology, Okayama University Medical School
Okayama, Japan (Director: Prof. S. Seno)

Received for publication, February 15, 1964

The incidence of leukemia is now increasing gradually year by year in several countries of the world as can be seen from the statistical investigations reported[1-5]. This is also the case in Japan[6-14]. This increase may be due to the increased detection rate by the improvement of diagnostic methods and by the development of the social security system, but there seems to be an actual increase in the number of the cases. According to the opinion of DOLL[15], the number of leukemia is increasing also in England and leukemia seems to be actually increasing at least in younger age, though the increase in older age appears to be indirect one, that is, due to the increased detection rate just mentioned. If the leukemia incidence is actually on the increase, it is a very serious social problem and the cause of it must urgently be attacked for finding the way to eradicate the very cause of this disease. In order to eliminate the indirect factors, which may lead to an erroneous judgment of the statistical data, autopsy cases have been observed, because in autopsy leukemias which are difficult to detect clinically can never be missed and the diagnosis is very reliable. From this standpoint, in this paper the observations on the autopsy cases in the past five years are reported for the purpose to get more reliable information whether leukemias have actually increased or not. Observations were also made with respect to sex, age and type of leukemias.

OBSERVATIONS

Prior to the demonstration of the detailed statistical works on autopsy cases it may be worthwhile to introduce briefly the population of Japan, its annual increase in recent years, and mortality rate. The population in Japan was about 91,000,000 in 1957 and it has increased by about 800,000 a year but the number of annual deaths has remained almost unchanged, about 700,000 per year[16]. The incidence of leukemia in 1958 was 2.64 per 100,000 population, which is 1.7 times that in 1951 and this means about 2,400 to 2,500 leukemic

Table 1 Changes in mortality from leukemia and lymphosarcoma for the period of years from 1951 to 1958. Mortality per 100,000 population.

Disease / Year	Leukemia	Lymphsarcoma
1951	1.58	0.52
1952	1.67	0.52
1953	1.90	0.61
1954	2.12	0.72
1955	2.28	0.79
1956	2.47	0.73
1957	2.43	0.81
1958	2.64	0.82
'51/'58	1 : 1.7	1 : 1.6

deaths per year in Japan (Table 1). In the last five years (1957—1961) 2,475 of autopsy leukemias including the leukemic and aleukemic tumors of hematopoietic organs have been reported[17]. Consequently, about 1/7 of the total leukemic deaths has been autopsied and this number will be enough to make some statistical observations.

In autopsy cases, too, both of actual autopsy number and the rate of leukemic numbers to the total autopsies have increased year by year (Table 2). Observations divided into each type of leukemias revealed that the increase is solely in acute leukemias while the other types of leukemia show

Table 2 The number of total and leukemia autopsy cases during the five years from 1957 to 1961.

Year	1957	1958	1959	1960	1961
Leukemia Autopsies (LA)	273	445	510	598	649
Total autopsy number (TA)	6, 391	9, 586	10, 427	11, 113	12, 483
LA/TA (%)	4.3	4.9	4.9	5.4	5.2

almost no increasing tendency both in actual number and in the rate to the total autopsy number (Fig. 1). Among acute leukemias, acute myeloid leukemia has a decidedly high incidence in Japan. Consequently, the increase in acute myeloid leukemia is mainly responsible for the increase of acute leukemias (Fig. 1).

The age distribution shows a higher rate of acute leukemia in younger age as in other countries[18], and acute myeloid leukemia is also high in incidence in younger age (Fig. 2). This signifies that the increase in acute leukemias as a whole is mainly attributable to the increase in leukemia in younger age.

The difference in the incidence as to sex has been observed and the leukemia incidence in male proved to be higher than that in female (Table 3). This coincides with the observations of leukemic deaths in Japan[6] as well as in

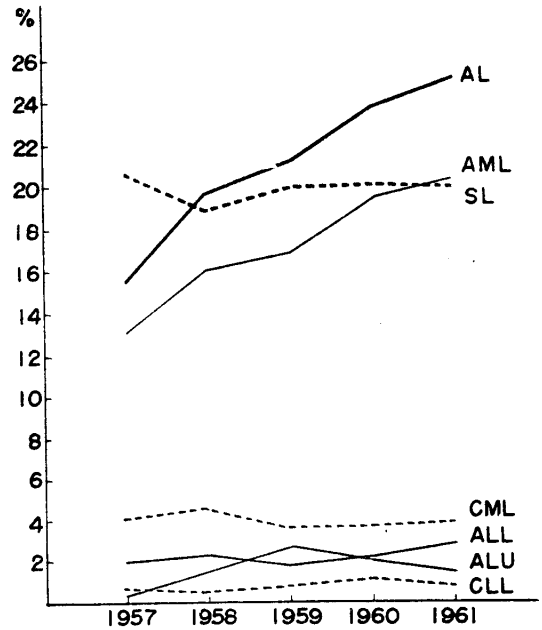

Fig. 1 Yearly change of the rate of autopsy number of leukemia in each type to the total autopsies. AL: Acute leukemia, AML: Acute myeloid leukemia, SL: Specific type of leukemia, ALL: Acute lymphatic leukemia, ALU: Acute leukemia of undifferentiated type, CLL: Chronic lymphatic leukemia, CML: Chronic myelogenous leukemia

Table 3 Autopsy number of leukemia (L), total autopsy number (A) and the ratio L/A in male and female (1957—1961)

Year		1957	1958	1959	1960	1961	Mean
Male	L	187	280	332	397	406	320
	A	4,026	5,771	6.015	6,904	7,694	6,082
	L/A (%)	4.6	4.9	5.5	5.8	5.3	5.3
Female	L	86	165	178	201	239	174
	A	2,365	3,329	3,785	3,987	4,588	3,610
	L/A (%)	3.6	5.0	4.7	5.0	5.2	4.8

other countries[19]. Further observations in detail by dividing into each leukemic type has revealed that acute myeloid leukemia is not concerned with the difference in sex. The main difference has been recognized in leukemia of specific type which is mainly composed of the leukemic and aleukemic tumors of hema-

topoietic organs, e. g. lymphosarcoma, reticulosarcoma, chloroma, myeloma, etc. (Table 4). These are rather low in incidence in younger age, and they

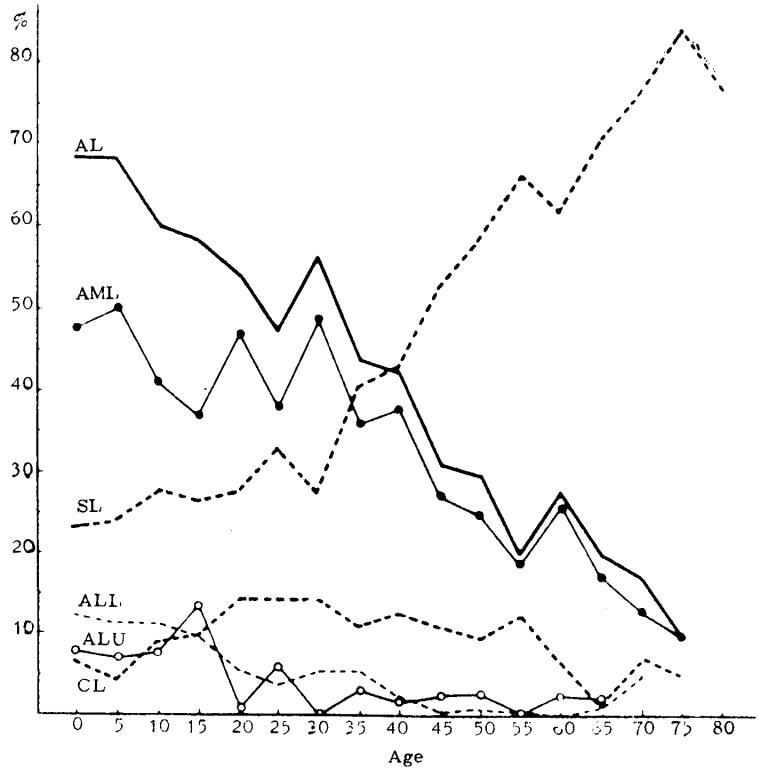

Fig. 2 Age distribution of acute, chronic and specific type of leukemias autopsied during five years (1957—1961). Each curve shows the percentage of the number of leukemia to the total number of leukemia autopsies in the corresponding age. For AL, AML, SL, ALL, ALU, and CL see Fig. 1.

Table 4 Incidence of each type of leukemia in male and female (1957—1961)

Sex \ Type		AL	AML	AFL	ALU	CL	CML	CLL	MoL	SL
Male	No.	197	159	28	10	38	32	6	11	164
	R (%)	0.65	0.52	0.09	0.03	0.12	0.10	0.02	0.04	0.54
Female	No.	119	94	11	11	25	20	5	8	90
	R (%)	0.64	0.52	0.06	0.06	0.14	0.11	0.03	0.04	0.49

		SL R	L	C	M	O
Male	No.	373	152	28	110	46
	R (%)	1.23	0.50	0.08	0.36	0.15
Female	No.	198	48	9	52	21
	R (%)	1.09	0.26	0.23	0.28	0.12

increase with advance in age (Fig. 2). Thus, it can be said that there is hardly any difference in the incidence of acute leukemia between male and female at least in the autopsy cases observed.

COMMENT

As just demonstrated the observations on the autopsy cases showed that the autopsy number of leukemic deaths is increasing year by year[20]. This coincides with the annual increase of leukemic incidence as observed in leukemic deaths in 100,000 population[6]. And yet the observations on the autopsy cases give a reliable information for the actual increment of leukemia. Data show that leukemia is increasing certainly by some unknown factor or factors. In contrast to observation in U. S. A.[1,2] where the leukemia in older age is increasing, the leukemia that is on the increase in Japan is acute leukemia in younger age both in male and female. In England the incidence of acute leukemia is increasing, though in adult age[3]. As the acute myeloid leukemia is extremely high in incidence among acute leukemias in Japan, the annual increase is mainly attributable to the increase in this type of leukemia in younger age. In the observations of autopsy cases the increased incidence of leukemia by the increased detection rate cannot be accounted as the factor misleading to an erroneous judgment is minimized. Nor is there any possibility that leukemias are antopsied in an especially higher rate in recent years than in the other diseases. Besides this, the decrease in deaths from other diseases that had been formerly the highest causative factors for death like tuberculosis and other infectious diseases, may be an indirect factor responsible for the increase in leukemic deaths as in other malignant neoplasms. This will be true in the death of adult to older age, but in younger age the situation is completely different from leukemia in those of older age, because the probability of suffering from leukemia in those who survived through the diseases will be less.

Therefore, it is reasonable to deduce that the leukemia incidence in children is actually increasing. Consequently, the annual increase of leukemia in Japan

will be an actual increase by unknown causative factors.

Among suspected factors leukemogenic virus may possibly be included. In some cases of animal leukemias, viruses are concerned but in human leukemia there seems to be no definitive evidence of virus involvement though some authors claim virus to be a causative factor[21, 22]. Besides virus, the ionizing radiation is concerned with the onset of leukemia in animal and it is also incriminated in human leukemia. A high incidence of leukemia among those handling X-rays suggests[23] that ionizing radiation should be an important factor for the induction of human leukemia. The higher incidence of leukemia among those exposed to the atomic bombs in Hiroshima and Nagasaki and the highest rate of acute myeloid leukemia also support this view[24–28]. The ionizing radiation in atmosphere will probably be increasing by repeated fission explosions.

Observations conducted on the incidence of leukemias by dividing the periods into the ones before and after the fission explosions may contribute to clarify whether or not the ionizing radiation would be a prbable cause, if the factors responsible for the increase of the detection rate are taken into consideration. The curve of leukemia incidence in Japan shows an incessant increase of the incidence but it shows a refraction at the Second World War into the age of nuclear fission[6]. In the former the increasing tendency was slow and gradual but in the latter it has been rather steep in the increasing curve. In the period before the War and the gradual improvement in the diagnostic method might have been concerned with the increase. But after the War the social security system has been set up widely, especially in the last several years, so that the increasing rate of detection of leukemias will not appreciably affect the statistical data. In spite of this the leukemia incidence has increased from about 2,200 cases to 2,700 in these five years. This means that an increase of 24.5 to 28.5 per 100,000 population. Indeed, the incidence of leukemias in Japan in 1957 was about 2.5 times that in 1947. During the same decade there was an increase of the leukemia incidence of about 1.6 times in the U. S. A. and Canada, and about 1.4 times in England and Denmark[6]. These data amply disclose how great is the increase in the incidenee of leukemias in Japan. All of these data together with those obtained from the observations on autopsied leukemias suggest that the increase in ionizing radiation in atmosphere is the most probable factor responsible for the rapid increase of leukemia incidence in recent years in Japan. This coincides with the view of CURT-BROWN and DOLL[3].

SUMMARY

For the purpose to know whether the annual increase of leukemia incidence

in Japan is due to some leukemogenic factors or due to the increased detection rate, the authors made some statistical survey of autopsy cases in which the diagnosis is reliable and not any type of leukemias escape the detection. The results showed that acute leukemias, which are found mostly in younger age, is actually increasing. In addition, it has been deduced that among the suspected factors the increase in ionizing radiation will be one of the most probable factors for the increase in leukemia incidence.

ACKNOWLEDGEMENT

We gratefully acknowledge the kind cooperation of staffs of pathological laboratories of universities and colleges by supplying us with the necessary data for the completion of this report.

REFERENCES

1. COOKE, J. V.: The occurrence of leukemia. *Blood* 9, 340, 1954
2. GUNZ, F. W. and HOUGH, R. F.: Acute leukemia over the age of fifty, A study of its incidence and natural history. *Blood* 11, 882, 1956
3. CURT BROWN, W. M. and DOLL, R.: Adult leukemia. Trend in mortality in relation to aetiology. *Brit. med. J.* 1, 1063, 1959
4. TING, N. and HWANG, T.: Leukemias in Chinese armed forces. Incidence and clinico-pathological study. *Acta Haem. Jap.* 21 (2) Suppl. 311, 1958
5. SACKS, M. S. and SEEMAN, I.: A statistical study of mortality from leukemia. *Blood* 2, 1, 1947
6. WAKISAKA, G.: Leukemia, a statistical investigation. Nippon Ketsuekigaku Zensho (Handbook of Hematology in Japanese) 5, 596, 1962
7. TAKEDA, K.: Geographical pathology of leukemia in Japan. *Acta* 16, 1629, 1960
8. WAKISAKA, G.: Clinical and statistical research of leukemia in Japan, especially in the Kinki district. *Acta Haem. Jap.* 21, (2) Supple. 240, 1958
9. SHIRAISHI, T.: Clinical and statistical research of leukemia in Hokkaido over the 7 year period 1931-1957, Ibid. 21 (2) Supple. 259, 1958
10. NAKAJIMA, A.: Statistical and clinical studies on leukemia of Kanto area, especially around Tokyo. Ibid. 269, 1958
11. OTA, K.: Clinical and statisticaI studies of leukemia in the Tokai district. Ibid. 279, 1958
12. HIRAKI, K.: Clinical and statistical research of leukemia occurring in Chugoku-Shikoku district of Japan. Ibid. 286, 1958
14. WAKISAKA, G., UCHINO, H., YASUNAGA, K., NAKAMURA, T., SAKURAI, M., MIYAMOTO, K., YOSHINO, T and MORIGA, M.: Statistical investigations of leukemia in Japan, *Acta Haemat.* in press
15. DOLL, R.: Paper read at VII International Congress for Geographical Pathology, 1963. Acta hemat, in press
16. Kôseinô Shihyo (Statistics of Public Health) Special issue in 1962 (in Japanese)
17. Annual of the Pathological Autopsy Cases in Japan, Ed. Japan. Soc. Pathol. Tokyo 1958—1962
18. WINTROBE, M. M.: Clinical Hematology, Lea and Febiger, Philadelphia, 1962
19. GILLIAN, A. G.: Age, sex and race selection at death from leukemia and the lymphomas. *Blood* 8, 693, 1953
20. SENO, S.: Statistical investigations of leukemia autopsies in Japan. *Acta Haemat*, in

press

21. DMOCHOWSKI, L.: Studies on submicroscopic structure of known or suspected origin, a review. *Blood* 13, 1017, 1958
22. BRAUNSTEINER, H. and PAKESCH, F.: Electron microscopic observations on leukemic cells, *Acta haemat.* 24, 64, 1960
23. WAKISAKA, G.: The effect of radiation on hematopoietic tissues with special reference to leukemia induced by radiation. *Hiroshima Igaku* 14, 916, 1961 (in Japanese)
24. BRILL, A. B., TOMONAGA, M., and HEYSSL, R. M.: Leukemia in man following exposure to ionizing radiation, a summary of findings in Hiroshima and Nagasaki and a comparison with other human experience. *Annals Intern. Med.* 56, 590, 1962
25. WATANABE, S.: On the incidence of leukemias in Hiroshimas during the past fifteen years from 1946—1960, *J. Rad. Res.* 2, 131, 1961
26. WATANABE, S., Ito, I., and MATSUBAYASHI, Y.: Statistical observations on leukemias in Hiroshima during the past fourteen years (1946—1959)
27. TOMONAGA, M.: Leukemia in Nagasaki atomic bomb survivors from 1945 through 1959. *Bull. Org. mond. Sante*, Bull. Wld. Hlth. Org. 26, 619, 1962
28. WATANABE, S., HIROSE, F., and MATSUBAYASHI, Y.: The incidence of leukemia in Hiroshima during the years from 1946 to 1960, Proc. 2nd Cong. Asia and Pacific Soc. Hematol. 81, 1962