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SHORT COMMUNICATION

Soluble interleukin-2 receptors in the serum of patients with Hodgkin's disease

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The mechanisms leading to the complex clinico-pathological picture in Hodgkin's Disease (HD) are poorly understood. In particular, the intimate nature and meaning of immunological abnormalities extensively reported in this disease, and the affiliation to a definite cellular lineage of Hodgkin (H) and Reed–Sternberg (RS) cells, are still a matter of debate (Hsu *et al.*, 1985; Stein *et al.*, 1985; Romagnani *et al.*, 1985; Kamesaki *et al.*, 1986). These latter cells, which are generally considered the malignant proliferating clone, although rather scanty within the involved tissues in most cases, seem to play a crucial role in the disease through a negative influence on the lymphoid environment. This eventually leads to the well known, yet unexplained, derangement of the immune system (Frydecka, 1985; Romagnani *et al.*, 1985).

It has been recently demonstrated that a soluble form of interleukin-2 receptors (sIL-2R), which retains the ability to bind IL-2, can be released by activated lymphoid cells (Rubin *et al.*, 1985). High levels of sIL-2R have also been found in the serum of hairy cell leukaemia (HCL) (Steis *et al.*, 1986; Chilosi *et al.*, 1986), whose cells are known to strongly express IL-2R (Korsmeyer *et al.*, 1983). In a previous report we demonstrated a strong cytoplasmic positivity for IL-2R in H and RS cells (Pizzolo *et al.*, 1984). In addition, activated lymphocytes expressing surface IL-2R have also been found in tissues involved by HD in higher proportion than in normal or reactive lymph nodes (Pizzolo *et al.*, 1984). All these considerations taken together, we investigated the presence of sIL-2R in the serum of patients with HD.

The study was performed on the serum of 23 patients with HD during the active phase of their disease (20 at diagnosis and 3 during the relapse). The stage of the disease, as defined according to the Ann Arbor classification, was assessed using standard procedures. The clinical findings of our patients are summarized in Table I. Patient and control sera, obtained from venous blood samples, were stored frozen until use. The levels of sIL-2R were measured with a commercial sandwich ELISA test kit (from T Cell Science, Cambridge, MA, USA), developed using two monoclonal antibodies directed against non-overlapping epitopes on the human IL-2R.

The mean sIL-2R values, obtained from 20 age-matched healthy individuals, were $248 \pm 124\ U\,ml^{-1}$. In 19/23 patients sIL-2R levels were higher than normal controls, the highest values being found in patients with constitutional symptoms (stage B) or relapsed (mean value: stage A = $815 \pm 628\ U\,ml^{-1}$; stage B + relapsed = $1{,}872 \pm 1{,}271\ U\,ml^{-1}$; $P < 0.05$) (Table I). All patients with normal values belonged to stage A group.

Our data indicate that the majority of patients with HD in active phase have increased values of sIL-2R in their serum, which correlate with the severity of the disease, as suggested by statistically significant higher values in stage B as compared to A. A statement on the possible correlation with other clinical characteristics, such as extension of the disease (stages I to IV), histological subtype, and presence of a bulky disease, can not be presently made due to the relatively small series of patients. Further observations and longitudinal studies will determine the value of our findings as a prognostic factor and as a biological tool for monitoring disease status and possibly the effect of therapy. In addition, the evidence herein provided of increased levels of sIL-2R seems relevant to an understanding of some biological aspects of the disease. In fact, the excess of sIL-2R released *in vivo* by chronically overstimulated cells might remove the available IL-2 and block the IL-2/IL-2R modulation necessary for a large number of biological responses. As a consequence, some IL-2 dependent phenomena (Farrar

Table I Soluble IL-2 receptor levels in the serum of patients with Hodgkin's disease

Patients	*Sex*	*Age*	*Histology*	*Clinical stage*	*sIL-2R U ml*$^{-1}$
STAGE A					
1	F	21	NS	II bulky	862
2	F	27	LP	I	325
3	M	34	NS	III	376
4	F	52	MC	I	245
5	M	69	NS	IV	771
6	F	18	NS	II bulky	2,300
7	M	27	NS	III	757
8	F	18	MC	III	1,376
9	M	52	NS	I	304
10	F	42	NS	IV	830
					mean ± s.d. = 815 ± 628
STAGE B					
11	F	20	NS	III bulky	1,534
12	F	33	NS	II	478
13	M	66	MC	IV bulky	2,192
14	M	39	NS	III	1,340
15	F	30	LP	III	631
16	M	40	MC	II	2,800
17	F	20	NS	II	881
18	F	31	NS	II bulky	4,800
19	M	59	MC	IV	1,487
20	M	75	LD	III	3,850
21[a]	M	42	NS	II bulky	960
22[a]	M	62	NS	II	1,850
23[a]	M	22	MC	IV	1,540
					mean ± s.d. = 1,872 ± 1,271

Mean values of sIL-2R ± s.d. in the serum of 20 healthy controls: $248 \pm 124\ U\,ml^{-1}$.

[a]Relapsed patients.

LP = lymphocyte predominance: NS = nodular sclerosis; MC = mixed cellularity; LD = lymphocyte depletion.

Stage A and B: absence and presence of constitutional symptoms, respectively.

Bulky = presence of bulky disease.

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et al., 1982; Smith & Cantrell, 1985) would be affected, including T-cell proliferation, cutaneous delayed type hypersensitivity, and regulation of NK activity. Indeed, most of these functions are impaired in HD (Frydecka, 1985; Romagnani *et al.*, 1985). An indirect support to this view comes from HCL, where the depressed NK *in vitro* activity, concomitant with high serum levels of sIL-2R, can be restored by the addition of exogenous IL-2 (Hooper *et al.*, 1986; Chilosi *et al.*, submitted). Also in line with the above considerations, evidence has been provided in HD of a serum factor which can inhibit the phytohaemagglutinin-induced transformation of normal lymphocytes (Scheurlen *et al.*, 1971). This factor is likely to correspond to the sIL-2R.

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