



## PALLIATIVE CARE CASE OF THE MONTH

“A middle aged woman with diffuse large B cell lymphoma  
in the ICU - is her prognosis good or bad? ”

by

Mamta Bhatnagar, MD

Volume 15, No. 47

April 2015

**Case:** GH was a 49-year-old woman who fell at home and developed weakness in bilateral lower extremities in the setting of a T8 vertebral fracture. This was later diagnosed as being from a high grade B-cell lymphoma. GH underwent spinal cord decompression followed by time in the ICU and oncology unit. Prior to transfer to a rehabilitation unit, she was treated with chemotherapy.

GH used to work in health care before she got sick and, according to her sister, had not been well for a year before admission. She had two children, one of whom was a teenager and lived with her. GH wanted to be with her child at home instead of going to rehabilitation. As her hospital stay progressed, GH became distressed about her slow recovery and inability to take care of affairs at home. Her personal coping skills were taxed by her diagnosis and treatment. She became irritable and angry when she actually felt sad and fearful because of what was happening to her.

Her rehab stay lasted five days before GH became septic and was transferred back to the Shadyside ICU. On day three of her ICU stay, palliative care was consulted for pain and symptoms, and we found her perseverating and pulling out her NG tube. We treated her delirium with IV Haldol and talked with the oncology and the critical care teams about her prognosis. The oncological opinion was that the patient's lymphoma was treatable as long as she could recover from her acute illness.

At a family meeting the family reiterated that the patient's goals were to live as long as she could for the sake of her children. That night the patient was intubated. A week later she was in multi-organ system failure, on dialysis, ventilator dependent and immunocompromised on multiple antibiotics for bacteremia. A follow-up family meeting was held at which the oncology staff, critical care and palliative care team members were present; the family reiterated their goal to continue current efforts.

On day 55 since her fall and diagnosis, GH developed arrhythmias felt to be due to an infiltrative process affecting her heart. At this point, GH was awake and wrote to the nurses that she wanted to stop all treatments. She remained consistent in her wishes, and she was terminally extubated with her family present. GH died 12 hours later in the ICU.

**Discussion:** Diffuse Large B-Cell Lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma, accounting for approximately 30% of all newly diagnosed cases and more than 80% of aggressive lymphomas.

Limited stage disease (Stages I, II and II bulky) is characterized by contiguous nodal disease on same side of diaphragm and/or single extra nodal site involvement. Advanced stage disease (Stages III and IV) includes patients with nodal involvement on both sides of the diaphragm and spleen involvement and additional non-contiguous extra lymphatic involvement. The diversity in clinical presentation and outcome, as well as pathologic and biologic heterogeneity, suggest that DLBCL comprises several disease entities with variable prognoses. Gene expression profiling has identified three major subgroups of DLBCL, termed germinal center B-cell like (GCB-DLBCL), activated B-cell like DLBCL (ABC-DLBCL), and primary mediastinal DLBCL (PM-BCL). Recent studies have shown better prognosis for the PM-BCL subtype as compared to GCB-DLBCL and ABC-DLBCL with survival rates 64%, 59% and 30% respectively.<sup>1</sup>

Therapeutically, prognosis has changed markedly with the addition of rituximab, a monoclonal antibody. Adding rituximab to CHOP (Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone) improves five-year survival rates to 58% from 45%. Approximately 10% of patients develop late relapse in 10 years, more people die from unrelated causes and 40% have disease progression.<sup>2</sup>

While the adoption of R-CHOP as the new standard of care has led to improved outcomes for this curable lymphoma, patients whose lymphoma is not cured by first-line therapy also have newer chemotherapy regimens which have led to improved outcomes. Five-year event free survival rates for patients with relapsed DLBCL are as low as 23% for patients with high-risk profile (short time to relapse, high disease burden, multiple chemotherapy regimens) or up to 59% among patients with chemo sensitive disease.<sup>3</sup>

Traditionally, the International Prognostic Index (IPI) has been used to predict prognosis in patients with DLBCL. It is based on the presence of negative prognostic markers such as Lactate Dehydrogenase, ECOG >2, age > 60years, Stage III-IV disease, more than one extra nodal site. Patients with three, four or five risk factors fall into a poor risk-group category with a long-term chance of cure of roughly 50%. The IPI cannot identify patients with survival rate less than 50%.<sup>4</sup>

GH's lymphoma was of the aggressive type with extensive atypia and proliferation on her biopsy (which has been correlated with presence of adverse genetic markers), Stage IV disease, LDH of 3,675 at the time of diagnosis and extra nodal involvement. Based on IPI, her risk profile was poor with a prognosis of roughly 50%. Her genetic profiling information was not available.

*Personal details in the case published have been altered to protect patient privacy.*

For palliative care consultations please contact the Palliative Care Program at PUH/MUH, 647-7243, beeper 8511, Shadyside Dept. of Medical Ethics and Palliative Care, beeper 412-647-7243 pager # 8513, Perioperative/ Trauma Pain 647-7243, beeper 7246, UPCI Cancer Pain Service, beeper 644-1724, Interventional Pain 784-4000, Magee Women's Hospital, beeper 412-647-7243 pager #: 8510, VA Palliative Care Program, 688-6178, beeper 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children's page 958-3844. With comments about "Case of the Month" call Dr. Robert Arnold at (412) 692-4834.



### (Discussion Continued)

The problem is the above information focuses on her long prognosis. In this case, the key question was her ICU prognosis. There is little data examining the course of DLBCL patients who have received R-CHOP and are subsequently in the ICU with multi-system organ failure. Most of the data mixes patients with solid tumors and “liquid” tumors. In a study conducted at seven academic, tertiary-care hospitals, overall hospital mortality of ICU patients with cancer exceeded 40%. The mortality of those requiring mechanical ventilation was nearly 70%, whereas almost 90% of cancer patients with poor neurologic function at ICU admission died before hospital discharge. Even for those patients who survive hospitalization, prognosis remains grim; approximately 75% of ICU survivors in one study lived less than three months after discharge.<sup>6</sup> The applicability of this data to our patient is unclear.

Common prognostic indicators such as Acute Physiology Score II, the Acute Physiology and Chronic Health Score II and the Mortality Probability Model II are not accurate in cancer patients as they underestimate mortality. The Cancer Mortality Model, on the other hand, overestimates mortality. Studies support that the need for mechanical ventilation, development of invasive fungal infection, septic shock, renal failure and declining functional status are adverse prognostic factors.<sup>7</sup>

**Case Conclusion:** For GH, the uncertainty in prognostication led to predictable discussions among the clinicians. Oncologists, focused on the long-term curability of the cancer; intensivists focused on the high mortality in cancer patients with MOSF and poor statistics in cancer overall.<sup>5</sup> Both parties’ views are accurate and reflect the difficulties in prognostication and lack of data. The family, not surprisingly, was torn between the two different points of view and focused on the long-term outcomes given the patient’s children. In taking care of this patient, I struggled with the patient’s suffering and that the dilemma of the family caught between the two prognostic views. It was only when GH made it clear that it was time to stop, and the situation was perceived as hopeless, that the course of her care shifted.

### References:

1. Diffuse large B-cell lymphoma subgroups have distinct genetic profiles that influence tumor biology and improve gene-expression-based survival prediction  
Silvia Bea , Andreas Zettl , George Wright , Itziar Salaverria , Philipp Jehn , Victor Moreno , Christof Burek , German Ott , Xavier Puig , Liming Yang , Armando Lopez-Guillermo , Wing C. Chan , Timothy C. Greiner , Dennis D. Weisenburger , James O. Armitage , Randy D. Gascoyne , Joseph M. Connors , Thomas M. Grogan , Rita Brazier , Richard I. Fisher , Erlend B. Smeland , Stein Kvaloy ,

Harald Holte , Jan Delabie , Richard Simon , John Powell , Wyndham H. Wilson , Elaine S. Jaffe , Emili Montserrat , Hans-Konrad Muller-Hermelink , Louis M. Staudt , Elias Campo , Andreas Rosenwald  
Blood Nov 2005, 106 (9) 3183-3190

2. Rituximab-CHOP Versus CHOP Alone or With Maintenance Rituximab in Older Patients With Diffuse Large B-Cell Lymphoma  
Thomas M. Habermann, Edie A. Weller, Vicki A. Morrison, Randy D. Gascoyne, Peter A. Cassileth, Jeffrey B. Cohn, Shaker R. Dakhil, Bruce Woda, Richard I. Fisher, Bruce A. Peterson and Sandra J. Horning  
JCO July 1, 2006 vol. 24 no. 19 3121-3127

3. Age-adjusted International Prognostic Index predicts autologous stem cell transplantation outcome for patients with relapsed or primary refractory diffuse large B-cell lymphoma  
Paul A. Hamlin , Andrew D. Zelenetz , Tarun Kewalramani , Jing Qin , Jaya M. Satagopan , David Verbel , Ariela Noy , Carol S. Portlock , David J. Straus , Joachim Yahalom , Stephen D. Nimer , Craig H. Moskowitz  
Blood Sep 2003, 102 (6) 1989-1996; 7

4. The revised International Prognostic Index (R-IPI) is a better predictor of outcome than the standard IPI for patients with diffuse large B-cell lymphoma treated with R-CHOP  
Laurie H. Sehn , Brian Berry , Mukesh Chhanabhai , Catherine Fitzgerald , Karamjit Gill , Paul Hoskins , Richard Klasa , Kerry J. Savage , Tamara Shenkier , Judy Sutherland , Randy D. Gascoyne , Joseph M. Connors  
Blood Mar 2007, 109 (5) 1857-1861;

5. Resolving Problems at the Intensive Care Unit/Oncology Unit Interface  
Stuart J. Youngner, Martha Allen, Hugo Montenegro, Jill Hreha, Hillard Lazarus  
Perspectives in Biology and Medicine Volume 31, Number 2, Winter 1988

6. Self-reported symptom experience of critically ill cancer patients receiving intensive care  
Nelson, Judith E. MD, JD; Meier, Diane E. MD; Oei, Erwin J. MD; Nierman, David M. MD; Senzel, Richard S. MRP; Manfredi, Paolo L. MD; Davis, Susan M. RN; Morrison, R. Sean MD  
Critical Care Medicine: February 2001 - Volume 29 - Issue 2 - pp 277-282

7. Performance of prognostic models in critically ill cancer patients – a review  
Sylvia den Boer<sup>1</sup>, Nicolette F de Keizer<sup>2</sup> and Evert de Jonge<sup>1</sup>  
Critical Care 2005, 9:R458-R463

*Personal details in the case published have been altered to protect patient privacy.*

For palliative care consultations please contact the Palliative Care Program at PUH/MUH, 647-7243, beeper 8511, Shadyside Dept. of Medical Ethics and Palliative Care, beeper 412-647-7243 pager # 8513, Perioperative/ Trauma Pain 647-7243, beeper 7246, UPCI Cancer Pain Service, beeper 644 –1724, Interventional Pain 784-4000, Magee Women’s Hospital, beeper 412-647-7243 pager #: 8510, VA Palliative Care Program, 688-6178, beeper 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children’s page 958-3844. With comments about “Case of the Month” call Dr. Robert Arnold at (412) 692-4834.