Chronic Viral Hepatitis in Cancer Patients Requires Personalized Management

By Bryan Tutt

Chronic viral hepatitis is life-threatening for many patients but curable or manageable for others. But in patients who have both viral hepatitis and cancer, cancer treatment may exacerbate the viral infection and lead to other complications, such as liver failure or even death.

Chronic infections with hepatitis B virus (HBV) or hepatitis C virus (HCV) are associated with the development of hepatocellular carcinoma (HBV or HCV infections account for 78% of cases worldwide). Other cancers are as common in patients with HBV or HCV as they are in the general population. And the prevalence of HCV and HBV make them an important public health concern.

According to the U.S. Centers for Disease Control and Prevention (CDC), between 800,000 and 1.4 million Americans are infected with HBV and 2.7–3.9 million with HCV. It is estimated that half of these people do not know they are infected because a person chronically infected with either virus can have a very low viral load, a normal serum alanine aminotransferase (ALT) level, and an absence of symptoms. The large population with undiagnosed HBV or HCV infection and the risks that cancer treatments pose for patients with the viruses make HBV and HCV important concerns in cancer care.
Chronic Viral Hepatitis in Cancer Patients

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Treating HCV

The high rate of chronic HCV infection and its frequent concurrence with cancer led physicians at The University of Texas MD Anderson Cancer Center to establish an HCV clinic in 2009. This was the first clinic in the United States devoted specifically to managing HCV infection in cancer patients. About 300 patients are seen at the clinic each year; most have cancers that are unrelated to their chronic HCV infection.

Because cancer usually is the more immediate threat, its treatment typically takes precedence in patients who also have HCV. “HCV treatment lasts 6–12 months; most of our patients do not want to delay cancer treatment that long, or their cancer is one that needs to be treated immediately,” said Harrys A. Torres, M.D., director of the HCV clinic and an assistant professor in the Department of Infectious Diseases, Infection Control, and Employee Health.

Dr. Torres works with oncologists to determine the HCV-related risks that may arise from their patients’ cancer treatments. For example, immunosuppression following stem cell or bone marrow transplantation can cause reactivation of the virus (i.e., sharp increases in the serum ALT level and viral load), as can treatment with monoclonal antibodies such as rituximab. Of greater concern is the hepatotoxicity of some antiviral drug regimens. Most chemotherapy drugs are processed in the liver and pose dangers to patients with cirrhosis, but the risks related to some treatment regimens are not well known. Therefore, Dr. Torres said, “We are studying what can happen with HCV in cancer patients and which chemotherapy regimens can be safely used.”

Once the immediate threat of cancer has been addressed, Dr. Torres focuses on the chronic HCV infection. The standard treatment for patients with HCV genotype 1 comprises pegylated interferon alfa-2a or -2b, ribavirin, and telaprevir or boceprevir. The latter two drugs are not approved for use in patients with other HCV genotypes, who receive interferon and ribavirin only. Whether a patient receives HCV treatment—and the timing of such treatment—depends on many factors. “We avoid concomitant HCV therapy and chemotherapy because interferon and ribavirin are myelosuppressive and cause anemia, neutropenia, and thrombocytopenia,” Dr. Torres said. Instead, many patients begin HCV treatment after the completion of chemotherapy or stem cell transplantation.

However, HCV treatment is not always delayed. “If a patient with HCV and hepatocellular carcinoma is recommended for a liver transplant, we begin HCV treatment while the patient is on the transplant list to eradicate the virus before the donor organ becomes available, thus preventing the infection of the new liver,” Dr. Torres said, adding that a study in this patient population was recently approved. “This will be the first clinical trial of HCV treatment from our institution,” he said. In this study, liver cancer patients from the largest liver transplant centers in the Texas Medical Center (The Methodist Hospital and St. Luke’s Episcopal Hospital) will be referred to MD Anderson’s HCV clinic for antiviral treatment before transplantation.

Immediate HCV treatment might also be recommended for a patient who needs chemotherapy with hepatotoxic drugs that would cause liver failure unless the virus is first eradicated.

A patient’s life expectancy may affect his or her decision to undergo HCV treatment. “The reason for HCV treatment is usually to prevent problems 10–20 years down the road,” Dr. Torres said. “A patient with metastatic cancer and a life expectancy of 5 years would not typically be a candidate for HCV treatment because the discomfort, adverse events, and inconvenience caused by the treatment would likely outweigh its benefits.”

Quality of life issues also may affect patients’ decisions. “I talk to my patients and tell them what side effects to expect from HCV treatment,” Dr. Torres said. These include flu-like symptoms and depression. “Some patients who have been through both chemotherapy and HCV treatment have told me that the HCV treatment is worse.”

Dr. Torres said that about 27% of his patients receive HCV treatment, which is similar to the treatment rate among HCV patients without cancer nationwide. The HCV cure rate among cancer patients is 30%–40%, which is lower than that in the general HCV patient population but similar to that in other immunocompromised patients. Dr. Torres said this rate may improve given the approval of the targeted drugs telaprevir and boceprevir about a year ago; it remains to be seen whether the drugs will produce a higher rate of lasting response among immunocompromised HCV patients.

Treating HBV

As is the case with HCV, monoclonal antibodies and other cancer treatments can reactivate chronic HBV infection. In fact, viral reactivation during cancer treatment is more likely among HBV patients than among HCV patients. Diagnostic criteria for HBV reactivation vary, but the first sign is an increase in the patient’s baseline viral load. This is followed by an increase in serum ALT.

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“Until we have further evidence, I can’t say for certain whether oncologists should screen all patients for HBV and HCV, but they should at minimum screen those with known risk factors.”

– Dr. Jessica Hwang
Managing Sleep Disorders in Cancer Patients

By Jill Delsigne

Quality sleep is essential to healing, to proper immune function, and even to mental health. Conversely, lack of sleep has been associated with depression, anxiety, and decreased cognitive function. In cancer patients, poor sleep reduces quality of life; nevertheless, most cancer patients do not mention sleep problems unless explicitly asked.

Estimates of the percentage of cancer patients affected by sleep disorders range from 30% to 88%. Sleep apnea is more common among cancer patients than in the general population, and cancer patients are twice as likely as people without cancer to experience insomnia.

The restless nights caused by sleep disorders can impair patients’ quality of life, immune systems, cognitive abilities, and abilities to function day to day. “Patients often say they feel like different people when they lose sleep; they struggle with poor concentration and memory,” said Dave Balachandran, M.D., an associate professor in the Department of Pulmonary Medicine at The University of Texas MD Anderson Cancer Center. “Daytime sleepiness affects their ability to function, affecting every aspect of their lives.” These effects can last far beyond treatment, becoming a chronic condition. Some breast cancer survivors, for example, have had sleep disorders up to 10 years after finishing treatment.

Despite the pervasiveness of sleep disorders in cancer patients, not much research is available on the relationship between cancer and sleep. MD Anderson researchers are leading the development of this field with the world’s first sleep center dedicated to cancer patients. At the sleep center, Dr. Balachandran and his colleagues are exploring the relationship between cancer and sleep, particularly whether conditions such as insomnia and sleep apnea are contributing factors to cancer development, symptoms of disease, or side effects of treatment. The researchers also are developing sleep disorder treatments tailored to cancer patients.

Sleep apnea

Sleep apnea has recently been shown to have a strong correlation with death from cancer. This is not surprising when one considers the prevalence of sleep apnea among cancer patients. Research done by Carmen Escalante, M.D., chair of the Department of General Internal Medicine, and Ellen Manzullo, M.D., a professor in the department, found that almost 30% of patients reporting cancer-related fatigue were diagnosed with sleep apnea.

Sleep apnea can result from several types of cancer treatment. Up to 80% of patients with head and neck cancer suffer from sleep apnea as a comorbidity or as a result of surgery or radiation therapy, according to the research of Saadia Faiz, M.D., an assistant professor in the Department of Pulmonary Medicine. Patients with breast cancer are particularly vulnerable to sleep apnea related to weight gain, which is a common side effect of breast cancer treatment. Narcotics and sleep medications given to relieve symptoms of any type of cancer also can contribute to sleep apnea.

Sleep apnea may accelerate cancer progression or interfere with cancer treatment. In vitro and animal studies have shown that intermittent hypoxia, mimicking the effects of the recurrent airway obstruction characteristic of sleep apnea, causes cancer cells to be more likely to proliferate.

Because sleep apnea is common in cancer patients, patients who report excessive sleepiness should be evaluated by a sleep specialist. If sleep apnea is a possible culprit, the patient may need to undergo polysomnography, an overnight test that monitors breathing, sleep stages, rapid eye movement, and other sleep metrics.

The standard treatment for sleep apnea is the continuous positive airway pressure (CPAP) machine. The CPAP technicians at MD Anderson’s sleep center specialize in helping cancer patients find the mask and system that work best for them. Patients with head and neck cancer, for example, may need an adjusted mask if the standard air pressure will interfere with a surgery site. Other strategies are employed to make CPAP tolerable for patients with dry mouth as a result of chemotherapy or radiation therapy. Tailoring CPAP therapy to patient-specific needs has enabled CPAP patients at the sleep center to consistently use their masks and sleep through the night, at a compliance rate well above the 50% compliance rate in the general population.

Insomnia

Insomnia, the most prevalent sleep disorder in the general population, also affects up to 80% of cancer patients. According to an MD Anderson study, 60% of patients who reported cancer-related fatigue were diagnosed with insomnia. Clinically, insomnia is diagnosed by the following criteria: taking more than 30 minutes to fall asleep or waking for more than 30 minutes during the night, having difficulty conducting daytime functions, and...
experiencing these disturbances at least 3 nights per week. The psychological stress of a cancer diagnosis can cause patients to lose sleep, as can schedule changes brought about by treatment. Patients requiring drug or radiation treatments at odd hours, for example, may find it extremely difficult to maintain a consistent sleep schedule.

The pain and other symptoms of the cancer itself and side effects of treatment—such as nausea, incontinence, or hot flashes—can also prevent patients from sleeping. In addition, medications to relieve other symptoms or to treat cancer can cause insomnia as a direct side effect. Inflammation, often the result of various types of treatment and of the cancer itself, also has been shown to affect the ability to sleep.

Radiation therapy, especially to the brain, can interfere with patients’ circadian rhythms and REM sleep cycles, inhibiting the signals for wakefulness and sleepiness. These signals are regulated by environmental cues known as zeitgebers. Zeitgebers include light, a regular meal schedule, social interactions, and daytime activity. Treatments such as light therapy and stimulant therapy can help regulate circadian rhythms and establish a regular sleep-wake schedule for patients with insomnia. Sleep medications are often given to treat insomnia in cancer patients, especially those with advanced disease who are near the end of life. However, sometimes sleep medications are contraindicated because of potential adverse drug interactions. And, according to Dr. Balachandran, sleep medication is at best a short-term solution. When possible, he prefers to help patients develop healthy sleep behaviors that will benefit them in the long term.

Cognitive behavioral therapy, considered the standard of care for insomnia in the general population, has also shown great promise for cancer patients. Cognitive behavioral therapy has been shown to help 70%–80% of patients in the general population who receive it and to reduce by half the need for sleep medications taken by cancer patients.

Cognitive behavioral therapy has multiple components—stimulus control, sleep hygiene, relaxation, and others—that can be tailored to a patient’s needs. People with insomnia often respond well to stimulus control therapy, which reconditions them to associate their bedrooms only with sleep. As patients learn healthy sleep hygiene (for instance, developing a relaxing bedtime ritual; getting up if sleep is difficult and only returning to bed when sleepy; and controlling environmental factors such as light, temperature, and noise), sleep comes to them more easily. Progressive muscle relaxation and guided imagery are often also very effective.

Depending on the severity of the insomnia, patients can work individually with a psychologist or sleep specialist, participate in group therapy administered by a trained nurse or counselor, or self-administer cognitive behavioral therapy.

Self-administered cognitive behavioral programs geared toward a general population are currently available online and on CD, and researchers are working on developing a tablet application for cancer patients that will guide them through self-administered cognitive behavioral therapy. “This application will take into account the unique issues and challenges that cancer patients face,” Dr. Balachandran said, “and the platform will make this type of therapy widely accessible.”

Helping patients find helpBecause quality sleep is essential to health and to recovery, several researchers have suggested that doctors ask cancer patients about sleep and fatigue at each medical visit and include sleep evaluation as part of the long-term follow-up. Patients often do not self-report these symptoms. In many cases, cancer patients with insomnia can benefit from referral to a psychologist or a sleep specialist.
Ex Vivo Umbilical Cord Blood Expansion Hastens Stem Cell Engraftment in Transplant Recipients

Engraftment of stem cells from umbilical cord blood can be hastened with pretransplantation expansion of the stem cells on a bed of mesenchymal precursor cells, according to a recent study.

The phase I/II trial analyzed engraftment results for 31 patients with hematologic cancers who had each received one expanded cord blood unit and one unmanipulated cord blood unit. These patients’ results were compared with the records of 80 patients who had received only the standard two units of unmanipulated cord blood.

“I believe we are witnessing a breakthrough in mantle cell lymphoma.”
– Dr. Michael Wang

In the units of expanded cord blood, the total number of nucleated cells increased by a median factor of 12, and CD34-positive cells, which are crucial for engraftment, increased by a median factor of 30. Among patients who received expanded cord blood, the cumulative incidence of neutrophil engraftment was 88% at 26 days and the cumulative incidence of platelet engraftment was 71% at 60 days; for the historical controls, those incidences were 53% and 31%, respectively.

Stem cell transplants usually involve bone marrow or peripheral blood from a donor, but matching donors are available for only about 25% of those needing such transplants. Cord blood stem cells, on the other hand, do not have to be as precisely matched to the patient, so cord blood can often be used for patients who do not have a matched donor.

Until now, the benefits of cord blood cell transplants have been counterbalanced by slow engraftment, which increases the risk of transplant-related complications. This slowness is attributable to the low number of hematopoietic stem cells per unit of umbilical cord blood. With ex vivo expansion, researchers were able to greatly increase the number of cord blood cells transplanted, reduce neutrophil and platelet recovery times, and increase the percentage of patients for whom successful engraftment took place.

The study’s report was published in the December 13 edition of the New England Journal of Medicine. Senior author Elizabeth Shpall, M.D., a professor in the Department of Stem Cell Transplantation and Cellular Therapy at The University of Texas MD Anderson Cancer Center, said, “Pretransplant cord blood expansion on mesenchymal stromal cells could become the new standard of care if our findings are confirmed in a randomized clinical trial.”

“Ibrutinib Shows Promise for Mantle Cell Lymphoma Treatment

An international phase II study of the experimental drug ibrutinib for the treatment of relapsed or refractory mantle cell lymphoma is showing durable responses with few side effects.

Mantle cell lymphoma is a rare subtype of B-cell lymphoma. Ibrutinib inhibits Bruton tyrosine kinase, which transduces signals from the B-cell receptor, a protein on the cell surface that enables B cells to bind to antigens. B-cell receptor signaling also plays an important role in the normal development of B cells. By inhibiting Bruton tyrosine kinase, ibrutinib causes cell death and decreases migration and adhesion of malignant B cells.

In the ongoing study, patients receive 560 mg of ibrutinib orally each day in continuous 28-day cycles until disease progression.

Rates of serious adverse events were low among the 111 patients in the interim safety analysis. Grade 3 or higher adverse events consisted of neutropenia in 11% of patients and anemia, diarrhea, dyspnea, pneumonia, and thrombocytopenia each in 5% of patients. These were similar to the safety data from earlier studies.

Of the 109 patients evaluable for efficacy, 47% had a partial response and 19% had a complete response. The median time this group of patients had been receiving ibrutinib was 6 months. Among the patients who had been receiving ibrutinib longest (median, 11 months), the complete response rate was 35%.

“What impressed me the most is the high complete response rate, which continues to improve with time,” said Michael Wang, M.D., an associate professor in the Department of Lymphoma and Myeloma and the director of the Mantle Cell Lymphoma Program at The University of Texas MD Anderson Cancer Center. “Ibrutinib is the safest drug we have for mantle cell lymphoma. Previously, such a rate could be achieved only with combination cytoreductive chemotherapy, which suppresses bone marrow and is toxic.”

Dr. Wang and his colleagues presented their interim results at the 54th American Society of Hematology Annual Meeting and Exposition in December. “I believe we are witnessing a breakthrough in mantle cell lymphoma,” Dr. Wang said. “This is great news for patients.”
Finding Information About Alternative Medicine

How to choose credible sources and avoid pitfalls

Many people are exploring natural or alternative medicine. Often they do so without consulting a physician, instead relying on the Internet for information. But many Web sites selling so-called healing products make unproven or false claims. Here, we share some trustworthy sources of information and tips to help you spot unreliable Web sites.

Dependable sources

Your doctor and his or her staff are valuable information sources because they are familiar with your health conditions and history. Don’t be nervous that your doctor will scoff if you ask about acupuncture, massage therapy, homeopathy, naturopathy, or herbal products; physicians, like the rest of us, are learning that some of these products and practices are helpful. In fact, many health care professionals use the term “complementary and integrative medicine” (CIM) instead of “alternative medicine” to emphasize the idea that these holistic treatments should be used in coordination with conventional medicine.

The University of Texas MD Anderson Cancer Center’s Integrative Medicine Program (www.mdamderson.org/cimer) offers general information about CIM and specific information about its role in cancer treatment. The program also hosts educational programs for physicians, patients, and the general public.

The U.S. National Institutes of Health operates several Web sites with useful information about CIM. The National Center for Complementary and Alternative Medicine (www.nccam.nih.gov) has information on a wide range of topics. For cancer-specific information, visit the National Cancer Institute’s Office of Complementary and Alternative Medicine (www.cancer.gov/cam). Reliable information about herbal products and nutritional supplements is available from the Office of Dietary Supplements (www.ods.od.nih.gov).

Accurate information about herbal medicine is also available through nonprofit groups such as the American Botanical Council (www.herbalgram.org) and the United States Pharmacopeial Convention (www.usp.org).

Professional organizations for CIM practitioners can help you find qualified practitioners in your area. Examples include the American Holistic Medical Association (www.holisticmedicine.org), the American Association of Naturopathic Physicians (www.naturopathic.org), the American Association of Acupuncture and Oriental Medicine (www.aaamonline.org), and the American College of Homeopathy (www.homeopathyusa.org).

Warning signs

Web sites operated by private companies should be viewed with caution. Some CIM companies offer high-quality products with proven benefits, but others sell products that are unproven or potentially harmful. Other companies may honestly believe in their product’s benefits but have no scientific proof to confirm these beliefs. Some signs of questionable CIM Web sites are:

• **Testimonials.** Comments from users who say the product worked are not proof of a product’s effectiveness. Consumers should be concerned if such testimonials are the only evidence offered. Clinical trials provide the most reliable form of proof.

• **Advertising a cure for a specific condition.** Although false advertising is illegal, some companies break the law, and others use misleading language and disclaimers. Unless a product is approved by the U.S. Food and Drug Administration to treat a specific condition, the product’s effectiveness probably has not been proven in clinical trials.

• **Secret ingredients.** Fraudulent sites often claim their products are the result of ancient remedies, secret recipes, miracle cures, or medical breakthroughs.

• **User fees.** Most legitimate sites will not charge users a fee to access health-related information, although some medical journals and consumer publications require a subscription.

• **Hard-sell tactics.** Limited-time offers and money-back guarantees are designed to encourage consumers to buy quickly instead of doing further research.

Other considerations

When viewing any Web site with CIM information, you may find it useful to ask the following questions:

• **Who runs this site?** Credible Web sites should have an “About Us” page that describes the organization and includes contact information.

• **Where does the information come from?** Medical statements should have references to original articles in medical journals.

• **How current is the information?** The articles or pages should indicate when they were last updated. If not, assume the copyright date at the bottom of the page to be the most recent date the content may have been reviewed.

These guidelines can help you avoid misleading information and dangerous products, but even a useful CIM product might not be for everyone. For example, a therapeutic massage might help someone with a strained muscle but hurt someone who has a medical device or implant. Herbal supplements may interact with prescription drugs. Your physician can help you make safe choices about CIM products and services.

— B. Tutt

FOR MORE INFORMATION

• Talk to your physician

• Visit www.mdamderson.org/cimer

• Call askMDAnderson at 877-632-6789

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among patients at risk for HBV,” she said. To determine which groups of cancer patients would benefit from screening, a prospective study is being planned that will screen all participants for HBV prior to cancer treatment and, once a large pool of data is available, apply models of different screening strategies. “We will enter several screening models to see whether screening according to certain risk factors or clinical predictors, like types of cancer or types of therapy, would have detected all the patients with HBV,” Dr. Hwang said. The study, which is funded by the National Cancer Institute, is planned to begin at MD Anderson, and Dr. Hwang hopes to expand the study to community oncology centers such as those in the Community Clinical Oncology Program. “We seek to find evidence that will provide cost-effective screening guidelines that can be incorporated into clinical practice,” she said.

“Until we have further evidence, I can’t say for certain whether oncologists should screen all patients for HBV and HCV,” Dr. Hwang said, “but they should at minimum screen those with known risk factors.” Dr. Davila agreed. She said, “If you think a patient has risk factors for viral hepatitis, please screen the patient.”

FOR MORE INFORMATION
Dr. Marta Davila 713-563-8906
Dr. Jessica Hwang 713-745-4516
Dr. Harrys Torres 713-792-6503

FURTHER READING

