

CANCER: KEYS TO SURVIVORSHIP - FIGHTING FATIGUE

CARSON PATTILLO, MPH: It's now my pleasure to introduce Ann Conkling-Walsh who will talk to us about treatment options for cancer-related fatigue.

Ann Conkling-Walsh is an autologous stem cell transplant coordinator at Yale-New Haven Hospital in New Haven, Connecticut. In 2002, Ms. Conkling-Walsh returned to Yale as the Clinical Project Coordinator for accreditation in the Yale Stem Cell Transplant Program for two years and as Clinical Nurse in the Medical Oncology Infusion Center for one year.

Ms. Conkling-Walsh held dual positions at the Stamford Hospital in Stamford, Connecticut, as Clinical Nurse Specialist in Oncology for 11 years and autologous stem cell transplant coordinator for eight years.

Early in her 25-year career, Ms. Conkling-Walsh held positions at Yale-New Haven Hospital for 10 years as staff nurse and assistant head nurse, on the Hematology/Oncology, General Medicine Unit as clinical instructor, and as staff on the medical Intensive Care Unit.

She worked on other health care facilities as a staff nurse in Boston, including Massachusetts General Hospital, Saint Elizabeth's Hospital, and the Boston Visiting Nurse Association. As a graduate student, she interned at the Dana-Farber Cancer Institute on the Bone Marrow Transplant Service.

Ms. Conkling-Walsh has been guest lecturer in the masters program at Yale University's School of Nursing since 2003, was a facilitator for *The Leukemia & Lymphoma Society's* national family support group program for three years, and was involved with seven cancer-related committees and boards at The Stamford Hospital for 10 years.

We're also thrilled to have Ms. Conkling-Walsh. Please help me welcome her.

ANN CONKLING-WALSH, RN, CNS: Thank you all for coming tonight. I'd like to thank *The Leukemia & Lymphoma Society* and certainly Ortho Biotech for sponsoring this program.

As Dr. Chu has mentioned, our talks somewhat overlap, so he very kindly covered treatment extensively, but I hope to focus on some of the additional treatment options that are open to patients and families. And I think what I'd like to emphasize to the social workers and the nurses tonight in the audience is that we play a key role in identifying a plan of care that is based on initially listening to our patients.

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ANN CONKLING-WALSH, RN, CNS: And as Dr. Chu has pointed out, the key is actually a symptom that they put up there as being more prevalent for patients than pain. So that's one point I do want to make tonight.

The objectives tonight are to recognize the common symptoms of cancer-related fatigue and to summarize some of the diagnostic criteria and the clinical assessment parameters for cancer-related fatigue. And then I will discuss the treatment options as well.

What is fatigue? It's really a frequent side effect of cancer and a common problem for patients undergoing cancer treatment with cytotoxic agents, biologic response modifiers, or radiation therapy. It is particularly prevalent with multimodality or dose-intense treatment protocols and in the setting of metastatic disease.

This definition was covered before, and again, it is a persistent and subjective sense of tiredness and weakness despite adequate rest, that interferes with usual functioning.

Although fatigue is consistently identified by patients as one of the most distressing symptoms associated with cancer and its treatment, it is consistently under-reported to health care providers and overlooked as a potentially treatable cause of treatment-related morbidity.

The prevalence of cancer-related fatigue is that it affects upwards of 17% to 90% of cancer patients overall, and it does affect greater than 75% of those with advanced cancer or bone metastases.

Clinicians may not recognize fatigue as a significant problem for the patient and be hesitant to discuss fatigue due to the lack of knowledge in this area or limited treatment options. Time constraints also likely play a part in the role we play in identifying this important symptom that patients bring to us.

There are a number of patient surveys that have been conducted in the last few years, and I'd like you to discuss three of them. In a study conducted by Vogelzang et al., 419 patients who were members of a 1,700 randomly selected American family group, were interviewed by telephone.

Fatigue was defined as a positive response to a single question, "Do you feel tired?" Of 419 patients surveyed, 74% reported fatigue at some point during

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ANN CONKLING-WALSH, RN, CNS: their disease, either during the treatment, and 32% reported daily fatigue. However, only 50% of the patients had discussed fatigue with their physicians and in only one-fourth of the cases was any intervention proposed.

Patients and oncologists disagreed on the importance of cancer-related fatigue and although oncologists believe that pain affected patients to a greater degree than fatigue, patients felt that fatigue adversely affected their daily lives more than pain.

In a study conducted by Curt, similar results were found in a second telephone survey of 379 patients. These patients had received chemotherapy with or without radiation. The patients were identified from a representative sample of 6,000 families obtained through the U.S. Bureau of Census.

Fatigue was defined in the same way as in the first study, meaning a positive response to, "Do you feel tired?" Patients reported fatigue as the symptom that was most affecting their quality of life, followed by nausea, depression, and pain.

The important component of this study that I thought was extremely interesting was the economic impact of cancer-related fatigue, which was considerable on these families. Of 177 employed patients, 75% of them changed their employment status as a result of fatigue, while 65% reported that their caregivers had to take at least one day off from work in a typical month.

And I think we see that in our clinical practice setting. A lot of our patients who are chronically ill and coming in for daily therapy or twice a week, are often accompanied by a family member. So the financial impact on families in relation to the fatigue is tremendous.

And in the final study by Eatock et al., comparable findings were also noted in a survey of patients and health care practitioners. And this was a study that was conducted by the All Ireland Fatigue Coalition. However, all of these surveys consist of retrospective cross-sectional data and are biased by recall and the use of non-validated diagnostic criteria.

What we don't know about cancer-related fatigue is the exact cause. And I think Dr. Chu presented all the existing potential causes of cancer-related fatigue, but we really don't know what the exact mechanism is today.

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ANN CONKLING-WALSH, RN, CNS: What we do know about it is that it's under-reported, it's identified, as I said earlier, as one of the most distressing symptoms. Different factors contribute to and add to fatigue. The levels vary from lack of energy to feeling wiped out. It is most common during active therapy but it may persist after treatment is completed.

It essentially affects the quality of life of patients and families, the physical, psychosocial, economic and occupational aspects of their lives.

The signs and symptoms that are associated with cancer-related fatigue are very descriptive. Difficulty climbing stairs or walking short distances, difficulty paying attention or concentrating, shortness of breath after light activity, difficulty performing simple tasks such as cooking or cleaning or showering, and unable to do as much during the day as they had prior to getting cancer.

Additional signs and symptoms include a desire to sleep more; trouble thinking, speaking or making decisions; impatience with family and friends; feeling like crying or feeling depressed; paleness or shakiness.

We currently do not have formal diagnostic criteria for cancer-related fatigue and those diagnostic criteria that have been developed are not in widespread use.

In 1998, a draft was proposed by the ICD910 criteria for cancer-related fatigue and although you probably can't read from this slide because it's a very tight slide, the initial proposed criteria were that a patient would have to have six or more of the following symptoms every day or nearly every day during the same two-week period in the past month. And at least one of the symptoms would be significant fatigue.

And the outcome of all the work that was done in this proposal was that no minimum number of diagnostic criteria are required to clinically diagnose cancer-related fatigue in clinical practice today. And formal diagnostic criteria, again I'm repeating, are not in widespread use.

Currently, what is in use in clinical practice, primarily for patients on clinical trials is a tool that we have, the National Cancer Institute toxicity grading scale. The tool allows us to grade, monitor, and consistently document levels of fatigue according to these descriptive areas. No fatigue is documented as zero. Increased fatigue over the baseline but not altering normal activities is graded as 1. A grade 2 fatigue toxicity is moderate fatigue, a grade 3 would be severe, and a grade 4, the patient would be bedridden.

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ANN CONKLING-WALSH, RN, CNS: If you're looking through medical records of patients who are on clinical trials, you will find these kinds of data, but in clinical practice, we are not routinely documenting patients' level of fatigue according to the NCI toxicity grading scale.

Dr. Chu spent a good portion of his talk on the clinical evaluation of patients who have fatigue and certainly we do know that because fatigue is subjective, the clinician has to rely upon the patient's self report to assess its presence and/or its severity, supported by the additional sources of information such as physical exam, laboratory data, or the descriptions of the family members. Patients should be actively screened for cancer-related fatigue at their initial clinic visit, at periodic intervals and as symptomology presents itself.

Again, I'm going to defer to Dr. Chu's talk where he was able to identify some of the current numeric scales that are being used to assess fatigue and certainly in addition to the NCI toxicity grading, in clinical practice, adopting the numeric scale would not only benefit patients, but would allow us to see trends in patients throughout their treatment and beyond.

I'm going to skip over some of this material.

Again, the assessment of treatable contributing factors includes looking at whether the patient is anemic, whether the patient has pain, emotional disturbance, sleep disturbance, nutritional issues, what is the activity level of the patient, and whether the patient has comorbid conditions.

In a study that was done in Texas, where, I think, since 1999, they've been piloting a focus clinic. Basically it's a symptom-management clinic where they isolated out patients who came in with a primary side effect related to treatment-of fatigue. And their initial diagnostic workup includes an electrolyte panel, chemistry panel, thyroid stimulating hormone studies, and a complete blood count. And these were done periodically as indicated.

The electrolytes are looked at two weeks prior to the appointment, the chemistry panel is done two weeks prior to the appointment. The TSH is evaluated one month prior to the appointment and the complete blood count two weeks prior to the appointment. But patients do not have to have these tests ordered if results are available within specified testing windows.

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ANN CONKLING-WALSH, RN, CNS: Etiology-specific treatments target potentially reversible causes. And there are some additional symptomatic approaches which currently are available to patients.

The treatment of anemia, as has been covered this evening, includes iron, folic acid, vitamin B-12 replacement, red blood cell transfusions, and the use of recombinant erythropoietin. In clinical practice, most of our patients refer to it as Procrit® (epoetin alpha) or Epogen® (epoetin alpha, recombinant). And today we have the availability since the year 2002, of the FDA-approved drug darbepoetin.

The efficacy of both these drugs is essentially the same. We know now that insurance companies are no longer denying patients receiving darbepoetin versus epo and I'll talk through one of the advantages of darbe versus epo as we go through the next few slides.

Both recombinant erythropoietin and darbepoetin do increase hemoglobin levels and reduce transfusion requirements and improve fatigue and overall quality of life. The dosing parameters are 10,000 units subcutaneous three times weekly or 40,000 units weekly.

What's important to just mention about this slide is that we now have practice guidelines that came from ASCO and ASH; and for nurses and physicians who are seeing these patients daily, the current dosing guidelines are based on these specific practice guidelines.

In addition, as I mentioned, one of the advantages of darbepoetin is that it is dosed less frequently than erythropoietin. So in terms of quality of life, if a patient had to be seen for the treatment of fatigue that was based on a diagnosis of anemia, the patient would potentially need to be seen in the clinic or a doctor's office three times a week, or weekly.

With the use of darbepoetin, it has a longer half-life, and subsequently they can be treated as infrequently as every four weeks. But in the initial therapy they start out receiving the drug every two weeks. And again, guidelines for the use of darbepoetin are currently published as well.

Some of the nonpharmacologic management around cancer-related fatigue involves education. And I think this is where all of us as health care practitioners play a tremendous role and have the responsibility of providing patients with strategies to minimize the risk of fatigue, and hopefully improve the quality of their lives.

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ANN CONKLING-WALSH, RN, CNS: Psychosocial interventions certainly have been identified in the literature as tantamount to improving patients' level of fatigue and Nora will be speaking to those issues later this evening. There is certainly a role for exercise. There is certainly a role for identifying patients sleep patterns, something that we can do about it. And there is a lot in the literature now, certainly Dr. Chu had alluded to it, about some of the alternative or complementary approaches. And we don't see anything in the fatigue literature about the herbal medications at this point, but we are seeing a lot in the literature for patients who choose to receive acupuncture and have found benefit.

I'm just going to primarily address the key bullet points of what we can teach patients in terms of ways of conserving energy. We need to assist patients to plan and organize what it is that they are doing, to pace themselves, to position themselves properly, to prioritize their activities.

When they're too tired to eat and they just don't feel like cooking, there are other members of the family that could take on those roles. They could shop at less busy times. We can provide information to patients around meal preparation, childcare, work, and leisure.

I'm going to touch on a few of these tonight, but your handout has them listed. And one of the things I can recommend to you in terms of where would you find this information, many of the professional websites including ONS.org as well as a lot of the patient websites that are open to them through the major cancer centers across the country, often list these conservation measures for patients to access themselves, and certainly for professionals as well.

Other ways to preserve energy would be teaching patients around bathing and grooming, some of the basic activities that they're involved with. Examples would be washing your hair in the shower rather than over a sink, using a terry robe instead of towels to dry off, use organizers to keep things within reach, using a chair in the shower or the tub. With respect to dressing, wearing loose clothing that is easier to put on and take off, and bringing your foot to your knee to put on socks and shoes so you won't have to lean over.

I think if there are any rehab specialists in the audience, a lot of what is being recommended for patients with fatigue is often utilized within the scope of their practice as well. Another is to wear slip-on shoes or shoes with Velcro® closures.

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ANN CONKLING-WALSH, RN, CNS: So these are very simple recommendations, but I think what's helpful to patients is if you can hand them a list that allows them to think about, "Now how am I going to conserve my energy?" It has been found to be very helpful.

With respect to housework, spread tasks over a week or a month and don't do it all in one day. Hire help for those that can. Use long-handled dusters, mops or dustpans. (Sounds like something I should be doing.) Use automatic washers and dryers if possible, and use lightweight irons.

Again, when we think about educating our patients and helping them understand ways to preserve their energy, a lot of what we're asking them to do is to change the role that they play within their families. And to the extent that many patients just by virtue of their disease process, by virtue of having to be tied to a health care facility, their role may have already changed within the family structure.

What I find helpful in working with the autologous stem cell transplant patients is to involve them in a family meeting periodically throughout the treatment course. It's very important for all of our patients who are undergoing chronic therapy to have their significant others present, not only at the time of diagnosis when they're being told about what the treatment course is going to be, but how will that treatment course impact their life?

And in fact, what kinds of planning do they have to do to ensure that their lives can go on with as minimal disruption as possible? But you can't have that meeting with the patient alone. You need to have that meeting with other family members or significant others present.

Some of the psychosocial interventions again, I know that Nora will be covering that this evening, include counseling for stress management, depression, and anxiety. Exercise has been shown to be tantamount in the improvement of patients' report of levels of fatigue. Patients who exercise during or after the completion of treatment have significantly reduced fatigue and emotional distress, decreased sleep disturbances, improved functional capacity, and better quality of life.

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ANN CONKLING-WALSH, RN, CNS: Sleep therapy is something that's being discussed in the nursing literature. Sleep disturbance associated with fatigue is often difficult to treat and manage. It may be influenced by numerous factors, including daytime naps, depression, anxiety, certain medications, sleep interruption due to increased urination or hot flashes, and evening food and beverage intake.

I was able to put together this chart for patient education with respect to good sleep hygiene. During the day you can recommend to your patients to exercise regularly, a 20-minute walk will help them relax and allow them to be more at ease in the evening, but not to do the exercise at night.

Limiting naps is something that is a hard concept to get across to patients who are not feeling exactly full of energy. If patients must nap, limit their naps to 30 minutes. Good sleep hygiene also includes before bedtime avoiding alcohol, caffeine, chocolate, and nicotine in the late afternoon or evening.

Limit liquids in the evening before going to bed so that they're not up urinating. Turn off the TV one hour before bedtime, listen to quiet music, or take a warm bath.

If you worry or you can't turn off your brain, when you try to sleep, make a list of things you need to do before you go to bed, then stop thinking about them. I think that applies to all of us.

At bedtime, patients should go to bed and get up at the same time every day, even on weekends. A bedtime snack of warm milk, turkey, or a banana may make you sleepy. And using the bedroom for sleep or sex, no reading, watching TV or working, comes recommended based on a lot of the data in the literature.

If the patient is a clock watcher, turn the clock so that you can't see its face. To fall asleep, lie in the position that you normally find yourself when you wake up. And go to bed at the same time with your spouse.

If you can't fall asleep, and if you haven't fallen asleep within 15 minutes, go to another room. Listen to quiet music, avoid things that stimulate your mind, read self-help books. It may help you feel drowsy, and go back to bed when you feel sleepy.

If you can't fall asleep, get up again and repeat as necessary. And if you wake up during the night, if you can't get back to sleep, follow the procedure again.

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ANN CONKLING-WALSH, RN, CNS: Another area that certainly Dr. Chu had touched on was the role of psychostimulants, antidepressants, and steroids. And although there were no controlled studies, evaluating the use of psychostimulants when I did my review, in patients with cancer-related fatigue, empiric administration may yield favorable results in some patients, particularly those who have sedation as a side effect of opioid therapy.

The drug Ritalin® (methylphenidate) had been mentioned tonight and Ritalin is essentially a CNS stimulant structurally similar to amphetamine. Cylert has a longer half-life, is also a CNS stimulant and Modafinil is a weight-promoting agent approved for narcolepsy. Since 1999 they've been using that as a treatment for narcolepsy.

Some more controlled studies need to be conducted, but this is showing up in the literature now and the reason I'm presenting it tonight is, I think if you are here learning to get some more information to teach your patients, or if you are here as a patient or caregiver, these are the kinds of things that are in the pipeline and that are being considered for use in cancer-related fatigue.

Antidepressants may be helpful when a patient has both fatigue and depression. For patients with insomnia, nortriptyline or amitriptyline may be useful. Case reports suggest efficacy of bupropion in patients with chronic fatigue syndrome, but no data are available in patients with cancer-related fatigue.

Anecdotal experience suggests that steroids may be beneficial for some patients with cancer-related fatigue. However, the side effects limit their long-term use. Steroids may be most helpful for patients with cancer-related fatigue who are in the terminal phase of advanced cancer.

So tonight, I had hoped to present the common symptoms of cancer-related fatigue and I offered a brief summary of some of the diagnostic criteria that have been developed but are not in widespread use. And we took a look at some of the treatment options that currently are identified as useful in cancer-related fatigue.

I think we still have a long way to go. One of the areas that I found of interest was in certain settings when we look at managing patients' symptoms, not just their disease process, we see the advent of very focused clinics where they're

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ANN CONKLING-WALSH, RN, CNS: providing symptom management alone. And as I mentioned earlier, at MD Anderson in Texas they have been running a fatigue clinic, I believe since 1999. And they're hoping to be able to publish some of their results with respect to whether or not focusing on symptoms makes a difference for patients with cancer-related fatigue.

Thank you very much.

CARSON PATTILLO: Thank you, Ann. Ms. Conkling-Walsh will also join us later during the question and answer session.