Eur J Cancer Clin Oncol, Vol. 22, No. 4, pp. 531–532, 1986.
Printed in Great Britain.

0277-5379/86$3.00+0.00

Letter to the Editor

Clinical Improvement and Partial Correction of the T Cell Defects of Acquired Immunodeficiency Syndrome (AIDS) and Lymphoadenopathy Syndrome (LAS) by a Calf Thymus Acid Lysate

GUIDO VALESINI,* VINCENZO BARNABA,* MASSIMO LEVRERO,* FRANCESCO BALSANO,* ORESTE SEGATTO† and PIER GIORGIO NATALI†

**Istituto Clinica Medica I, Univ. of Rome 'La Sapienza' and †Lab. Immunologia Ist. Regina Elena for Cancer Research, Rome, Italy*

ALTHOUGH thymic hormone treatment in AIDS patients has been found so far to lack therapeutic efficacy, a recent report by Mascart-Lemone *et al.* [1] has shown that the synthetic penta-peptide TP-5 resembling thymopoietin in its biological activity was capable of restoring the proliferative response and to reverse the inhibition of T lymphocytes functions in three AIDS patients.

We report here the changes in peripheral blood lymphocytes subpopulations and functional activities observed in one AIDS patient and two LAS patients following treatment with a calf thymus acid lysate (Thymomodulin 'Leucotrofina' Ellem SpA, Milano, Italy). The rationale for using this thymus extract was based on its property to induce Thy 1–2 antigen expression in murine splenic null cells [2] and modulate human T cell phenotypic maturation in the thymic as well as extra-thymic compartment (Segatto *et al.*, submitted for publication).

The AIDS patient was the first case reported in Italy [3] fulfilling the CDC diagnostic criteria.

He was a 42-year-old Caucasian heterosexual man with oral Kaposi's sarcoma. The two LAS patients were both very active Caucasian homosexuals. The first was a 25-year-old male resident of New York who had moved to Rome 6 months previously, the second a 28-year-old male with several North American partners. Both patients presented with generalized lymphoadenopathy, fever, episodic diarrhoea, weight loss and severe asthenia of four months duration.

All patients were administered Thymomodulin in the amount of 20 mg IM for 30 days, then 60 mg orally for 60 days. Peripheral blood mononuclear cell phenotype and functional tests were performed before and at the end of treatment. Table 1 summarizes the results of this study.

Using a battery of commercially available monoclonal antibodies to lymphoid cell subsets all three patients displayed a variable degree of depletion of T lymphocytes. While T4 helper T cell subset showed a significant reduction in all three cases, the cytotoxic-suppressor T8 population was reduced in the AIDS patient and slightly increased in the two LAS patients.

These variations of T cell subsets were consistently associated with a significantly depressed T4/T8 cell ratio.

Proliferative response to different lectines showed a consistent depression in mitogenic response to PHA in all patients. ^{3}H-thymidine incorporation in presence of PWM was significantly lower than control in the AIDS patient and in one of the LAS affected individuals. ConA mitogenic activity was found depressed only in the two LAS patients.

All three patients' sera contained antibodies to HTLV-III when tested by indirect immunofluorescence on HT9 infected cells.

Accepted 15 October 1985.
Address correspondence to: Pier Giorgio Natali, M.D., Lab. Immunologia, Ist. Regina Elena, V.le Regina Elena, 291, 00161 Rome Italy.
This work was supported by PF "Oncologia" CNR.

Following treatment with Thymomodulin all three patients showed an increase in peripheral blood T3 positive lymphocytes and in the number of T4 helper-inducer subset; the suppressor-cytotoxic subset on the other hand almost doubled in the AIDS patient while underwent opposite quantitative variations in the two LAS patients. Despite these non-concordant variations, the T4/T8 value showed a highly significant increase toward normality in all three patients.

In vitro responsiveness to mitogens displayed invariably various degrees of increase following treatment except in the AIDS patient where ConA *in vitro* responsiveness was of significant lower level.

The *in vitro* IgG synthesis was persistently high before and after treatment.

All these laboratory findings were paralleled by clinical improvement represented by disappearance of fever and asthenia and objective reduction of the lymphoadenopathy. No side effects were observed during the treatment period.

The present results show that a relatively crude calf thymus acid hydrolysate endowed with the ability to induce human T cell phenotypic maturation, is capable of partially restoring the T cell imbalance and proliferative response present in AIDS and LAS patients studied.

Because male homosexuals have been found to lack circulating levels of some thymic hormone [4] it does not come unexpected that administration of thymic extracts and/or factor/s may correct some of the cellular defects of these patients. Thymomodulin appears to contain factors which can regulate T cell population homeostasis as well as functional activity.

At the present we are monitoring whether the effects of Thymomodulin on the T cell compartment are time-limited and whether patients with AIDS and LAS have distinct long-term responses to the pharmacologic activity of this thymic extract.

Table 1.

Patient No.	1		2		3		Normal values
Diagnosis	AIDS		LAS		LAS		
Clinical features	Kaposi's Sarcoma		Lymphoadenopathy, Weight loss, fever		Lymphoadenopathy, Weight loss, fever		
	(1)	(2)	(1)	(2)	(1)	(2)	
T3 cells per mm^3(*)	314	626	1009	1289	882	1378	1290 ± 90
T4 cells per mm^3 (*)	19	222	401	835	321	711	835 ± 55
T8 cells per mm^3 (*)	260	412	606	378	545	666	468 ± 34
T4/T8	0.07	0.54	0.66	2.2	0.58	1.05	1.76 ± 0.24
Proliferation to PHA (†)	15.4	20.3	23.4	50.3	5.2	20	99 ± 6.7
Proliferation to PWM (†)	5.5	11.2	18.2	22.5	8.3	17.5	20.7 ± 5.3
Proliferation to ConA (†)	27	16.4	13.7	21.3	9.3	17.5	25 ± 4.8
In vitro IgG synthesis ng/ml	20,000	13,500	n.t.	n.t.	19,000	17,000	1196 ± 32

(1) Before, and (2) after treatment

(*) By Indirect Immunofluorescence

(†) Incorporation of ^{3}H-thymidine of 10^3 stimulated cells cpm × 10^3. Triplicate cultures

REFERENCES

1. Mascart-Lemone F, Huygen K, Clumeck N, Brenez D, Bolla K, Duchateau J. Stimulation of cellular function by thymopoietin (TP-5) in three AIDS patients. *Lancet* 1983, **ii**, 735–6.
2. Twomey JJ, Kouttab NM. Selected phenotypic induction of null lymphocytes from mice with thymic and nonthymic agents. *Cell Immunol* 1982, **72**, 186–194.
3. Rezza G, Ippolito G, Marasca G, Greco D. AIDS in Italy. *Lancet* 1984, **ii**, 642.
4. Dardenne M, Bach JF, Safai B. Low serum thymic hormone levels in patients with acquired immunodeficiency syndrome. *N Engl J Med* 1983, **309**, 48–49.