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Association between non-insulin dependent diabetes mellitus and non-Hodgkin's lymphoma

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of diabetes in the second group was significantly increased (table). The prevalence of diabetes in patients with extranodal lymphoma in the head, nose and sinuses, central nervous system, and orbit was particularly increased, with a ratio of observed to expected cases of diabetes of 7.3 (95% confidence interval 3.51 to 11.2, $P < 0.0001$). In contrast, the correlation coefficients between diabetes and other factors were 0.001 (-0.0029 to 0.0049) for age, 0.006 (-0.016 to 0.028) for body mass index, and -0.057 (-0.19 to 0.078) for sex.

Cases of diabetes mellitus observed in 133 patients with lymphoma compared with those expected in general population

Lymphoma	No of cases		Ratio of (95% confidence interval) of observed cases to expected cases	P value
	Observed	Expected		
Nodal (n=74)	8	7.03	1.14 (0.35 to 1.92)	0.74
Extranodal (n=59)	18	5.52	3.26 (1.75 to 4.77)	<0.0001

The onset of diabetes in all 26 cases was in adulthood. All cases were type II non-insulin dependent diabetes mellitus, 23 of which were controllable with diet alone.

Comment

The association between diabetes mellitus and lymphoma was first suggested by Stowens.⁴ This association, however, was not confirmed by another study.⁵ Few studies have been published on the differences in characteristics or prognostic factors between patients with nodal lymphoma and those with extranodal lymphoma, and the findings of these were not clear.¹ The present study found that the prevalence of diabetes was high in patients with extranodal lymphoma, especially lymphoma in the head, nose and sinuses, central nervous system, and orbit.

We cannot clearly explain why diabetes is often found in patients with extranodal lymphoma, but a genetic association may exist between the extranodal lymphoma and the locus of type II non-insulin diabetes mellitus. Further study of genetic markers may show further differences between extranodal lymphoma and nodal lymphoma.

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Nodal and extranodal lymphomas are considered to be distinct entities on the basis of histological distribution, response to chemotherapy, and prognosis.¹ The risk of non-Hodgkin's lymphoma is significantly increased in patients in an immunosuppressive state,² and diabetes mellitus impairs the immune response to bacterial infections.³ We therefore retrospectively investigated the prevalence of diabetes mellitus in patients with nodal and extranodal lymphomas to determine whether the risk of lymphoma is increased in patients with diabetes.

Patients, methods, and results

From 1986 to 1993, 160 patients with nodal and extranodal lymphoma, excluding those who were positive for human T cell leukaemia/lymphoma virus type I antibody, were treated at Kobe University School of Medicine Hospital. No patients were positive for HIV-1 antibody. We excluded 27 patients (21 with nodal lymphoma, six with extranodal lymphoma) because adequate data were not documented. Thus 133 patients (74 with nodal lymphoma and 59 with extranodal lymphoma) remained in the study. The median age at diagnosis was 62 in patients with nodal lymphoma and 60 in patients with extranodal lymphoma. The distributions of age, sex, and histological findings were not significantly different between the group of patients with nodal lymphoma and the group with extranodal lymphoma except that the prevalence of patients with a follicular-type lymphoma was higher in the first group. The body mass index (weight (kg)/(height (m)²)) was 21.8 (SD 2.90) in the group of patients with nodal lymphoma and 22.6 (3.58) in the group with extranodal lymphoma.

We calculated the number of patients in each group expected to have diabetes, using the age and sex specific prevalence of diabetes reported by the ministry of health and welfare. We calculated the confidence intervals of the ratios of observed to expected cases and we tested the equality of the numbers observed and the numbers expected by assuming that the observed numbers had a normal distribution. A two sided test was used.

Diabetes was diagnosed in eight of the 74 patients with nodal lymphoma and in 18 of the 59 patients with extranodal lymphoma. In the first group no increase occurred in the ratio of observed to expected cases of diabetes, while the ratio of observed to expected cases

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