

Title: Impact of Brain Tumor and Its Treatment on the Physical and Psychological Well-being, and Quality of Life amongst Pediatric Brain Tumor Survivors

Introduction

Significant improvement in the medical technology and childhood cancer treatment have led to a marked increase in pediatric brain tumor survival rate. Yet, improved survival inevitably accompanied with tremendous adverse disease- and treatment-related sequelae which can have lifelong implications on pediatric brain tumor survivors (PBTS). A considerable body of evidence shows that PBTS are more susceptible and vulnerable to experience physical, neurocognitive, psychological sequelae, due to the fact that the permanent neurologic damage to the developing young brain (Anderson et al., 2001; Monje and Fisher, 2011; Shah et al., 2015)

Alarming, these adverse late-effects can appear at the time of diagnosis or emerge at any time along the continuum of survivorship (Macartney et al., 2014a). The combined effect of these sequelae across multiple domains can consequently cause devastating effect on PBTS' overall quality of life (QoL) (Gunn et al., 2016; Kyung et al., 2013).

Risk of depression identified as the most prevalent psychiatric late-effect encountered by PTBS (Carpentier et al., 2003). Of particular note, PBTS reported more depressive symptoms when compared to other childhood cancer survivors and

the healthy norms (Shah et al., 2015). Evidence indicates that more depressive symptoms experienced by the brain tumor patients could be attributed to the combined effect of cancer diagnosis with comparatively poor prognosis, worry for brain tumor recurrence, and impaired physical, neurocognitive and psychosocial functioning result from the sequelae caused by brain tumor and its treatment (Gurney et al., 2009). Higher risk of depression was found to have close association with poorer clinical outcomes (Mainio et al., 2005), lower self-esteem, poorer QoL (Zeltzer et al., 2009) and higher tendency of suicidal ideation (Recklitis et al, 2010).

Aside from higher risk of depression, intruded self-esteem was also another pronounced psychiatric condition exhibited by PBTS (Hörnquist et al., 2015). This can be explained by the apparent changes in survivors' physical appearance which are common physical sequelae in PBTS. The persistent and visible changes may include presence of persistent visible scars and lesions, hair loss or even long-term alopecia, head or neck disfigurement and short stature (Gurney et al., 2003; Kinahan et al, 2012). These changes in survivors' physical appearance can intrude their self-esteem due to the distorted body image (Hörnquist et al., 2015). Altered self-esteem can also pose a negative impact on survivors' QoL (Hörnquist et al., 2015) and create other psychological problems including depression, anxiety, and suicidality (Moksnes and Espnes, 2012). Taken all these together, the QoL of PBTS has been severely

influenced as evident by the poor QoL scores reported by PBTS in studies conducted in the West (Aarsen et al., 2006; Meeske et al., 2004; Wu et al., 2007).

Nevertheless, a review of literature notes that the documented impact of brain tumor and its treatment on the physical, psychosocial and QoL among Hong Kong Chinese PBTS remains unclear. Although there exists evidence addressing the psychological well-being of PBTS in the West, the findings may not be applicable to Hong Kong due to the markedly cultural difference in terms of distinct philosophies of care and treatment, which lead to different disease experience and response for patients in Hong Kong and the West (Chung et al., 2014). It is essential, therefore, prior to design any appropriate interventions for the Hong Kong Chinese PBTS, the impact of brain tumor and its treatment should be examined. This study aimed to explore the impact of brain tumor and its treatment on psychological well-being and QoL of Hong Kong Chinese PBTS. The objectives were to:

- (1) assess depressive symptoms, self-esteem, and QoL of Hong Kong Chinese pediatric brain tumor survivors
- (2) compare depressive symptoms, self-esteem, and QoL between Hong Kong Chinese PBTS and survivors of other pediatric cancers
- (3) understand how brain tumor and its treatments influence PBTS' physical and psychosocial well-being, and QoL.

Methods

Study design and sample

A cross-sectional study was conducted. Children who attended the scheduled medical follow-ups in the pediatric outpatient clinic and met the inclusion criteria were invited to participate in this study. The inclusion criteria of the study were as follows: (1) Hong Kong Chinese pediatric brain tumor and other types of childhood cancer survivors, (ii) aged between 7 and 16 years, (iii) can speak Cantonese and read Chinese, and (iv) had completed the cancer treatment for at least six months. We excluded survivors with cognitive and learning impairment, and those with evidence of tumor recurrence and secondary malignancies.

In Hong Kong, an average of 25 and 145 children and adolescent with ages 0 to 19 years were newly diagnosed with a pediatric brain tumor and other types of childhood cancer, respectively (Hospital Authority: Hong Kong Cancer Registry, 2017). To enhance the generalizability of the study findings, a convenience sample of 77 PBTS and 80 survivors of other childhood cancer were recruited.

Study instruments

Demographic sheet

A demographic sheet was developed to collect participants' demographic data, clinical characteristics and medical history. Data such as sex, age, parents' education

attainment, age at diagnosis, treatment modality received, and time since treatment completed were recorded.

The Chinese version of the Center for Epidemiological Studies Depression Scale for Children (CES-DC)

Depressive symptoms of the participants were measured using the Chinese version of the CES-DC. It is a commonly used tool in assessing the number of depressive symptoms of children and adolescent (Radloff, 1977). It consists of 20 fully standardized items which are rated on a 4-point Likert scale regarding the participants' feelings and experiences of last week. Scores may range from 0 to 60. Higher scores indicate a higher level of depression. A cut-off score of the scale is 16, indicating the children or the adolescents are currently experiencing a significant level of depressive symptoms. The CES-DC demonstrated good internal consistency with a Cronbach's alpha coefficient of 0.82, and satisfactory convergent with $r = 0.63$ and discriminant validity with $r = - 0.52$ (Li et al., 2010a).

The Chinese version of the Rosenberg self-esteem scale (RSES)

The Chinese version of the RSES was used to evaluate the participants' self-esteem. It is a tool designed to assess the global self-esteem of children (Philips et al., 2008) and adolescent (Byrne, 2000). The scale encompasses 10 items, rating on a 4-point Likert scale (1= "strongly disagree", 2= "disagree", 3= "agree", 4 = "strongly agree").

Scores ranging from 10 to 40, in which higher scores indicate higher levels of self-esteem. The results of psychometric properties test of the Chinese version of RSES showed that its internal consistency was good, with a reported Cronbach's alpha coefficient of .84 and discriminant validity with $r = -0.52$ (Li et al., 2010a).

The Chinese version of the Pediatric QoL Inventory 4.0 Generic Core Scale (PedsQL 4.0)

To measure the participant's QoL, the Chinese version of the PedsQL 4.0 was used.

The scale contains 23 items which are categorized into four dimensions, namely physical, emotional, social and school functioning. The participants were asked to response on how much of a problem as stated in each item they have been experienced over the last month using a 5-point Likert scale from 0 (never a problem) to 4 (almost always a problem). The PedsQL scores range from 0 to 100, with higher scores indicating a better health-related QoL (Varni et al., 2001). The psychometric properties of this scale have been empirically tested with the internal consistency of an alpha coefficient 0.86 and test-retest reliability ranged from $r = 0.65$ to $r = 0.81$ (Chan et al., 2005).

Semi-structured interview

To gain a better understanding of Hong Kong Chinese PBTS' physical, psychosocial well-being and QoL, a one-to-one semi-structured interview was conducted.

Participants were randomly selected for the interview from all the PBTS participated in this study according to the serial codes generated by a computer until data saturation was achieved. An interview guide was developed and used throughout the interview process. Examples of the questions include: What is your pediatric cancer experience? How does the brain tumor and its treatment impact your daily life? Follow-up probes were then used, such as “Why do you feel like this?”, “How is that?”, and “Could you give me some example?”

Data collection procedures

Prior to the commencement of the study, ethical approval was gained from the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster. After checking the eligibility of the children based on the inclusion and exclusion criteria of the study, written consent from the children's parents was obtained. Meanwhile, children were invited to put their names on a specially designed assent form to indicate their voluntary participation in the study. Both children and their parents were assured of complete anonymity and their voluntary participation in the study. A set of structured questionnaires comprising a demographic sheet, the Chinese version of CES-DC, RSES, and PedsQL 4.0 was distributed and completed by the participants. In addition, all interviews were conducted by a qualified research nurse. The interviews were audio-taped with

consensus by the participants. Each interview lasted for about 30 minutes.

Data analysis

SPSS version 23.0 for Windows (IBM Corp., Armonk NY, USA) was used for data analysis. Independent *t*-test and chi-squared test were used to compare the demographics and clinical characteristics between survivors of pediatric brain tumor and survivors of other childhood malignancies. The means, standard deviations, and range of scores of the CES-DC, RSES and PedsQL 4.0 were calculated by the descriptive statistics. An Independent *t*-test was used to assess the difference in mean scores of the CES-DC, RSES and PedsQL 4.0 between groups. Additionally, the interrelationships among the demographics and clinical characteristics of the participants and the scores of the CES-DC, RSES and PedsQL 4.0 were investigated using the Pearson product-moment correlation coefficient.

For analyzing the qualitative data, Colaizzi's seven-step method was employed (Colaizzi, 1978). Firstly, the researchers got familiar with the qualitative data by reading through the transcripts repeatedly and listening to the audiotapes of the interviews. Then, significant statements which were related to psychological well-being were identified and extracted. Next was to formulate meanings from the significant statement extracted to further reflect the informant' intents. To ensure consistency, comparisons were continually made between the original transcripts and

the identified meanings throughout the process. Afterwards, the researchers clustered these identified meanings into different themes. Finally, the findings were organized into in-depth descriptions of the phenomena and were summarized into short and dense statements which were then returned to the available informants to verify the accuracy of the findings that represent the informants' experience.

Results

The results indicated that the two groups were similar in regard to most of the demographic and clinical characteristics, including sex, age, time since treatment completed and educational attainments of parents, except for the type of treatment received (Table 1). Of 80 survivors of other childhood cancer, a majority of them suffered from leukemia (33.8%), followed by lymphoma (20.0%) and osteosarcoma (12.5%). The mean time since treatment received of PBTS was 30 months. Table 2 shows that PTBS had statistically significantly higher means of the depressive symptoms, and lower means of self-esteem and QoL when compared to survivors of other childhood cancer. Over 70% of PBTS scored at or above the cutoff score of 16 as measured by the CES-DC, indicating that a majority of PBTS are potentially at risk for depression. The interrelationships among the demographics and clinical characteristics and the scores of the CES-DC, RSES and PedsQL 4.0 are showed in Table 3. The results indicated that there were statistically significantly high negative

correlations between CES-DC and RSES scores, and CES-DC and PedsQL scores.

These findings indicated that a greater number of depressive symptoms was associated with lower level of self-esteem and QoL. Statistically significantly high positive correlation was found between the RSES and PedsQL scores, indicating that higher level of self-esteem was associated with better QoL. Furthermore, there were statistically significantly small positive correlations between types of treatment received and CES-DC scores, and time since treatment completed and CES-Dc scores.

A total of 16 interviews were conducted. The impact of brain tumor and its treatment on PBTS's daily life were categorized into four major themes, including physical, psychological, social and school functioning. In general, almost all informants expressed that brain tumor and its treatment exert devastating impact on multiple domains, including physical, neurocognitive, psychological and social functioning, thereby leading to decrement of their QoL.

Regarding the impact of brain tumor on PBTS' physical well-being, fatigue and headache were the frequently reported physical issues by PBTS that disrupting their daily functioning. One informant said, "I always feel tired easily, I can't complete the tasks that my classmates can do during the sports lesson in school, it makes me feel frustrated." Another survivor said, "Headaches really bother me a lot, it will get worse

if I engaged in a physical activity.” Reduced functional capacity such as limb weakness and imbalance gaits were also reported by a few informants, which making them become more dependent on others in daily life.

In respect to the psychological domains, a substantial proportion of informants expressed that they often experience low or depressed mood and stress. Some explained that these originated from the fear of cancer recurrence. One survivor said, “Although the doctor told me that I have been cured, I worry about the brain tumor may come to me again, it was really scary, and I don’t think I could bear with it once more.” A few older PBTS felt depressed and worried about their future as they perceived themselves as less capable than their healthy counterparts. An older survivor claimed, “...I am quite useless, I can’t foresee my future, sometimes I asked myself try not to think about it, but when I realize that all my friends are more capable than me, this feeling just pops up randomly and make me feel so depressed and stressful.” While some stated that they felt inferior and depressed because of their visible and persistent change in physical appearance, such as scars and hair loss. One informant said, “I am so ugly because of the surgical scar at the back of my skull which unfortunately can’t be covered by my hair, though my parents and friends always tell me that I’m not, I know they just want to comfort me, I feel depressed about it.” Similarly, some survivors reported low-esteem due to a lack of personal

achievement after their cancer diagnosis. One informant said, “I am not as good as my siblings and peers, it seems that I don’t have any achievement throughout my life, sometimes I think I am a useless person at all.”

For the social domain, most informants experience difficulties in making friends and maintaining relationship with others because of the limited functional capacity which restricted their daily engagement in social activities with their friends. One survivor said, “Because of the limited functional capacity, I can’t hang out and play with my friends most of time, I feel like so far apart from them, it makes me down.”

While for the family aspect, most informants report close family relationship and showed appreciation of love and support gained from their significant ones. One survivor claimed, “I am so blessed to have such a family which is full of tremendous love and support, this makes me stronger to fight against the on-going challenges.”

Finally, for the school domain, poor academic performance was one of the major concerns expressed by most survivors. One informant expressed, “I feel a significant decline in my learning capability, I always get poor results from the tests and examinations, which make me feel very disappointed and distressed. I think my parents are dissatisfied with my performance too.”

Discussion

The results of the current study showed that over 70% PBTS were at risk of

depression and they experienced significant greater depressive symptoms when compared with survivors of other childhood cancer. Compared to the results of a local study which measured the depressive symptoms of Hong Kong Chinese healthy schoolchildren with similar ages, only 30% of schoolchildren exhibited certain number of depressive symptoms (Li et al., 2010b). The findings of the present study were in accord with the findings from the previous studies conducted in the West, showing that PBTS reported significantly higher depressive scores when compared with survivors of other pediatric cancers and their healthy peers (Shah et al., 2015). Noteworthy, PBTS in this study presented a higher risk of depression when compared to only 19% PBTS in the West (Shah et al., 2015).

There are some possible reasons to explain why there is a discrepancy in the occurrence and severity of depressive symptoms between Hong Kong and the Western counties. First, Chinese children might be affected by their cultural characteristics of fatalism, hence they might tend to perceive themselves as incapable to control their fate. In addition to the cultural factor, the paucity of psychosocial support for PBTS in Hong Kong seems to be another plausible reason explaining the significantly higher percentage of Hong Kong Chinese PBTS who were at potential risk of developing depression. In Hong Kong, whilst regular medical follow-up is provided for PBTS throughout their survivorship, physiological care and monitoring

and prevention of cancer recurrence receives the most attention (Li et al., 2012). It is disconcerting to recognize the relative absence of social group and community support available for PBTS in Hong Kong. Unlike Hong Kong, Western countries have abundant resources and supporting strategies to promote psychological well-being among children and adolescents that have survived brain tumors and their family members. A vast range of free services targeting on the enhancement of PBTS' psychological well-being and QoL are provided by numerous organizations in the West. These include social network support groups (A Kids' Brain Tumor Cure Foundation, 2018), physical and psychosocial support programs, such as rehabilitation therapy, music therapy, yoga, and special educational program led by qualified teachers (Memorial Sloan Kettering Cancer Center, 2018). All these psychosocial supports are believed to exert positive effect on ameliorating disease and treatment-related sequelae, thereby eliminating on-going life challenge faced by PBTS and ultimately enhancing the psychological well-being and QoL among PBTS (Decker, 2007).

Consistent with the studies conducted in Western countries (Essen et al., 2000; Zeltzer et al., 2009), the results of the present study revealed that greater number of depressive symptoms was strongly associated with lower self-esteem and QoL. It is therefore vital for healthcare professionals to carefully monitor the occurrence of

depressive symptoms in PBTS and to implement early interventions that can help reduce their depressive symptoms so as to enhance their self-esteem and QoL.

Results from the qualitative interviews revealed the deleterious impact of brain tumor and its treatment on PBTS' physical, psychological, social and school functioning. Of particular note, most PBTS expressed psychological distress in relation to the disease burden on their physical, social and school domains. In respect of the physical well-being, headache, fatigue and reduced functional capacity were the common physical sequelae reported by PBTS. The results were in accord with a previous qualitative study conducted in the West (Macartney et al., 2014b).

Concerning the psychological aspect, most PBTS exhibited feelings of fear, depressed mood and intruded self-esteem. Fear originated from cancer recurrence, which is an extremely stressful events for the children and adolescents, who are with limited cognitive capacity to cope with it. It is noted that depressed mood and low self-esteem were co-occurred, as most of PBTS in the qualitative interviews reported depressed mood also exhibited low self-esteem. A lack of personal achievement seems to be one of the dominant reasons making PBTS feeling depressed and having low self-esteem. Therefore, future studies can explore and develop some, appropriate interventions in strengthening their sense of achievement, thereby making them feel capable in achieving certain task and, hence boosting their self-esteem. Regarding the social

aspect, most PBTS encountered difficulties in making friends and maintaining friendship due to limited functional capacities in participating in social activities. This somehow exerts negative effect on their psychological well-being as peer support was found to be associated with lower level of depression among Hong Kong Chinese adolescents (Chang et al., 2018). Brain tumor and its treatment also impact on the academic functioning of PBTS due to the decline in learning capability, such as poor concentration and memory loss. The failures encountered in their academic field may further exaggerate the psychiatric condition of depressive symptoms and further intrude their self-esteem.

Implications for practice

The psychological sequelae presented by PBTS should warrant immediate attention and effort from the healthcare professionals to monitor and alleviate by developing an effective intervention specifically for this population. Additionally, this study gives a valuable insight for the health care professionals that when planning an intervention in improving PBTS' QoL, it is necessary to incorporate strategies that target on reducing depressive symptoms and enhancing self-esteem of PBTS. Moreover, the findings of this study could enhance the accountability and responsibility of the healthcare professionals that they should pay close attention and prospectively monitor the adverse psychological late-effect posed by brain tumor and treatment during the

routine medical follow-up to detect the problem as early as possible. Furthermore, healthcare professional should play a proactive role in empowering and advocating PBTS' well-being alongside their survivorship through collaborating with non-governmental organizations, educational sectors and governmental policymaker to provide support and help for PBTS and their caregivers to eradicate on-going challenges throughout their cancer journey.

Limitations

There are several limitations in the current study. First, the generalizability of the findings was limited due to the use of convenience sampling and all data was collected in one setting. Second, this study only examined the impact of brain tumor and its treatment on survivors' well-being from the children's perspectives. However, parents may play influential roles in shaping their children's development, hence, future studies may gain a more in-depth understanding about the impact of brain tumor on PBTS from the parents' perspectives. Moreover, temporality is uncertain due to the cross-sectional design. It is recommended to conduct a longitudinal study to determine if brain tumor and its treatment have long-lasting effect on physical, psychosocial and QoL among Hong Kong Chinese PBTS.

Conclusion

This study has addressed a literature gap by showing that Hong Kong Chinese PBTS

have poorer psychological well-being, in terms of depressive symptoms and self-esteem, and more severely compromised QoL compared with that of other childhood cancer survivors and their healthy counterparts. It is vital for healthcare professionals to develop and implement interventions which target on reducing depressive symptoms, enhancing self-esteem and QoL among Hong Kong Chinese PBTS.

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Table 1. Demographic and clinical characteristics by groups ($N = 157$).

| | n (%) | | χ^2 | p -value |
|---------------------------------|--|--|------------|-------------------|
| | Survivors of childhood brain tumor ($n = 77$) | Survivors of other childhood cancer ($n = 80$) | | |
| Sex | | | 0.36 | .55 ^{ns} |
| Male | 46 (59.7) | 43 (53.8) | | |
| Female | 31 (40.3) | 37 (46.3) | | |
| Treatment received | | | 60.95 | .00 |
| Surgery | 26 (33.8) | 7 (8.8) | | |
| Radiotherapy | 7 (9.1) | 4 (5.0) | | |
| Chemotherapy | 0 (0.0) | 44 (55.0) | | |
| Mixed method | 44 (57.1) | 25 (31.3) | | |
| Time since treatment completed | | | 1.57 | .91 ^{ns} |
| 6-12 months | 26 (33.8) | 22 (27.5) | | |
| 13-24 months | 15 (19.5) | 17 (21.3) | | |
| 25-36 months | 9 (11.7) | 10 (12.5) | | |
| 37-48 months | 7 (9.1) | 8 (10.0) | | |
| 49-60 months | 6 (7.8) | 10 (12.5) | | |
| >60 months | 14 (18.2) | 13 (16.3) | | |
| Parents' educational attainment | | | 2.43 | .49 ^{ns} |
| Primary school or below | 6 (7.8) | 8 (10.0) | | |
| Lower secondary school | 18 (23.4) | 24 (30.0) | | |
| Upper secondary school | 32 (41.6) | 24 (30.0) | | |
| Tertiary education | 21 (27.3) | 24 (30.0) | | |
| | Mean (SD) | | t -value | p -value |
| Age of children (years) | 11.77 (2.93) | 11.70 (2.84) | 0.14 | .89 ^{ns} |

ns, not significant at $p > .05$.

*Group comparisons t -test for continuous and χ^2 for nominal and categorical variables.

Table 2. Mean scores and standard deviations for the CES-DC, RSES and PedsQL 4.0 of survivors for pediatric brain tumors and survivors of other childhood cancer ($N = 157$).

| | Mean (SD) | | <i>t</i> -value | <i>p</i> -value |
|---------------------|---|--|-----------------|-----------------|
| | Survivors of pediatric brain tumor (<i>n</i> = 77) | Survivors of other childhood cancer (<i>n</i> = 80) | | |
| Depressive symptoms | 20.35 (6.64) | 15.24 (6.95) | 4.71 | .00* |
| Self-esteem | 23.84 (5.11) | 26.94 (4.13) | -1.18 | .00* |
| QoL | 66.60 (12.44) | 70.57 (11.30) | -2.10 | .04 |

* $p < .001$

Table 3. The intercorrelation coefficients among the CES-DC scores, RSES scores, PedsQL 4.0 scores, age, sex, diagnosis, type of treatment received, time since treatment completed, and parents' education attainment among PBTS ($n = 77$)

| | A | B | C | D | E | F | G | H |
|------------------------------------|-------|-------|-------------------|-------------------|--------------------|--------------------|-------------------|---|
| Age (A) | 1 | | | | | | | |
| Sex (B) | 0.16 | 1 | | | | | | |
| Types of treatment received (C) | 0.01 | -0.10 | 1 | | | | | |
| Time since treatment completed (D) | 0.19 | 0.18 | 0.15 | 1 | | | | |
| Parents' educational level (E) | -0.04 | -0.05 | -0.15 | -0.12 | 1 | | | |
| CES-DC (F) | -0.01 | 0.04 | 0.29 ^a | 0.24 ^a | -0.17 ^a | 1 | | |
| RSES (G) | -0.04 | -0.20 | -0.18 | -0.19 | 0.15 | -0.76 ^a | 1 | |
| PedsQL 4.0 (H) | 0.02 | 0.003 | -0.14 | -0.13 | 0.17 | -0.68 ^a | 0.69 ^a | 1 |

^a Significant at $p < 0.01$