Statistical Study on Malignant Melanoma in Japan (1970-1976)

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OHSUMI, T. and SEIJI, M. *Statistical Study on Malignant Melanoma in Japan (1970-1976)*. Tohoku J. exp. Med., 1977, 121 (4), 355-364 — The authors reported in 1972 a statistical study based on 501 cases of malignant melanoma. As continuous study this review was carried out on 456 cases of melanoma which were reported during six years between 1970 and 1976. These two studies showed quite similar results as follows: (1) Yearly incidence of malignant melanoma indicated a definite upward trend and the average number of patients was 71.1 per year. (2) Distribution by age showed one peak in the seventh decade. (3) Sex ratio was 1.1: 1. (4) The number of cases per total population in Japan showed great increase in over fifth decades and two peaks in the 7th and 8th decades. (5) Average age of the onset of all melanoma was 51.6 years old, while, that of brain and spinal cord melanoma was 25.4 years old. In the skin melanoma with preexisting pigmented skin lesions, the median age of the onset of primary melanoma on the foot was 38.7 years old and that of originated melanoma except foot was 65.9 years old. (6) Incidence of the melanoma was high in the sole considering the number of melanocytes per unit skin area. (7) Metastasis of eye melanoma was low (23%). ——— melanoma

In 1972, the authors reported on "Statistical Study on Malignant Melanoma in Japan (1961-1970)". As continuous study this statistical study on 456 cases of malignant melanoma reported in Japan during the last 6 years from 1970 to 1976 was carried out. The incidence of malignant melanoma among Japanese has been thought to be significantly low as compared with that of Caucasians. It was reported that the racial ratio between Caucasians and other races was 250:1. In our country, however, the incidence of malignant melanoma indicates a definite upward trend in recent years. There is no difference in the number of melanocytes per unit area of the particular skin area among white and black races, but the amount of melanin produced differs in races. Pigment cells from which malignant melanoma derives are seen in skin or mucous basal cell layer, dermis, hair follicles, meninges encephali or chorioides. There seemed to be a parallel relationship between the incidence of melanoma and the number of melanocytes in the particular skin area except on the sole where an incidence of melanoma was exceptionally high on the bases of the number of melanocytes per unit skin area.

Malignant melanoma has been classified in many ways according to their

clinical and/or pathological characteristics. Recently, however, it was classified into the following major three groups by Mihm et al. (1971); (1) lentigo maligna type, (2) superficial spreading type, (3) nodular type, and (4) undeterminate type. All forms differ in their mode of onset, course and prognosis, and each has distinctive clinical and histopathological appearances. So, statistical studies on each individual type of malignant melanoma will be carried out in future according to this classification.

MATERIALS

As a follow-up study, the statistical work was carried out on all cases of malignant melanoma reported in the *Japan Centra Revuo Medicina*, which is a journal abstract covering almost all medical journals published in Japan. This particular statistical review was made of each original journal, quoted *Japan Centra Revuo Medicina* from March 1970 through July 1976, between volumes 255 and 322. All of 456 cases seemed to have occurred in Japanese because of no case of foreigner. Occasionally a particular case was reported independently in the different journals and in this study such overlapped cases were seen over 110 cases. In order to carry out the more precise study we tried as much as possible to eliminate these overlapped cases by checking up the individual original journals in which the cases were reported.

RESULTS AND DISCUSSION

Numbers of malignant melanoma between 1961 and 1976

The histogram (Fig. 1) shows the yearly incidence of melanoma between 1961 and 1976. White columns indicate the number of melanoma collected in the previous report (Seiji and Ohsumi 1972) and zebra columns the number of this report. In the previous statistics, the yearly incidence of melanoma revealed a definite upward trend every year up to 1967. However, as Fig. 1 shows, there was one peak in 1967, and after 1969 it was within a limited range. The abnormal

Fig. 1. Yearly incidence of malignant melanoma. 1961 Mar.~ 1976 July.

upward trend seen between 1965 and 1967 may indicate that a great interest was focused on malignant melanoma in these years because the new, stimulative clinico-pathological studies were being carried out on malignant melanoma during those years in the U.S.A. and Australia. After 1975 there seems to show a slight upward trend ranging between 70 and 90 cases per year. This review study deals only with the reported cases in *Japan Centra Revuo Medicina* so that the cases were recorded on the reported year, but in order to analyze the yearly incidence it would be much better to count the year of an onset of the melanoma instead of recording the year when the cases were reported. Unfortunately it was almost impossible to do so because of the nature of this kind of journal.

Age and sex distribution

Fig. 2 gives the sex and age distribution of 456 cases. White columns indicate the numbers of male and zebra ones those of female. In the previous report there were two peaks in the fifth and seventh decades in male and one peak in the seventh decade in female. However, this figure shows only one peak in the seventh decade in both male and female.

Fig. 3 presents a comparison of the incidence of malignant melanoma by sex in three statistical studies which reported by Yoshida in 1955, Kukita et al. in 1961 and Seiji and Ohsumi in 1972 and the present study. The sex ratio of our 957 cases was 1.1:1 and the ratio of four reports was 1.27:1. The incidence of melanoma seems to be slightly higher in the male group than in the female. The sex ratio of obduction in Japan is reported to be 10: 7, and it may be concluded that the mortality of female is low or the number of female obduction small. The average incidence per year shows a great increase in the latest group among these four generations and the latest average per year of 456 cases shows 71.1 cases per year.

Fig. 2. Distribution of 456 cases of malignant melanoma according to age and sex. 1970 Mar.~ 1976 July.

Fig. 3. Comparison of the incidence of malignant melanoma by sex among the four statistical studies.

Table 1 presents a relationship between the age distribution of malignant melanoma and of population and shows a relationship between the incidence of melanoma by age per ten thousand of population in Japan in 1971. And this table indicates a great increase over the fifth decade and there appears to be two peaks in the seventh and eighth decades.

Location

Table 2 elucidates the locations of the primary lesion by sex during 1961 March and 1976 July and Table 3, during 1970 March and 1976 July. There are a few differences in these two tables. In the sex ratio, genital organ and anorectum are

TABLE 1. Relationship between the age distribution of malignant

	0-9	10-19	20-29
(1) Number of malignant melanomas	10	10	27
(2) Number of malignant melanomas per year	1.77	1.77	4.77
(3) Japanese population in 1971*	174×10^5	164	198
(4) $\frac{\text{Malignant melanomas}}{100,000} = \frac{(2)}{(3)} \times 10^5$	0.010	0.011	0.024

* *Kosei no Shihyo* (Jap.), edited by Kishi, T., Kosei Tokei Kyokai, Tokyo, 1968-1975,

TABLE 2. Incidence in location of the primary lesions and the sex ratio (1961 Mar.~ 1976 Jul.)

Location	Number of patients	%	Male	Female	Unknown
Skin	313	32.7	171	122	20
scalp, face or neck	49	5.1	22	24	3
trunk	68	7.1	40	22	6
upper extremity	43	4.5	20	23	—
lower extremity	147	15.4	84	52	11
unknown	6	0.6	5	1	—
Mucosa	259	27.1	95	114	50
nose	84	8.8	38	30	16
mouth	134	14.0	48	53	33
pharynx	4	0.4	1	2	1
genital organ	37	3.9	8	29	—
Others	332	34.7	154	132	46
brain or spinal cord	58	6.1	30	15	13
eye	205	21.4	94	78	33
gastrointestinal tract	65	6.8	27	38	—
lung	4	0.4	3	1	—
Unknown	53	5.5	21	14	18
Total	957	100.0	441	382	134

more frequent sites in female than male; on the other hand, trunk and lower extremity in male. According to the statistical study on obduction in the last 10 years (Mori 1971), the most frequent site of involvement was skin and the least was eye. This low incidence of the eye melanoma mortality may be due to the following reasons; usually they will be found in the early stage and treated immediately, in most cases radically such as extraction of the eye bulb. Among the eye melanoma, chorioides is the most common site of involvement, that is, 107 out of 205 cases reported during 1961 March and 1976 July. Shinbo et al. (1970) reported that 80% of the primary melanomas of eye were chorioides melanomas.

Nasal and oral malignant melanoma is one of the most common melanomas in Japan. As has been pointed out by Shimizu et al. (1972), the initial symptom of nasal melanoma may be epistaxis or nasal obstruction, and nasal melanomas have often been reported too. Among oral melanoma, palate melanoma was 20 cases

melanoma and of population (1970 Mar.~ 1976 Jul.).

Age						Total
30-39	40-49	50-59	60-69	70-79	80-	
45	73	87	92	48	10	402
8.00	12.9	15.4	16.3	8.49	1.77	71.1
169	137	94	69	36	10	1050 × 10 ⁵
0.047	0.094	0.16	0.24	0.24	0.18	0.0677

TABLE 3. *Incidence in location of the primary lesions and the sex ratio (1970 Mar.~ 1976 Jul.)*

Location	Number	%	Male	Female	?	Average of age	Number
Skin	170	37.3	95	64	11	49.8	154
scalp, face or neck	20	4.4	12	8	—	39.1	20
trunk	37	8.1	20	13	4	39.8	33
upper extremity	24	5.3	10	14	—	49.9	22
lower extremity	83	18.2	48	28	7	56.8	78
unknown	6	1.3	5	1	—	41.	1
Mucosa	124	27.2	45	62	17	56.5	108
nose	47	10.3	19	18	10	56.0	38
mouth	49	10.8	19	23	7	58.6	42
pharynx	2	0.4	1	1	—	60.0	2
genital organ	26	5.7	6	20	—	53.7	26
Others	146	32.0	66	63	16	50.2	130
brain or spinal cord	21	4.6	12	4	5	25.4	17
eye	85	18.6	33	40	12	50.5	73
gastrointestinal tract	37	8.1	18	19	—	60.2	37
lung	3	0.7	3	—	—	62.3	3
Unknown	16	3.5	6	4	6	44.7	10
Total	456	100.0	212	193	51	51.62	402

out of 49 cases and gingiva or alveolar 19 cases. As Chaudhry et al. (1958) pointed out, frequent sites were hard palate, gingiva and soft palate and lower jaw was uncommon site. Oral melanoma with preexisting pigmentation was seen frequently. Out of 94 cases, Takagi et al. (1972) reported 34 cases of oral melanoma with preexisting pigmentation and secondary pigmentation was observed in 28 cases. Table 2 presents the average age of 402 cases.

In the previous report, the incidences of brain and spinal cord melanoma by age showed a peak in the third decade. In this paper, 21 cases (male 12, female 4, unknown 5) were described and the median age was 25.4 years old and the age distribution was as follows:

Age	0-9	10-19	20-29	30-39	40-49	50-59	60-	Unknown	Total
Number	4	1	6	3	—	3	—	4	21

Gibson et al. (1957) reported that the 4th decade was most frequent in the Western countries. Takeda et al. (1974) reported that the diffuse black pigmentation was seen in meninges encephali in 42 out of 43 cases in Japan, and in 14 cases among them a deposit was observed in hemisphaerium.

The average age of trunk and face melanomas was 39.5 years old and this was low next to that of brain and spinal cord melanomas.

Table 4 shows the locations of the primary lesions of the lower extremity. The most frequent site of involvement was sole.

The relationship between the onset of melanoma and the distribution of melanocytes in the skin of the different parts of the body is shown in Table 5. As

TABLE 4. *Incidence in location of the primary lesions of lower extremity (1961 Mar.~ 1976 Jul.)*

Location	Number	%	Male	Female	Unknown
Thigh	16(7)	10.9	7	6	3
Knee	5(2)	3.4	1	3	1
Leg	17(11)	11.5	10	7	—
Back of foot	6(5)	4.1	4	2	—
Toe	27(15)	18.4	16	7	4
Sole	75(43)	51.0	46	26	3
Unknown	1(—)	0.7	—	1	—
Total	147(83)	100.0	84	52	11

() ; 1970 Mar.-1976 Jul.

TABLE 5. *Relationship between the site distribution of malignant melanoma and the number of melanocytes per unit skin area in patients over 15 years old (1961 Mar.~ 1976 Jul.)*

Site	(1) Number of patients	(2) Percentage of (1)	(3) Proportion of skin area in different parts of the body	(2)/(3)	Number of melanocytes per mm ²
Scalp, face & neck	48(19)	16.4%	10.0%	1.64	1400-1930
Arm	12(5)	4.1	14.3	0.29	1160
Hand	27(16)	9.3	5.1	1.81	1120
Trunk	57(29)	19.5	23.7	0.82	890
Genital organ (♂)	7(5)	2.4	0.5	4.79	2100-2380
Thigh, knee & leg	36(17)	12.3	39.6	0.32	1130
Foot (except sole)	33(20)	11.3	4.0	2.83	1420-2840
Sole	72(40)	24.7	2.8	8.81	1680
Total	292(151)	100.0%	100.0%		

() ; 1970 Mar.-1976 Jul.

has been reported, melanoma occurred predominantly on the sole. It was reported that 86% of the skin melanomas were found on lower limbs in the East and Central Africa and almost of these were seen on the sole and 30% of the skin melanomas occurred on lower limbs among Caucasians. While the incidence of melanoma of lower extremity in Japanese was 45% among 313 cases of skin melanoma and 51% of the disease on lower extremity were seen in sole; therefore, the type of melanoma in Japanese may be different from that in African's.

Metastasis

Table 6 gives the incidence of metastasis of malignant melanoma by sex and age, and Table 7 gives the frequency of metastasis by site primarily affected during 1961 March and 1976 July. Age distribution pattern was similar to that of the previous report. The site distribution pattern also showed similar tendency, and a high incidence (over 60%) of metastasis was recognized in the melanomas affected primarily on the trunk, lower limbs and gastrointestinal tract, while the lower frequency of metastasis was observed in cases of eye melanoma (23%) (Table 7).

TABLE 6. *Incidence of metastasis of malignant melanoma*

Sex		0-9	10-19	20-29	30-39
Male	metastasis (+)	2	4	6	14
	meta. (-) or (?)	2	3	12	9
Female	metastasis (+)	3	1	4	11
	meta. (-) or (?)	2	1	5	11
Unknown	metastasis (+)	1	—	—	—
	meta. (-) or (?)	—	1	—	—
Total	metastasis (+)	6	5	10	25
	meta. (-) or (?)	4	5	17	20
Total		10	10	27	45

TABLE 7. *Incidence of metastasis of malignant melanoma by site primarily affected (1961 Mar.~ 1976 Jul.)*

Location	Metastasis (+)	Meta. (-), (?)	Total
	Number (%)		
Skin	184(59)	129	313
scalp, face or neck	24(49)	25	49
trunk	45(66)	23	68
upper extremity	25(58)	18	43
lower extremity	84(57)	63	147
unknown	6(100)	—	6
Mucosa	121(47)	138	259
nose	42(50)	42	84
mouth	62(46)	72	134
pharynx	1(25)	3	4
genital organ	16(43)	21	37
Others	112(34)	220	332
brain or spinal cord	16(28)	42	58
eye	48(23)	157	205
gastrointestinal tract	45(69)	20	65
lung	3(75)	1	4
Unknown	33(62)	20	53
Total	450(47.0)	507	957

This might be due to the fact that the radical treatment, mostly eye extraction, was performed in the early stage. The average period between the eye extraction and the metastasis was reported to be 46 months.

Age distribution of skin malignant melanoma with preexisting pigmented skin lesions

Table 8 shows the age distribution of 154 cases of skin malignant melanoma with and without preexisting pigmented skin lesions. The average age of foot melanoma with preexisting pigmented skin lesions was 65.9 years old, which was considered to be significantly higher compared with the median age of 402 cases of

by sex and age (1970 Mar.~ 1976 Jul.)

Age							Total
40-49	50-59	60-69	70-79	80-89	90-99	Unknown	
20	22	31	13	1	—	4	117
11	25	20	8	2	2	1	95
17	19	24	14	—	1	1	95
23	21	17	13	4	—	1	98
2	—	—	—	—	—	11	14
—	—	—	—	—	—	36	37
39	41	55	27	1	1	16	226(49.6%)
34	46	37	21	6	2	38	230(50.4%)
73	87	92	48	7	3	54	456

TABLE 8. Age distribution of skin malignant melanoma with preexisting pigmented skin lesions (1970 Mar.~ 1976 Jul.)

	Age										Total
	0-	10-	20-	30-	40-	50-	60-	70-	80-	90-	
1. Scalp, face & neck	—	3	1	1	2	1	—	1	—	1	10
2. Arm	—	—	—	1	1	—	—	—	—	—	2
3. Hand	—	—	—	1	1	1	2	—	—	—	5
4. Trunk	2	2	2	7	4	2	3	—	—	—	22
5. Thigh, knee & leg	1	1	1	1	1	1	—	—	—	—	6
6. Foot	—	—	—	—	1	1	3	3	—	1	9
7. Total (except foot)	3	6	4	11	9	5	5	1	—	1	45
8. Total	3	6	4	11	10	6	8	4	—	2	54

Age average			Preexisting pigmented skin lesions		
Pigmented skin lesion		Total		Skin malignant melanoma	Skin malignant melanoma except foot
(+)	(-)				
1. 41.0			Nevus pigmentosus	14	13
2. 40.0			Compound nevus	3	3
3. 53.8			Blue nevus	1	1
4. 36.7			Pigment fleck	20	13
5. 28.8			Lentigo	16	15
6. 65.9	59.1	60.1			
7. 38.7	57.0	43.4			
8. 43.2	53.4	49.8	Total	54	45
(54 cases)	(100 cases)	(154 cases)			

all melanoma collected. However, that of skin melanoma with preexisting pigmented skin lesions except foot was 38.7 years old. In other words, among the skin melanoma with preexisting pigmented skin lesions, the foot melanoma was more severe in older age; on the other hand, the skin melanoma except foot appeared in much younger generation. The designations of the pigmented skin

lesions were exactly listed up in Table 8 as they were described in the original reports. Most of these pigmented skin lesions were reported to have existed for more than five years.

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