

Curcumin as an Alternative Medicine for Terminal Stage Endometrial Cancer Patient (Case Report)

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ABSTRACT

Curcumin has historically been used in anti-cancer therapies. However, the anti-metastatic effect and molecular mechanism of curcumin in endometrial carcinoma (EC) are still poorly understood. In this case, the patient administrated with 1,000 mg curcumin as an alternative medicine after completed operation and chemotherapy. To evaluate the effect of Curcumin as an alternative medicine after completed operation and chemotherapy of endometrial carcinoma. A 62 years old woman has been diagnosis with stage IV B endometrial cancer and was treated with Radical Hysterectomy and Omectectomy on April 18th 2016. Patology result was endometrial carcinoma type endometrioid. After the operation, Paxus Carboplatin chemotherapy had been given for six series and finished on August 2016. In our experience, the life expectancy after completed surgical procedure and chemotherapy is not more than one year. This condition could make patient fell hopeless and ask for alternative treatment. In this case, the woman was administrated with 1,000 mg curcumin everyday which was started before the operation and continued after completed chemoterapy. During our observation, we found no side effect of using curcumin as an alternative medicine. She has free of any complaints in the year 2017. The relapse of endometrial cancer was found in July 2018. During 2018, we performed secondary debulking and continued with six series of Paxus Carboplatin chemotherapy. During 2018 until she died on January 28th 2019, her condition got worse. In this case, we have an experience using curcumin as an alternative medicine for terminal stage endometrial cancer patient which may increase the life expectancy for more than one year. Eventhough we could not cure the patient, but we have an opportunity to prolong her life expectancy for more than 2 years with one year free of any complains. We have to conduct more research in curcumin as an alternative medicine for endometrial cancer patient to get more data of the efficacy of curcumin.

Keywords: *Curcumin, endometrial cancer*

1. INTRODUCTION

Endometrial cancer (EC) is a group of epithelial malignancies that occurs in the endometrium of perimenopausal or postmenopausal women [1]. In the US alone, uterine cancer is the fourth most diagnosed type of cancer in women [2]. Data from Indonesian Academic Hospital in the year 2007 showed that uterine cancer is the third most diagnosis gynecology type of cancer after cervical cancer and ovarian cancer [3]. Data from the population-based cancer registry in Jakarta Province showed that uterine cancer is one of the leading cancers among females with incidence rate is 1.76 per 100,000 females in 2005-2007 [4].

Intrusive interventions are the usual approach for the treatment of endometrial carcinoma such as surgery (mainly hysterectomy and salpingo-oophorectomy) and other alternatives or complimentary treatments including radiation therapy (brachytherapy or external beam radiation therapy), chemotherapy, and hormone therapy [2]. *Todo et all* reported that the survival rate of lymphadenectomy is

restricted in low-risk patients; however, in intermediate or high risk patients, complete or systematic lymphadenectomy in both the pelvic and para-aortic regions has substantial therapeutic effects [5]. In terminal stage patient, the intrusive interventions have low sucessfull result but the side effect increases among most of the patient.

With the exponential advancement of science, new promising therapies are being developed to treat different types of cancers, and among these remedies herbal medicine is being taken into serious consideration [2]. Curcumin, a widely used in Chinese herbal medicine, has historically been used as anti-cancer therapies [6]. Curcumin has been demonstrated to have an anti-tumor activity but the underlying molecular mechanisms are not fully uncovered [7]. The anti-metastatic effect and molecular mechanism of curcumin in endometrial carcinoma are also still poorly understood [6].

In clinical scenario during treatment of cancer patients, some clinicians and researchers use curcumin combined with chemotherapy and radiotherapy as the most common modalities for the treatment of cancer. Experimental studies have shown that inflammation plays a central role in tumor

resistance and the incidence of several side effects following both chemotherapy and radiotherapy. Inflammation resulting from radiotherapy and chemotherapy is responsible for adverse events such as dermatitis, mucositis, pneumonitis, fibrosis, and bone marrow toxicity [8]. Curcumin has found to be cytotoxic and exerted chemopreventive activities in nature to a wide variety of cancer cell lines and animal tumor models via multiple molecular mechanisms targeting all stages of carcinogenesis [9][10].

Curcumin, 1,7-bis (4-hydroxy 3-methoxy phenyl)-1,6-heptadione-3,5-dione or diferuloylmethane is a dietary phytochemical obtained from the dried rhizomes of plant Turmeric (*Curcuma longa*). The rhizome of this plant is also referred to as “root” and is the most useful part of the plant for culinary and medicinal purposes. Turmeric has been used traditionally in the Indian system of medicine “Ayurveda” as an antiseptic, wound healing, and anti-inflammatory agent. The characteristic yellow colour of the turmeric is due to the curcuminoids present in it, namely curcumin (1), demethoxycurcumin (2), bisdemethoxycurcumin (3) and cyclocurcumin (4). Curcuminoids presents in 3–5% of turmeric, and acts as major biologically active ingredient. It is insoluble in water and soluble in ethanol and acetone [11]. In Indonesia turmeric (*C. domestica* Val., syn. *C. longa* L.) is known under about 80 different local names, of which *kunir* and *kunyit* are most commonly used. *Curcuma* species grow more or less everywhere in Indonesia below 600 meters, cultivated as well as uncultivated, and thus are widely available. Turmeric is used in traditional Indonesian herbal medicine and found in practically every herb drink preparation [12].

After completed surgical, chemotherapy and radiotherapy are used as treatments for cancer. Both doctor and patient will follow-up the side effect of the treatment and possibility of recurrency. For the most patient, this condition leads to be a psychological problem caused by uncertain situation of their disease. During waiting period, most of the patient try to use herbal therapy. Curcumin is one of the choice among the cancer patients.

Eventhough curcumin in theorytical and laboratory result showed as a promising ingredient to cure variaty of cancer, it is still not enough sample in clinical scenario to prove the hypotesis. In this case, we would like to report our experience by using curcumin as an alternative medicine for terminal stage endometrial cancer patient.

2. METHOD

A 62 years old woman had been diagnosis with stage IV B endometrial cancer and was treated with Radical Hysterectomy and Omectectomy on April 18th 2016. Patology result was endometrial carcinoma type endometrioid. After the operation, double agent Paxus and Carboplatin chemotherapy had been given for six series and finished on August 2016. In our experience, the life expectancy after completed surgical procedure and chemotherapy is not more than one year. This condition

could make patient fell hopeless and ask for alternative treatment. In this case, the woman was administrated with 1,000 mg curcumin everyday which was started before the operation and continued after completed chemotherapy. During our observation, we found no side effect of using curcumin as an alternative medicine. She has free of any complaints in the year 2017. The relapse of endometrial cancer was found in July 2018. During 2018, we performed secondary debulking and continued with six series of double agent Paxus and Carboplatin chemotherapy. During 2018 until she died on Januari 28th 2019, her condition got worse. In this case, we have an experience using curcumin as an alternative medicine for terminal stage endometrial cancer patient which may increase the life expectancy for more than one year. This is a case report without personal data or personal figures of the patient. Therefore no ethical approval is required

3. RESULTS AND DISCUSSION

Hopelessness is the main situation concerned in most of advanced stage of cancer patients such in this case. Event the patient followed all of the modalities for the treatment of cancer. Most patients will think of alternative treatment to increase their survival. Without guidance from clinician, Indonesian cancer patient will go to traditional healers. Most of the traditional healers that usually without any scientific backgrounds, would promote a herbal remediance. They also promote herbal remediance without explanation of side effects for the body.

As a clinician, we administrated this patient with curcumin as an alternative medication for her advanced stage of endometrial cancer. The curcumin that we used already standarise by the farmacology industry and approved by Indonesian agency of drug and food control (BPOM). Curcumin in this case was already prepared as tablet to be convenient for daily use of the patient.

Our main aim of using curcumin is to protect the patient from side effect of chemotherapy Paxus and Carboplatin. Tan and Norhaizan reported that chemotherapy is responsible for adverse events such as dermatitis, mucositis, pneumonitis, fibrosis, and bone marrow toxicity [9]. Lantika *et al* reported that main side effect during chemotherapy process using Paxus and Carboplatin is nausea and vomiting which found in 50% of patients [13]. Chemotherapy-induced liver damage in cancer patients may occur during chemotherapy or after the total course. Although liver function impairment may be reversed in some patients after the treatment, abnormal liver function may lead to an interruption of anti-tumor therapy and jeopardize the prognosis of patients [14]. Curcumin has also been used to support liver function and to treat jaundice in both Ayurvedic and Chinese herbal medicine [15]. Tang results provided novel insights into therapeutic mechanisms of curcumin in inhibiting Hepato Cellular Carcinoma activation and intervening liver fibrogenesis associated with nonalcoholic fatty liver disease (NAFLD) and/or nonalcoholic steatohepatitis (NASH) [16]. In this case we did not find any liver function impairments during and after

Paxus and Carboplatin chemotherapy. This clinical case results support other research of the potential effect of curcumin to protect liver. Nausea and vomiting during chemotherapy course were also not so severe.

Our second aim in this clinical case is to increase survival rate and prolong for the possibility of disease recurrence. In this clinical case patient has diagnosed with stage IVB endometrial carcinoma. Based on our experience at Sanglah Hospital, the survival rate of terminal endometrial carcinoma patient is not more than one year. In some cases patient could not complete chemotherapy course caused by side effect of using Paxus and Carboplatin, which are the first line chemotherapy. In this clinical case by using curcumin as an alternative medicine, patient could complete first course chemotherapy of Paxus and Carboplatin in 2016 and continue with one year of free clinical manifestations or complains of the endometrial cancer in 2017. The relapse of endometrial cancer was found in July 2018. During 2018, we performed secondary debulking and continued with six series of double agent Paxus and Carboplatin chemotherapy until she died on January 28th 2019.

Eventhought the patient died on January 28th 2019 but the survival rate was increase dramatically for more than two years and prolonged relapse of endometrial cancer for more than one year. Condition in this case is not by accidental but it must have a scientific background to explain the improvement of the patient. We perform journal review to get the answer.

Although cancer is treated by surgery, radiotherapy, immunotherapy or gene therapy, separately or in combination, still chemotherapy plays crucial role for the treatment of cancer; particularly to inhibit invasion and metastasis. Therefore, there is a continuous need to search new anticancer agents to prevent invasion and metastasis and subsequently to reduce cancer-related mortality. Current research in this field directs to identify potent anti-invasive and anti-metastatic novel chemotherapeutics. A qualitative estimate states that about 25% drugs are still directly derived from the Mother Nature and 74-80% of all cancer drugs have the origins from natural products such this curcumin tablet is made by natural product modification. Of the 1,355 new entities introduced as therapeutics between 1981 and 2010, 71% were natural products or natural product derived compounds [17].

One of natural product derived compounds is curcumin. Curcumin has shown to be successful in several types of cancer lines, mainly because of its ubiquitous action on different modulator of anti-cancer effects. Curcumin alone or in combination is non toxic and is proposed to accentuate the therapeutic efficiency of chemotherapeutics by inhibiting ABC efflux transporter. Curcumin inhibits tumor growth by arresting cell cycle progression, inducing apoptosis, inhibiting the expression of anti apoptotic proteins, inhibiting multiple cell survival signaling pathways and their cross-communication, and modulating immune responses. All these properties make curcumin a promising drug for mono or combination therapy [18].

Eventhough curcumin is a promising drug for mono or combination therapy for endometrial cancer, it is still not

enough research in human. Research cautiously extrapolate results from experiments which were done either *in vitro* or *in vivo* in rodents, zebrafish and human beings drawn the conclusions curcumin has a significant effect on endometrial carcinoma where it exhibited pro-apoptotic, anti-proliferative, and anti-migratory activities of endometrial tumor cells [1],[2][6][19][21].

In this clinical case we could not prove with pathways of curcumin treatment lead to increase the patient survival rate dramatically for more than two years and prolong relapse of endometrial cancer for more than one year. Within observation in this clinical case supports that curcumin is a promising drug for mono or combination therapy, especially after standard modality therapy such as surgery, chemotherapy, and radiotherapy.

4. CONCLUSION

Eventhough we could not cure the patient, but we have an opportunity to prolong her life expectancy for more than 2 years with one year free of any complains.

5. RECOMMENDATION

We have to conduct more research in curcumin as an alternative medicine for endometrial cancer patient to get more data of the efficacy of curcumin.

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