Original Study

Impact of Routine Surveillance Imaging on Outcomes of Patients With Diffuse Large B-Cell Lymphoma After Autologous Hematopoietic Cell Transplantation

Narendranath Epperla,[1] Namrata Shah,[1] Mehdi Hamadani,[1] Kristin Richardson,[3] Jonathan T. Kapke,[2] Asmita Patel,[5] Sravanthi P. Teegavarapu,[5] George Carrum,[6] Parameswaran N. Hari,[1] Sai R. Pingali,[5] Reem Karmali,[4] Timothy S. Fenske[1]

Abstract

A majority (71%) of DLBCL relapses after auto-HCT are detected by routine surveillance imaging. Overall, there appears to be limited utility for routine imaging after auto-HCT except in select cases where earlier detection and salvage therapy with allogeneic HCT is a potential option.

Background: For patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), autologous hematopoietic cell transplantation (auto-HCT) is commonly used. After auto-HCT, DLBCL patients are often monitored with surveillance imaging. However, there is little evidence to support this practice. **Patients and Methods:** We performed a multicenter retrospective study of DLBCL patients who underwent auto-HCT (n = 160), who experienced complete remission after transplantation, and who then underwent surveillance imaging. Of these, only 45 patients experienced relapse after day +100 after auto-HCT, with relapse detected by routine imaging in 32 (71%) and relapse detected clinically in 13 (29%). **Results:** Baseline patient characteristics were similar between the 2 groups. Comparing the radiographic and clinically detected relapse groups, the median time from diagnosis to auto-HCT (389 days vs. 621 days, $P = .06$) and the median follow-up after auto-HCT (2464 days vs. 1593 days $P = .60$) were similar. The median time to relapse after auto-HCT was 191 days in radiographically detected relapses compared to 492 days in clinically detected relapses ($P = .35$), and median postrelapse survival was 359 days in such patients compared to 123 days in patients with clinically detected relapse ($P = .36$). However, the median posttransplantation overall survival was not significantly different for patients with relapse detected by routine imaging versus relapse detected clinically (643 vs. 586 days, $P = .68$). **Conclusion:** A majority (71%) of DLBCL relapses after auto-HCT are detected by routine surveillance imaging. Overall, there appears to be limited utility for routine imaging after auto-HCT except in select cases where earlier detection and salvage therapy with allogeneic HCT is a potential option.

Clinical Lymphoma, Myeloma & Leukemia, Vol. ■, No. ■, ■-■
Keywords: Auto-HCT, Clinical, DLBCL, Radiographic, Relapse

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma, accounting for approximately 30% of all non-Hodgkin lymphoma cases in the United States each year. This translates into 20,000 to 22,000 new cases of DLBCL diagnosed each year.[1,2] Currently there is a lack of consensus

[1]Division of Hematology and Oncology
[2]Department of Medicine, Medical College of Wisconsin, Milwaukee, WI
[3]Department of Medicine
[4]Division of Hematology, Oncology, and Cell Therapy, Rush University Medical Center, Chicago, IL
[5]Division of Hematology and Oncology, Houston Methodist Cancer Center, Houston, TX
[6]Center for Cell and Gene Therapy, Baylor College of Medicine, Texas Children's Hospital and Houston Methodist Hospital, Houston, TX

Submitted: Jun 16, 2016; Revised: Aug 13, 2016; Accepted: Aug 18, 2016

Address for correspondence: Timothy S. Fenske, MD, Division of Hematology and Oncology, Medical College of Wisconsin, 9200 W Wisconsin Ave, Milwaukee, WI 53226
Fax: (414) 805-4624; e-mail contact: tfenske@mcw.edu

2152-2650/$ - see frontmatter
http://dx.doi.org/10.1016/j.clml.2016.08.018

regarding optimal method and frequency of radiographic imaging surveillance for DLBCL patients whose disease is in remission.[3-7] The current National Comprehensive Cancer Network and European Society of Medical Oncology guidelines recommend surveillance computed tomographic (CT) scans for the first 2 years after completion of front-line therapy.[8,9] In contrast, the 2014 Lugano classification system advises against routine surveillance imaging.[10] In addition, in a recent population-based study that compared surveillance strategies for DLBCL in first complete remission (CR) in Denmark and Sweden, no survival benefit was associated with surveillance imaging.[11]

Importantly, radiation exposure from surveillance imaging is not trivial, with a potential risk of secondary malignancies. According to some estimates, 0.4% to 2% of cancers in the United States may be related to radiation exposure from CT scans.[12-14] In addition to the radiation exposure, routine surveillance imaging can lead to significant patient anxiety, false-positive findings, unnecessary invasive procedures to follow-up on incidental findings, and a considerable increase in health care cost.[4,15,16]

While there is a growing literature suggesting a lack of clinical benefit of surveillance imaging for DLBCL in first CR, little is known about the potential value of surveillance imaging for patients with relapsed and refractory DLBCL who experience a CR after autologous hematopoietic cell transplantation (auto-HCT). In this setting, there is a considerably higher risk for relapse[17] compared to patients in first CR. As a result, surveillance imaging would be more likely to detect relapse and lead to earlier initiation of salvage therapies, which could theoretically lead to improved outcomes. Surveillance imaging is currently a standard practice at many transplant centers. However, this practice is not evidence based, has not been shown to improve overall survival (OS), and may pose a risk to patients as a result of radiation exposure.

We therefore conducted a multicenter retrospective study of a cohort of DLBCL patients who experienced a CR after auto-HCT and then underwent routine surveillance imaging. We sought to define how many surveillance imaging studies were obtained, how often relapses were detected by surveillance imaging versus clinically (based on signs, symptoms, or laboratory findings), and whether survival either from the time of transplantation or after detection of relapsed disease was improved if relapse was detected by imaging versus clinically.

Patients and Methods

Eligibility Criteria

Adult patients who underwent auto-HCT between January 2000 and December 2013 at 3 participating academic tertiary-care medical centers (Medical College of Wisconsin, Milwaukee, WI; Medical Center, Chicago, IL; and Houston Methodist Hospital, Houston, TX) were identified. The Medical College of Wisconsin Scientific Review Committee and the institutional review boards at all 3 sites approved this study.

To be eligible for the study, the patients must have experienced CR (confirmed by CT and/or positron emission tomographic [PET] scan) on their first posttransplantation evaluation, typically conducted between days 60 and 100. Patients were selected after screening for eligibility criteria. After retrospective chart review, the patients were classified into 2 groups: those who never experienced relapse and those who did. The latter group was further categorized as clinical versus radiographic relapse, which was based on how the relapse was detected. Patients were classified as having a clinical relapse if the relapse was initially detected based on signs, symptoms, physical examination findings, or laboratory abnormalities. Patients were classified as having a radiographic relapse if the relapse was detected solely by planned surveillance imaging in the absence of signs, symptoms, physical examination findings, or laboratory abnormalities.

A total of 209 patients with relapsed or refractory DLBCL who underwent auto-HCT were identified using these search strategies. Patients who experienced CR after first-line therapy and then underwent up-front auto-HCT without any evidence of relapsed or refractory disease were not eligible. A total of 194 patients had evaluable data after excluding 15 patients with insufficient information. Additionally, 34 patients were excluded (8 as a result of death or being lost to follow-up, and the remaining 26 as a result of disease progression or relapse before day +100 evaluation), leaving 160 patients who met the inclusion criteria. Of these, 45 patients experienced relapse after day +100 after auto-HCT. Disease relapse in 13 patients was detected clinically; in the remaining 32 patients, relapse was detected by routine imaging (Figure 1). Patients in the clinically detected relapse group comprised those who presented with relapse in between radiographic surveillance. At all participating transplant centers, the intended mode of surveillance was history, physical examination, and laboratory studies, as well as CT or PET/CT scans obtained at 3- to 6-month intervals during the first 3 years after auto-HCT.

Study End Points

The primary objective of our study was to compare OS between patients whose relapse (after day +100 after auto-HCT) was detected clinically versus those whose relapse was detected radiographically (on routine surveillance imaging). Secondary objectives were to determine the median time to relapse and posttransplantation relapse survival between patients whose relapse was detected clinically versus those whose relapse was detected radiographically as well as to determine the number of surveillance imaging studies performed in patients who never experienced relapse after auto-HCT.

OS was defined as the time from auto-HCT to date of death or last follow-up. Time to relapse was defined as time from auto-HCT to the date of relapse. Postrelapse survival was defined as time from relapse (after auto-HCT) to date of death or last follow-up.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics. Comparisons were made between the clinically and radiographically detected relapse groups by the Wilcoxon rank sum test for continuous variables and the Fisher's exact test for categorical variables. The log rank test was used to compare the survival distribution (OS and posttransplantation relapse survival) between these 2 groups.

Results

Patient Characteristics

Table 1 lists the patient-related, disease-related, and treatment-related variables of the entire group, while Table 2 compares the