Leukemia autopsies in Japan

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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.
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\textsuperscript{1-5}. This is also the case in Japan\textsuperscript{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\textsuperscript{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\textsuperscript{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.

<table>
<thead>
<tr>
<th>Year</th>
<th>Leukemia</th>
<th>Lymphosarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>1951</td>
<td>1.58</td>
<td>0.52</td>
</tr>
<tr>
<td>1952</td>
<td>1.67</td>
<td>0.52</td>
</tr>
<tr>
<td>1953</td>
<td>1.90</td>
<td>0.61</td>
</tr>
<tr>
<td>1954</td>
<td>2.12</td>
<td>0.72</td>
</tr>
<tr>
<td>1955</td>
<td>2.28</td>
<td>0.79</td>
</tr>
<tr>
<td>1956</td>
<td>2.47</td>
<td>0.73</td>
</tr>
<tr>
<td>1957</td>
<td>2.43</td>
<td>0.81</td>
</tr>
<tr>
<td>1958</td>
<td>2.64</td>
<td>0.82</td>
</tr>
</tbody>
</table>

\[ \frac{51/58}{1: 1.7} \quad 1: 1.6 \]

In the last five years (1957—1961) 2,475 of autopsy leukemias including the leukemic and aleukemic tumors of hematopoietic organs have been reported. 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 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, 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 as well as in Japan.

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

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

<table>
<thead>
<tr>
<th>Year</th>
<th>1957</th>
<th>1958</th>
<th>1959</th>
<th>1960</th>
<th>1961</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>187</td>
<td>280</td>
<td>332</td>
<td>397</td>
<td>406</td>
<td>320</td>
</tr>
<tr>
<td>A</td>
<td>4,026</td>
<td>5,771</td>
<td>6,015</td>
<td>6,904</td>
<td>7,694</td>
<td>6,082</td>
</tr>
<tr>
<td>L/A (%)</td>
<td>4.6</td>
<td>4.9</td>
<td>5.5</td>
<td>5.8</td>
<td>5.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>86</td>
<td>165</td>
<td>178</td>
<td>201</td>
<td>239</td>
<td>174</td>
</tr>
<tr>
<td>A</td>
<td>2,365</td>
<td>3,329</td>
<td>3,785</td>
<td>3,987</td>
<td>4,588</td>
<td>3,610</td>
</tr>
<tr>
<td>L/A (%)</td>
<td>3.6</td>
<td>5.0</td>
<td>4.7</td>
<td>5.0</td>
<td>5.2</td>
<td>4.8</td>
</tr>
</tbody>
</table>

other countries. 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

![Graph showing 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)

<table>
<thead>
<tr>
<th>Type</th>
<th>AL</th>
<th>AML</th>
<th>AML</th>
<th>ALU</th>
<th>CL</th>
<th>CML</th>
<th>CLL</th>
<th>MoL</th>
<th>SL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>No.</td>
<td>R (%)</td>
<td>No.</td>
<td>R (%)</td>
<td>No.</td>
<td>R (%)</td>
<td>No.</td>
<td>R (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>197</td>
<td>0.65</td>
<td>159</td>
<td>0.52</td>
<td>28</td>
<td>0.09</td>
<td>10</td>
<td>0.03</td>
<td>38</td>
</tr>
<tr>
<td>Female</td>
<td>119</td>
<td>0.64</td>
<td>94</td>
<td>0.52</td>
<td>11</td>
<td>0.06</td>
<td>11</td>
<td>0.06</td>
<td>25</td>
</tr>
</tbody>
</table>
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. This coincides with the annual increase of leukemic incidence as observed in leukemic deaths in 100,000 population. 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. 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. 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 autopsied 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. 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 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. 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 probable 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. 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. These data amply disclose how great is the increase in incidence 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.

SUMMARY

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

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