2-Chlorodeoxyadenosine treatment for cutaneous T-cell lymphoma

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Abstract

The primary cutaneous lymphomas are often indolent but difficult to treat. In the early stages psoralen and ultraviolet-A therapy is the standard treatment whereas at the tumor stage chemotherapy (e.g. pegylated doxorubicin) is often used for debulking. The purine analog 2-chlorodeoxyadenosine (2CdA) acts in non-Hodgkin's lymphoma and has been used in our center for the treatment of advanced primary cutaneous T-cell lyphomas (CTCL). Here, we report on the efficacy and side effects of 2CdA in six patients with CTCL. One patient died owing to myelosuppression. Partial responses were seen in four cases but full remission was observed in only one case. We concluded that 2CdA has a limited usefulness in the management of advanced CTCL.

Introduction

A purine analog 2-chlorodeoxyadenosine (2-CdA) has been accepted as the treatment of choice in hairy cell leukemia and low-grade non-Hodgkin's lymphomas. It has also been recommended in stage IV A/B of cutaneous T-cell lymphomas (CTCL), along with chlorambucil, liposomal doxorubicin, CHOP polychemotherapy, denileukin difitox, and others.[1-11] The aim of our study was to analyze the efficacy and side effects of 2CdA treatment for CTCL.

Materials and Methods

We treated six CTCL patients (five with *mycosis fungoides*; four in stage IIB, one in IVB, and one with peripheral cutaneous T-cell lymphoma (PTCL), unspecified) with 2CdA (pulses of 0.12 mg/kg/day/5 days).[10,12-20] The patients failed standard therapies including glucocorticoids, retinoids, methotrexate, radiotherapy, and phototherapy. The efficacy of the treatment was established based on the clinical evaluation of skin lesions and internal involvement.

Results

The patients received 1-8 pulses of 2CdA (Table 1, Figures 1-4). One patient achieved total remission (patient 46/F, Figure 2A and B), lasting six months. Partial remission was achieved in four cases. Progression of the disease during treatment appeared in one case (patient 71/F, Figure 4). One patient died because of myelosupression and staphylococcal sepsis just after the second pulse with 2CdA (patient 43/F, Figure 1). We tried to avoid the

Table 1. Characteristics of the patients.

Age/Gender	Diagnosis and stage[1]	Duration of the disease	Previous treatment
43/F (Fig. 1)	MF IIB	13 mth	Prednison, PUVA, RePUVA cyclofosphamid
46/F (Fig. 2A, B)	MF IVB	31 mth	PUVA
46/F	PTCL	6 mth	Acitretin
65/F (Fig. 3A, B)	MF IIB	6 mth	acitretin, acitretin + MTX
58/M	MF IIB	16 mth	Acitretin, MTX, local electron beam therapy (Department of Radiotherapy)
71/F (Fig. 4A, B)	MF IIB	4 yr	Prednisone, MTX, UVB311, acitretin, bexaroten (severe side effects: total skin peeling, bullae, and progression of the disease to MF IV)

MF, *mycosis fungoides*; PTCL, primary cutaneous peripheral T-cell lymphoma.

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Key words: 2-chlorodeoxyadenosine (2CdA), cutaneous T-cell lymphoma, mycosis fungoides, Sézary syndrome, treatment, side effect.

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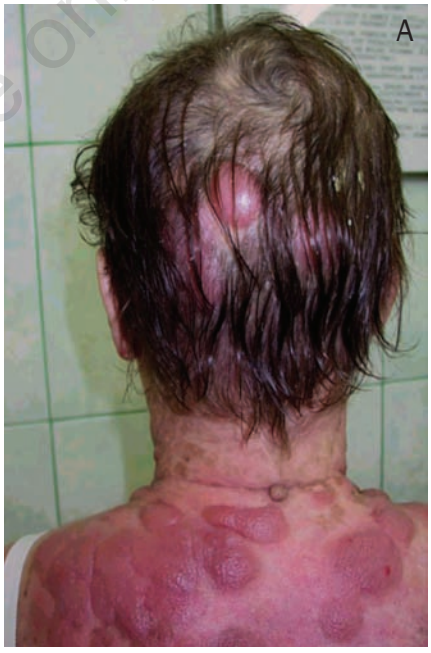

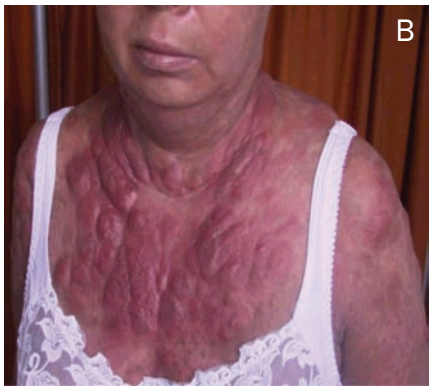

Figure 1. (A and B) Before 2CdA treatment: patient died of *S. aureus* sepsis after the second pulse.

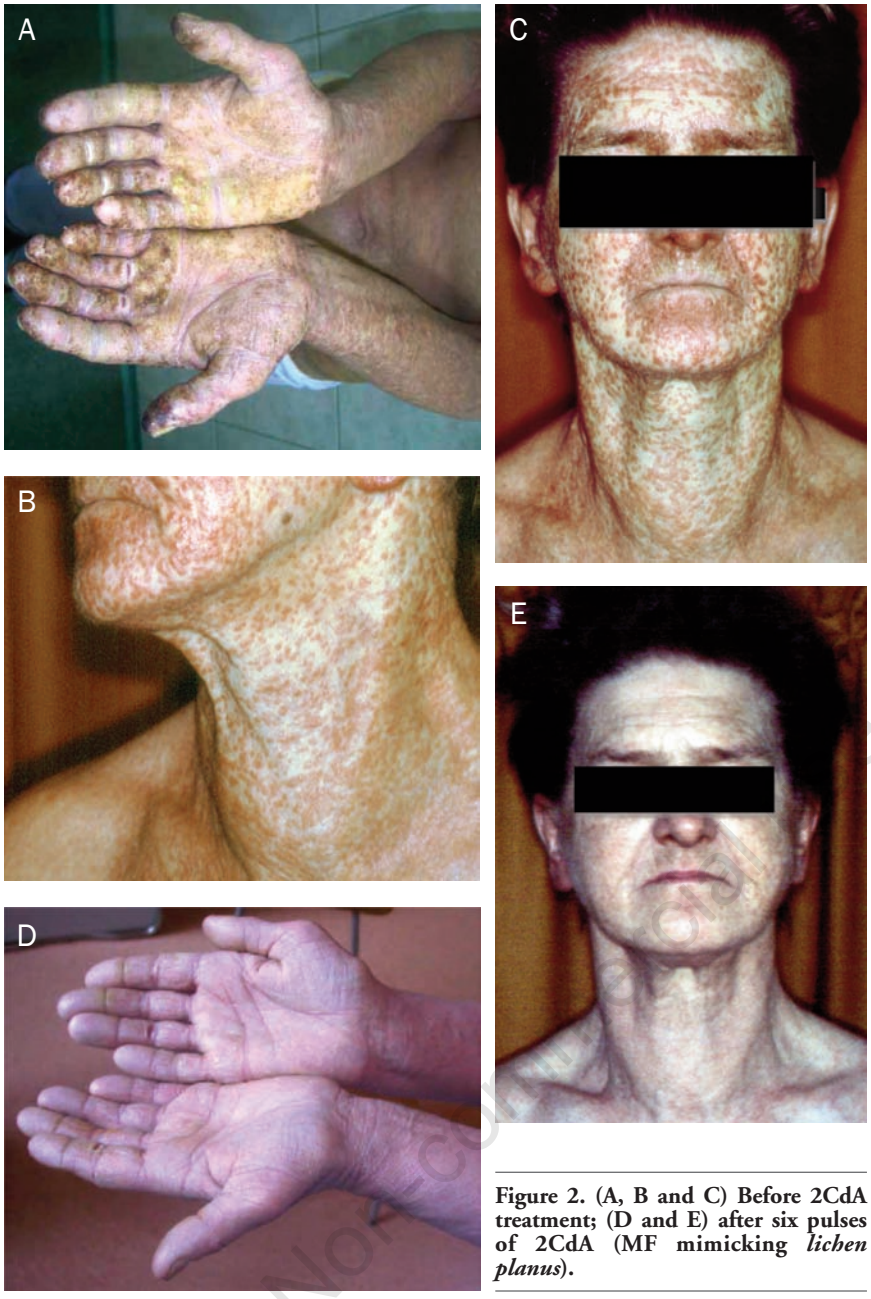

Figure 2. (A, B and C) Before 2CdA treatment; (D and E) after six pulses of 2CdA (MF mimicking *lichen planus*).

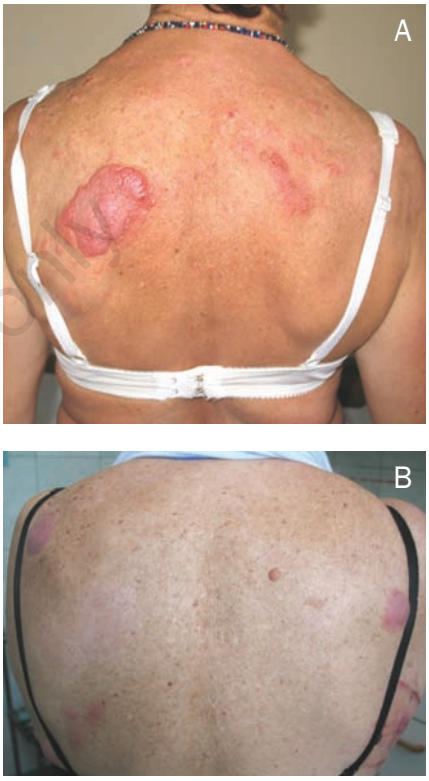

Figure 3. (A) Patient 65/F before2CdA treatment; and (B) after treatment (remission but new tumors have appeared).

Table 2. Response to 2-chlorodeoxyadenosine.

Patient	No of cycles/dose per cycle (1 cycle = 5 d)	Duration of the cutaneous response	Lymph node status (response)	Outcome
43/K (Fig. 1)	2/0.12 mg/kg (7 mg/d)	No response	Slight	Death because of *S. aureus* sepsis
46/K (Fig. 2A-E)	8/0.12 mg/kg (7 mg/d)	6 mounth	Total	Death because of dissemination of MF (6 mth after end of 2CdA)
46/K	3/0.12 mg/kg (8 mg/d)	6 mounth	Total	Death, metastasis of lymphoma to central nervous system
65/K (Fig. 3A, B)	6/0.12 mg/kg (7 mg/d)	2 weeks	Moderate	Progressive disease
58/M	6/0.12 mg/kg (13 mg/d)	8 mounth	Not applicable	Progressive disease
71/K (Fig. 4A, B)	1/0.12 mg/kg (7 mg/d)	Progressive disease	Not applicable	Progressive disease

Response: slight, <25%; moderate, 25-50%; significant, 50-75%; total, 100%; PTCL, primary cutaneous peripheral T-cell lymphoma.

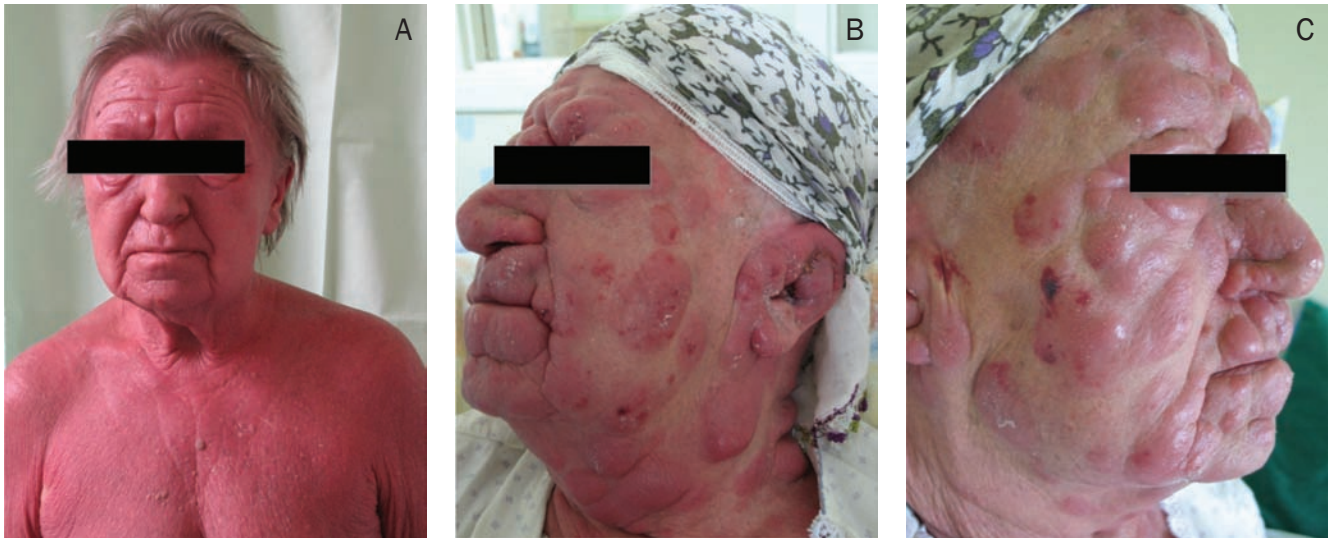

Figure 4. (A) Patient 71/F before 2CdA treatment; and (B, C and D) after one pulse of 2CdA treatment: rapid progression just after the treatment showing *faces leonona*. This was followed by seven pulses of CHOP with only 7-10 days' lasting remission, then by TSEB.

infections by chemoprophylaxis with co-trimoxazol and acyclovir during and after 2CdA treatment. One patient died because of progression of the lymphoma to the central nervous system a few months after the end of treatment (patient 46/F with PTCL). The other two patients achieved partial remission and required further chemotherapy (Table 2).

Discussion

2CdA therapy was mostly well tolerated in view of the known side effects (Table 4) although one patient died just after the second pulse because of myelosupression. The observed remissions were short-lasting. Table 3 shows the experience with 2CdA in other

Table 3. Response to 2-chlorodeoxyadenosine in CTCL patients – results from different centers and from the Dermatological Department, Gdansk, Poland.

	Number of patients	Complete (%) remission	Partial remission (%)	No response (%)
Bouwhius *et al.*, 2002, USA[3]	6	13	50	37
Kuzel *et al.*, 1996, USA[12]	21	14	14	72
Saven *et al.*, 1992, Canada[25]	16	20	27	47
Rummel *et al.*, 1998, Germany[20]	66	38	ND	ND
Kay *et al.*, 1992, Canada[9]	40	20	22.5	57.5
Kong *et al.*, 1997, USA[11]	24	12	12	76
O'Brien *et al.*, 1994, USA[23]	22	18	23	59
Dept. of Dermatology, Poland (present report)	6	33	50	17

ND, no data.

Table 4. Dose-dependent side effects after 2-chlorodeoxyadenosine, based on data in the literature[8,13,21-23]

Side effect	Time of appearance (*)
Headache (22%, 7% >2nd week)	Immediate
Erythema (5-27%, 10% >2nd week)	Early
Nausea (0-28%)	Immediate
Myelosupression (neutropenia, thrombocytopenia, lymphocytopenia)	Early, distant, late
Cutaneous side effects, including panniculitis (19%)	Immediate
Paraparesis, tetraparesis (rare)	Distant
Hyperuricemia	Immediate
Renal finction disturbances (rare)	Early
Fever (46%)	Immediate
Fatigue (45%, 11% >2nd week)	Immediate

*The time of side effects' appearance: immediate, hours; early, days, weeks; distant, weeks, months; late, months, years.