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MID- AND POST-ABVD GALLIUM SCANNING PREDICTS FOR RECURRENCE IN EARLY-STAGE HODGKIN'S DISEASE

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Purpose: To determine the efficacy of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) for patients with Hodgkin's disease and to identify predictors of outcome with this regimen.
Methods: Between 1987 and 1998, 175 patients with Stage I-IV Hodgkin's disease received ABVD as part of initial treatment. Overall survival (OS), freedom-from-treatment-failure (FFTF), and progression-free survival (PFS) were calculated using the Kaplan-Meier technique. Log–rank tests were used to identify univariate predictors of OS, FFTF, and PFS. Specifically, restaging gallium scan results and clinical response after chemotherapy were separately evaluated.
Results: The median follow-up time was 64 months. The 5-year OS, FFTF, and PFS rates were 90%, 85%, and 82%, respectively. For Stage I-II patients, restaging gallium scan results and clinical response after chemotherapy were highly predictive of OS, FFTF, and PFS ($p < 0.0001$). Other significant predictors for higher OS included age <50 ($p = 0.002$), female gender ($p = 0.047$), and absence of B symptoms ($p = 0.043$). Of the 20 patients with a positive restaging gallium scan, 4 received high-dose therapy and 16 continued with conventional-dose therapy or received no further treatment. Of these 16 patients, 11 (69%) were disease-free at last follow-up.
Conclusions: Although a positive mid- or postchemotherapy gallium scan was an adverse prognostic factor for OS, FFTF, and PFS, continued treatment with conventional-dose therapy may be adequate in selected patients with positive scans.

Hodgkin's disease, Doxorubicin, Bleomycin, Adriamycin, Vinblastine, Dacarbazine, Gallium scannings.

INTRODUCTION

Historically, radiation therapy alone has been the mainstay of treatment in patients with early-stage Hodgkin's disease. For patients with advanced-stage disease, the introduction of the combination chemotherapy regimen mechlorethamine, Oncovin, procarbazine, and prednisone (MOPP) in the mid-1960s substantially improved the cure rates of these patients (1). The Adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) regimen was initially introduced as a form of second-line therapy in patients who had a poor response to, or relapsed after, MOPP chemotherapy (2–5). Randomized studies subsequently showed that ABVD-containing regimens were superior to MOPP as first-line treatment for both advanced-stage and early-stage Hodgkin's disease (6–8). Given that, along with its substantially lower myelosuppressive and leukemogenic effects and the preservation of patient fertility, ABVD is currently the most widely accepted chemotherapy regimen for Hodgkin's disease.

There is a considerable amount of retrospective information available on prognostic factors and long-term treatment outcome of patients with Hodgkin's disease (9–14). However, most of these studies consist of a heterogenous patient population treated with radiation therapy with or without various types of chemotherapy. In this study, we identified a cohort of patients who all received ABVD as part of initial treatment. We sought to determine the long-term efficacy of ABVD with or without radiation therapy and to evaluate treatment-related toxicities in patients who received ABVD for their Hodgkin's disease. In addition, predictors of treatment outcome, including clinical and radiographic response to chemotherapy, were evaluated.

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Table 1. Patient characteristics

		Number (%)
Age at diagnosis		
Mean	29.9	
Median	30	
Range	9–71	
≤50		166 (95)
>50		9 (5)
Gender		
Female		82 (47)
Male		93 (53)
Clinical stage		
I		14 (8)
II		125 (71)
III		17 (10)
IV		19 (11)
B symptoms		
Yes		66 (38)
No		109 (62)
Mediastinal disease		
None		32 (18)
<34%		89 (51)
≥34%		54 (31)
Number of sites		
0–3		121 (69)
≥4		54 (31)
Histology		
Lymphocyte predominant		3 (2)
Nodular sclerosing		148 (85)
Mixed cellularity		18 (10)
Unclassifiable		6 (3)

METHODS AND MATERIALS

Patient characteristics

Between 1987 and 1998, 175 patients with Hodgkin's disease received ABVD as part of initial treatment. Patient characteristics are summarized in Table 1. Median age at presentation was 30. A total of 139 patients (79%) had Ann Arbor clinical stage (CS) I-II disease, and 36 patients (21%) had CS III-IV disease. B symptoms were present in 66 patients (38%). Fifty-four patients (31%) had large mediastinal lymphadenopathy, defined as the width of the mediastinal mass greater than one-third of the maximum thoracic diameter, and 54 patients (31%) had four or more sites of disease at presentation. Histologic classification for all patients was confirmed by hematopathologists at the treating hospital.

Treatment

All 175 patients received ABVD as part of initial treatment. The median number of cycles of chemotherapy was 6 (range, 1–10), with 33 patients receiving less than 6 cycles and 134 receiving 6 or more cycles of chemotherapy. The total number of cycles of chemotherapy in the remaining 8 patients was unknown. Consolidative radiation therapy was added in 146 patients (83%), whereas 29 patients (17%) were treated with chemotherapy alone. Among the 139 patients with CS I-II disease, 90% received consolidative radiation therapy and 58% of the 36 patients with CS III-IV disease received radiation therapy. All patients treated with radiation therapy underwent simulation and received treatment on 4-MV to 6-MV linear accelerators for mantle and pelvic fields and 6- to 15-MV linear accelerators for paraaortic irradiation. Twenty-one patients (14%) received subtotal nodal irradiation, 91 patients (62%) received mantle radiation therapy (inclusion of bilateral neck, bilateral axillae, mediastinum, and bilateral hila), 28 patients received involved-field irradiation to the mediastinum (19%), and 6 patients received radiation therapy to sites other than the chest region (4%). The median dose of radiation to the mediastinum was 3660 cGy (range, 1500–4320 cGy). The prescribed radiation doses were normalized to the central axis. Because of reduced scattered dose from the lung blocks, the lower mediastinum typically received approximately 7% less than the prescribed dose. Only 3 patients received whole-lung radiation therapy (2%).

Restaging gallium

Gallium scan for restaging midway through chemotherapy was performed in 91 patients, and postchemotherapy gallium scan was performed in 119 patients. Because this cohort of patients was treated at a time before positron emission tomography scanning was available at our institution, none underwent positron emission tomography scan for restaging. Thirty patients had mid-chemotherapy gallium scan only, 58 had postchemotherapy gallium scan only, and 61 patients had both mid- and postchemotherapy gallium scans. One hundred forty-nine patients (85%) underwent at least one gallium scan either mid-chemotherapy or postchemotherapy. Seventeen patients (15%) did not have a gallium scan for restaging, and in 9 patients, it is unknown whether any restaging gallium scan was performed. Patients with a positive restaging gallium scan at the end of the ABVD chemotherapy were managed in one of the following ways: proceeded with radiation therapy as planned (8), received additional chemotherapy or radiation therapy (6), underwent high-dose therapy with stem-cell rescue (4), or had no further treatment (2).

Clinical response after chemotherapy

Clinical response after chemotherapy was determined based on computed tomography (CT) scan findings or by physical examination at the end of the ABVD chemotherapy, using guidelines developed by the International Workshop on Response Criteria for non-Hodgkin's lymphoma (15). A complete response (CR) was defined as a negative physical examination and residual disease of 1 cm or less. A complete response/unconfirmed (CRu) was defined a >75% reduction in tumor volume, with residual disease of 2 cm or less. A partial response (PR) was defined as >50% reduction in tumor volume. Stable disease was defined as <50% reduction in tumor volume. Progressive disease was defined as an increase in the size of initial disease or development of new sites of disease. Relapsed disease was defined as further disease progression or appearance of new sites of disease after a response had been achieved with the initial course of treatment.

Statistical analysis

Overall survival (OS), freedom from treatment failure (FFTF), and progression-free survival (PFS) were calculated using the Kaplan-Meier technique. OS was defined as the time from Hodgkin's disease diagnosis to death or last follow-up. PFS was defined as the time from Hodgkin's disease diagnosis to relapse or death from any cause without documented relapse. FFTF was defined as the time from Hodgkin's disease diagnosis to relapse. Log–rank tests were used to identify univariate predictors of OS, FFTF, and PFS. Two-sided Fisher's exact tests were performed to determine if there was an association between pulmonary complications and various patient or treatment factors.