

Nutritional Supplementation and Fatigue in a Patient with Adenoid Carcinoma

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Abstract: Fatigue is commonly experienced by a number of patients with differing types of cancers who are undergoing various treatments including radiotherapy. While the etiology of radiation induced fatigue is not known, there is much speculation as to its causes and as a result, its treatment. The case of a 43-year-old, otherwise healthy male, recently diagnosed with adenoid carcinoma is evaluated and reviewed. After diagnosis, he underwent surgery to remove the tumor, and received a total amount of 6000 cGy for 42 days and initiated nutritional supplementation with Propax. His radiotherapy was well tolerated with no significant adverse events. Based on patient surveys, his fatigue scores significantly improved even as his radiation treatments progressed. Patient diaries report him to be optimistic and in otherwise good health. He has been able to return to a lifestyle similar to that before diagnosis of his cancer. Although randomized, blinded, clinical studies are pending, nutritional manipulation may improve the quality of life for patients by decreasing the fatigue and malaise commonly encountered in cancer patients.

Introduction

Fatigue is a common complaint of oncology patients who undergo radiotherapy⁽¹⁻⁵⁾. Even though it commonly occurs, it is not well understood and there are numerous theories regarding its severity and prevalence in a patient's daily routine⁽⁵⁾. While as many as 32% of cancer patients report that fatigue adversely affects their lives, it is recognized by only about 76% of oncologists⁽⁵⁾. Of more importance, both patients and physicians report fatigue to be a more prominent adverse event than pain. This is especially interesting given that 74% of patients believe fatigue is an untreatable adverse event that must simply be endured⁽⁵⁾.

The factors that affect the level of fatigue in patients with cancer have not been formally recognized. However, Smets et al evaluated fatigue in patients undergoing radiation and compared it with fatigue in the general population. Both disease-free and cancer fatigue was significantly associated with differences in gender, physical distress, pain, sleep quality, functional disability, psychological distress and depression⁽⁶⁾. Thirty-four percent of cancer patients reported fatigue to be more severe than was expected and 39% listed fatigue as one of the most problematic symptoms of the radiation treatments⁽⁶⁾.

As evasive as its etiology, recognized or approved treatments appear to be even more illusive. It is not surprising then that healthcare providers continue to struggle with a variety of quality of life issues (including fatigue). As a result some clinicians may consider nutritional supplements to increase the body's inherent defenses against disease, medications, and the assault of aggressive radiation.

Objective

To evaluate the effectiveness of nutritional supplementation for decreasing fatigue in an adenoid cystic carcinoma undergoing surgery and radiation.

Case History

A previously healthy 43 year old male was diagnosed in January 1999 with asymptomatic adenoid cystic carcinoma. In February he complained of nasal stuffiness and a lump on the side of his nose. CT of chest, abdomen, and pelvis were negative for metastasis. At this time aggressive excision with reconstruction was recommended. Alternative treatments included radiotherapy and hyperthermia.

He acknowledged an anaphylactic allergic reaction and rash to penicillin. Medications included alprazolam and Ambien at bedtime as needed. He denied any significant past medical history. However, past surgical history included PRK to both eyes approximately 1 year ago, bilateral inguinal hernia repair at 10 years of age, and correction of undescended testicle at 12 years of age. It is not known if the undescended testicle resulted from the hernial surgery. He denied tobacco use and reports occasional alcohol consumption. Family history significant for controlled Chronic Lymphocytic Leukemia for his 70 year-old father.

Initial physical examination acknowledged a well developed, well nourished and vigorous appearing male in no acute distress. The patient reported his energy level was appropriate and experienced no headache or migraines. He had no complaints of blurred vision, photophobia, or diplopia. However, he did report visual changes when looking upward to the extreme. He had no hearing changes, shortness of breath, chest pain, or changes in appetite or bowel habits. There was no report of neuromuscular pain or weakness.

His skin texture and color were normal without rash, cyanosis, or petechiae. External examination reported a atraumatic, normocephalic patient without deformity. There was no lesions or blood noted in the oral cavity. Additionally, no jugular venous distension of the neck was noted. Evaluation of lymph nodes reported no submandibular, cervical, or supraclavicular adenopathy. Review of cardiac, respiratory, and neurologic systems were insignificant.

A CT and MRI of the head and neck performed in January 1999 confirmed a 3 - 4 cm mass that filled most of the right nasal cavity with extension through to the subcutaneous skin of the face. Although the orbit itself appeared normal, initial invasion of the orbital bony floor was suspected. In addition, there was extension into the maxillary sinus. He was diagnosed with adenoid cystic carcinoma (Stage T4N0M0) of the right maxillary sinus.

In February, patient underwent facial degloving and surgical excision of the tumor. During the surgery, a gingivobuccal incision from the left to right premolars and down to the maxillary bone was performed. A Dingman elevator was used to elevate the periosteum and soft tissue on the left and right sides of the anterior face of the maxilla carefully preserving the infraorbital nerve. The margin of the piriform aperture was identified and incisions were made to enter the nasal floor and midline across the nasal spine. Since CT had revealed tumor invasion into the nasal bone and frontal processes of the maxilla, visualization of the septum was obtained. However, examination of the mucoperichondrium and cartilaginous septum confirmed the absence of tumor invasion into the septum. At this time, osteotomies, similar to those performed during medical rhinoplasty, were performed. The tumor was then removed without difficulty and hemostasis was controlled through bipolar cautery. Multiple sections were obtained for

biopsy. Microscopic description reported lamellar bone infiltrated by adenoid cystic carcinoma with prominent desmoplastic reaction. The neoplasm was composed mostly of monotonous round blue cells that revealed ovoid nuclei with vesicular chromatin. The cytoplasm was present with closely packed cells arranged in large solid sheets and nests. There were scattered tumor nests with several small lumina formations, some with central necrosis. Scattered mitotic figures were also present.

Laboratory values (potassium, sodium, chloride, CO₂, BUN, serum creatinine, albumin, total bilirubin, alk phos, and AST) were normal. However, glucose levels were elevated on 2 consecutive days while protein and calcium were decreased. Complete blood count summaries can be found in figure 1. Only hemoglobin and hematocrit reductions appeared slightly abnormal.

The septal bone was harvested for reconstruction surgery post evaluation of tissue biopsies. The final analysis of the frozen sections was negative for tumor. After surgery he was transferred to the medicine floor with a nasal splint. He did very well post operatively. By day 2 he was tolerating a soft diet. He had minimal edema on day 3 and was able to tolerate oral foods well. He remained afebrile and was discharged home on hydrocodone for pain and clindamycin empirically for infection. Once he was at home, he began nasal treatment with steam and irrigation.

He tolerated his first radiation treatment in March (11th) without any difficulty and received his last treatment in on April 21 (Total dose of 6000 cGY for 42 days). During radiation, he complained of early morning nausea that was relieved with sleep and treated with lorazepam 1mg 3 times daily, headache that was treated with hydrocodone, and dry eyes relieved with refresh P.M. drops. He also had some ophthalmic discharge that was treated with gentamicin ophthalmic ointment. A well tolerated diet included cottage cheese, ice cream, saltine crackers, and fresh fruits. He requested a refill of a sedative, Ambien 10mg HS prn, that he had been taking chronically for about a year. The physician discussed the hazards of chronic use with the patient but did not want to add additional stresses on him. They agreed to initiate tapering of the Ambien in anticipation of discontinuation post radiation treatments. He complained of somnolence produced by the lorazepam but continued to take it as prescribed for the nausea. Two weeks after completion of his radiation therapy, right nasal obstruction with epiphora was noted. He reported thick mucous bilaterally; but otherwise was doing well. He continued to steam and irrigate using Bag Balm ointment intranasally. Early in his radiation treatment he recorded in his patient survey for fatigue that he was generally very active (professionally and personally). He also noted that the fatigue he was experiencing was having a "dramatic" impact on his energy level. In addition, he found it was harder to concentrate as a result. Nutritional supplementation of Propax (3 packs per day) was initiated in late June. He reported an improvement in his fatigue levels by day 5 of nutritional therapy with Propax and that he was able to tolerate the nutritional therapy without stomach upset. This trend in improvement continued through day 35 where he indicated that fatigue no longer affected his daily life. He noted dramatic improvements in his overall condition and that he able to work 10 -12 hours daily. (See figure 2 for fatigue survey).

In July of 1999, he developed adhesions and stenosis of the sinuses that produced chronic sinusitis. He was given the antibiotic, Septra, for the infection. However, he complained of vomiting and stomach cramping. The Septra was discontinued and he was given Ceclor 500mg B.I.D for 14 days. He also complained of nasal dryness for

which a waterpik system was presented. He returned to surgery in late July for re-biopsy of the nose to rule out tumor recurrence. During this procedure uncinata processes, purulent ethmoid material and anterior ethmoid cells were removed from the right nasal cavity. Significant scar tissue was also removed from the right inferior nasal cavity. Diseased mucosa of the right ethmoid was drained and removed. Additional biopsies were obtained to evaluate for recurrence of the tumor. Pathology of the specimen reported chronic sinusitis with inflammatory polyps and increased eosinophils. Based on his fatigue survey results, he was able to tolerate the antibiotics (without stomach upset) much better than he had previously been able to tolerate. Seven months post radiation treatment, no major fatigue was reported. He continues to work 10 - 12 hours daily and credits Propax in making a significant difference in his cancer treatment regimen.

In mid August, he was healing well with no evidence of tumor recurrence. In addition, he had decreased supplementation of Propax to only one pack daily and continued to maintain a significantly reduced level of fatigue as indicated on his patient fatigue survey.

Discussion

There are fundamental biochemical differences in the composition of membrane lipids (glycosphingolipids and phospholipids) between tumor cells and normal cells^(7,8,9,10,11). These differences may result from the aggressiveness of a specific tumor to deplete the normal phospholipids of a normal cell membrane in exchange for extrinsic phospholipids. Since phospholipids maintain membrane integrity, regulate enzyme activities and processes, and possess other specific functions, reduced levels may limit metabolic activity and available energy^(12,13,14,15,16).

Similarly, as tumor cells sequester large amounts of phosphatidyl choline, an imbalance in choline homeostasis may result that could lead to muscle fatigue as a result of decreasing plasma, brain, and muscle choline. This may account for the malaise and chronic fatigue reported to accompany certain types of cancers. Therefore, oral exogenous supplementation may provide some benefit for fatigue. Studies by Haubrich⁽¹⁷⁾ and Cohen⁽¹⁸⁾ reported that oral administration of choline can elevate plasma brain and neuronal choline concentrations to release acetylcholine in the neuromuscular system. Since muscle function decreases during choline deficiency⁽¹⁹⁾, supplementation with phosphatidyl choline may compensate for the deficiency⁽²⁰⁾.

In addition, the protective effects of fat-soluble and other natural antioxidants are well known⁽²¹⁾. These antioxidant defenses are important in determining immune cell integrity and functionality of membrane lipids, cellular proteins, and nucleic acids. Additionally, antioxidants are believed to control signal transduction and gene expression in immune cells⁽²²⁾. There are several stages where antioxidants may control the progression and malignancy of disease. Antioxidants may also provide protection even when cancer-infected viral activity is present⁽²²⁾.

Therefore, dietary introduction of these nutrients may stimulate host immunological defenses and damage malignant cells directly by cycling with consequent oxygen radical production. The unique dietary supplement, Propax, addresses the nutritional concerns of oncology patients without resorting to mega dosing as in many immunosuppressive types of disease states. The formulation is composed of the complete antioxidant group and trace minerals, combined with water-soluble nutrients

and essential fatty acids. To aid in the production of ATP, the formulation also includes phospholipids & creatinine, creatinine phosphate, tyrosine, and alpha glutarate. Finally, the formulation utilizes a unique delivery system that mimics the way the body utilizes nutrients by improving cell maintenance and metabolic activity of normal cells⁽²³⁾.

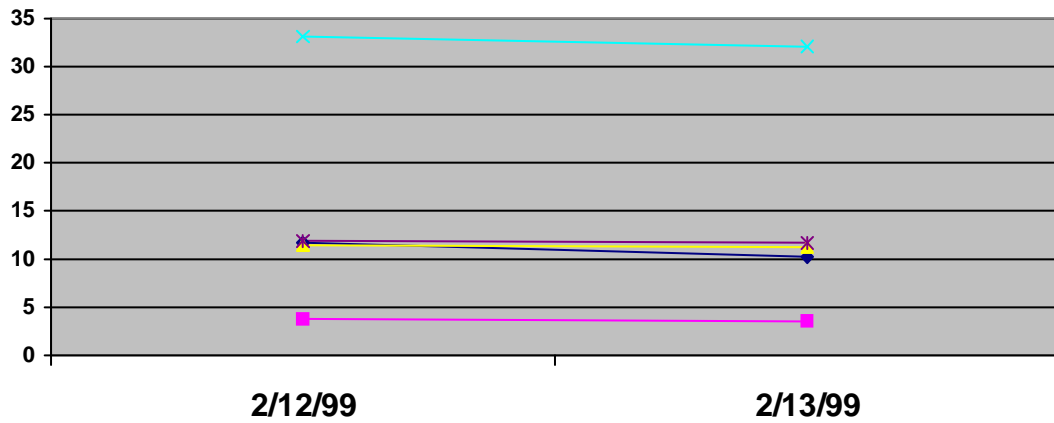
Radiation in combination with surgery is considered standard of therapy for adenoid cystic carcinoma and has been associated with better survival outcomes^(24,25,26). However, radiotherapy is associated with several physical and psychological symptoms, especially during treatment periods⁽²⁷⁾. Evidence suggests fatigue may be more profound upon completion of therapy as opposed to its initiation⁽²⁸⁾. However, this was not the case for the patient discussed here. His fatigue actually improved throughout his radiation therapy.

The pain and fatigue as experienced by this patient is not uncommon⁽²⁹⁾. Both of these physical symptoms improved over the course of treatment. Additionally, sleep disturbances similar to that encountered by this patient is also common and may require a sedative to facilitate sleep⁽³⁰⁾. Although predicting symptoms like fatigue in patients is difficult, evidence does suggest that a patient's understanding of fatigue and physical condition pre-treatment with radiation may also affect the perception of fatigue as experienced by the patient⁽³¹⁾. This may have contributed to the positive results of this study as his general mental well-being throughout radiation therapy was optimistic. This is supported by the recent work of Lilleby et al who stressed a significant importance on the overall general well being of patients. In fact, general quality of life issues such as physical function, emotional function and fatigue were of greater significance to the patient than other issues like sexuality or probability of infection⁽³²⁾. Lovely and colleagues concluded similar results by reporting an inverse relationship between quality of life and fatigue⁽³³⁾.

These properties may be of benefit in treating the fatigue and malaise commonly seen in patients with immunosuppressive disease, similar to the one previously described. Although, well-controlled, blinded, clinical studies are required to draw definitive conclusions on the effectiveness of nutritional supplements like Propax, it may correlate with the positive results for decreased fatigue and stomach upset experienced by the patient.

Figure 1. Summary of differentials during treatment regimens.

Summary of CBC parameters



Fatigue Survey During Treatment

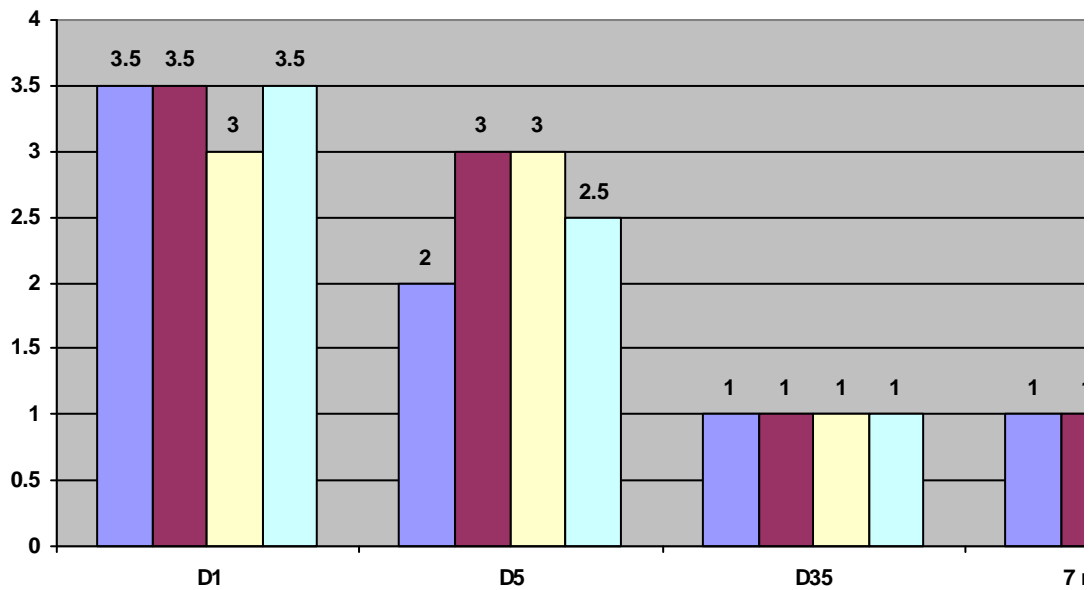


Figure 2. Summary of fatigue indicators per patient survey.

Legend: 1 = Does your tiredness / fatigue keep you from doing your housework / job/ work?
 2 = Does your fatigue keep you from your social life?
 3 = Do you take naps everyday because of tiredness / fatigue?
 4 = Does your fatigue interfere with your mental focus?

Rated 1 thru 5:
 1 = None of the time
 2 = Part of the time
 3 = Half of the time
 4 = Most of the time
 5 = All of the time

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