

Lung Cancer in a Male Smoker Treated by Adjunct Nutritional and Phyto-Therapy

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Abstract: Current understanding of the aetiology of lung cancer suggests that oxidative stress is strongly implicated in its pathogenesis with both internal cellular production of free radicals and external carcinogens such as from tobacco smoke. Other risk factors include family history, exposure to radiation, chronic obstructive pulmonary disease, overweight, chronic inflammation, and poor dietary habits. Patients' survival rates have not changed appreciably suggesting that Western conventional therapeutic advances have been rather slow. This case study shows how a well-designed nutritional and phyto-therapy may offer an effective adjunct treatment for non-small cell lung cancer (NSCLC). The protocol included dietary and lifestyle modifications as well as the use of evidence-based nutraceuticals and herbs. The terminal cancer patient in question was diagnosed by his oncologist as being cancer-free after five months or so. According to ANMP (www.anmp.org.my), such a protocol treats, controls, and/or prevents chronic metabolic disorders such as cancer by impacting on the patient's physiological, hormonal, and/or immune functions.

Keywords: Non-small cell lung cancer, angiogenesis, metastasis, cachexia, anorexia, nutritional therapy, CT scans and chest X-rays, adjunct cancer therapy.

CASE PRESENTATION

Samuel Q., age 51 and a senior radiology technician employed at a major government hospital, was referred by a family friend to seek 'alternative' or complementary therapy(ies) for his end-stage non-small cell lung cancer (NSCLC) after conventional therapy failed to arrest its progression since it was first diagnosed at stage II some four months earlier. He suffered persistent cough, shortness of breath, wheezing and occasional chest pain. He was unclear as to what extent his accumulated occupational hazard and smoking contributed to his conditions. A senior physician at the same hospital had earlier diagnosed him as having bronchitis and alveolitis (inflamed alveoli or air sacs). After taking cough mixtures for two months and not recovering, he had a chest radiograph done which showed some abnormal mass in his lungs. A computerised tomography (CT)-guided biopsy confirmed his worst fear. Within two days he was placed on radiation cum chemotherapy. Although surgery would be a common way to treat adenocarcinoma lung cancer, he was advised otherwise. However, his lung malignancy progressed to the terminal stage after sixteen weeks. Besides reducing the number of cigarette smoked, he was told by his oncologist that he could "eat or drink almost anything" as he pleased. However, his appetite deteriorated within six weeks after he developed anaemia resulting apparently from damage inflicted to

his bone marrow by chemotherapy received. His serum ferritin level was significantly elevated as indicated on Table 1. With significant weight loss, he felt rather weak and feared that his cachexia (physical wasting syndrome) might worsen.

The patient had been a smoker for the past twenty years or so. He claimed that long working hours promoted his smoking habit and elevated his mental stress over the past decade when he took on a more senior position at his present hospital. There was no family history of lung cancer. However, he admitted that his dietary habits were far from ideal.

Consequently, the dietary plan recommended included these food items:

- (a) Cruciferous vegetables such as cabbages and broccoli as well as bean sprouts: steamed or lightly cooked, served two or more times daily. These may protect against cancer cells proliferation. Generally, the more quality vegetables are consumed by lung cancer patients, the longer they seem to live [1]. There seems to be a significant association between the highest flavonoid intake from vegetables and berries and reduced risk of developing lung cancer [2]. Sulforaphane, an isothiocyanate (sulfur-containing compound) present in some cruciferous vegetables, possesses anticancer properties [3].
- (b) Leafy vegetables and plant sterols and sterolins from sources such as rice bran, sesame seeds, sunflower seeds, pumpkin seeds, pearl barley,

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Table 1: Extracts from Serum Test Results for the First Six Months of 2011-2012

	Nov	Jan	Mar	May
CEA (<5ng/ml)	121.0	71.2	25.5	5.2
CA 125 (<35U/ml)	163	94	35	4.6
hs-CRP (<1mg/L)	30.5	12.2	10.9	3.5
HbA1c (<5.1%)	7.1	6.8	6.5	6.1
Fasting glucose (83mg/dl)	145	114	109	94
Cortisol (50-230ng/ml)	228	205	177	112
Free T3 (1.6-3.6pg/ml)	1.8	2.1	2.2	2.5
DHEA-S (0.32-3.80ug/ml)	0.49	0.87	1.12	1.45
Haemoglobin (>12.5g/dl)	9.3	10.6	11.5	11.9
TRBC (>4.5mm ³)	3.1	4.2	4.6	4.7
Serum Ferritin (20-300ug/L)	1254	1159	973	529
Lymphocytes (20-45%)	16	20	28	29
(25(OH)D (>30 ng/mL)	15	31	52	67

soy beans, and soy products: lightly cooked, two or more servings daily. There is growing epidemiologic evidence that increased intake of phytoestrogens are associated with decreased risk of lung cancer [4]. Fresh orange-yellow corn is a rich source of lutein [5], which protects against lung cancer [6]. Green leafy vegetables are rich in folate, which deficiency could predispose individuals toward developing lung cancer [7].

- (c) Pumpkin and carrot: steamed or lightly cooked, two or more servings daily. These are some of the richest source of alpha carotene, which protects against lung cancer. Extensive studies confirm free radicals are involved in the initiation and promotion of cancer [8-10]. Consequently, low plasma levels of dietary antioxidants are correlated with increased cancer mortality rates [11, 12]. Lung cancer risk can be significantly lowered in patients who consumed a diet high in a variety of carotenoids [13].
- (d) Red tomatoes or tomato paste added to cooking or soup daily. A diet high in tomatoes may reduce overall incidence of cancer by some 50% [14] including cancer of the lung [13]. Furthermore, the flavonoid lycopene can double the protective capacity of carotene [15].
- (e) Spices added to daily cooking. Onions contains quercetin, which like antiestrogen drug tamoxifen has similar affinity to type II estrogen binding

sites in NSCLC cell lines and hence it could regulate their growth [16]. Turmeric contains curcumin, which is able to positively affect gene transcription and to induce cancer cell apoptosis (programmed cell death) [17].

- (f) Nuts: raw or lightly cooked, served two or more times per day. Brazil nuts are very rich source of selenium, which deficiency increases the risk of fatal cancer [18]. However, due to its possible toxicity at very high dosage [19], a food source for this micro-nutrient is recommended. Selenium could offer a 50% reduction in overall cancer death rate [20] and could decrease lung cancer risk by up to 50% [21]. Just two quality Brazil nuts daily provide some 200mcg selenium sufficient to effect this risk major reduction [22]. A higher dietary intake of d-alpha-tocopherol and other mixed tocopherols such as from raw nuts and seeds could also cut the risk of lung cancer by 55% [23] and this vitamin is especially protective for smokers [24].
- (g) Fresh organic berries and fruits such as blueberry, kiwi, bell pepper and guava: two or more servings daily. These are some of the richest sources of ascorbic acid, which is negatively associated with most cancers [25].
- (h) Fish such as mackerel, wild salmon, cod, or anchovy: steamed and served daily. These fatty seafood are rich in omega-3 fats needed to reverse cachexia by inhibiting LMF (lipid

mobilizing factor) produced by the developing tumour, which causes direct breakdown of the patient's adipose (fat) tissues [26].

- (i) Food rich in L-tryptophan such as soy isolate, organic lean poultry, leafy vegetables, legumes, and seeds: lightly cooked and served two or more times per day. This essential amino acid is a precursor to the neurotransmitter serotonin, which is then converted to the neurohormone melatonin [27], which can enhance the patient's survival [28].

The beverages recommended were:

- (a) Yellow (Chinese) or Green (Japanese tea: three to four cups a day after meal. This beverage could prevent further development of tumours by blocking angiogenesis (growth of new blood vessels) [29]. It has chemo-preventive properties and it may reduce the dosage of chemotherapy drugs used by enhancing their cytotoxicity [30]. These teas could also block or reduce absorption of iron from food.
- (b) Malaysian cocoa, low fat, powdered: two or more cups a day. This beverage has as much or higher level of antioxidants than tea or red wine [31] useful for lowering oxidative stress.

The patient was advised to drastically reduce or avoid these food items:

- (i) Red meat and processed meat such as burgers, sausages, and canned meat. Intake of these meat sources may be positively associated with lung cancer, with individuals in the highest quintile of processed meat intake having a 16% elevated risk for lung cancer [32]. Besides being a generator of damaging free radicals and lipid peroxidation, excess iron from these meat sources promotes malignant cell DNA (deoxyribonucleic acid) replication.
- (ii) Bottled omega-6 polyunsaturated fatty acids such as those from corn oil, sunflower oil, safflower oil, and soy oil since these are easily oxidised as well as being used by the body to produce arachidonic acid and pro-inflammatory prostaglandins leading to accelerated tumour growth [33] or carcinogen-induced, pre-cancerous lesions [34]. However, our body needs small quantity of non-oxidised omega-6 for it to function efficiently.

- (iii) Refined sugars, soft drinks, fruit drinks, packaged fruit juices and refined carbohydrates such as toasted cereals, bread, instant breakfast cereals, tidbits, biscuits and noodles. Cancer or tumour cells are primarily sugar metabolisers [35] in an anaerobic environment. Hyperglycemia also increases the pro-inflammatory process and it adversely affects the patient's immune system [36].

The phyto-extracts prescribed for this patient were:

- (a) *Astragalus membranaceus extract* (standardised to 15% astragaloids): one gram three times a day. This root extract has immunologic benefits by stimulating macrophage and natural killer cell activity and inhibiting T-helper cell type-2 cytokines. It combines well with chemotherapy to enhance its effectiveness [37]. Astragaloids stimulate immuno-competent cells and can, depending on dosage used, reduce side effects in patients on chemotherapy [38].
- (b) *Artemisia annua* herbal tea: 4 cups a day. This widely-grown Tropical herb could be used together with elevated levels of transferrin in drug-resistant lung cancer [39]. Its active components such as triterpene and sesquiterpene are able to destroy cells in NSCLC [40]. When taken in sufficient dosages, their effectiveness may be comparable with other standard chemotherapy drugs used to combat cancer but with the distinct advantage of rather low toxicity [41].

These nutrients were prescribed to be taken with meals containing some fats/cooking oil:

- (1) *Co-enzyme Q10 (ubiquinone)*: 100mg three times a day since its levels tend to be significantly lower in patients suffering from cancers [42- 44].
- (2) *Malaysian wild pollens*: one teaspoon three a day. This supplementation is a rich source of multivitamins/minerals/ antioxidants/enzymes, which intake is associated with improved survival and quality of life in NSCLC patients [45]. In addition, NSCLC patients who take quality vitamin supplements and/or with higher circulating blood folate concentrations are more likely to be long-term survivors [46].
- (3) *Soy isoflavones (standardised to 25% genistein)*: 500mg three a day. Phyto-nutrient such as

genistein may reverse radio-resistance and chemo-resistance in cancer cells [47]. It induces apoptosis in NSCLC cells through a gene p53-independent pathway and, thus, acts as an anticancer agent [48]. Genistein in isoflavones antagonises estrogen-and androgen-mediated signaling pathways in the processes of carcinogenesis [47]. Furthermore, it has antioxidant properties and is a potent inhibitor of angiogenesis and metastasis [49]. Antiangiogenic therapy is a useful weapon in the treatment of solid tumours, including non-small cell lung cancer [50].

- (4) *Curcuma longa* extract (standardised to 90% curcumin with 2.5% pepper oil): 1.5g three times a day can inhibit cancer at its initiation, promotion and progression stages of development [51]. It is a cyclooxygenase-2 (COX2)-inhibitor and it possesses both anti-inflammatory and antioxidant properties [52]. It may substantially enhance chemotherapy drug Vinorelbine-mediated apoptosis in lung cancer cells [53].
- (5) *Quercetin/bromelain* 3:1: one gram three times a day to help inhibit cell proliferation and may induce apoptosis *via* caspase-3 cascade in the human lung cancer [54].
- (6) *Red grapes extracts* [standardised to 50% resveratrol (3,5,4'-trihydroxy-trans-stilbene)]: 500mg three times a day could enhance cell killing by conventional cancer treatment, with a sensitiser enhancement ratio of up to 2.2. Resveratrol enhances the radiosensitivity of lung cells by inhibiting the DNA transcription factor NF-kappaB [55]. This antioxidant is known to interfere with all three stages of carcinogenesis. It also possesses anti-angiogenic properties [56] and enhances functions of cellular mitochondria [57] for improved energy production.
- (7) *Shark cartilage* (powdered, hydrosoluble): two grams in gel capsules three times a day could slow or inhibit growth of tumors through anti-angiogenesis [58-61] with little or no toxicity. The link between angiogenesis and tumour progression is strong [62]. Bioavailable shark cartilage can inhibit proliferation of blood capillaries induced by tumours [63, 64].
- (8) *Vitamin D*: 4,000IU twice times a day. Its mechanisms of action include inhibition of cell

proliferation, stimulation of apoptosis, suppression of inflammation, and inhibition of tumour angiogenesis, invasion, and metastasis [65].

- (9) *Ultra Refined Anchovy Fish Oil* [Eicosapentaenoic acid (EPA) 500mg: docosahexaenoic acid (DHA) 200mg]: one gram gel capsule three times a day. This supplement may result in increased chemotherapy efficacy without affecting the toxicity profile and may contribute to increased patient survival [66]. Fish oil can improve the quality of life parameters in patients with NSCLC [67] and it is negatively associated with lung cancer [68]. Its EPA interferes with multiple mechanisms implicated in the pathogenesis of cachexia [69].

PATHOGENESIS

Cancer is characterised by uncontrolled cell growth that may consume the patient through malnutrition, organ failure or infection which it is capable of inflicting. NSCLC is an adenocarcinoma of the glandular tissue that begins in the cells that line the alveoli and produce substances such as mucus. It accounts for more than 80% of all lung cancer cases [70] with overall 5-year survival rate of just 16% [71]. While persistent cough and shortness of breath are common signs of NSCLC, the presence of chronic obstructive pulmonary disease can raise risk of lung cancer by up to 450% [72].

Cigarette smoke generates significant amount of oxidative stress and is widely viewed as the principal risk factor for the development of lung cancer [73-75] accounting for up to 90% of lung cancer incidence [76] since cigarette smoke contains more than 60 known carcinogens [77]. While some researchers claim that in the absence of cigarette smoking lung cancer would be a rare disease [78], about 50% of all women with lung cancer worldwide are non-smokers [79]. Perhaps, their higher body mass index raises their risk of malignancies [80]. The neoplastic process is also associated with inflammation [81] and occupational exposure to arsenic [82].

Second-hand smoke may cause lung cancer in life-long non-smokers. Risk increases with the amount and duration of tobacco inhaled. Similar to many other cancers, lung cancer is initiated by activation of oncogenes or inactivation of tumour suppressor genes [83]. There may be significant associations between Cytochrome P450 1A1 gene polymorphisms (CYP1A1)

and lung cancer [84, 85], while some studies found no significant associations [86]. However, lung cancer seems to be more strongly associated with Cytochrome P450 1B1 gene polymorphisms (CYP1B1) [87, 88]. Several other genetic polymorphisms are associated with lung cancer such as genes coding for interleukin-1 [89], apoptosis promoters such as caspase-8 [90], and DNA repair molecules such as XRCC1 [91]. People with these polymorphisms may be more likely to develop lung cancer after exposure to carcinogens.

Dietary factors have been proposed as potential risk modulators, with antioxidants vitamins A, C and E as having a protective effect [92]. Indeed, between 50% and 90% of all cancers could be prevented with skilfully and individually designed nutrition [93]. Many cancer patients die from malnutrition and/or infections both of which are linked to improper nutrition. Change in nutritional status is significantly associated with change in quality of life and change in lean body mass [94]. Cachexia not only shortens survival rates in patients, but also any positive response to chemotherapy is significantly reduced [66]. Even gradual weight loss has been identified as an indicator of poor prognosis in cancer patients [95]. Unfortunately, some 60% of lung cancer patients have already experienced a significant weight loss at time of their first diagnosis [96], defined as at least a 10% loss of body weight over a six months' period [97]. Proper nutritional therapy helps cancer patients maintain their appropriate body weight and nutrition stores while offering improved quality of life [98]. However, there may be other physiological issues affecting patient's nutritional status such as indigestion, hypometabolism, food malabsorption and obstructions [99].

Unfortunately, even with the best supportive care alone, patients with metastatic NSCLC have a median survival period of just 4 to 5 months and a one-year survival rate of approximately 10% [100]. Over the past two decades, chemotherapy for NSCLC has raised average survival of patients by just two months [101]. A recent study showed only 1.5% of Australian patients with NSCLC benefited from chemotherapy [102]. The need for an integrative therapy is evident.

SCREENING PITFALLS

Computed tomography (CT) scans and chest X-rays have been promoted for lung cancer screening, but studies have yet to show if such screening saves lives since they can be associated with significant false-positive rates [103]. Current evidence does not seem to

support lung cancer screening using chest radiography, sputum cytology, or even low-dose CT as studies investigating the application of these screening techniques have not reported improved survival benefits [104].

The exhaled breath analysis may be a promising tool [105]. It is a non-invasive approach for the detection of biomarkers associated with oxidative stress in the respiratory tract and has previously being shown to measure differences in levels of oxidative stress or inflammatory markers in patients with various respiratory conditions such as asthma, chronic obstructive pulmonary disease and bronchiectasis [106, 107].

Efforts are in progress to develop more noninvasive diagnostics for lung cancer using techniques such as detection of methylated tumour DNA in sputum, serum proteomics, mRNA or microRNA (endogenous RNAs involved in regulating gene expression) profiling in peripheral blood, and exhaled volatile markers [108]. Although each of these approaches has its own merits, none has yet passed the exploratory stage [109].

CASE DIAGNOSIS

Besides comprehensive history taking, diagnosis was greatly facilitated by the numerous test reports which the patient regularly sent in for review. Although in many similarly advanced NSCLC cases, chemotherapy seems to improve survival and is therefore widely used as first-line treatment [110], the patient in question seemed rather unwell for any further treatment using this approach. Indeed, he was advised by the hospital oncologist that he was free to use any other treatment option. Periodic blood tests showed an anaemic state and progressively elevated serum ferritin levels while his tumour protein markers CA-125 and CEA (Carcino-embryonic Antigen) levels rising rapidly over the past eight weeks or so. These are considered useful clinical markers for monitoring therapeutic outcome [111].

The high fatality is linked partly to the fact that the majority of the lung cancers are diagnosed at their late stages with the conventional treatment outcome being suboptimal [112]. Close to 70% of lung cancer patients present with locally advanced or metastatic disease at the time of their diagnosis [113].

The patient showed signs of cachexia, which was manifested as weight loss with significant depletion of

both his adipose tissue and lean muscle mass. This condition alone is estimated to be the immediate cause of death in up to 40% of cancer patients [114].

A major obstacle to this nutritional therapy is anorexia (loss of appetite or desire to eat), which the patient claimed was the result of his chemotherapy. This condition is a most common side-effect in individuals with widely metastatic disease [115] because of physiologic alterations in metabolism during carcinogenesis. It tends to hasten the course of cachexia [96].

The patient's tumour/cancer and inflammatory markers improved significantly, so was his diabetes, serum ferritin levels, and anaemia. The Oncologist's Report issued by the hospital dated May 19, 2012 indicated tumour remission to stage 1 and absence of malignancy. The patient continued with the recommended nutritional therapy, which outcome thus far suggested an effective adjunct therapy to initiate NSCLC remission. It was, however, uncertain if this natural therapy would achieve similar results for other terminal lung cancer patients. A large cohort of patients with similar conditions has to be studied to throw more light on the merits of offering this adjunct therapy on a wider scale.

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