

Clinical Pearls

This column is featured in every issue of the Cancer Strategies Journal, edited by Dwight McKee, MD. Do you have a Clinical Pearl that you would like to share with our readers? Please forward them to editorial@cancerstrategiesjournal.com.



All of the bulleted points below are from the integrative cancer medicine practitioners who participate in the Mederi Foundation Monthly Roundtable discussions...

- In treating patients with metastatic cancers and who have high ceruloplasmin levels, we may need to consider using TM (compounded ammonium tetrothiomolybdate) during our treatment, to limit the angiogenic effects of copper. Of course, it is advisable that when we use TM in such settings, that the patient be on a good food and oral herbal and supplement program. If patients are receiving chemotherapy, the ceruloplasmin (Cp) should not be lowered below the low normal range (18-20 mg/dl), otherwise bone marrow may not recover well enough from chemotherapy treatments. Lowering Cp to low normal can improve chemosensitivity of tumors; this has been most well documented for sensitivity of ovarian cancer to platinum based chemotherapy. (ref)
- In treating patients who are her2positive, with trastuzumab (Herceptin®), consider using more olives and sulfurophane-based foods in the diet (brassica vegetables, onions, garlic). Resveratrol, honokiol, quercetin, red clover isoflavones and soy isoflavones also help to prevent tumor resistance to trastuzumab from emerging, by helping to maintain expression of the important tumor suppressor gene known as PTEN.
- When we add lapatinib as an oral agent in treating her2neu positive cancers, the advantage is that lapatinib crosses the blood-brain barrier better than does trastuzumab, or TDM-1. TDM1 is Herceptin bound to a cytotoxic agent derived from a tree that grows in harsh environment. Lapatinib is a tyrosine kinase inhibitor with many applications in her2neu positive cancers. Also, lapatinib also helps with her1 or EGFR receptor positive cancers, as it is a dual EGFR and Her-2/neu inhibitor.
- Putting 1 tsp of glycine in tea in treating patients with cancer is sometimes very useful, not only because it helps in building glutathione, but also because glycine lowers tumor growth, and it helps build GABA, to help relax overanxious patients who by this anxiety are contributing to adrenal stress. Use the glycine with chamomile tea, and consider adding rose petals, particularly useful at bedtime.
- In patients with cancer who have high CRP and/or sed rate, make sure to watch the 1,25 (OH) Vitamin D level as well as the 25 (OH) Vitamin D level if we are adding Vitamin D to their oral program. High 1,25 Vitamin D levels can lead to hypercalcemia and its resultant complications like kidney stones. Herbs such as celery root, hydrangia, and gravel root are very useful in these situations, to ionize the calcium and thus help prevent such complications, but its best to avoid high 1,25 di-OH vitamin D levels and hypercalcemia.
- Squamous cell cancers are not highly sensitive to chemotherapy. The response rate is not uncommonly under 50%. It is advisable to check EGFR expression levels on biopsy slides and if positive, to consider the use of weekly cetuximab in-

fusions (an anti-EGFR monoclonal antibody), along with a strong oral program, in such patients. Most of these patients, especially with cervical cancers, have upregulated COX-2 and mTor pathways, so consider botanicals and food changes to address these imbalances, to make therapies more effective.

- IGF-1 pathways often drive squamous cell cancers, so make sure to use good insulin regulating herbs, nutrients, and foods in such patients: bitter melon, cinnamon in good amounts (several grams a day), gymnestre sylvestre, alpha lipoic acid, berberine, and jerusalem artichokes; for patients with excess body fat, exercise and a whole foods diet with no sugars, and a small amount of low glycemic carbohydrates, rich in proteins and healthy fats is also essential for controlling insulin and IGF-1 levels.
- What foods are good to add to a patient program in order to strengthen lung energy? Pears and persimmons. Also root vegetables, miso, and mushrooms build lung energy. This is important in patients with primary lung cancers or metastatic lung cancers. Herbally, ella champagne (sp?) is often indicated as a primary herb in a patient herbal formula. If patients are melancholic, also consider adding cordyceps, licorice, mullein, and small amounts (1-2%) of pulsatilla and bryonia
- If a patient has a tendency to have a lot of phlegm, consider, beyond eliminating dairy foods, the following: serrapeptidase enzyme, as well as N-acetyl cysteine, a demulcent tea, and inulin, as expectorants
- In spite of what a patient thinks and feels, or what they have been told by their oncologists, never assume that the patient is going to pass on before doing a thorough patient evaluation and research. Look for vitality and the spark of will to live, in their eyes, as well as their digestive power.

EEG Biofeedback Has Potential for 'Chemo-Brain'

Data from a pilot study support the hypothesis that EEG Biofeedback has potential for reversing or reducing the cognitive sequelae of cancer treatment ('chemo-brain'). 23 women previously treated with chemotherapy for breast cancer, and with documented cognitive impairment received two 33-minute neurofeedback training sessions each week for ten weeks. Neurofeedback was delivered via Zengar NeuroOptimal Professional equipment, a systemic approach that provides concurrent feedback on EEG activity in 16 standard time-frequency envelopes.

Larger-scale studies with placebo groups are needed to confirm this result and to explore whether EEG biofeedback, administered concurrently with cancer treatment, might reduce the incidence or severity of cognitive impairment.

Dr. Ross reports consistently positive results with this modality in his practice

Ref: Efficacy of EEG Biofeedback in Addressing Cognitive Dysfunction in Cancer Survivors. Jean Alvarez, David L. Granoff, Allan Lundy

From Warren Ross, MD, Ellicott City, MD

GBM and the Ketogenic Diet

Management of GBM has been difficult using standard radiation with temozolomide. The ketogenic diet is used commonly to treat refractory epilepsy in children and, when administered in restricted amounts, can also target energy metabolism in brain tumors. We report the case of a 65-year-old woman who presented with progressive memory loss, chronic headaches, nausea, and a right hemisphere multi-centric tumor seen with magnetic resonance imaging (MRI). Following incomplete surgical resection, the patient was diagnosed with glioblastoma multiforme expressing hypermethylation of the MGMT gene promoter.

Prior to initiation of the standard therapy, the patient conducted water-only therapeutic fasting and a restricted 4:1 (fat: carbohydrate + protein) ketogenic diet that delivered about 600 kcal/day. The patient also received the restricted ketogenic diet concomitantly during the standard treatment period. The diet was supplemented with vitamins and minerals. Steroid medication (dexamethasone) was removed during the course of the treatment.

After two months treatment, the patient's body weight was reduced by about 20% and no discernible brain tumor tissue was detected using either FDG-PET or MRI imaging. Biomarker changes showed reduced levels of blood glucose and elevated levels of urinary ketones. MRI evidence of tumor recurrence was found 10 weeks after suspension of strict diet therapy.

This is the first report of confirmed GBM treated with standard therapy together with a restricted ketogenic diet. As rapid regression of GBM is rare in older patients following incomplete surgical resection and standard therapy alone, the response observed in this case could result in part from the action of the calorie restricted ketogenic diet. Further studies are needed to evaluate the efficacy of restricted ketogenic diets, administered alone or together with standard treatment, as a therapy for GBM and possibly other malignant brain tumors.

Nutr Metab (Lond). 2010 Apr 22;7:33. doi: 10.1186/1743-7075-7-33. Metabolic management of glioblastoma multiforme using standard therapy together with a restricted ketogenic diet: Case Report. Zuccoli G, Marcello N, Pisanello A, Servadei F, Vaccaro S, Mukherjee P, Seyfried TN.

From Mark Bricca ND, L.Ac., Ashland, OR

Endometriosis Is An Inflammatory Syndrome

I have had great success using Inflammaway, Honokiol and Cell Guardian (Natura Health Products), limiting estrogenic foods and instructing patients about environmental chemicals, personal care products that contain estrogenic chemicals.

From Nalini Chilkov L.Ac. OMD, Santa Monica, CA

Fasting As Part Of Cancer Treatment

Short-term fasting (48 hours) was shown to be effective in protecting normal cells and mice but not cancer cells against high dose chemotherapy, termed Differential Stress Resistance (DSR), but the feasibility and effect of fasting in cancer patients undergoing chemotherapy is unknown. Here we describe 10 cases in which patients diagnosed with a variety of malignancies had voluntarily fasted prior to (48-140 hours) and/or following (5-56 hours) chemotherapy. None of these patients, who received an average of 4 cycles of various chemotherapy drugs in combination with fasting, reported significant side effects caused by the fasting itself other than hunger and lightheadedness. Chemotherapy associated toxicity was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) of the National Cancer Institute (NCI). The six patients who underwent chemotherapy with or without fasting reported a reduction in fatigue, weakness, and gastrointestinal side effects while fasting. In those patients whose cancer progression could be assessed, fasting did not prevent the chemotherapy-induced reduction of tumor volume or

tumor markers. Although the 10 cases presented here suggest that fasting in combination with chemotherapy is feasible, safe, and has the potential to ameliorate side effects caused by chemotherapies, they are not meant to establish practice guidelines for patients undergoing chemotherapy. Only controlled-randomized clinical trials will determine the effect of fasting on clinical outcomes including quality of life and therapeutic index.

Safdie, Dorff, Quinn, et al. Fasting and cancer treatment in humans: A case series report. Aging. 2009 December; 1(12): 988-1007.

From David Lerner L.Ac., Olympia, WA

Treatment of Multiple Myeloma By Herbal Formula, Herb Isolates and Injection

Multiple myeloma (MM) is one of several diseases that are collectively known as plasma cell dyscrasias. In general, the term myeloma refers to cancer of special types of white blood cells called plasma cells (Medifocus, 2013). Prototypic drugs thalidomide, bortezomib, and lenalidomide have been used for the treatment of this disease (Raab et al, 2009).

TCM adjunctive approaches have been shown of value. Oral administrations of Huang-Lian-Jie-Du-Tang along with compounds isolated from the herbs have been shown to have an anti-proliferative effect (Ma et al, 2005). *Scutellaria baicalensis* (S.B.), a key herb, inhibits myeloma cell lines (Kumagai, et al, 2007) and contains a number of compounds. SB isolates Wogonin (Zhang et al, 2007), Baicalein (Liu et al, 2009), Baicalin (Huang et al, 2012), and Berberine (Wu et al, 1998; Hu et al, 2013) have been shown to inhibit growth through apoptosis and suppress NF- κ B nuclear translocation.

Simultaneous use of IM Artesunate (ART) increases the efficacy of the herbs and isolates. ART is a potential drug for treatment of multiple myeloma (Holien et al, 2013) and can block ERK1/2 activation, down-regulate VEGF and Ang-1 expression and inhibit angiogenesis (Chen et al, 2010). ART decreased the level of NF- κ B p65 protein in the nucleus, while increased the level of I κ B α protein in the cytoplasm. (Li et al, 2009).

While the combinations described have not been trialed, the protocol has been clinically effective and non-toxic.

Formula:

- Huang Lian (*Rhizoma Coptidis Recens*)
- Huang Qin (*Radix Scutellariae Baicalensis*)
- Huang Bai (*Cortex Phellodendri*)
- Zhi Zi (*Fructus Gardeniae Jasminoidis*)

Chen H, Shi L, Yang X, et al. Artesunate inhibiting angiogenesis induced by human myeloma RPM18226 cells. Int J Hematol. 2010 Nov;92(4):587-97. doi: 10.1007/s12185-010-0697-3.

Holien T, Olsen OE, Misund K, et al. Lymphoma and myeloma cells are highly sensitive to growth arrest and apoptosis induced by artesunate. Eur J Haematol. 2013 Jul 22. doi: 10.1111/ejh.12176.

Hu HY, Li KP, Wang XJ, et al. Set9, NF-kappaB, and microRNA-21 mediate berberine-induced apoptosis of human multiple myeloma cells. Acta Pharmacol Sin. 2013 Jan;34(1):157-66. doi: 10.1038/aps.2012.161.

Huang Y, Hu J, Zheng J, et al. Down-regulation of the PI3K/Akt signaling pathway and induction of apoptosis in CA46 Burkitt lymphoma cells by baicalin. J Exp Clin Cancer Res. 2012 May 20;31:48. doi: 10.1186/1756-9966-31-48.

Kumagai T, Muller CI, Desmond JC, et al. Scutellaria baicalensis, a herbal medicine: Anti-proliferative and apoptotic activity against acute lymphocytic leukemia, lymphoma and myeloma cell lines. Leukemia Research 31 (2007) 523-530

Li S, Xue F, Cheng Z, et al. Effect of artesunate on inhibiting proliferation and inducing apoptosis of SP2/0 myeloma cells through affecting NF-kappaB p65. Int J Hematol. 2009 Nov;90(4):513-21. doi: 10.1007/s12185-009-0409-z.

Continued at www.cancerstrategiesjournal.com/ReferencesVolume1Issue4.pdf

From Daniel Weber Ph.D., Sydney, Australia