to be risk factors for HCL. Recently, an elevated risk for developing HCL has been reported in farmers.[1,2] Familial HCL, defined as the occurrence of HCL among numerous first degree family members, has previously been reported in only seven families.[4-10] Analyzing the HLA typing in these families, similarities has been found in the HLA types, raising the possibility that HCL is an HLA-linked disease. In contrast, no specific HLA antigens have been found in unrelated cases of HCL, but an increased frequency of B17 and DR11 antigens compared to those found in the normal Caucasian population, has been recorded.[11] In familial cases, there were different haplotypes reported to be specific for the disease: type A1 A3 B8 B149; type A1 B78; type A3 A9 B7 Cw610; type A3 B3 B7 DR2 7; type A2 Bw4 Bw62(15)Cw1DR4 DRw53 DQ33; and type A3 B7 or A2 Bw4 and Bw64. It is interesting that the type A3 B7 and A2 Bw4 Bw6 were reported in various cases and the type Bw6 was common in all the cases reported by two authors.[4,5] The hypothesis that HCL is an HLA-linked disease was, therefore, considered, but not proven.

We present two patients (father and son); HLA typing of our patients showed the haplotype A80 B45 Bw6 Cw6 DR9 DR53 DQ2. This haplotype has not previously been seen in reported cases of familial HCL. The father's HLA showed an interesting association of HLA type A2Bw4Bw6, previously reported.[4,5] We feel that our findings strengthen the possible association between these antigens and the development of HCL. However, environmental factors could play a role in the genesis of HCL within families. It has recently been published that the most frequent occupation among 48 Swedish men and women with HCL was farming or gardening (31%) (39% of the men).[2] Our two patients were farm workers exposed to suspected carcinogens. The existence of some HLA antigens in common suggests a familial predisposition to the disease,[3] however, familial HCL is not associated with a specific HLA haplotype; the role of an environmental risk factor, to which the affected members of the families were exposed, cannot be excluded either.

Key words

Familial hairy cell leukemia, hairy cells, HLA typing, HLA-linked disease

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Tumor burden and serum level of soluble CD25, CD8, CD23, CD54 and CD44 in non-Hodgkin's lymphoma

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We studied the value of soluble CD25, CD8, CD23, CD54 and CD44 serum levels as tumor burden markers in lymphoma. Soluble CD25 compared with the others sCD and the usual serum factors (albumin, lactate dehydrogenase, β_2-microglobulin, uric acid and C-reactive protein), showed the strongest correlation with the Ann Arbor stage and the number of affected localizations. sCD25 level is the most sensitive serum marker for tumor burden in lymphoma.

Tumor burden is an important prognostic factor in lymphoma.[1] Tumor burden is roughly approximated by physical examination, bone marrow biopsy and imaging techniques. Estimating tumor burden by a non-invasive method is an old interest in oncology. Over the last decade, the measurement of soluble receptors levels has been explored as an additional tool for the assessement of tumor burden and prognosis in patients with lymphoma.[2,3] Several investigations in different histologic subtypes of non-Hodgkin's lymphoma (NHL) have demonstrated the good association between soluble serum interleukin-

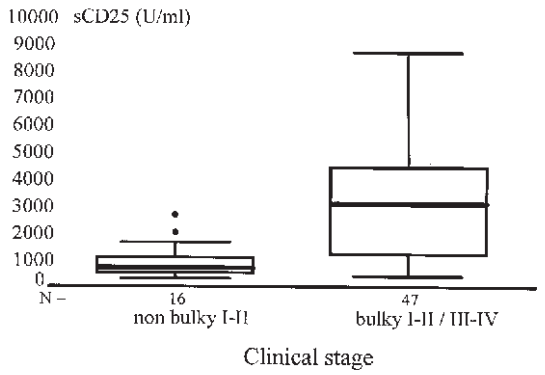

Figure 1. Serum sCD25 levels in relation to clinical stage. All patients with non bulky I-II stage had a serum sCD25 level < 3,000 U/mL. The highest value in the NHL group is not showed. The center line represents the median.

2 α receptor (sCD25) level and the tumor burden.[4,5] Soluble sCD25 was considered the most sensitive serum marker for tumor burden in lymphoma.[6] Others soluble receptors seem to be associated with tumor burden, e.g. sCD8,[7] sCD23,[8] sCD54[9] and sCD44,[10] and interesting biological-clinical correlations have been established in chronic lymphocytic leukemia.[11,12] The value of these new serum factors for estimating tumor burden had not been evaluated versus soluble CD25.

We measured serum levels of sCD25, sCD8, sCD23, sCD54 and sCD44s at diagnosis in 63 adults patients with NHL diagnosed from January 1991 to July 1994. Patients with clinical evidence of acute infection were not included in this study. The extent of disease, evaluated according to standard criteria, was expressed by the Ann Arbor stage system, and by the number of affected nodal or extranodal localizations. The histologic specimens were revised according to the updated Kiel classification. The series included 30 patients histologically classified as having low-grade NHL, and 33 patients classified as having high-grade NHL. Patients with chronic lymphocytic leukemia, hairy cell leukemia and Waldenström disease were excluded from analysis. Serum samples were also taken from 49 healthy adult persons (controls). The measurements were performed by enzyme-linked immunosorbent essay with commercially available kits: sCD25, sCD8 and sCD23 came from T Cell Science, sCD44 and sCD54 from Bender Medsystems.

Serum values of sCD25, sCD8, sCD54 and sCD44 were elevated in NHL in comparison with normal controls ($p < 0.0001$; see Table 1). Values of sCD25 were markedly increased, in contrast the median of sCD23 in NHL was not different from that in the control group. Of the sCD molecules, only sCD25 and sCD8 showed significant differences between stages I-II and III-IV (see Table 1). Nevertheless no cut-off for sCD25 or sCD8 could separate the patients well according to the stage. When we associated the stage with the presence of bulky disease, sCD25 showed some discriminant utility (see Figure 1): all patients with non bulky I-II stage (16 cases) had a sCD25 < 3000 U/mL. Nevertheless, 22 out of 47 with extended disease (bulky I-II and III-IV stages) also had a serum sCD25 < 3000 U/mL ($p = 0.0002$, chi-square test). Among sCD molecules, sCD25 showed the stronger correlation with the Ann Arbor stage, the number of affected localizations (nodal, extranodal and total), and

Table 2. Correlations between serum sCD levels and clinical parameters in NHL patients.

	sCD25 *p*	*sCD8* *p*	*sCD23* *p*	*sCD54* *p*	*sCD44* *p*	*LDH* *p*	*β_2m* *p*
High-grade NHL group							
Ann Arbor stage	**	ns	ns	*	*	**	*
Number localizations	**	*	ns	**	*	**	*
LDH	**	**	ns	**	**	-	**
β2-microglobulin	**	**	ns	**	**	**	-
Low-grade NHL group							
Ann Arbor stage	*	ns	ns	ns	ns	ns	ns
Number localizations	*	*	ns	ns	ns	*	*
LDH	**	ns	ns	**	*	-	*
β2-microglobulin	*	**	ns	ns	*	*	-

Spearman´s rank correlation is showed by the p value (two tailed).
**p ≤ 0.05; ** p≤ 0.01; ns: not significant (p > 0.05).*

Table 1. Serum sCD in NHL patients according to Ann Arbor stage.

	No. of cases	*sCD25 (U/mL)* *median*	*p*	*sCD8 (U/mL)* *median*	*p*	*sCD23 (U/mL)* *median*	*p*	*sCD54 (ng/mL)* *median*	*p*	*sCD44 (ng/mL)* *median*	*p*
Control vs NHL											
Control	49	385	< 0.0001	370	< 0.0001	140	ns	248	< 0.0001	502	< 0.0001
NHL	63	1,757		655		174		550		894	
Ann Arbor stage											
I-II	24	789	0.0006	544	0.0144	128	ns	502	ns	856	ns
III-IV	39	3,174		810		214		600		976	

Levels of sCD are shown as median. ns: not significant (p > 0.05).

the serum levels of lactate dehydrogenase (LDH) and β_2-microglobulin (β_2m), as shown in Table 2. Of all the serum factors studied, i.e. the sCD and the usual serum markers (LDH, β_2m, albumin, uric acid and C-reactive protein), sCD25 also showed the strongest correlation with tumor burden (data about albumin, uric acid and C-reactive protein are not shown in Table 2).

In conclusion, serum levels of sCD25, sCD8, sCD54 and sCD44 are roughly proportional to the burden of neoplasia, but sCD25 is clearly more sensitive as a marker of tumor burden than others sCD. sCD25 is also clearly a more sensitive marker of tumor burden than usual serum factors. Measurements of sCD25 can be indicated for stage assessment in all patients with NHL.

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Key words

Serum markers, tumor burden, sCD25, sCD8, sCD23, sCD54, sCD44, non- Hodgkin's lymphomas.

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Thyroid volume is progressively reduced as a sequela of neck irradiation for childhood Hodgkin's disease

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Thyroid volume reduction was observed, among 25 subjects off-therapy after Hodgkin's disease. The volume reduction was related to dose (p=0.014) and time from radiotherapy (p=0.01). The correlation was very specific since all patients with reduced volume had hypothyroidism, but not very sensitive since 25% of subjects with thyroid dysfunction had normal gland volume.

As the thyroid gland is frequently within the field of neck irradiation for Hodgkin's disease (HD), patients treated in this way may have an increased risk of secondary thyroid carcinoma.[1-3] It is, therefore, recommended that the follow-up of these patients includes thyroid ultrasound examination[4,5] and monitoring of thyroid hormones.[6] We followed-up 25 children who had been treated for Hodgkin's disease; 22 of them received neck irradiation, while performing thyroid ultrasound screening, we also measured the gland volume, and this information was compared with that of the thyroid function.

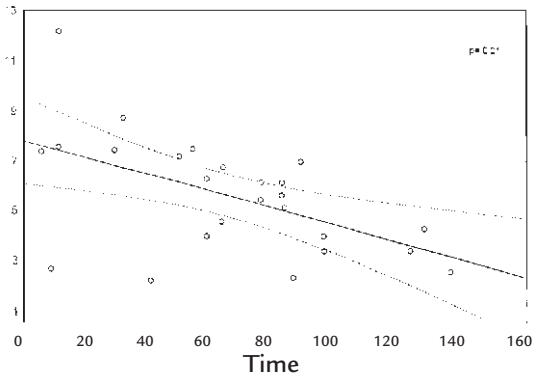

Figure 1. Regression line and 95% CI of the thyroid volume measured by us in patients evaluated at different times after completion of treatment for childhood Hodgkin's disease.