

What makes the symptom free for the cancer patient in oldest old without treatment? Case Reports in a Long term care facility

Kazue Takayanagi^{1*} and Yoshikuni Sato²

- 1 Ohshu Medical Foundation, Healing Environment Society and Academy of Laughter, Nippon Medical School, Japan
- 2 Ohshu Medical Foundation, Japan Surgical Society, Healing Environment Society, Japan

Abstract

Background: Oldest old cancer patients without treatment in our long-term-care facility, where laughter therapy is used, lived happily and longer with neither any major complaint nor individual symptoms. We would like to report on these cases.

Methods and Findings:1 A 97 year female, with hepatocellular carcinoma, symptom free, expired by stroke. A CT showed that the tumor had grown double in size compared with its size two years ago. Tumor markers were extremely high.

2 A 79 year male with severe dementia gradually lost weight within 7 months although he had a good appetite. Abdominal ECHO and CT proved a cystic malignant tumor in the liver with cholelithiasis without symptom. High CA19-9 was noticed. He had no weight gain for four months although his appetite was the same as before.

3 An 86 year female with a long standing schizophrenia had a malignant lymphoma of the stomach confirmed by biopsy 3 yrs 3 m ago. She had severe anemia and needed several blood transfusions. Her anemia improved after the transfusions. She had a cheerful character after she suffered from herpes zoster.

4 A 95 year female, who had a right lung partial lobectomy at her 68 yr against cancer, showed left side lung mass for 4 years but was symptom-free. After 4 years, the tumor mass maintained its size but pleural effusion and thickness were seen by CT. Her high CEA suggested carcinoma of left lung.

In all cases, families preferred conservative management only as patients may not have fully understood their own physical situation. They lived happily in this facility, where laughter therapy was applied.

Limitation occurs because of case reports. Epidemiologic surveys nationwide are requested.

Conclusion: There were four reported untreated cases of symptom-free cancer oldest old patients. All cases had a good appetite, cheerful, with or without dementia, and lived for an average of 2 and half years.

Psychologic effects may have contributed to the symptom-free feature of the tumor. We treated several other symptom-free cancer survivors who lived happily in this facility. A further understanding of the mechanism behind this rare phenomenon may provide new strategies for management of cancer. Similarly, research on the effect of deciding on the treatment is, likewise, warranted.

Keywords: Cancer survivors; Oldest old; Without treatment; Long-term-care facility; Laughter therapy; Dementia

Corresponding author: Kazue Takayanagi

✉ takayanagikazue@gmail.com

Director, Ohshu Medical Foundation, President, Healing Environment Society and Academy of Laughter, Lecturer, Nippon Medical School, Japan

Tel: +81 3-3822-2131

Introduction

In general, a patient with cancer suffered from some serious symptom, gradually weakens and expires.

In our "Seiwaen", a long-term care facility, we had 96 patients of which 15 of them were cancer survivor patients. Our facility provided residence and rehabilitation to the elderly or "guests" earlier discharged from semi-acute hospitals. After, they returned to their own homes or nursing homes. In the facility, a routine laughter therapy was implemented with the guests who were already in various levels of dementia.

The guests without dementia, including cancer survivors, took routine laughter therapy, as well as study classes with laughter.

We would like to report four cases in our facility that has the following issues:

Cancer patients, who are symptom-free with worsening malignancy, and: Cancer survivor without treatment. This paper is a report with a general discussion on the status of cases of oldest old symptom-free, and untreated cancer survivors.

Cancer survivors who had dementia did not feel stressed as much as the ordinary cancer survivors did. The character of the patients, as well as degree of dementia may have contributed to the results. However, our guests with cancer were oldest old and were living happily, even with untreated cancer [1,2]. This psychiatric status may enhance immunity. Immune response may take a role for spontaneous regression or symptom-free status [3,4]. Caregiver's health implications of health observations of cancer survivors is more likely due to their personal experience with cancer patients, i.e., stressful, rather than simply the patients' disease status [5]. These results suggest that psychosocial variables, especially coping strategies, play an important role in determining the immunological response [6].

We had four un-treated cancer patients who were symptom-free and live happily in our facility, where laughter was applied. Further understanding behind this rare phenomenon may provide new strategies for management of cancer.

Methods

All guests in Seiwaen, a long-term-care facility, ranked by dementia severity using the Hasegawa Dementia Scale (HDS) from 0 (complete dementia) to 30 (normal), were studied. HDS, a simple intelligence test, was often used along with the MMSE in Japan [4]. The cut-off value was 20/21.

We reported four cases of symptom-free cancer patients without treatment. The tumor grew bigger and the physical signs were supposed to be worse, although those clinical appearances were symptom free or rather getting better.

Results

Figure 1 showed four cases at the onset of malignancy and **Figure 2** showed the end stage or the latest status of cases.

Case 1: Female, 97 years

A 95 years female was diagnosed cholangitis and hepatocellular

carcinoma which occupied 40% of right lobe of the liver at I Hospital on March, 2009 (**Figure 1a**). No treatment for cancer was done. The patient became a resident of our facility on May 10, 2010. One year later, she suffered from cholangitis and treated with antibiotics. She became sociable with a positive outlook, interested in music and always sang songs. Her HDS improved from 9 on admission to 13 on May18, 2011.

Then patient suddenly had a stroke on October 16, 2011. Abdominal CT showed enlarged tumor occupied 90% of the right lobe of the liver, right pleural effusion, and diaphragmatic invasion of the tumor (**Figure 1b**). Tumor markers were extremely elevated: α FP was 4750, DUPAN-2 was 300, PIVIK (ECL) was 4870 and CA19-9 was 53.2. She did not show any digestive symptoms including jaundice until expired on October 20. She was cancer symptom-free for two years and 7 months.

Case 2: Male, 79 years

He had cerebral infarction with left paralysis. He lost 11kg in six months. ECHO showed a parenchymal mass inside the delated gall bladder apart from gall stones in the gall bladder (**Figure 2a**).

A cystic mass 21.5 x 21.0 mm in right lobe of the liver with irregular lesion in 40.5 x 23.1 mm in low density was seen in CT (**Figure 2b**). The tumor invaded to the caudate lobe. Tumor marker was elevated as CEA: 9.5 ng/ml, CA19-9: 178 U/ml. The patient's liver function test was within normal and Hb was 11.5 mg/dl. Cystic malignancy of liver was strongly suspected.

The HDS of the patient was 0 and family refused for the further therapy. He had an excellent appetite since young up to present. He did not show any digestive problem including cholangitis although his plain X-P showed Chilaiditi syndrome. He has maintained his present weight for the last six months (**Figure 2c**).

Case 3: Female, 87 years

The patient has been suffered from schizophrenia since 1972, chronic heart failure, and hypertension since 2003. The patient has had gastric bleeding since February 7, 2012 and needed several blood transfusions. Endoscopy was done and primary gastric diffuse large B-cell lymphoma (PGDLCL) was diagnosed histologically (**Figure 3a**). Family, a nurse, prefer the best supportive therapy rather than chemotherapy. On **March 29, 2013**, her Hb was 5.4 mg/dl requiring blood transfusion. Follow-up endoscopy revealed hemorrhagic lymphoma in the stomach on Sept.10, 2013 (**Figure 3b**).

The patient was admitted to our long-term-care facility on August, 2014. Her Hb was 11.8 mg/dl. She suffered from herpes zoster in the thigh on August 2014. Since then, she never complained any digestive disorder and kept good appetite. She changed her behaviour and had a positive outlook. Her Hb improved to 14.8 mg/dl on March, 2015 without any treatment, although her HDS dropped down from 20 to 8 in 8 months. Endoscopy proved enlarged ulceration of the tumor at June 4, 2015. She is happy 43 months after the onset.

Case 4: Female 95 years

The patient had r-upper lobectomy against lung cancer at her

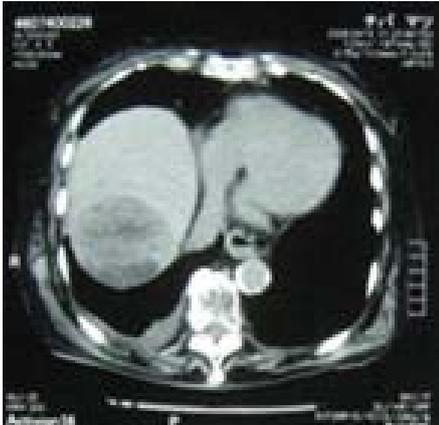


Figure 1A,1B Case 1 female, 97 yr: A female was diagnosed cholangitis and hepatocellular carcinoma which occupied 40% of right lobe of the liver in CT at I Hospital on March, 2009 at her 95 yr.
b. Abdominal CT showed enlarged tumor occupied 90% of the right lobe of the liver on October 16, 2011.



Figure 2A,2B,2c a: Case 2, male 79 years: ECHO showed Parenchymal mass inside the dilated gall bladder apart from gall stones which based at the gall bladder at March3, 2015.
b: A cystic mass in the right lobe continued to lower section to the caudal lobe in CT at March3, 2015
c: An irregular lesion was seen to have continuity within 40.5 x 23.1 mm in low density were seen in CT.



Figure 3A,3B a: Case 3, female, 87 years: Biopsy by gastric endoscopy proved diffuse large B-cell lymphoma at March 24, 2012.
b: Endoscopy showed hemorrhagic and enlarged ulceration of multiple lymphoma of stomach at June 4, 2015.

67 year old. The patient had history of cerebral palsy at 88 yr and cholangitis in 89ys. Left lung cancer was diagnosed accidentally by CT and family refused any treatment for the patient (**Figure 4a**). Her HDS was 20 and she was admitted to a long-term care facility. She suffered from dementia with Lewy

Bodies in her 90 and HDS dropped down to 7. She kept singing songs and talking in air.

Cancer was 1.7 cm in diameter and has spread to the main bronchus and is less than 2 centimetres below where the trachea joins the bronchus and the chest wall. Left posterior pleural

effusion and thickness were seen with tumor on plain chest X-ray on May 20, 2015. CT scan on June 3, 2015 revealed same size of tumor with accumulated pleural effusion and thickened pleura (Figure 4b). Stage IIB lung cancer were diagnosed.

The patient had mild anemia as Hb: 11.1 mg/dl and tumor marker was high in CEA: 9.4, suggested she had malignant tumor of lung. The patient did not show any cough or shortness of breath. Her SPO2 was 98% 78 months after the discovery of the second lung mass.

Discussion

Four untreated cancer survivors in oldest old with symptom-free were reported. Their natural history of cancer progressed but showed symptom -free. In all cases, families had a prerogative to decide on the treatment and conservative management were taken. The following are some possibilities.

1. Progress of disease is slower in oldest old.
2. The symptoms were anemia and weight loss. The patients could have missed the signs because of dementia.
3. All of them had mild dementia and received laughter therapy. They were not interested to dwell on their own physical problems except feeding.
4. All cases had no metastasis although the tumor itself progressed locally. Lymphatic or haematogenous metastasis hardly occurred in oldest old.

The direction of the proliferation of the tumor, such as no bile duct obstruction, is the important symptom-free factor [7].

Histology of the tumor might take a role for symptom-free [8] Immune modulation may work for symptom-free. Infections may contribute to the etiologic pathway and/or be markers of underlying immune modulation in lymphoma cases. In our case the subject had herpes zoster after confirmed diagnoses and improved anemia. Precise elucidation of these mechanisms may provide important clues for understanding how immune disturbance contributes to lymphoma [9].

In general, prognosis of early lung cancer that did not receive treatment is not good [10]. However, they are a report that absence of symptom at diagnosis is a favourable prognostic factor for patients with non-small cell lung cancer regardless whether treatment was performed [11].

The primary limitation of our study is the case reports. Studies with larger samples are warranted, as such studies would improve the precision of estimates of parameters and effect sizes, increase power to detect more subtle effects, and enhance generalizability (e.g., dementia and laughter therapy). Clearly there is a need for further research focused on factors contributing to dementia beyond the informed consent and research examining the connections among stress, dementia, immunity, and health outcomes.

Heron described a representation of the natural history of cancer without treatment [12]. The localized cancer might have less chance for easy doubling to bring any symptom like our four cases.

Anorexia may be the consequence of chemotherapy or psychological disorders induced by announcement about cancer. Laughter therapy or dementia without chemotherapy might work on prevention of anorexia in our cases. Premature satiety, nausea, and loss or change in sense of taste and smell were not recorded as well.

Cachexia or general state alteration including major weight loss was seen in Case 2 only. He could have diversion of the normal metabolism with secretion of cytokines with a necrotic effect, although he himself did not complain about cachexia and a malaise subsequently. Other various factors, such as mass effect of the tumor, direct effect on the digestive tract and previous poor alimentation, have not been incriminated in our cases.

In general, elderly has been identified as a poor prognostic factor in diffuse large B-cell lymphoma [13]. However, in our case3, auto-immune diseases during B lymphoid tumors might be the etiology of relieve the severe anemia [13].

These were indeed cancerous tumors, but ones that caused



Figure 4A,4B a: Case 4, female, 95 years: A mass 1.7 cm in diameter (arrow) was seen in the plain chest X-day at April 13, 2012.
b: CT scan on June 3, 2015 revealed same size of the tumor with accumulated pleural effusion and thickened pleura.

no symptoms and were unlikely ever to become deadly, the researchers said [14,15].

Cancer cells in the oldest old might have less energy to promote proliferation to the host. In this series, we have cancer cases with local invasion such as lymph node swelling and pleural effusion. Hematogenous metastasis may cause worse effect for the patient which causes some symptom.

Detailed informed consent was not done because of dementia and by family's decision. It might work to the lively life of their own. Further research on the effect of treatment decision-making for these patients is warranted.

What makes symptom-free for the cancer patient in oldest old without treatment? The common subjective symptoms of cancer are anorexia, pain and malice. In our cases, tumor invasion preferentially follows less resistant zones: organ capsules, nerve sheaths and small vessels. They work for symptom-free as pain or some symptom due to space occupying lesion.

Dementia and laughter therapy might work as good influence to the symptom-free of cancer patient. Laughter is not only a physical reaction, but also a part of human behavior regulated by the brain, helping humans clarify their intentions in social interaction and providing an emotional context to conversations.

Laughter regulates immunes and gene expression [16] Rhythmical movement of the diaphragm by laughter enhance serotonin, dopamine, emotional movement enhanced oxytocin, morphine, relaxed sympathetic nerves. NK cell activity improves by the laughter [17].

In our laughter therapy, we did not used the procedure for the

guest to suffer from embarrassment, apology, or confusion such as nervous laughter or courtesy laugh [18,19]. The guests and staff were happy and praise each other. The laughter therapy is for the guests and staff to be happy [20].

Further understanding of the mechanism behind this rare phenomenon may provide new strategies for management of cancer. Further research on the effect of treatment decision-making for these patients is warranted.

Conclusion

Psychologic effects may have contributed to the symptom-free feature of the tumor. We treated several other symptom-free cancer survivors who lived happily in this facility.

Four untreated cases of symptom-free cancer oldest old patients were reported. All cases had a good appetite, cheerful, with or without dementia, and lived for an average of 2 and half years. Some of the emotional benefits include diminishing anxiety or fear, improving overall mood, and adding joy to one's life. All guests with dementia did not feel stress or anxiety levels to cope with their terminal illness unless they have no symptoms.

Furthermore, laughter therapy can be a significant enhancement to their life. A further understanding of the mechanism behind this rare phenomenon may provide new strategies for management of cancer. Similarly, research on the effect of deciding on the treatment is, likewise, warranted.

Acknowledgment

We would like to extend our appreciation to Professor C. Maesawa for histological advice he had provided.

References

- 1 Takayanagi K, Sato Y (2015) Do Cancer survivors, including those with multiple primary cancers, live longer when in a long-term-care facility?-Possibility of Harmless Cancer in Oldest Old-Jacobs. *Journal of Cancer Science and Research*: In press.
- 2 Takayanagi K, Sato Y (2013) Clinical manifestation and outcome of oldest old patients with cancer. *Jpn Hosp* 47-51.
- 3 Kim SB, Kang W, Shin SH, Lee HS, Lee SH, et al. (2015) Spontaneous neoplastic remission of hepatocellular carcinoma. *Korean J Gastroenterol* 65: 312-315.
- 4 Mizuno T, Ishigaki M, Nakajima K, Matsue T, Fukushima M, et al. (2013) Spontaneous remission of epstein-barr virus-positive diffuse large B-cell lymphoma of the elderly. *Case Rep Oncol* 6: 269-274.
- 5 Gregorio SW, Carpenter KM, Dorfman CS, Yang HC, Simonelli LE, et al. (2012) Impact of breast cancer recurrence and cancer-specific stress on spouse health and immune function. *Brain Behav Immun* 26: 228-233.
- 6 Pulgar Á, Garrido S, Alcalá A, Reyes del Paso GA (2012) Psychosocial predictors of immune response following bone marrow transplantation. *Behav Med* 38: 12-18.
- 7 Luigi B, Giovanna B, Stefano G, Fabio F, Gianni Z, et al (1992) Natural history of small untreated hepatocellular carcinoma in cirrhosis: A multivariate analysis of prognostic factors of tumor growth rate and patient survival. *Hepatology* 16: 132-137.
- 8 Devaney K, Goodman ZD, Ishak KG (1994) Hepatobiliary cystadenoma and cystadenocarcinoma. A light microscopic and immunohistochemical study of 70 patients. *Am J Surg Pathol* 18: 1078-1091.
- 9 Anderson LA, Atman AA, McShane CM, Titmarsh GJ, Engels EA, et al. (2014) Common infection-related conditions and risk of lymphoid malignancies in older individuals. *Br J Cancer* 110: 2796-2803.
- 10 Henschke CI, Yankelevitz DF, Libby DM, Pasmantier MW (2006) Survival of patients with stage I lung cancer detected on CT screening. *N Engl J Med* 355: 1763-1771.
- 11 In KH, Kwon YS, Oh IJ, Kim KS, Jung MH, et al. (2009) Lung cancer patients who are asymptomatic at diagnosis show favorable prognosis: A Korean Lung Cancer Registry Study. *Lung Cancer* 64: 232-237.
- 12 HERON JF (2009) Cancer natural history-www.oncoprof.net website http://www.oncoprof.net/Generale2000/g01_HistoireGenerale/gb01-hg13.html, Last update 15 June 2009
- 13 Ogura M (2010) Treatment for the elderly with malignant lymphoma, *Jap. Elderly Medical Journal* 47: 271-275.
- 14 USA today (2013) Harmless lung cancer? Many tumors not lethal www.usatoday.com/story/news/nation/2013/12/.../lung-cancer/3927909/ 2013/12/09
- 15 Noji S, Takayanagi K (2010) A case of laughter therapy that helped improve advanced gastric cancer. *Jpn Hosp* 29: 59-64.
- 16 Hayashi T, Urayama O, Kawai K, Hayashi K, Iwanaga S, et al. (2006) Laughter regulates gene expression in patients with type 2 diabetes. *Psychother Psychosom* 75: 62-65.
- 17 Sakai Y, Takayanagi K, Ohno M, Inose R, Fujiwara H (2013) A trial of improvement of immunity in cancer patients by laughter therapy. *Jpn Hosp* 53-59.
- 18 Takayanagi K, Shimura T, Iwabuchi K, Fujiwara H, Ohnishi J, et al. (2012) Laughter education for implementation of the smile-sun method to promote natural healing in public and healthcare facilities. *Jpn Hosp* 57-61.
- 19 Takayanagi K (2011) Effect on self-esteem of workshop to induce laughter through praise. *Jpn Hosp* 61-65.
- 20 Takayanagi K, Matsuoka H, Ishii K (2013) The Smile-Sun Method (SSM): Procedures For Enhancing Interpersonal Skills And Producing Affective Change.