Clinical Significance of Non-Hodgkin's Lymphoma with an Irregular, Non-Contrast-Enhanced Area

Yasuhiro Saitoh,* Masayuki Mineta, Tomonori Yamada, Dalhei Yoshikawa, Hiroshi Yoshida, and Tamio Aburano

Department of Radiology, Asahikawa Medical University and Hospital, Asahikawa, Japan

Background: An irregular, non-contrast-enhanced area shown on postcontrast computed tomography (CT) or postcontrast magnetic resonance imaging (MRI) in cases of non-Hodgkin's lymphoma (NHL) may indicate that the primary tumor has a high degree of malignancy. This study was planned to determine whether this indicated a poor prognosis.

Methods: Fifty-six patients with NHL (32 males and 24 females) underwent diagnostic imaging; the internal characteristics of the primary lesion were evaluated retrospectively by 2 radiologists. Postcontrast CT with 2 mL/kg of contrast medium was performed in 46 cases during the equilibrium phase, and postcontrast MRI was also performed in 10 cases by the spin echo method following an 0.1 mmol/kg intravenous injection of gadopentetate.

Results: Ten (17.8%) of the 56 cases with NHL showed an irregular non-contrast-enhanced area. The 5-year survival rate for cases with homogeneous enhancement was 77.5%, while the actuarial survival rate at 44 months for cases with an irregular non-contrast-enhanced area was 25.4% (P < 0.005). From the results of multivariate analysis using Cox's regression model for 11 factors (internal characteristics, sex, age, clinical stage, primary site, size, lactic dehydrogenase value, systemic symptoms, cell marker, histopathologic criteria, and therapy), symptoms (P = 0.0001) and internal characteristics (P = 0.0164) were selected as the variants affecting the prognosis. No correlations were found between internal characteristics and other variants.

Conclusion: Contrast CT or MRI should be evaluated before treatment, as the presence of an irregular non-contrast-enhanced area indicates a poor prognosis.

INTRODUCTION

Several reports have shown that lymphomas with an irregular, non-contrast-enhanced area inside the lesion have a higher malignancy and a poorer prognosis than lymphomas that show homogeneous contrast enhancement on computed tomography (CT) or magnetic resonance imaging (MRI). However, there has been insufficient investigation concerning the correlation to other background factors such as clinical stage, lesion size, and primary site, and concerning the independence of non-contrast-enhanced areas as a prognostic factor. In this paper, we report the results of multivariate analysis performed to determine the clinical significance of image findings showing an irregular, non-contrast-enhanced area inside a lesion that has been diagnosed as non-Hodgkin's lymphoma (NHL).

PATIENTS AND METHODS

NHL was histopathologically diagnosed in 56 patients, who had CT and MRI scans before treatment. Patient characteristics are shown in Table 1. The patients were 32 males and 24 females, with an age distribution of 10 to 84 years (mean, 58.6). The distribution of clinical stages, according to the Ann Arbor classification, were stage I, 19 cases; stage II, 19 cases; stage III, 8 cases; and stage IV, 10 cases. The histopathologic criteria were based on the working formulation.

There were 4 methods of treatment: radiotherapy alone, radiotherapy followed by chemotherapy, chemotherapy followed by radiotherapy, and chemotherapy alone. Patients in the radiotherapy alone group and radiotherapy followed by chemotherapy group were irradiated locally at a dose of 60 gray/30 fractions/6 to 7
weeks (60 Gy/30 f/6 to 7 wk), generally with cobalt 60 gamma rays. Subsequent chemotherapy consisted of 3 to 5 courses of mainly vincristine, cyclophosphamide, procarbazine, and prednisone (VEPP) or cyclophosphamide, vincristine, and prednisone treatment. In the groups in which chemotherapy was performed first or only chemotherapy was performed, the treatment consisted of 2 to 7 courses of bleomycin, doxorubicin, cyclophosphamide, vincristine, and prednisone; cyclophosphamide, doxorubicin, vincristine, and prednisone; or prednisone, methotrexate, calcium leucovorin, doxorubicin, cyclophosphamide, and etoposide with cytaBOM (proMACE-cytaBOM: prednisone, calcium leucovorin, doxorubicin, cyclophosphamide, cytarabine, pepleomycin, vincristine, and methotrexate). In these groups, the dose of radiation, given after chemotherapy, was 40 Gy/20 f/5 wk.

Diagnostic imaging was performed on all patients before treatment, and the internal characteristics of the primary lesion on CT and MRI images were evaluated retrospectively by 2 radiology specialists. CT images were used for the evaluation in 46 cases, and MRI images were used in 10 cases in which no CT scan had been performed. For the CT imaging, 2 mL/kg of nonionic contrast medium was used, and the CT was performed during the equilibrium phase. A 1.5 T superconducting machine was used for MRI, which was also performed in the equilibrium phase by the spin echo method at T1-weighted imaging (TR 500 ms/TE 15 ms) following an 0.1 mmol/kg intravenous injection of gadopentetate. A T2-weighted imaging was not used as a rule for evaluation reference.

Statistical Analysis
Statistical significance was determined by the chi-square test (including a correction factor) and Fisher's direct probability method. We used the Kaplan-Meier method for calculating the survival rate, the log-rank test for assessing significant differences, and Cox's multiregression life table for multivariate analysis. A difference of $P < 0.05$ was considered to be statistically significant.

RESULTS
A CT scan showing a homogeneous contrast enhancement inside a lesion and an MRI scan showing an irregular, non-contrast-enhanced area inside a lesion are depicted in Figs. 1 and 2, respectively. Ten of the 56 patients (17.9%) in this study showed an irregular, non-contrast-enhanced area inside the lesion.

As for the relation between the presence or absence of a non-contrast-enhanced area and a complete remission after treatment, the results showed that a complete remission was not obtained in 8.7% (4/46) of the patients with a homogeneous contrast area. In patients with a non-contrast-enhanced area, the percentage of...