Successful Treatment of Oxaliplatin-Induced Peripheral Neuropathy with Naturopathy
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First line chemotherapy regimens for colon cancer include FOLFOX (leucovorin, 5-fluorouracil, and oxaliplatin). This combination of medications, more significantly oxaliplatin, has been linked to peripheral neuropathy. For patients with previous active lifestyles, peripheral neuropathy can cause a decreased quality of life. In addition, there are many other side effects of FOLFOX including nausea, diarrhea, and weight loss. Significant peripheral neuropathy in patients undergoing FOLFOX therapy may occur spontaneously after oxaliplatin infusions are discontinued. Current literature supports the need to clinically evaluate peripheral neuropathy in patients undergoing FOLFOX chemotherapy, but few studies have shown an effective way to treat the peripheral neuropathy experienced by many patients.1,2 Standard of care for chemotherapy-induced peripheral neuropathy (CIPN) includes dose reduction and/or discontinuation of the suspected neurotoxin. Such dose-limiting effects are poor prognostic indicators and often negatively affect a patient’s long-term survival.
Patient H is a 43-year-old male diagnosed with stage IV colon cancer in December 2003. After H was diagnosed he was treated with 20 cycles of FOLFOX (December 2003–October 2004). The FOLFOX was tolerated moderately well. The oxaliplatin dose was 85 mg/m² throughout the 20 cycle course. In February 2004, before the fifth cycle of FOLFOX, the oncologist referred H to the Integrative Medicine clinic; the referral was due to H’s desire to continue with the chemotherapy protocol with goals including weight optimization and alleviation of side effects from the medications causing decrease in daily activities and decreased quality of life.

The Integrative Medicine clinic is staffed with an internist, naturopathic doctors, acupuncturists, massage therapists, and a nutritionist. H saw Dr. Ken Weizer, a board certified Naturopathic Doctor (ND). H presented with chief complaints of weight loss over two months totaling 10% of body weight, nausea, diarrhea, and peripheral neuropathy. On exam, chemotherapy-induced peripheral neuropathy (CIPN) was assessed as paresthesia in the fingertips for 2–3 days post chemotherapy before complete resolution. However, the CIPN by the ninth cycle of FOLFOX was lasting a full week after chemotherapy treatments and the paresthesia progressed to include all fingers and toes. The CIPN subsequently progressed from the tips of the fingers and toes to involving the entire digits with mild to moderate pain and was affecting the patient’s activities of daily living (ADL). The CIPN associated with oxaliplatin is cumulative and dose dependent. The CIPN was graded using a subjective pain scale and through patient interview with specifics determined regarding location, duration, and effects on ADLs. There is controversy regarding the most sensitive scale to evaluate peripheral neuropathy, and many of the scales do not take into account ADLs, therefore in H’s case, no objective scale was used to evaluate the neuropathy.

H was given a protocol to follow with goals of alleviating side effects; the modalities included nutrition, hydrotherapy, supplements, and exercise. A whole foods diet was implemented for weight optimization. The diarrhea was treated with eating organic yogurt and kefir as a source of probiotics. L-glutamine powder 7 g/d was recommended for rebuilding the gut as well as treating diarrhea. Zinc gluconate 20 mg/d was added for the restoration of taste. The CIPN was treated with Neurosol at one softgel twice daily. The hydrotherapy consisted of home treatments including warming socks and gloves nightly to increase peripheral circulation and Epsom salt soaking baths twice weekly. The exercise protocol was a daily walk for 20 minutes.

When H presented for the 11th cycle of FOLFOX, the peripheral neuropathy had completely resolved as determined by patient interview before administration of the chemotherapy. At this point H had received a cumulative dose of oxaliplatin of approximately 850 mg/m². The dose-limiting neurotoxicity occurs with a cumulative dose between 780 and 850 mg/m² in oxaliplatin treatment. At no point during the remaining nine cycles (cycles 12-20) did H present with complaints of CIPN. The CIPN treatment of Neurosol and home hydrotherapy was continued throughout the FOLFOX treatment and discontinued after the last cycle of FOLFOX, October 2004. (Figure 1)

H had excellent partial remission and was switched to irinotecan and bevacizumab, and later cetuximab. The partial remission continued through June 2005. Unfortunately, by October 2005 the cancer was found to be progressive as evidenced by CT scan and CEA (carcinoembryonic antigen) levels rising. At this point, a second round of FOLFOX (13 cycles) was started April 2006. The oxaliplatin dose was 85 mg/m² with a cumulative dose of approximately 1000 mg/m². On two of the cycles the oxaliplatin dose was reduced to 75 mg/m² due to neutropenia, but not reduced due to neurotoxicity or CIPN. H resumed a similar protocol as for the first FOLFOX treatment, including the same diet therapy of whole foods and yogurt, and a meal of organic liver and onions 1-2 times weekly to guard against chemotherapy-induced anemia. Other therapies included Epsom salt baths, Neurosol (one softgel bid), omega-3 fish oil capsules, and one tablet of silymarin 80% bid (equal to 56mg silymarin/tab).

The use of silymarin is currently in question with regards to potential interactions from hepatic metabolism of other medications the patient may be on. The specific concern is that silymarin modulates the activity of cytochrome P450 enzymes and may increase the levels of toxic medications in a patient. The silymarin was prescribed for liver health due to the progressive metastatic cancer in the liver. The FOLFOX combination contains three medications, none of which are hepatically cleared, so the use of silymarin was not contraindicated in this patient.

Since H began naturopathic integrative care his weight stabilized and was considered healthy for his height (+/- 5 pounds) for 15 months while undergoing chemotherapy. In addition, the patient experienced a complete elimination of the CIPN. The Neurosol was discontinued after recovery from the neuropathy and this symptom had not returned.
as of December 2006. H has had regular bowel movements without significant constipation or diarrhea with the exception of chemotherapy days when he experienced one day of diarrhea that affected daily activities. This is a reduction from seven days of diarrhea post chemotherapy before initiating integrative medical care.

In August and September 2006, while undergoing FOLFOX treatments, H enjoyed fishing trips to British Columbia and a vacation to Puerto Vallarta. H has had enough energy to be able to exercise and take pleasure in life. After the 13th cycle of FOLFOX in October 2006, H met with the oncologist and in a review of symptoms had no fevers, unusual anorexia, weight loss, peripheral neuropathy, unusual aches or pains, anxiety, depression, or rashes.

There are limitations to this case report. No validated tools were used to objectively evaluate the quality of life, ADLs, and CIPN. The data was retrieved through interview and chart notes from the physicians caring for H. In summary, during the naturopathic care that the patient received, H experienced a reduction in all major side effects from the chemotherapy, increased quality of life as evidenced by the ability to not only leave the house, but also to take vacations and engage in hobbies that were previously difficult.

**DISCUSSION**

This case provides evidence that both an MD and an ND can work together with excellent results and have a synergistic relationship. There was a transparency of care as communication between the two physicians was always open. The oncologist was able to provide the chemotherapeutic agents for the cancer at the optimal dose due to the adjunct care. Maintaining the optimum dose is ideal if the tumor is responding, and physicians may be discouraged in reducing the dose due to toxicity. The ND, with simple therapeutics, was able to maintain H’s vitality as the cancer treatments progressed.

**REFERENCES**


4. Each Neurosol softgel is composed of gamma-linoleic acid (GLA) from borage seed oil 160mg, vitamin A from beta-carotene 2000 iu, vitamin C from Ultrapotent C (Metagenic product) 133mg, niacin (as niacinamide ascorbate) 10mg, vitamin B6 as pyrrololine HCl 25mg, folic acid as 5-formyl tetrahydrofolate 267mcg, vitamin B12 as methlycobalamin 167mcg, and intrinsic factor (porcine) 6.7mg. For more information see www.metagenics.com. Accessed May 6, 2008.


At a cumulative dose of 1170 mg/m², oxaliplatin neurotoxicity in the form of sensory symptoms with functional impairment occurs in about 50% of patients.8 The neuropathy can present in two distinct forms. The first is an acute neuropathy triggered by cold characterized by peripheral nerve hypersensitivity which is reversible after cessation of treatment. The second form is a chronic form which is similar to other platinum-based chemotherapeutic agents, however the onset is more rapid and produces distal dysesthesias and paresthesias of gradually prolonged duration that occur between treatment cycles with increasing intensity with the cumulative dose. 9 10 H had both forms of CIPN.

Although there was a variety of therapeutics in the treatment protocol, Neurosol was the only supplement solely directed at the CIPN. Since Neurosol is not under FDA approval, many medical doctors may be wary of advising patients of its use. Further, as a supplement, many insurance companies will not compensate the patient for the cost of natural health products. Another drawback to using these products is that it may also be difficult to locate a specific supplement. A bottle of 60 capsules can be purchased for an average price of $36.00.