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Basic Original Report

Radiation pneumonitis in pediatric Hodgkin lymphoma patients receiving radiation therapy to the chest

Gary D. Lewis MD [a, b, c], Jennifer E. Agrusa MD [d], Bin S. Teh MD [b], Maria M. Gramatges MD, PhD [d], Viral Kothari MD [e], Carl E. Allen MD, PhD [d], Arnold C. Paulino MD [c,*]

[a]*Department of Radiation Oncology, The University of Texas Medical Branch at Galveston, Galveston, Texas*
[b]*Department of Radiation Oncology, Houston Methodist Hospital, Houston, Texas*
[c]*Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas*
[d]*Division of Pediatric Hematology and Oncology, Baylor College of Medicine, Houston, Texas*
[e]*Department of Pediatric Pulmonary Medicine, Baylor College of Medicine, Houston, Texas*

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Abstract

Purpose: The purpose of this study is to determine the incidence of radiation pneumonitis (RP) in children receiving radiation therapy (RT) for Hodgkin lymphoma (HL).

Methods and patients: A retrospective chart review was conducted of pediatric HL patients who received multiagent chemotherapy followed by RT to any part of the chest. The National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03, was used to determine the RP grade. Parameters analyzed included sex; age; bleomycin dose; and RT dosimetric variables such as mean lung dose (MLD), mean individual (i; right vs left) lung dose or iMLD, V5 to V25, and individual lung V5 to V25.

Results: From 2008 through 2016, 54 children with HL received RT to the chest and had follow-up and dosimetry information. All patients received induction chemotherapy; the most common regimen was Adriamycin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide–based chemotherapy (n = 48). All received a prescribed dose of 21 Gy in 14 fractions. Median follow-up from completion of RT was 39.5 months. Three of 54 patients (5.6%) or 3 of 108 (2.8%) lungs developed RP; 2 lungs had grade 1, whereas 1 had grade 2 RP. RP was seen only in patients with MLD >12.4 Gy (P = .009), V5 >66% (P = .033), V10 >55% (P =.015), V15 >45% (P =.005), and V20 >32% (P =.007). Likewise, RP was only seen in lungs with iMLD >13.8 Gy, iV5 >75% (P =.02), iV10 >64% (P =.02), iV15 >47% (P < .005), and iV20 >34% (P =.003).

Conclusions: RP in pediatric HL patients is an uncommon complication. MLD, iMLD, V5-V20, and iV5-iV20 correlated with RP.

Introduction

Radiation oncologists often use adult dosimetric parameters to help guide treatment planning in children with cancer. Although there is adequate information on the

Conflicts of interest: None.

* Corresponding author. Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Box 97, Houston, TX 77030.

E-mail address: APaulino@mdanderson.org (A.C. Paulino).

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incidence and risk factors for radiation pneumonitis in adults,[1] information is limited in children. The existing limited data suggest the rates of pediatric radiation pneumonitis are lower compared with adults, possibly from lower radiation therapy (RT) doses used and different risk factor profiles.[2,3] For example, unlike adults, children are less likely to be exposed to environmental insults such as smoking and asbestos, which may compromise the integrity of the lung. Most of the existing data with regard to RT parameters that influence the development of pneumonitis has been in patients with lung cancer, a substantial proportion of whom have a history of smoking.

The determination of lung dosimetric parameters specific to children may allow for improved radiation treatment planning for pediatric Hodgkin lymphoma (HL) patients also receiving pulmonary-toxic systemic therapy. We hypothesize that dosimetric parameters may have an influence on the development of radiation pneumonitis in children with HL. We performed this study to determine the incidence of radiation pneumonitis (RP) in the pediatric population receiving RT and bleomycin-containing chemotherapy for HL.

Methods and patients

Patient and treatment characteristics

This retrospective study was approved by the Baylor College of Medicine Institutional Review Board. Overall, 72 patients were identified based on a retrospective review of patients diagnosed with HL and treated with RT from June 2007 to May 2016. Four patients did not have RT directed to the chest and 14 patients did not have adequate dosimetry data or minimum follow-up of 1 year after RT. Fifty-four pediatric patients had sufficient dosimetry data and follow-up information to be included in the current analysis. Baseline patient characteristics including age, sex, and Ann Arbor stage were recorded. The median age was 15 years (3-18 years). There were 29 girls and 25 boys. All patients received induction chemotherapy with a regimen that included bleomycin (median dose 60 IU/m^2; range, 45-80 IU/m^2). The most common chemotherapy regimen was Adriamycin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide (n = 48). Overall, 45 patients (83.3%) received 4 cycles of chemotherapy. RT was initiated approximately 3 weeks after completion of the last cycle of chemotherapy. All patients received external beam RT with photons after computed tomography (CT) scan simulation. Simulation imaging included the entire bilateral lungs. Treatment planning was performed using Philips Pinnacle TPS (Philips Medical Systems, Andover, MA). The guidelines for target delineation used on these patients are based on Children's Oncology Group protocols because many of these patients were enrolled on the AHOD0031, AHOD0831, or AHOD1331 protocols. Those who were not enrolled also followed the same RT guidelines. In these guidelines, lung heterogeneity correction was used. The clinical target volume and planning target volume margins were also per protocol.[4]

All patients received a prescribed dose of 21 Gy in 14 fractions to the involved sites of disease. In addition, 6 patients also received concurrent, low-dose, bilateral whole lung irradiation to a prescribed dose of 10.5 Gy in 14 fractions. RT was delivered via 3-dimensional (3D) conformal RT (CRT) in 43 patients and intensity modulated RT (IMRT) in 11 patients.

Radiation pneumonitis grading

Radiation pneumonitis data were collected retrospectively from review of the medical record. Toxicities were evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03, to determine the RP grade (grade 1: asymptomatic, clinical or diagnostic observations only, intervention not indicated; grade 2: symptomatic, medical intervention needed; grade 3: severe symptoms, oxygen indicated; grade 4: life-threatening respiratory compromise including tracheotomy and intubation; grade 5: death). All grades of RP were considered clinically significant. The diagnosis of RP was based on the appropriate clinical symptoms with corresponding radiographic changes within the radiation field without evidence of other competing diagnoses. Two authors agreed independently with regard to the presence of pneumonitis and its corresponding grade.

RT dosimetric analysis

Right, left, and total lung volumes were contoured on the patient's CT scan simulation imaging. Contoured lung volumes did not include the intrathoracic lymph nodes being treated. Differential and cumulative dose-volume histograms of the total lung volume were calculated without excluding the overlapping planning target volume. Mean total lung dose (MLD), mean individual (right vs left) lung dose (iMLD), and volume of both and individual lungs receiving a dose of 5 Gy (V5 and iV5), 10 Gy (V10 and iV10), 15 Gy (V15 and iV15), 20 Gy (V20 and iV20), and 25 Gy (V25 and iV25) were collected for analysis.

Statistical analysis and follow-up

The χ^2 and Fischer exact tests were used to compare the proportion of patients who developed pneumonitis according to sex, age ($\leq$14 vs >14 years), bleomycin dose ($\leq$60 vs >60 IU/m^2), and RT parameters such as MLD, iMLD, V5, iV5, V10, iV10, V15, iV15, V20, iV20, V25, and iV25. Cutoffs for age and bleomycin dose were