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Intermittent Leukapheresis: An Adjunct to Low-dose Chemotherapy for Sézary Syndrome

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McEvoy MT, Zelickson BD, Pineda AA, Winkelmann RK. Intermittent leukapheresis: An adjunct to low-dose chemotherapy for Sézary syndrome. Acta Derm Venereol (Stockh) 1989; 69: 73–76.

Eleven patients with Sézary syndrome were treated with intermittent leukapheresis in addition to low-dose chlorambucil and prednisone. The results were as good as or better than those with chemotherapy alone. We believe the combined program with continuous leukapheresis to be optimal therapy but note that intermittent treatment offers some benefit for patients. *Key words: Cytapheresis; Apheresis; Lymphapheresis; Erythroderma.* (Accepted May 11, 1988.)

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Treatment of Sézary syndrome has included multiagent systemic chemotherapy (1–3), psoralen and ultraviolet light A therapy (PUVA) (4, 5), topical application of nitrogen mustard (5), electron beam irradiation (6), and administration of anti-thymocyte globulin (7). All of these are relatively ineffective, aggravating, or only of short-term value. Low-dose chlorambucil and prednisone treatment of Sézary syndrome has produced remissions and partial remissions, and it remains the basic treatment against which other programs should be measured (8). We compared data on 11 patients treated with intermittent leukapheresis in addition to low-dose chlorambucil and prednisone and on patients treated with low-dose chemotherapy alone.

MATERIALS AND METHODS

We retrospectively reviewed the treatment and the clinical course of 11 patients with Sézary syndrome who were treated with intermittent leukapheresis in combination with low-dose prednisone and chlorambucil between 1977 and 1987. In these 8 men and 3 women, the mean (± SD) age at onset of erythroderma was 54.1±14.4 years and the mean age at diagnosis of Sézary syndrome was 56.5±12.2 years. Survival was measured from the onset of erythroderma to death or the present time.

The diagnostic criteria for Sézary syndrome were 1) erythroderma, 2) circulating Sézary cell counts of 15% or more of the total leukocyte count or an absolute count >1 000/μl on a number of occasions, and 3) subepidermal lymphocytic band-like infiltrate in the skin with varying numbers of cerebriform Sézary cells.

Leukapheresis was given two or three times per week during hospitalization, at 48–72-h intervals. Two different centrifugation devices were used—the Fenwall CS 3000 continuous-flow cell separator, and the COBE (IBM) 2997 continuous flow cell separator. The mean number of treatments given was 8.8 (range, 2 to 28). The majority of the patients received less than 10 treatments. The procedure was well tolerated.

All patients received prednisone (20 mg/day) and chlorambucil (4 mg/day). The dose of prednisone was decreased or discontinued when improvement permitted. Relapses were treated with topical corticosteroids and wet dressings, reinstitution of leukapheresis, and continuation of the prednisone and chlorambucil.

Eight patients had failed to respond to alternative regimens prior to referral (Table I). Three patients received PUVA for various periods, without improvement. Radiotherapy was given to 3 patients—2 received electron beam irradiation (1 386 cGy and 850 cGy), and one patient received palliative irradiation for a poorly differentiated lymphocytic lymphoma that developed late in the course of his disease. Four patients had received topical or systemic chemotherapy. One patient who was referred with a presumed diagnosis of pityriasis rubra pilaris had been treated with methotrexate. One patient received mechlorethamine topically, and two patients were treated with polychemotherapeutic regimens (COPP, Cytoxan, Oncovin, procarbazine, and prednisone; CHOP, Cytoxan, hydroxydaunorubicin, Oncovin, and procarbazine).

Treatment response was assessed as either complete (absence of symptoms [pruritus, scaling, poor temperature control] and erythroderma with sustained decrease in Sézary cell count to <1 000/μl) or partial (relief of symptoms and resolution of erythroderma but Sézary cell count >1 000/μl).

RESULTS

Eight of 9 patients followed from onset of erythroderma survived 5 years or more, giving a 5-year survival rate of 89%. Two patients have been followed for less than 5 years. Only one of 7 patients has survived for more than 10 years, giving a 10-year survival rate of 14%.

Two patients achieved complete remission and 9 showed partial response with 50–80% improvement. Among those with partial response, the mean time to relapse was 12 months (range, 4 to 48 months).

At the time of review, 6 of the 11 patients had died. The mean interval between onset of erythroderma and death was 8.0±6.5 years (Table II). The mean interval between onset of symptoms and death was 11.4±6.5 years. The data from an earlier study from this Department are presented in the table for comparison. The mean intervals between onset of eryth-

Table I. *Previous treatments given to 8 Sézary syndrome patients*

Treatment	No.
PUVA	3
Chemotherapy	
Single agent	1
Multiple agents	2
Mechlorethamine topically	1
Radiation	3

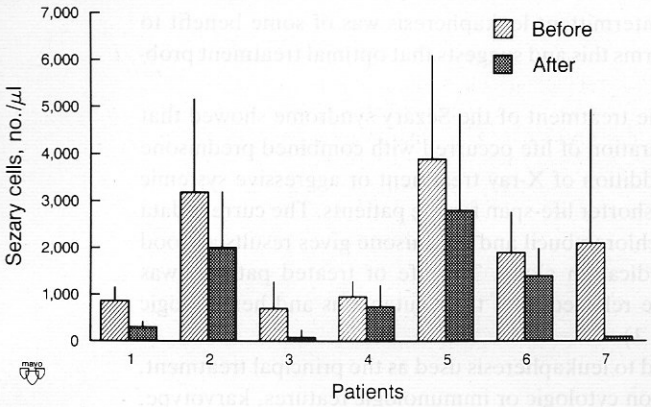

Fig. 1. Sézary cell counts before (diagonal hatching) and after (cross hatching) leukapheresis, shown as mean ± SD for each patient.

roderma and death and between onset of symptoms and death are similar in both study populations. The causes of death were myocardial infarction in one patient, pneumonia in one, unidentified sepsis in 3 (one patient had lymphoma and one had cardiac and renal failure), and undetermined in one.

Five patients were living at the time of the study. The mean interval between onset of erythroderma and follow-up was 5.8±3.6 years. The mean time between onset of symptoms and follow-up was 7.9±5.3 years. Survivals from onset of symptoms to date were similar in both studies. For survival from onset of erythroderma, 3 of our present patients have lived longer than the range set by the earlier population (7.5, 8.6, and 9.0 years vs. 7.2 years). One of this group has been in remission for 6 years and has been off all therapy for 1 year. Four are in partial remission and continue on prednisone and chlorambucil. There was no difference between the doses of chlorambucil and prednisone used in this and in the earlier study.

Circulating Sézary cells were measured before and after leukapheresis (Fig. 1). There was a significant reduction in the mean number of circulating Sézary cells after leukapheresis.

DISCUSSION

Edelson et al. (9) described a patient with Sézary syndrome who improved after leukapheresis. Winkelmann et al. (10) reported an early experience at Mayo and in Paris with this treatment for Sézary syndrome. Revuz et al. (11) noted complete remissions during continuous biweekly and weekly leukapheresis for Sézary syndrome. The earlier Mayo ex-

Table II. *Survival data in two studies*[a]

	Survival interval (mean ± SD), yr			
	Alive		Dead	
From onset of:	Prior study (n=7)	Present study (n=5)[b]	Prior study (n=20)	Present study (n=6)[b]
Erythroderma	4.6±2.6	5.8±3.6 (3)	6.2±2.6	8.0±6.5 (1)
Symptoms	8.1±5.7	7.9±5.3 (0)	8.3±3.2	11.4±6.5 (2)

[a] Present study and Winkelmann et al. (8).
[b] Numerals below in parentheses are number of values outside the range found in the prior study.

perience gave some indication that even intermittent leukapheresis was of some benefit to the patients. Our current larger study confirms this and suggests that optimal treatment probably should include leukapheresis.

The previous summary (8) of data on the treatment of the Sézary syndrome showed that significant increases in remission and in duration of life occurred with combined prednisone and low-dose chlorambucil therapy. The addition of X-ray treatment or aggressive systemic chemotherapy was associated with a much shorter life-span for the patients. The current data show that intermittent leukapheresis plus chlorambucil and prednisone gives results as good as or better than those with the oral medication alone. The life of treated patients was lengthened, their itching and redness were relieved, and their cutaneous and hematologic values returned to or toward normal (Fig. 1).

Not all Sézary syndrome patients respond to leukapheresis used as the principal treatment, as in the report by Revuz (12). No studies on cytologic or immunologic features, karyotype, or staging have given predictable measures of response or non-response to leukapheresis (13). All of the patients in our series had at least a short-term response, and we believe that, when used with the prednisone and chlorambucil program, leukapheresis may be the best current treatment for Sézary syndrome. If continuous leukapheresis is not possible, intermittent treatment can still provide some benefit in all but the most severe cases in the stage of T-cell leukemia/lymphoma.

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