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ORIGINAL RESEARCH REPORT

Utility of routine surveillance imaging for diffuse large B-cell lymphoma post autologous transplant: A single center experience

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Abstract
Surveillance scans after autologous stem cell transplant (auto-HCT) for patients with relapsed/refractory (RR) diffuse large B Cell lymphoma (DLBCL) have no proven survival benefit. We studied survival differences among patients with RR DLBCL post auto-HCT whose recurrences were detected clinically versus with routine surveillance imaging. Among the 139 patients with RR DLBCL that underwent auto-HCT from 2000 to 2014 at our institution, 37 relapsed: 21 clinical and 16 radiological. The median time to progression was 167 days for the clinical cohort and 565 days for the radiological cohort ($p = 0.03$), and median overall survival (OS) was 587 days and not reached, respectively ($p = 0.006$). Most patients with relapsed DLBCL after auto-HCT were diagnosed clinically and were likely to be detected earlier and have a shorter OS. Relapse in patients with aggressive disease will likely be detected when clinically apparent, and the outcome of these patients is independent of the way the relapse is diagnosed. Thus, universal scanning after auto-HCT appears to have little benefit.

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Introduction

Diffuse large B-Cell Lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL), comprising approximately 30% of all NHL cases in the United States each year [1,2]. For the 20,000–22,000 new patients with DLBCL each year, the introduction of rituximab to chemotherapy regimens has provided improved results with complete response ranging from 75 to 80% [3–7]. However, up to one-third of patients have disease that relapses after primary therapy or is refractory to initial treatment [7].

The standard of care for relapsed or refractory DLBCL is salvage chemotherapy followed by autologous stem cell transplantation (auto-HCT). This course of treatment is based on the results of a trial showing high-dose chemotherapy and auto-HCT provided a significantly better progression free survival (PFS) and overall survival (OS) in subjects randomized to this therapy compared to those receiving chemotherapy alone [8]. Even with this treatment, relapse or disease progression remains a frequent occurrence at 50–60 percent [4,9,10].

Consequently, DLBCL patients routinely receive radiologic surveillance imaging with CT or PET/CT after auto-HCT. Recently the frequency, method, and even need for radiologic imaging surveillance for DLBCL patients whose disease is in remission after primary therapy has come into question. Both the National Comprehensive Cancer Network and the European Society of Medical Oncology guidelines continue to recommend surveillance computed tomographic (CT) scans no more than every 6 months for the first 2 years after completion of frontline therapy [11,12]. However, the 2014 Lugano classification system advises against routine surveillance imaging [13]. An increasing number of recent studies have shown no OS or PFS benefit associated with surveillance imaging [14–23]. Furthermore, routine surveillance imaging carries with it well known risks of radiation including an increasing incidence of secondary malignancies [24–26].

Although the evidence disputing the clinical benefit of surveillance imaging for DLBCL in first complete response (CR) continues to mount, there is a paucity of data concerning the potential benefit of surveillance imaging for patients with relapsed and refractory DLBCL who experience a CR after auto-HCT. Epperla et al. conducted a multi-center retrospective review examining DLBCL patients who received routine surveillance imaging after complete response from auto-HCT. This study found no significant survival benefit for surveillance imaging, but it did suggest potential value of routine imaging after auto-HCT in select cases where earlier detection and salvage therapy with allogeneic HCT would be an option as the majority of relapses (71%) were detected by radiologic imaging [18]. Despite a lack of evidence, surveillance imaging remains standard practice in the United States, creating increased radiation exposure, health care costs, and unnecessarily invasive follow-up procedures for patients [16,21,23,27–29].

Therefore, we conducted a retrospective study of a cohort of all DLBCL patients at our institution who received auto-HCT from 2000 to 2014 and then relapsed. Our patients were divided into two cohorts, those whose relapse was diagnosed 'clinically' and those whose relapse was diagnosed 'radiographically', and their characteristics and outcomes were compared.

Patients and methods

Patient selection

We performed a retrospective review of all patients with relapsed or refractory DLBCL who had received auto-HCT for treatment at the University of Kansas Cancer Center from 2000 to 2014. Approval from the University of Kansas institutional review board was obtained prior to data collection.

Eligibility criteria for our study thus included all patients aged 18 or greater with a diagnosis of relapsed/refractory DLBCL that were undergoing autologous transplant at our institution from 2000 to 2014.

After screening for eligibility criteria, patients were selected and baseline clinical, laboratory, and treatment data were collected from their medical records using a systematic approach. Selected patients were initially divided into two groups consisting of those who never relapsed and those who did. The latter group was further divided into patients whose relapse was determined clinically versus radiographically (see Fig. 1).

Clinical progression of disease was defined as tumor progression detected or suspected based on signs, symptoms, physical examination findings, or laboratory abnormalities. Usual signs and symptoms observed were those classical of disease recurrence such as night sweats, fevers, weight loss, palpable masses, organomegaly or signs or symptoms localizing to a particular area of the body where relapse was suspected. Laboratory findings observed were those suspicious or consistent with disease progression such as abnormalities on routine blood counts, chemistry, erythrocyte sedimentation rate, or an elevated lactate dehydrogenase (LDH) or uric acid.

Radiographic progression of disease was defined as tumor progression detected exclusively by predetermined

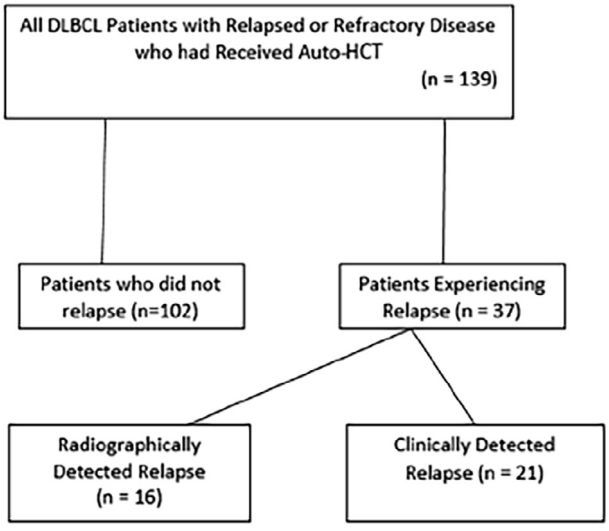

Fig. 1 Consort diagram outlining the study.

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