

Mental health among young adult survivors of childhood cancer and their siblings including posttraumatic growth

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Abstract

Background Few studies have addressed the mental health status of young adult childhood cancer survivors (CCSs) and their siblings (SIBs). This paper focuses on depression, anxiety, posttraumatic stress symptoms (PTSS), and posttraumatic growth (PTG) among Japanese CCSs and their SIBs.

Methods Adolescent and young adult CCSs ($n=185$), in remission for more than 1 year, their SIBs ($n=72$), and general controls (CONTs) ($n=1,000$) completed anonymous self-report questionnaires for depression, anxiety, PTSS, and PTG. The physicians in charge also completed an anonymous disease/treatment data sheet.

Results CCSs were approximately 8 years old at diagnosis and approximately 23 years old at the time of the survey. Their diagnoses included leukemia (57%), lymphoma (12%), and solid tumors (30%). Thirty-eight percent underwent surgery and 25% received stem cell transplantation. No significant differences were found between CCSs and CONTs in terms of depression and anxiety. CCSs had significantly more PTSS and had remarkably greater PTG compared to CONTs. Although no significant differences were found between SIBs and CONTs regarding depression, anxiety, or PTSS, female SIBs exhibited greater PTG compared to female CONTs. **Conclusion** To empower CCSs, they should be evaluated periodically regarding PTSS and PTG and should be provided

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appropriate care and feedback. The fact that the mental health status of young adult SIBs was similar to CONTs at 15 years after their siblings' diagnoses may help reassure parents who worry about mental health among the siblings of an affected child during and after his/her treatment.

Keywords Childhood cancer · Mental health · Posttraumatic growth · Survivor

Introduction

Childhood cancer that was uniformly fatal 40 years ago can now be cured with an overall success rate approaching 80% [1]. As the number of childhood cancer survivors has risen dramatically, health and quality of life of long-term survivors following successful treatment has become a significant clinical concern. The clinical goal is to achieve successful treatment with fewer late effects along with the establishment of a risk-based follow-up system after treatment [2]. The Childhood Cancer Survivor Study (CCSS), a large scale study conducted in North America that includes approximately 20,000 childhood cancer survivors diagnosed between 1970 and 1986 and about 5,000 siblings of the survivors, has recently published its findings as a review series in the May 2009 issue of the *Journal of Clinical Oncology* [3]. In addition to the CCSS in North America, a large cohort study has been conducted in the UK [4].

Unlike the UK, where children with cancer are treated in large-scale childhood cancer centers, almost all children with cancer in Japan are treated at regional hospitals [5]. Moreover, few pediatricians in Japan had discussed the prognosis with the child due to the unwillingness of the parents to reveal the truth to the child [6, 7]. For these reasons, it has been difficult to perform long-term follow-up of childhood cancer survivors in Japan. In recent years, pediatricians have adopted a more positive attitude towards revealing the truth to children with cancer regarding their prognosis, and there has been an increased focus on the importance of long-term follow-up of childhood cancer survivors (CCSs) in Japan [8].

Two study groups, comprising a large number of pediatricians from many hospitals, have collaborated for the first time in a cross-sectional research to study the physical health status and quality of life among CCSs in Japan. Ishida et al. [9] reported the details of the research protocol, which was developed with reference to the CCSS in North America [10] and the UK [4]. Although mental health status was studied in two previous CCSS [11, 12], neither posttraumatic stress symptoms (PTSS) nor posttraumatic growth (PTG) were the focus of these studies. In this study, we investigate depression and anxiety as well as PTSS as potential late effects on mental health [13]. We

also investigate PTG as another reaction to the stresses of survivorship based on the description of Barakat et al. [14]. Eligible participants in our study included CCSs and their siblings (SIBs).

The purpose of this paper, therefore, is to describe the status of depression, anxiety, PTSS, and PTG among CCSs and SIBs.

Methods

Participants

Participants were recruited by their physicians from participating hospitals that agreed with the purpose of the present study. Inclusion criteria were as follows: (1) 16 years of age or older at the time of the survey; (2) survival of more than 5 years after cancer diagnosis and continued remission lasting more than 1 year without any anticancer therapy; (3) knowledge (of both CCS and SIB) of the true cancer prognosis; (4) guardian (parent) provided informed consent for participation in the study; and (5) CCS and SIB provided informed consent for participation in the study.

Patients were excluded if (1) the attending physician felt that the study might affect the patient adversely; (2) the patient had health problem(s) that did not originate in childhood cancer and it was obvious that these health problem(s) interfered significantly with everyday activities and social life; or (3) it was considered too difficult for the patient to complete the self-report questionnaires.

Sample sizes were calculated so that a statistically significant level regarding the difference in the status of physical disability between CCSs and SIBs would be reached based on CCSS results. The target sample sizes were 200 for CCSs and 50 for SIBs (α error 0.05, Power 0.8). Additionally, a matched control group (CONTs) was recruited from a list of individuals registered for internet surveys conducted by a research company. CONTs comprised individuals with no history of childhood cancer or siblings with any history of cancer who matched the CCS group in terms of region of residence, gender, and age. The sample size of this control group was computed so that differences in mental health status between the CCSs/SIBs and the CONTs could be identified by reference to the previous studies [15–17]. The consequent target sample size was 1,000.

Procedure

The study was conducted from August 1, 2007 to March 31, 2009. Guardian's (parental) consent was obtained when the subject was younger than 20 years of age. In addition,

the following measures were taken to ensure that no pressure was applied by the physicians in charge to encourage CCSs, SIBs, or their parents or guardians to participate in the study and that subjects' privacy was protected: (1) the questionnaire as well as the disease/treatment data sheet was assigned an identification number and the subjects remained anonymous; (2) CCSs and their SIBs whose parents or guardians provided consent to the study were given information about the study by their physicians in charge, and CCSs and SIBs who agreed to participate in the study completed the questionnaires and mailed them to the research center (YI) by themselves; and (3) the CCSs' physicians in charge completed the disease/treatment data sheets regarding diagnoses, treatment, and late effects by referring to the CCSs' medical records after obtaining the CCSs' consent. The physicians sent the data sheets to the research center by fax.

Some participants sent the written consent sheets to the branch office (KK), as required by the Institutional Review Boards and Ethics Committees of some participating hospitals. Until the termination of the current study, the written consent sheets were maintained in the branch office, which is independent of the research center, to protect the participants' privacy.

Measurements

The questions were modeled after the questionnaire used by CCSS in North America [10] and the questionnaire used by the British CCSS [4], as well as the questionnaire used by the After Completion Therapy Clinic (ACT) at St. Jude Children's Research Hospital [18]. The physicians in charge were responsible for recording the diagnosis, treatment, and late effects of CCSs. The following measures were used for assessment of mental health.

The Japanese version of the K10 (K10-J)

The K10 was developed using the item response theory by Kessler et al. [19]. A Japanese version was developed by Furukawa et al. in the World Health Organization (WHO) World Mental Health Survey Japan [20]. The K10 is a 10-item self-report screening instrument for mood and anxiety disorders based on the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) [21]. Symptoms (e.g., feeling so sad that nothing can cheer you up) are rated on a five-point Likert scale for frequency of occurrence (from 1 (never) to 5 (all the time)) during the past 30 days. A score of 15 or above was used as the cutoff point for identifying those at high risk for mood and anxiety disorders [20]. Cronbach's alpha coefficients for this scale among the CCS, SIB, and CONT groups in the current study were 0.93, 0.92, and 0.94, respectively.

The Japanese version of the impact of event scale-revised (IES-RJ)

The Impact of Event Scale-Revised (IES-R) is a 22-item self-report instrument [22]. The items reflect the DSM-IV. Cluster criteria for PTSD include intrusion, avoidance, and hyperarousal. Symptoms are rated on a five-point Likert scale for the degree of distress caused by the symptom during the previous week (from 0 (none) to 4 (extreme)). High scores indicate a high degree of symptoms of PTSD. The Japanese version of the IES-R was developed by Asukai et al. [15].

We asked CCSs and SIBs to what extent they were troubled by their own or their siblings' illness and treatment. In addition, we asked the CONTs as to whether they had ever experienced any major stress event in their lives. We then continued to ask those who answered in the affirmative additional questions such as "What was the major stress event?" (using a list developed by Taku [23]), "When did it happen?" and "How did it trouble you?". The list was developed for Japanese adolescents and includes 13 life stressors that adolescents are likely to experience. Descriptive statistics were computed with the assumption that those who answered in the negative ("I haven't") scored zero for all items in the IES-RJ.

Weiss [24], who developed the IES-R, stated that the scale has no "cutoff" points and that it should not be used as a proxy for the diagnosis of PTSD. On the other hand, Asukai et al. [15], who developed the Japanese version, found that it could be used for survivors with PTSD symptoms (PTSD + partial PTSD) using a 24/25 cutoff. We used this cutoff to compare the proportion of high scores between groups in the current study. Cronbach's alpha coefficients for this scale among CCSs, SIBs, and CONTs in the current study were 0.94, 0.92, and 0.97, respectively.

The Japanese version of posttraumatic growth inventory (PTGI-J)

PTG was assessed using the Japanese version of the Posttraumatic Growth Inventory (PTGI-J) [16]. The PTGI-J was developed to achieve the greatest possible semantic and content equivalence to the original PTGI [17]. The original PTGI is a 21-item scale that measures the degree of positive changes experienced in the aftermath of a traumatic event. The PTGI consists of five subscales: Relating to Others (e.g., "I better accept needing others"), New Possibilities (e.g., "I developed new interests"), Personal Strength (e.g., "I discovered that I'm stronger than I thought I was"), Spiritual Change (e.g., "I have achieved a better understanding of spiritual matters"), and Appreciation of Life (e.g., "I have a greater appreciation for the value of my own life"). We used the original 21-item

version with five subscales, whereas Taku et al. [16] omitted three items from the original 21 items in the PTGI-J through a factor analysis of the data from a Japanese college student sample. Items were rated on a 6-point Likert scale, ranging from 0 (do not agree at all) to 5 (strongly agree).

We asked CCSs how much their way of life was affected as a result of the illness and treatment they experienced, and asked SIBs how much their way of life was affected as a result of the illness and treatment their siblings experienced. We also asked the CONTs how much their way of life was affected as a result of experiencing the major stress event. Therefore, in the CONTs, the PTGI-J was applicable only for those participants who had experienced any major stress event. Cronbach's alpha coefficients for this scale among the CCS, SIB, and CONT groups were 0.94, 0.96, and 0.95, respectively.

Analysis

We first compared those who answered the questionnaire to those who did not in terms of their demographic characteristics and medical information. Then we examined demographic characteristics of the CCSs, SIBs and CONTs by computing descriptive statistics. Finally, we compared CCSs and SIBs with the CONTs, taking gender into consideration (in terms of the K10-J, the IES-RJ and the PTGI-J scores), since it was generally believed that women scored higher than men with regards to depression or PTSS. For the categorical items, either χ^2 test or Fisher's exact test was used. For the ordinal and continuous variables, the Mann-Whitney *U*-test was performed. For multiple comparisons, Bonferroni's adjustment was used. These statistical analyses were performed using SPSS software version 12.0 J (SPSS, Inc., Chicago, IL, USA).

Ethical consideration

The study protocol was reviewed and approved by the Institutional Review Boards and Ethics Committees of 12 hospitals, including five educational hospitals, three general hospitals, two cancer centers, and two children's hospitals.

Results

Characteristics of the participants

The physicians in 12 hospitals asked 261 CCSs to participate in our research study. One hundred and eighty-nine (72.4%) of them returned the answer sheets to the research center. For the SIBs, on the other hand, the questionnaire was distributed to approximately 138 people. Seventy-four SIBs (an estimated 53.6%) returned the answer sheets.

Of the 189 CCSs who participated in the research, we excluded 4 people because one survivor was 20 years old at the time of diagnosis, one had his/her mother answer for him/her, and two suffered from another disease that might have affected their QOL. Thus, 185 (70.9%) CCSs were included in the analysis. We also excluded 2 of the 74 SIBs because they were younger than 16 at the time of the research, resulting in the inclusion of a total of 72 SIBs (an estimated 52.2%) in the study.

When comparing those who answered to those who did not, we found that women were more likely to answer the questions ($p=0.001$), but there was no significant difference in terms of age at the time of the research, diagnosis, year at diagnosis, type of cancer, type of treatment, and whether late effects or relapse had occurred (Table 1).

The age of the participants in all three groups was approximately 23 years old at the time of the research, but the female SIBs were approximately 2 years older (Table 2). In addition, there were more married females in the SIB group than in the CONT group. One of the demographic features of the CCSs was the lower number of full-time desk workers compared to the CONTs; however, there was no significant difference in annual income between the two groups.

Cancer diagnoses were all made between 1979 and 2003 (median: 1992), and hematological malignancies comprised 129 cases (69.2%) (Table 1). Regarding treatment, the combination of chemotherapy and radiation was the most popular treatment combination and was applied to 73 cases (39.5%). Surgery was performed in 70 cases (37.8%) and hematopoietic stem cell transplantation was conducted in 46 cases (24.9%). In addition, among CCSs, 34 cases (18.4%) experienced recurrence of the disease, and 103 cases (55.7%) had late effects according to physicians' reports.

Depression and anxiety

K10-J score was higher for females than for males in the CCS and CONT groups (Table 3). No significant differences were found in K10-J score between the CCS/SIB group and the CONT group for both females and males. On the other hand, the proportion of participants whose K10-J scores were 15 or above was greater in females compared to males only in the CONT group. In addition, the proportion of participants whose K10-J scores were 15 or above was smaller in the SIB group compared to that in the CONT group for males.

Posttraumatic stress symptoms

In the CONT group, 658 participants answered that they had experienced any major traumatic event. Of these, only

Table 1 Comparison between participants and non-participants among childhood survivors

		Participants <i>n</i> =185		Non-participants <i>n</i> =65 ^a		χ^2 (<i>P</i> -value)
		<i>n</i>	%	<i>n</i>	%	
Gender	Female	108	58.3	22	33.8	0.001
Age at time of research	16–19	47	25.4	19	29.2	0.438
	20–24	75	40.5	29	44.6	
	25–29	38	20.5	13	20.0	
	30–40	25	13.5	4	6.2	
Age at time of diagnosis	0–5	70	37.8	29	44.6	0.106
	6–12	69	37.3	28	43.1	
	13–18	46	24.9	8	12.3	
Year at diagnosis	1979–1983	12	6.5	5	7.7	0.952
	1984–1988	37	20.0	14	21.5	
	1989–1993	62	33.5	23	35.4	
	1994–1998	41	21.9	13	20.0	
	1999–2003	33	18.7	15	23.1	
Diagnosis	ALL	81	43.8	32	49.2	0.865
	AML	21	11.4	6	9.2	
	MDS/other blood cancers	4	2.2	2	3.1	
	Malignant lymphoma	23	12.4	7	10.8	
	Neuroblastoma	11	5.9	6	9.2	
	Brain tumor	10	5.4	0	0.0	
	Bone tumor	10	5.4	3	4.6	
	Rhabdomyosarcoma	8	4.3	1	1.5	
	Langerhans cell histiocytosis	4	2.2	3	4.6	
	Wilms tumor	4	2.2	1	1.5	
	Hepatic tumor	1	0.5	2	3.1	
	Others	8	4.3	2	3.1	
	Treatment	Chemotherapy	182	98.4	65	
Radiation		113	61.1	35	53.8	0.307
Operation		70	37.8	21	32.3	0.425
Stem cell transplantation		46	24.9	18	27.7	0.653
Outcome	Recurrence	34	18.4	10	15.4	0.586
Late effects	Exist	103	55.7	39	60.0	0.545

^aNo information of the others (*n*=7) is available

19 participants selected “admission to hospital or severe disease” as the most stressful event in their lives. The events most commonly selected by participants were “occupational problems or money-related troubles” (*n*=125), “relationship problems” (*n*=96), “love problems” (*n*=94), “academic problems” (*n*=91), “bullying” (*n*=73), “separation or divorce of parents, disease of a family member, or an accident experienced by a family member” (*n*=64), and “bereavement” (*n*=43). The mean age when they experienced the events was 18.9 years (SD: 5.66) and an average of 5.42 years (SD: 5.18) had passed since the event at the time of the survey. The other 342 participants answered that they had not experienced a major traumatic event.

The IES-RJ scores of females (both total and all subscales) were higher compared to males only in the CONT group (Table 3). When the IES-RJ scores of the CCS group were compared to those of the CONT group, total IES-RJ score and the “hyperarousal” score were significantly higher in the CCS group compared to the CONT group for females, while total IES-RJ score and the scores of all three subscales were significantly higher in the CCS group compared to the CONT group for males. In addition, when the IES-RJ scores of the SIB group were compared to those of the CONT group, the “hyperarousal” score was lower in the SIB group compared to the CONT group for females.

The proportion of participants whose IES-RJ scores were 25 or above was greater for females compared to males

Table 2 Demographic data

	Female						Male					
	CCSs		SIBs		CONTs		CCSs		SIBs		CONTs	
	<i>n</i> =108		<i>n</i> =42		<i>n</i> =584		<i>n</i> =77		<i>n</i> =30		<i>n</i> =416	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Age at time of research												
mean ± SD (median)	23.2±4.9	(22)	25.6±5.5	(23.5)	23.9±5.4	(23)	23.1±5.1	(22)	24.3±4.6	(24)	23.8±5.8	(23)
16–19	28	26	3 *1	7	145	25	19	25	4	13	102	25
20–24	41	38	20	48	228	39	34	44	12	40	187	45
25–29	25	23	11	26	134	23	13	17	10	33	69	17
≥30	14	13	8	19	76	13	11	14	4	13	58	14
Educational achievement												
Less than high school	2	2	2	5	36	6	5	6	0	0	29	7
High school	39	36	7	17	190	33	26	34	11	37	120	29
College/vocational school	33	31	13	31	114	20	14	18	7	23	36	9
University	33	31	17	40	229	39	29	38	11	37	213	51
Graduate school	1	1	3	7	15	3	3	4	1	3	18	4
Marital status												
Single	90	83	26 †1	62	464	79	68	88	28	93	375	90
Married	15	14	15	36	110	19	9	12	2	7	38	9
Divorced	0	0	1	2	8	1	0	0	0	0	2	0
Other	1	1	0	0	2	0	0	0	0	0	1	0
Occupation												
Student	42 †2	39	13 †3	31	224	38	35 †4	45	11 †5	37	204	49
Part-time worker	10	9	6	14	52	9	34	44	3	10	15	4
Full-time desk worker	16	15	7	17	200	34	11	14	11	37	125	30
Medical worker	16	15	0	0	25	4	5	6	0	0	2	0
Full-time laborer	3	3	1	2	2	0	11	14	2	7	18	4
Other	7	6	6	14	0	0	2	3	3	10	0	0
Unemployed	13	12	9	21	81	14	10	13	0	0	52	13
Annual income (JPY) ^a												
<1 million	62	57	29 *2	69	328	56	49	64	11	37	246	59
1–2 million	26	24	5	12	88	15	7	9	4	13	41	10
2–3 million	11	10	3	7	94	16	10	13	8	27	39	9
3–5 million	6	6	3	7	69	12	9	12	4	13	68	16
5–8 million	1	1	0	0	4	1	0	0	2	7	20	5
≥8 million	0	0	0	0	1	0	1	1	0	0	2	0

*1 and *2: Significant difference between SIBs and CONTs by Mann-Whitney *U* test. *P*=0.029 and 0.039, respectively

From †1 to †5: Significant difference between CCSs or SIBs and CONTs by Fisher's exact test. *P*=0.043(†1) and 0.000(†2, †3, †4, and †5), respectively

^a 1 JPY(Japanese yen) = 0.0109526 USD(US dollars), 1 million JPY=10,953 USD, 8 million JPY=87,621 USD (monthly average rate in January, 2010)

only in the CONT group. In addition, the proportion of participants whose IES-RJ scores were 25 or above was not significantly different in the CCS (23.4% for females and 16.9% for males) and SIB groups compared to the CONT group for both females and males.

Posttraumatic growth

In the CONT group, 658 participants completed the PTGI-J. The total score and three subscales of the PTGI-J for females were higher than those for males in the CONT

Table 3 Mental health among CCSs, SIBs, and CONTs

	CCSs				SIBs				CONTs			
	n	mean	SD	median	n	mean	SD	median	n	mean	SD	median
Female												
K10	105	8.58	8.16	6.00 *1	41	6.85	7.19	4.00	584	9.14	8.91	7.00 *2
K10≥15	24	%	22.9	%	6	%	14.6	%	136 †1	%	23.3	%
IES_R	107	16.42	16.67	11.00 †1	41	9.00	11.51	4.00	584	15.91	19.70	7.50 *3
IES_R≥25	25	%	23.4	%	5	%	12.2	%	154 ‡2	%	26.4	%
IES_R_intru	107	0.76	0.82	0.50	41	0.45	0.61	0.25	584	0.70	0.92	0.25 *4
IES_R_avoid	107	0.74	0.75	0.50	41	0.49	0.65	0.38	584	0.79	0.96	0.38 *5
IES_R_hyper	107	0.74	0.88	0.50 †2	41	0.24	0.46	0.00 †7	584	0.67	0.97	0.17 *6
PTGI	102	50.50	24.45	47.50 †8	40	37.60	24.65	37.50 †20	423	27.69	22.94	22.00 *7
PTGI_ReO	107	2.47	1.29	2.14 †9	41	1.97	1.39	2.00 †21	423	1.32	1.25	1.00 *8
PTGI_NewP	106	2.59	1.36	2.80 †10	41	1.69	1.33	1.60	423	1.44	1.34	1.20 *9
PTGI_Pers	103	2.19	1.28	2.00 †11	40	1.57	1.27	1.25	423	1.26	1.24	1.00 *10
PTGI_SpiC	107	1.38	1.28	1.00 †12	41	0.90	1.01	0.50	423	0.78	1.06	0.50
PTGI_AppL	107	2.98	1.32	3.00 †13	41	2.46	1.52	2.67 †22	423	1.54	1.22	1.33
Male												
K10	77	6.35	6.69	4.00	29	6.21	6.44	5.00	416	6.20	7.83	3.00
K10≥15	10	%	13.0	%	3 ^a	%	10.3	%	61	%	14.7	%
IES_R	77	13.07	13.15	8.00 †3	30	6.37	8.53	2.50	416	9.61	16.20	0.00
IES_R≥25	13	%	16.9	%	2	%	6.7	%	58	%	13.9	%
IES_R_intru	77	0.61	0.65	0.38 †4	30	0.28	0.51	0.06	416	0.43	0.76	0.00
IES_R_avoid	77	0.61	0.68	0.38 †5	30	0.30	0.36	0.19	416	0.48	0.81	0.00
IES_R_hyper	77	0.56	0.62	0.33 †6	30	0.29	0.41	0.00	416	0.39	0.75	0.00
PTGI	73	50.68	24.98	51.00 †14	28	31.04	26.20	29.50	235	23.49	22.69	16.00
PTGI_ReO	77	2.57	1.30	2.71 †15	30	1.44	1.36	1.14	235	1.05	1.18	0.71
PTGI_NewP	75	2.47	1.34	2.40 †16	29	1.41	1.38	1.00	235	1.25	1.31	0.80
PTGI_Pers	76	2.21	1.35	2.13 †17	29	1.47	1.32	1.25	235	1.04	1.15	0.50
PTGI_SpiC	77	1.37	1.23	1.00 †18	30	1.02	1.26	0.50	235	0.79	1.13	0.00
PTGI_AppL	76	2.96	1.24	3.00 †19	30	1.90	1.20	2.17 †23	235	1.37	1.22	1.00

From *1 to *10: Significant difference between females and males by Mann-Whitney U test. $p=0.049(*1)$, $<0.001(*2, *3, *4, *5, *6)$, $0.007(*7)$, $0.002(*8)$, $0.045(*9)$, and $0.018(*10)$ respectively

From †1 to †23: Significant difference between CCSs or SIBs and CONTs by Mann-Whitney U test with Bonferroni adjustment for multiple tests. $p=0.034(†1)$, $0.013(†2)$, $<0.001(†3, †4)$, $0.001(†5)$, $<0.001(†6)$, $0.028(†7)$, $<0.001(†8-†19)$, $0.026(†20)$, $0.007(†21)$, $<0.001(†22)$, and $0.042(†23)$, respectively

‡1 and ‡2: Significant difference between females and males by Fisher's exact test. $p=0.001(‡1)$ and $p<0.001(‡2)$, respectively

^a Significant difference between SIBs and CONTs by Fisher's exact test with Bonferroni adjustment for multiple tests. $p<0.001$

group (Table 3). The total score (47.50 for females and 51.00 for males) and all the subscales of the PTGI-J in CCS group, for both females and males, were significantly higher than those in the CONT group ($p < 0.001$ for all). On the other hand, the total score and the score of “Relating to Others” of the PTGI-J for females in the SIB group were significantly higher than those in the CONT group, and the score of “Appreciation of Life” for both males and females in the SIB group was significantly higher than that in the CONT group.

Discussion

This paper presents a description of the status of young adult CCSs and SIBs in Japan with regard to depression, anxiety, PTSS, and PTG. Young adult CCSs suffered the same level of depression and anxiety as CONTs, but showed a higher level of PTSS compared to CONTs. In addition, the CCSs reported greater PTG compared to the CONTs. Moreover, this study revealed that the mental health status of young adult SIBs was not significantly different from that of the CONTs after approximately 15 years since the diagnosis of their siblings. Female SIBs in particular showed greater PTG compared to female CONTs.

The CCSS has previously indicated that females are significantly more likely to develop symptoms of depression than males among long-term survivors of childhood leukemia, Hodgkin’s disease, and non-Hodgkin’s lymphoma and their siblings [25]. In the current study, however, females were significantly more likely to indicate symptoms of depression than males only in the CCS and CONT groups. This difference between the CCSS and the current study may have resulted from the sample size of the SIB group in the current study.

Moreover, the CCSS revealed that long-term survivors of childhood brain cancer or childhood solid tumors and their siblings reported significantly lower levels of depression and anxiety compared to population norms [26, 27]. In the current study, participants in both the CCS and SIB groups reported the same level of depression and anxiety as participants in the CONT group. We also found that the proportion of suspected mood or anxiety disorders in female CCSs, male CCSs, and female SIBs in the present study were not significantly different from those observed in the CONT group. Only in male SIBs was the proportion of suspected mood or anxiety disorders significantly smaller than those observed in the male CONTs.

Eight previous studies have focused on PTSS among young adult CCSs [28–35]. However, we cannot strictly compare the status of PTSS between the current study and previous studies because the IES-R was not used previous-

ly. The study by Langeveld et al. [33] (the largest of these seven studies) reported that female CCSs had significantly greater total IES scores [36] compared to male CCSs. In the current study, the difference in the scores between females and males was significant only in the CONT group. The sample size of CCSs and SIBs may have been too small to determine any gender differences.

Previous studies using a validated schedule of structured or semi-structured interviews or the IES have shown that the prevalence of PTSD ranged from 6.2% [32] to 21.6% [31]. The proportion of participants in the present study whose IES-RJ scores were 25 or above was comparable to previous studies.

Although the proportion of participants whose IES-RJ scores were 25 or above was not significantly different between the CCS and CONT groups, the median of the total IES-RJ score of the CCS group was higher than that of the CONT group. Unlike cancer-related trauma among CCSs, the majority of the most stressful events selected by participants in the CONT group were not considered life-threatening events. In addition, cancer-related trauma among CCSs was more likely to be repeated and complicated than trauma experienced by CONTs [32, 37]. Therefore the level of PTSS among CCSs was considered higher than that of CONTs even at approximately 15 years after the diagnosis.

There have been no studies which have focused on PTSS among young adult siblings of CCSs. Therefore, the current study is the first to reveal that the health status of young adult siblings is at the same level as the CONTs from a PTSS standpoint.

The concept of PTG is that of a positive psychological change experienced as a result of a struggle with highly challenging life circumstances [38]. The positive consequences of childhood cancer have been studied from various perspectives, but a majority of the results have indicated that survivors do not differ from comparison groups [39]. Although some researchers used the concept of benefit finding [40, 41], which does not require an assumption of prior experience of traumatic stress, we adopted the concept of PTG. As the framework of PTSS fits childhood cancer survivors and their families [13], we consider that the concept of PTG is also appropriate for them.

There are a large number of studies regarding PTG among breast cancer survivors [42], but there are few studies focusing on PTG among CCSs. Barakat et al. [14] described adolescent survivors’ reports of positive changes in themselves, their relationships, and their life goals following successful treatment for childhood cancer under the concept of PTG. However, there has been no study regarding young adult CCSs and PTG. Thus, our study is the first to report the status of PTG among young adult CCSs and their siblings.

We found that CCSs showed remarkably significant PTG compared to the CONTs. In addition, female SIBs also experienced greater growth compared to female CONTs. The PTGI have often been used in previous studies on breast cancer survivors. These studies reported a greater total PTGI score compared to our findings. For example, Cordova et al. [43] and Weiss [44] reported a mean total PTGI score among breast cancer survivors of 64.1 and 60.2, respectively. However, the mean age of their samples was 54.7 and 52.9 years old, respectively, and majority of them were Caucasian. On the other hand, Taku et al. [16], the developer of the PTGI-J, reported that mean total PTGI-J score was 38.9 among Japanese undergraduate students aged 18 to 25 years with various trauma. Considering these previous studies, our results appear to demonstrate that young adult CCSs in Japan have greater PTG.

There are several limitations of our study. First, despite the fact that we are the first multi-centered study in Japan, the sample size may have limited the study's power and obscured possible effects which may have been revealed with a large sample size, especially regarding gender differences. Second, most of the participating hospitals belonged to a study group for childhood hematological malignancies, and the ratio of solid tumors was therefore small compared to those in the national register of treatment research projects for pediatric chronic specified disease [45]. Third, this investigation centered only on those patients who received long-term follow-up by their attending pediatricians. Negative responses may therefore have been underestimated and positive responses may have been overestimated. Fourth, the duration between age at the time of diagnosis and age at the time of the research was approximately 15 years among the CCSs and the time after a traumatic life event was 5 years among the CONTs. Although we asked CCSs about the changes they experienced as a result of the illness and treatment they received, their answers may have included natural growth.

Despite these limitations, this study clarifies the status of young adult CCSs and SIBs with regard to depression, anxiety, PTSS, and PTG. These results suggest that CCSs should be evaluated periodically with regards to PTSS and PTG, and that they should be provided appropriate care and feedback. In addition, these results will also help to reassure parents who are worried about the mental health of the siblings of the affected child during and after his/her treatment.

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