

Naturopathic oncology: An emerging discipline

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As cancer care becomes increasingly interdisciplinary, the need for quality, regulated, and responsible integration of physician-level practitioners has become critical. Naturopathic oncology has risen to meet this calling. As an emerging specialty, it is poised to lead the swell of interest and information regarding nonconventional approaches to treat the person with cancer. As consumers and practitioners realize this surge, it is imperative such medicine be presented to the patient with diligence and accountability.

Naturopathic medicine is a distinct system of health care and distinguished by the principles that underlie and determine its practice. These principles are based on objective observation of the nature of health and disease, and are continually reexamined in the light of scientific advances.¹ Methods used are consistent with these principles and are chosen on the basis of patient individuality. Such principles are *vis medicatrix naturae* (the healing power of nature), *primum non nocere* (first do no harm), prevention, *tolle causam* (treat the cause), *tolle totum* (treat the whole person), and *docere* (doctor as teacher). Naturopathic oncology is simply the precepts of naturopathic medicine applied to the treatment of people with cancer.

The main focus of naturopathic oncology is enhanced survival and quality of life, for the person with cancer, through appropriate and effective integration of its practice into cancer care. Various factors have caused a large thrust toward alternative or nonconventional medicine in oncology. This is potentially dangerous for patient and doctor as the choice of a qualified practitioner comes into question. Regulation of the nonconventional oncology industry is tantamount to patient safety and efficacy. Due to the industry boom, *docere* has become increasingly important; that is, professional education, such as board certification in naturopathic oncology, knowledge of the principles and practice of oncology, clinical experience, and effective comanagement within a medical team. Moreover, education of the public is as important as education of physicians. As a practitioner of naturopathic oncology, I often need to make patients aware that ignorance is not bliss and address the following key educational issues.

- Just because something is natural, does not necessarily mean it is beneficial, effective, safe, or appropriate.
- Justify confidence in your practitioner: Ask questions about his or her experience and knowledge base.

- The Internet can be a source for inaccurate and deceptive information. Be careful what you read and make sure you research companies that make claims with little or no substantiation for their products. Often, to promote a product, companies will offer empty patient testimonials mysteriously bereft of critical information regarding the case and lack third-party independent literature.
- Many patients seeking naturopathic consultation object to conventional treatments for fear of toxicity—the adage commonly mentioned by such a cohort: “Chemotherapy and radiation are poisons and kill the good cells too.” Patients need to be educated about the rationale behind this and why such an effect is, in the end, appropriate.
- In medicine, it is difficult to “compare apples to apples.” Many times, patients with friends or family members who had a difficult time with, or ineffective consequences from, conventional oncology will refuse such approaches for themselves. Because most patients are not medically trained, they are unable to understand the uniqueness of their individual case.
- “Boosting” the immune system is not always the answer and might sometimes be inappropriate.

As a distinct discipline, naturopathic oncology seeks to integrate with the conventional model of patient care, not rise above it. I have found the majority of my patients are interested in the integrative approach to their treatment, allowing the beneficial interaction of therapies within such a paradigm. There have been numerous instances such co-treatment has resulted in an overall improved clinical outcome for patients. Based on my experience, I have found people with cancer who undergo an integrative treatment plan generally fare better than people who do not. Many patients, for instance, have to truncate or postpone their cytotoxic or radiotherapeutic treatments secondary to toxicity. Because this is not desirable for patient or physician, integrative treatment—by increasing toleration and decreasing the side effect profile of conventional treatments while not interfering with them—can prevent such interruptions and keep patients on the original schedules. Not only does this provide better quality of life for the patient, it creates an easier flow of office logistics as well. Furthermore, when patients understand such benefits there becomes less potential for them to draw away from standard therapy.

With its strengths, naturopathic oncology has its weaknesses. Most important is the general perception of the field by other physicians. Credibility is one obvious reason there has been a general reluctance on the side of traditional physicians to collaborate with naturopathic practitioners. Standards of practice are crucial to any discipline. Naturopathic physicians are the highest-trained practitioners with the broadest scope of practice in non-pharmacologic patient management. To answer the credibility issue, The Oncology Association of Naturopathic Physicians was established to create and maintain such standards. Its mission: to advance the philosophy, science and practice of naturopathic oncology. Its primary function is educational. The OncANP has two arms: the Oncology Academy of Naturopathic Physicians, a membership organization; and the American Board of Naturopathic Oncology, the body which will soon grant board certification in naturopathic oncology. Other functions of OncANP include development and maintenance of a repository of information and knowledge about naturopathic oncology, promotion of clinical research in naturopathic oncology, provision of advanced and continuing education in naturopathic oncology, facilitation of the standardization of instruction of oncology at naturopathic medical schools, and provision for a forum of enhanced communication among health care providers regarding naturopathic oncology. OncANP is a recognized affiliate of the American Association of Naturopathic Physicians, the national group representing the profession of naturopathic physicians licensed or eligible for licensing as naturopathic doctors.

Practicing naturopathic oncology

A philosophical pillar of naturopathic oncology is constant reverence for the beauty and mystery of the human experience. As a physician, I consistently strive for effective communication with my patients and those who accompany them to my office. In a sense, communication becomes a modality. A good treatment plan begins with educating the patient and the caregivers. When the basis of the conventional and adjunctive naturopathic treatment plan is well understood—not just from a mechanistic perspective, but how the specific plan applies to each individual patient—one will be more accepting of the plan. Such understanding and acceptance can potentially improve the efficacy of the treatment.

Each new patient or new problem presents a new and interesting mystery to engage. Take for instance a 62-year-old woman with an initial diagnosis of HER2-negative, estrogen-receptor positive breast cancer, stage 3 disease. Such a patient might undergo mastectomy and lymphadenectomy followed by chemotherapy and radiation. Tolerance for such a regime will depend partially on the following factors: age, performance status prior to treatment, overall life patterns, and which agents are employed.

One patient could have a more difficult time with a standard allopathic regimen than another; for instance, a first-line anthracycline-containing protocol. This is where naturopathic oncology can effectively aid conventional oncology for the better overall welfare of the patient, as exemplified above. On successful completion of the conventional oncology plan, naturopathic oncology becomes concerned with continuance of care to support the vitality of the patient and offers evidence-based recommendations to reduce the risk of recurrence. It is in this setting that the wholeness which is integrative oncology resides and where naturopathic oncology makes its first strides.

For example, fatigue is a common problem for people with cancer, regardless of their treatment regime, and it is not uncommon for patients to have increased fatigue after treatment begins. Fatigue can be debilitating and act as the cause for other complications of disease management as patients progress through their regime. In a population-based survey of people with cancer,² 78% of patients surveyed experienced fatigue; 61% felt the fatigue adversely affected their lives; 74% considered fatigue a symptom to endure; only 27% reported receiving treatment for fatigue.

Not only can fatigue be cumulative and increase over time,³ but cancer-related fatigue is the most frequently reported symptom of cancer and cancer treatment. It can significantly impair patients' quality of life.⁴ Given the data mentioned above combined with pure clinical experience, there is a high likelihood this patient will develop fatigue. Thus, treatment strategies to prevent or combat mental or physical fatigue should be employed, but tailored to the patients' mechanism of fatigue. Clinical experience shows fatigue is an inherently subjective and multidimensional condition, the causes of which can include anemia, micro- or macronutrient depletion, release of various metabolites from the tumor necrosis, cytokine disruptions, depression, muscle weakness, weight loss, disrupted oxygen supply, or disrupted sleep patterns.

As a result of this persistent, debilitating, and sometimes mysterious condition, people with cancer are turning to nonconventional solutions. Practitioners of naturopathic oncology investigate the situation from a physician-level perspective and integrate appropriate treatment measures to correct problems safely and effectively, without disruption to the traditional treatment plan. Also, by observing the clinical course of her disease and the unknowns that accompany it, this application of the principles of naturopathic intervention will allow ongoing individualization of her treatment plan.

Many practitioners and patients are familiar with the notion of nutritional supplementation, and this subject serves well to augment the description of naturopathic oncology. To resume the case at hand, an argument can be made for the use of the oral supplement, melatonin.

Melatonin has been available in the United States since 1988 and is probably best recognized as a sleep aid. Humans naturally produce and secrete melatonin via regulation by the circadian clock in the suprachiasmatic nucleus of the hypothalamus and under perception of darkness. In essence, melatonin is the chemical expression of darkness. The utility of melatonin as a therapeutic agent transcends its popularity as a sleep-inducing agent.

For the patient described in this article, melatonin could serve multiple functions. Should the patient be or become fatigued secondary to a sleep disturbance, melatonin might provide therapeutic benefit because multiple problems can arise when one begins to lack sleep. Second, should she receive an anthracycline, melatonin can provide her with hematological benefit: a 1999 Phase 2 study evaluated 14 women with metastatic breast cancer and persistent thrombocytopenia treated by weekly epirubicin at 25 mg/m² IV + 20 mg of melatonin given orally every evening starting 7 days prior to chemotherapy. Patients were considered evaluable when they received at least four cycles of chemotherapy. The induction phase with melatonin induced a normalization of platelet number in 9 of the 12 evaluable patients, and no further platelet decline occurred in chemotherapy.⁵ This clearly demonstrates how the co-administration of a nutritional supplement can help patients decrease treatment interruptions and realize chemotherapy when adverse side effects might otherwise obviate their appropriate treatment. Furthermore, upfront use of melatonin in this or similar scenarios might make the appropriate treatment more inviting to an otherwise skeptical patient. To boot, it is plausible to extend the utility of melatonin across the spectrum of valuable anthracyclines.

Continuing, melatonin could have additional benefits for this patient. The following argument not only has value for this case, but yields a general expression of what type of in-depth investigation and knowledge is generated about nutritional supplements. Melatonin has direct oncostatic properties. One known mechanism of malignant cell metabolism is via the EGFR/MAPkinase pathway. Such a pathway begins with the

metabolism of an omega-6 essential fatty acid, linoleic acid (LA). Metabolism of LA by 15-lipoxygenase yields 13-hydroxyoctadecadienoic acid, which can directly activate the EGFR/MAPkinase cascade leading to cell proliferation. However, when melatonin sits in its receptor on a cancer cell, it stimulates a G-protein coupled receptor leading to suppression of tumor cyclic adenosine monophosphate (cAMP) production. Suppression of cAMP leads to suppression of LA uptake by the tumor, and thus can markedly attenuate tumor growth. Additionally, LA can downregulate melatonin receptors on cells.⁶

To attend naturopathic medical school, applicants complete the same science premedical requirements required by conventional schools of medicine. Naturopathic medical schools are 4-year, graduate level, federally and regionally accredited institutions. The first two years are comparable to conventional medical school, emphasizing basic medical sciences. The second two years concentrate on clinical sciences, focusing on natural therapeutics. Students also receive supervised clinical training in outpatient clinics and preceptorships with other licensed physicians. At graduation, naturopathic physicians have completed more than 4,800 hours of naturopathic medical education.

The Naturopathic Physicians Licensing Examination is the standard used by all licensing jurisdictions for naturopathic physicians in North America. It includes five basic science exams—anatomy, physiology, pathology, biochemistry, microbiology and immunology—taken after the first two years of naturopathic medical school. The clinical science examinations are taken following graduation and include clinical and physical diagnosis, laboratory diagnosis and diagnostic imaging, botanical medicine, pharmacology, nutrition, physical medicine, homeopathy, minor office procedures, psychology and lifestyle counseling, and emergency medicine. Individual jurisdictions might give additional examinations in jurisprudence, homeopathy, acupuncture, obstetrics, and minor surgery.

Naturopathic physicians practice in virtually every state and Canadian province as well as many foreign countries, under various legal provisions. At this writing, U.S. states and territories that license NDs are Alaska, Arizona, California, Connecticut, District of Columbia, Hawaii, Idaho, Kansas, Maine, Montana, New Hampshire, Oregon, Puerto Rico, Utah, U.S. Virgin Islands, Vermont, and Washington State. The Canadian provinces that license NDs are Alberta, British Columbia, Manitoba, Ontario, and Saskatchewan.

Downregulation of melatonin receptors in this case could become problematic—not only from the adverse-effects aspect mentioned previously, but because of the potential role of melatonin as a participant in the hormonal realm. Take, for instance, the effects of melatonin on MCF-7 cells: Melatonin does not bind directly with an estrogen receptor (ER) or interfere with the binding of estradiol to the ER. But melatonin can downregulate ER- α expression on breast cancer cells, inhibit binding of estradiol-ER complex binding to the estrogen response element in the DNA, and counteract the stimulatory effect of estradiol on

cell invasiveness on MCF-7 cells.⁷ Melatonin has also been shown to inhibit aromatase.⁸ Furthermore, women with ER+ breast tumors can have low melatonin levels compared to controls. The lower those levels, the higher the number of estrogen receptors on their cells.⁹ Additionally, when estrogens are bound to the ER, adenylate cyclase is activated, thereby inducing production of cAMP which can be counteracted by melatonin as above.⁷

The knowledge base on melatonin provides an excellent framework from which to derive integrative protocols. Supplementation of the capsule form of melatonin certainly makes sense, and a dietary program would certainly be developed for this particular patient which would restrict the intake of LA and include foods, such as red cherries, high in melatonin.

A similar argument can be made for the use of coenzyme Q₁₀ (CoQ₁₀) supplementation for this case. It is common industry knowledge that anthracyclines can cause damage to the myocardium, hence the reason behind the functional testing of the organ prior to such therapy. The mechanism by which has now been elucidated by laboratory methodology and elegantly described in a recent publication.¹⁰ I paraphrase it here: Unique to cardiac mitochondria is an NADH dehydrogenase present at the cytosolic side of the inner membrane; other tissue mitochondria only have such NADH dehydrogenase complexes present on the inner or matrical aspect of the inner membrane. To come in contact with the inner mitochondrial matrix a molecule would have to be lipophilic—and doxorubicin is not. Because doxorubicin is allowed entrance to the mitochondrial cytosol, when in the cytosol of a cardiac mitochondrion it will encounter the cytosolic NADH dehydrogenase. Such an encounter will reduce doxorubicin to its semiquinone. This semiquinone undergoes auto-oxidation to form the fully reduced dihydroquinone. These reactions create a destabilized metabolite and eventually a sugar moiety is cleaved forming the doxorubicin aglycone. The highly lipophilic aglycone penetrates the inner membrane and displaces CoQ₁₀ from its place in the electron transport chain (ETS). In the ETS, CoQ₁₀ is normally an electron acceptor and donor, whereby it transfers an electron from complex I and II to complex III. However, the aglycones, instead of transferring to complex III, transfer electrons directly to molecular oxygen, thereby creating superoxide radicals. Through a series of reactions, the superoxides are converted into hydroxyl radicals which places the cardiac myocytes in an environment of high oxidative stress. This, in addition to the impaired energy production capacity of the cell brought on by the interrupted ETS, likely accounts for the cellular damage and noted post-doxorubicin EKG changes.

Conclusion

When provided with enough proper cofactors, the human body can produce its own CoQ₁₀. But this

capacity becomes inversely proportional with age. Thus, in keeping with the precepts of naturopathic medicine and those of general cardiac health for a populous of patients with advancing age, dietary strategies replete with foods high in CoQ₁₀ are pragmatic. This of course would ensure better chronic, low-level CoQ₁₀ availability but might not be adequate to safeguard against an acute “hit” such as that experienced by the heart in the presence of doxorubicin. Thus begs the notion of CoQ₁₀ supplementation as part of an integrative, doxorubicin-containing protocol. Which, because CoQ₁₀ is an antioxidant, begs the further question and well-known argument: Should antioxidants be used alongside chemotherapy? Although this article is not the forum to introduce a subject so deserved of a weighted colloquy, one would wonder if co-administration of CoQ₁₀ could prevent or reduce cardiotoxicity while preserving or enhancing the anthracycline effect. If so, perhaps higher dosages could be given with improved responses.

Hence the notion “from great debates can come great medicine.” Great medicine is defined by its benefit to humankind whether it be improved survival time, decreased pain, improved quality of life, or some other measurable and meaningful instance. And greatness often starts with hypotheses represented by mere paper and culture dish which, when taken to the clinic, become live with rich personal interaction. Such interaction brings excitement to the future of the art of medicine delivering one from the boring rote-dom of yawful prescribing. A deliverance that once realized and once actualized can foster greatness. For greatness is born of great deeds. And great deeds in medicine are born of raw physician talent embraced by the unwavering courage of our patients. It is in this realm that naturopathic oncology awaits to transcend its mystery and emerge as a true discipline. ♦

References

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