CASE STUDY

66-YEAR-OLD MAN WITH FEBRILE NEUTROPENIA

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BACKGROUND

A 66-year-old white male with a history of chronic lymphocytic leukemia (CLL) transformed to a diffuse large-cell lymphoma presents to the hospital with febrile neutropenia. He was diagnosed with CLL in 2000 after presenting with fatigue and palpable lymph nodes. He had received numerous chemotherapy regimens and continues to require chemotherapy for control of his disease. In 2005, he presented with fevers, night sweats, and weight loss and was noted to have a transformation to an aggressive diffuse large-cell lymphoma. Eight days before this presentation, the patient received cyclophosphamide, doxorubicin, vincristine, and prednisone chemotherapy plus rituximab (R-CHOP).

PAST MEDICAL HISTORY

The patient was diagnosed with CLL in 2000 and was treated with 4 cycles of fludarabine with no response. He was subsequently treated with rituximab 3 times a week for 4 weeks, with a partial response that lasted 5 months. He then received alemtuzumab for 11 weeks from 2001 to 2002, resulting in another partial response. In 2002 to 2003, the patient received 6 cycles of rituximab and fludarabine and achieved a partial response. The patient then received multiple cycles of pentostatin, cyclophosphamide, and rituximab. The patient exhibited a nodal response, but he was noted to have persistent cytopenias. With his recent transformation, his hematologist has now decided to use 6 cycles of R-CHOP scheduled every 21 days in an attempt to control his disease.

FAMILY HISTORY

The patient was married with 3 children. He had a history of appendicitis with an appendectomy performed in 1988. The patient’s mother had a history of breast cancer diagnosed at age 58 years. He had no other family history of cancer.

PHYSICAL EXAMINATION

On this presentation the patient appeared thin, pale, diaphoretic, and fatigued. Physical examination revealed the following: height 5’7”; weight 120 lb; venous/systolic blood pressure 92/40 mm Hg; body temperature 41°C; heart rate 124 beats per minute; respiratory rate 26 breaths per minute; and oxygen saturation 93%. Chest radiograph showed bilateral axillary and mediastinal adenopathy and atelectasis bilaterally in the lower lobes. Computed tomography (CT) scan showed moderate ascites, splenomegaly, and para-aortic and mesenteric lymphadenopathy.

LABORATORY STUDIES

Laboratory studies in the hospital were as follows: sodium 136 mEq/L; potassium 4.6 mEq/L; blood urea nitrogen 31 mg/dL; creatinine 0.9 mg/dL; glucose 121 mg/dL; chloride 97 mEq/L; calcium 8.9 mg/dL; total bilirubin 2.9 mg/dL; magnesium 1.8 mEq/L; albumin 2.0 g/dL; urinalysis unremarkable; white blood cell count 160/mm³, with 80% lymphocytes; hemoglobin 9 g/dL; mean cell volume 95.8 FL; and platelet count 26 000/mm³.

DIAGNOSES ON HOSPITAL ADMISSION

The patient was admitted for treatment of febrile neutropenia. Peripheral intravenous access was obtained after hospital admission. No obvious source of infection was noted. Blood cultures x2, urinalysis, chest radiograph, and chest and abdominal CT were obtained and a pneumonia was identified. The patient was started on cefepime 2 g every 8 hours intravenously, and 3 g piperacillin/0.375 g tazobactam (Zosyn; Wyeth, Madison, NJ) every 6 hours intravenously upon admission to the hospital.

MEDICAL ONCOLOGY CONSULTATION

A diagnostic tap was performed to obtain ascitic fluid. The cultures showed no infection.

HOSPITAL COURSE

The patient responded well to intravenous anti-
otics during his hospital course and was discharged after 5 days. He required a central venous access device for continued antibiotic treatment of pneumonia upon discharge. Home care follow-up was required for the antibiotic infusions. While hospitalized, the clinical nurse specialists performed a risk assessment on the patient and discussed improvements in supportive care with the physician team. Pegfilgrastim 6 mg subcutaneously and darbepoetin alfa 4.5 µg/kg every 2 weeks subcutaneously were prescribed as part of the patient's care going forward as per the current National Comprehensive Cancer Network (NCCN) guidelines. The NCCN guidelines also mention a clinical trial under way at the time of publication exploring dosing darbepoetin alfa every 3 weeks. The results of this trial were recently presented at the 2005 American Society of Clinical Oncology 41st Annual Meeting. The data showed most patients, regardless of baseline hemoglobin, achieved and maintained the target hemoglobin with 3-week dosing. The study concluded that darbepoetin alfa 300 µg every 3 weeks was well tolerated and effective for achieving and maintaining evidence-based target hemoglobin levels in patients with chemotherapy-induced anemia. Based on this data, darbepoetin alfa might alternatively be dosed in this type of patient every 3 weeks, allowing coordination of chemotherapy and growth factor administration and decreasing the number of office visits.

OUTPATIENT COURSE
As an outpatient, he completed a 10-day course of antibiotics without difficulty. Darbepoetin alfa treatment started in the hospital was to be administered every 2 weeks. Pegfilgrastim will be given with the next cycle of R-CHOP. A nutritional consultation was obtained while in the hospital, and was to continue with his follow-up visits.

DISCUSSION
Upon examination of this patient's medical record, it is apparent that his supportive care treatment has been inconsistent. For most of his initial treatments, despite his age and the intensity of his chemotherapy treatments, he did not receive growth factor support. He has received multiple transfusions to support his low hemoglobin and platelet counts. The patient reported feeling fatigue “pretty much since diagnosis” with very low energy levels. He reported frequent infections and had been taking prophylactic oral antibiotics (ciprofloxacin 500 mg 2 times a day, amoxicillin 875 mg 2 times a day, and dapsone 100 mg once a day) for most of the past year. He reported some sporadic growth factor use (filgrastim) and states, “My doctor tells me when to take it based on my symptoms.” He further stated, “When I do the filgrastim, it is usually just every other day that I give myself shots.”

Up to this point, the patient had never received a red blood cell growth factor. This patient's risk factors for anemia include age, current treatment regimen, past history of blood transfusions, and past history of myelosuppressive therapy. Elevation of the hemoglobin level to a target of 11 to 12 g/dL is recommended and may increase quality of life and decrease fatigue. Risk factors substantiating the use of neutrophil colony-stimulating factors for this patient include age, cancer diagnosis, chemotherapy regimen, history of febrile neutropenia with past chemotherapy regimens, chronic cytopenias, malnutrition, and abnormal liver function. According to Groopman and Itri, the CHOP chemotherapy regimen studied in 212 patients with non-Hodgkin's lymphoma resulted in a 49% incidence of grade 1 or 2 anemia and a 17% to 79% incidence of grade 3 or 4 anemia. In addition, as stated in the NCCN Myeloid Growth Factor guidelines, R-CHOP is associated with an intermediate risk of febrile neutropenia (10%–20%). Alternative dosing for filgrastim, as was being done in this case, is not recommended at this time and may have provided insufficient support.

This patient is a prime example of how a risk assessment program and the use of evidenced-based practice guidelines could have possibly prevented hospitalization and subsequent complications. Although this patient's disease was being controlled, thus the treatment was considered palliative, we know that preventing adverse effects of chemotherapy has a major impact on a patient's quality of life and can possibly prevent life-threatening complications.

REFERENCES