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Prednimustine in Mycosis Fungoides: A Report from the Scandinavian Mycosis Fungoides Study Group

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Abstract. Prednimustine, a chlorambucil ester of prednisolone, was administered orally to 5 patients with mycosis fungoides in advanced tumour stage. Partial remission was obtained in 2 of the patients. However, we do not consider the agent to be particularly advantageous for the treatment of mycosis fungoides.

Key words: Mycosis fungoides; Prednimustine

Hitherto, systemic chemotherapy of late stage of mycosis fungoides has had only a slight or transient effect (3, 7). Chlorambucil combined with prednisone, however, is highly effective even in small doses in the treatment of the Sézary syndrome, regarded by many as the leukemic variant of mycosis fungoides (9). Few reports exist of its use in mycosis fungoides, but none of them with encouraging results.

Recently, a chemical combination of chlorambucil and prednisolone has appeared in the form of prednimustine, LEO 1031 (4), the chlorambucil ester of prednisolone. After absorption it is split into the active components chlorambucil and prednisolone. For reasons unknown, prednimustine can be administered in far higher doses than can chlorambucil and prednisolone given as separate drugs, and in equipotent doses it is less toxic than either of the two compounds. However, an unexplained, delayed bone marrow toxicity has been reported, possibly a result of accumulation of the drug.

Prednimustine has proved capable of inducing and maintaining remissions in various forms of lymphoma (8), leukemias (1, 2) and in metastasising mammary carcinoma (5). Previously, prednimustine has been administered occasionally to mycosis fungoides patients (6). We therefore considered it of interest to examine the effect of this drug in more advanced stages of mycosis fungoides.

PATIENTS

Five patients with mycosis fungoides, in stages III to V according to the staging criteria of the Scandinavian Mycosis Fungoides Study Group (7), have been treated with prednimustine (Table 1). The age range of the patients was 48 to 90 years and the duration of the disease 1–13 years. All the patients had previously been treated with topical X-ray irradiation, topical nitrogen mustard or PUVA and two of them had also received various forms of systemic chemotherapy. At the onset of therapy the disease was in its active phase in all patients.

TREATMENT

Prednimustine was given orally as tablets of 20 or 100 mg active drug, roughly estimated to contain 50% chlorambucil and 50% prednisolone. Prednimustine was given in a dose of 120 mg/m² daily for 5 days, followed by a rest period, and repeated every third week. The dosage had to be reduced in 2 cases.

Prior to therapy and at weekly intervals during the treatment period the following parameters were measured: hemoglobin, erythrocytes, thrombocytes, leukocytes, differential count, serum creatinine, serum uric acid, aspartate-amino-transferase (ASAT), alanine-amino-transferase (ALAT), alkaline phosphatases, serum bilirubin.

RESULTS

The treatment was given for a total of three to eight cycles. In 2 patients prednimustine induced partial

Table 1. *Five patients with mycosis fungoides treated with prednimustine*

Stage III: cutaneous tumours; stage IV: lymph node involvement; stage V: involvement of internal organs. All stages histologically verified. PR: partial remission (improvement by more than 50%); NC: no change; PD: progressive disease. All changes compared with the situation at commencement of treatment

	Patients					
	P. K.	E. U.	P. H.	A. B.	I. C.	E. P.
Age	48	63	70	90	46	74
Sex	M	F	M	F	F	F
Stage	III	III	III	III	IV	V
Therapeutic effect						
Initially (2-3 m)	NC	PD	PD	NC	PR	PR
Late (4 m)	-	-	-	-	PD	PD

remission (Table 1). In the remaining 3 patients the disease was either unaffected or progressed during the treatment, which therefore had to be abandoned.

Side effects

Three patients developed late bone marrow toxicity with leukopenia and thrombocytopenia after 2-4 weeks of therapy. The leukopenia lasted for 6 weeks in one of them. One patient experienced a transient psychotic episode during the treatment, and another patient hallucinated. In these 2 patients the medication could be continued after dosage reduction. Four patients complained of insomnia during the 5-day treatment periods. No change in the liver parameters was observed.

COMMENT

Despite promising results in various lymphomas (8), leukemias (1, 2) and solid tumours (5), prednimustine has more or less failed in the treatment of cutaneous mycosis fungoides lesions. The effect on lymph nodes, however, seems to be somewhat better. Prednimustine has not so far been used in the Sézary syndrome, where it might be expected to be more efficacious, since chlorambucil combined with prednisone even in low doses is able to induce and maintain remission for long periods (9). The toxicity of the drug has been slight, but the delayed bone marrow toxicity has caused some concern, as also has the psychotic episode in one patient.

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