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Letter to the Editor

Treatment of Widespread Skin Infiltration in Acute Myeloblastic Leukaemia with Superficial Penetrating Whole Body Electron Beam Therapy

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IMPROVEMENTS in the chemotherapy of acute myeloblastic leukaemia (AML) during the past two decades have led to increased remission rates and prolongation of median survival times and, as a result, extra-medullary leukaemic deposits are being more frequently observed. One commonly involved site is the skin, and either discrete nodules or generalised rashes may develop while a patient is in apparently complete remission and receiving maintenance chemotherapy. Such deposits almost certainly comprise a reservoir of cells assistant to the drugs being used and, rather than attempting to choose alternative systematic chemotherapy, consideration should be given to the use of radiotherapy. Superficial penetrating electron beams (electron shower or bath) offer a highly specific means of treating skin infiltrates which need not interfere with maintenance chemotherapy, since the depth/dose can be adjusted to spare the bone marrow. Despite the obvious attractions this form of radiotherapy offers in the treatment of leukaemic skin infiltrates, there have been few reports of its use [1]. We describe two patients treated in this manner.

Patient 1

Prior to his diagnosis, this 44-year-old male had a 1-cm diameter skin nodule on his chest wall which was faintly red, fixed to skin, non-tender and shown by excision biopsy to be a leukaemic nodule. Marrow aspiration at diagnosis showed more than 90% blast cells with fine azurophilic granules which gave a positive reaction with Sudan Black but were negative with P.A.S. The course of the patient's disease was monitored by blood and bone marrow blast cell counts, as shown in Fig. 1. Three weeks after his fourth consolidation course of cytosine arabinoside and thioguanine, fixed, non-tender skin nodules began to appear which were again shown to be leukaemic infiltrates by excision biopsy. At the same time, he developed a proptosis of the left eye which was assumed to be due to a retrobular deposit.

His chemotherapy was changed and he received 16 Grays to the left retrobular area which led to resolution of the proptosis. Despite a fall in his marrow blast cells from 29 to 8% the skin nodules failed to respond, and at the nadir of his leucopenia blast cells appeared in his peripheral blood. It seemed possible that his skin infiltrates were acting as a reservoir of leukaemic cells and it was decided to attempt to eradicate them with superficial penetrating electron beams immediately following a second course of chemotherapy. A 6-MeV Linear Accelerator was used to generate electrons and over a five week period he received 16.5 Grays to his total body surface, shielding only his head, hands and feet. Full exposure of all surfaces was obtained by the method of multiple beams as described by Karzmark [2] and Ste-

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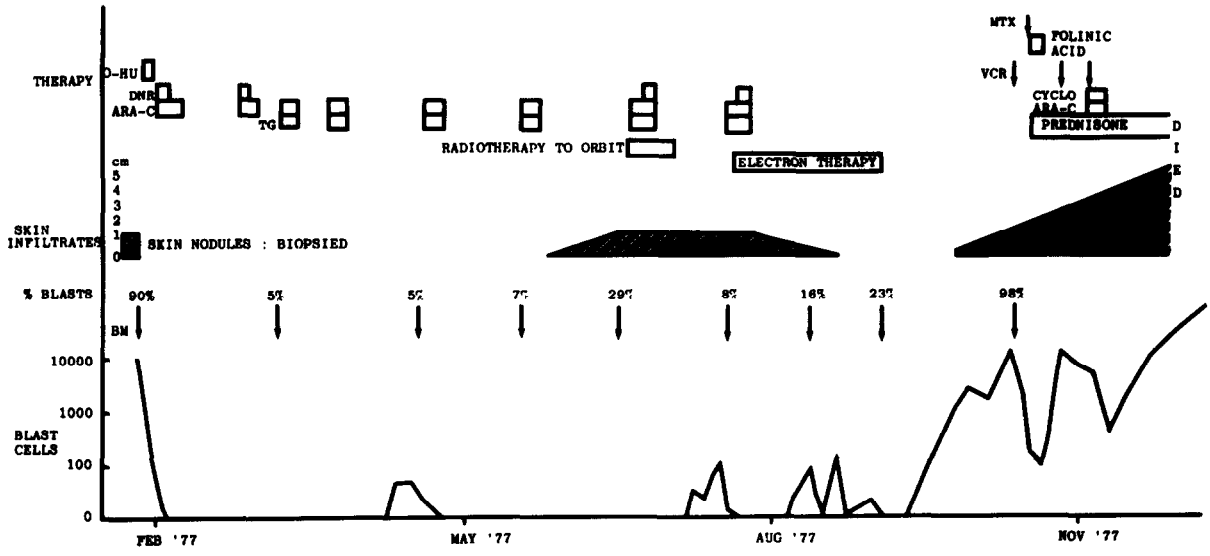

Fig. 1. *Haematological, dermatological and therapeutic details of Patient* 1. *Abbreviations: O-HU, hydroxy urea; ARA-C, cytosine arabinoside; DNR, daunorubicin; TG, thioguanine; VCR, vincristine; MTX, methotrexate; CYCL, cyclophosphamide.*

wart [3] (details shown in Table 1). Following this treatment, most nodules had totally regressed and he was clinically well. The marrow blast cells had risen to 23% and as his leukaemia was clearly resistant, he was given no further chemotherapy at this stage. A few weeks later he developed multiple nerve root involvement with severe hyperaesthesia, with skin involvement in two forms—a diffuse thickening of the skin associated with an unpleasant itching sensation, and maculo-papular nodules which increased gradually in size. At this time, a change occurred in the morphology of the patient's leukaemic cells—a steadily increasing number of large monocytoid cells with basophilic cytoplasm was noted. These cells were P.A.S.-positive and showed surface staining with fluorescent anti-γ and anti-κ sera (Hoechst), which was resynthesised when the cells were incubated *in vitro* for 2 hr 15 min at 37°C after trypsinisation (Table 2). Because these findings suggested a transformation of his disease, he was treated with vincristine, methotrexate, cyclophosphamide and prednisone but with minimal effect on his leukaemic deposits and blast cells.

Patient 2

A 49-year-old female was diagnosed as having AML and brought into remission without difficulty (Fig. 2). After the fifth course of maintenance chemotherapy, bone marrow confirmed continuing remission, but shortly afterwards she noticed multiple areas of erythematous raised nodules on her back, legs, breasts and abdomen. Skin biopsy showed infiltration of the dermis and subcutis with primitive mononuclear cells. She was given 13 Grays of electron beam therapy (Table 1) to her total body surface, excluding head, fingers and toes, over 22 days, with a satisfactory resolution of her skin lesions. Although she also developed neurological complications while remaining in marrow remission, her skin remained clear of infiltration up to her death nineteen months after her initial diagnosis, a finding confirmed at autopsy.

DISCUSSION

Whole body medium energy electron beam therapy has been available for almost two decades. Its main use has been in treating patients with mucosis fungoides and other

Table 1. *Depth/dose details of whole body electron beam therapy*

Patient	Total dose (Grays)	Depth (cm)	Penetration (%)	No. of treatments	Period (days)
1	16.5	1.6	80	12	35
2	13	1.2	80	9	22

Table 2. Leucocyte studies in Patient 1: percentage of cells positive with FITC antisera after trypsinization and resynthesis

Cells	Surface immunoglobulin chain							E rosette +ve cells (%)
	γ	μ	α	δ	ε	κ	λ	
Blasts	67	0	0	0	0	53	0	0
Lymphocytes	25	0	0	0	0	11	0	7

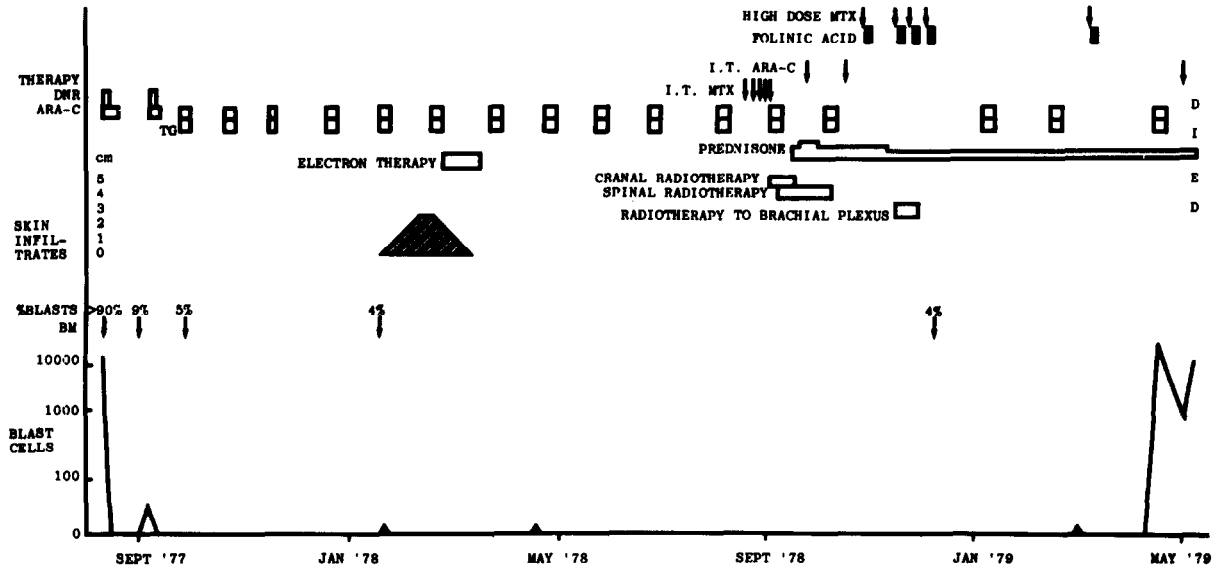

Fig. 2. Haematological, dermatological and therapeutic details of Patient 2. Abbreviations: as for Fig. 1.

lymphomas with generalised skin involvement. The degree of penetration of the electron beam is dependent on the energy of the electrons, which can be adjusted so that a satisfactory dose may be administered to the dermis and subcutis, while deeper tissues, including bone marrow, receive only a small fraction of the dose. This technique caused regression of skin nodules in both patients. In patient 1, where our experience suggested that skin infiltrates may act as reservoirs of leukaemic cells capable of re-entry into the circulation, the effect was unfortunately short-lived, but in patient 2, the nodules did not re-occur in the fourteen months following electron beam therapy, despite CNS and systemic relapse.

The emergence of new clones in acute leukaemia is a well-recognised phenomenon, and such populations are in general characterised by the loss of specific characteristics [4]. The opposite happened in the new clone identified in Patient 1 showing P.A.S. positivity and endogenously synthesised γκ surface immunoglobulin, features of lymphoid cells specifically B cell in type. It is now recognised that a proportion of patients with chronic granulocytic leukaemia undergoing acute transformation acquire cells with lymphoid markers [5] but we know of no instance of this being described in acute myeloblastic leukaemia.

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