

# Total Skin Electron Beam Therapy As Part Of A Therapeutic Regimen For Leukemia Cutis: A Case Report And Review Of Literature

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## Abstract

Leukemia cutis (LC) is a rare clinical presentation of acute myeloid leukemia (AML). We report a 26 year-old female patient presented with widespread skin infiltration and raised hyperpigmented lesions which appeared 7 months after AML diagnosis. The skin lesions had been refractory to several single or combination treatments. The patient was treated with total skin electron beam therapy (TSEB). She received 19.5 Gray (Gy) in 18 fractions followed by boost to underdosed skin areas. The skin lesions disappeared completely with no severe acute toxicities. Upon completion of TSEB, patient initiated total body irradiation (TBI) before stem cell transplantation (SCT).

## CASE REPORT

A 26 years-old AML female patient presented with skin lesions and breast mass. Bone marrow aspiration and peripheral blood smear confirmed diagnosis of acute monoblastic leukemia. The molecular and cytogenetic analysis revealed a normal karyotype, nucleophosmin 1 (NPM1) mutation, negative promyelocytic leukemia retinoic protein acid receptor a (PML-RARa) translocation t (15;17), FMS-like tyrosine kinase-3 gene (FLT3) -TKD wild-type mutation and negative FLT3-ITD. Analysis of cerebro-spinal fluid showed no evidence of malignancy. She was treated with intensive induction and consolidation chemotherapy with Gemtuzumab ozogamicin and all-trans retinoic acid (ATRA) in the context of AML-SG 09-09 Arm a clinical study. She achieved complete remission as confirmed by bone marrow aspirate after 1, 2 and 4 months.

Two months after starting the third consolidation chemotherapy she was found to have several raised, pigmented, painless, firm nodules that appeared first on her left upper arm and then appeared on her back, face and lower limbs (Figure1). Punch biopsy of the lesion on her left upper arm revealed AML skin infiltration. A few days later the fourth bone marrow aspirate was diagnosed of relapse with a finding of 40% monoblasts. She was then treated with intrathecal methotrexate and remission induction chemotherapy with idarubicin, etoposide, cytarabine, ATRA

(ICE-A regimen) but the skin findings were progressive. Therefore, preliminary phase chemotherapy treatment with cytarabine was performed for 5 days. One month later, she received a second cycle. As a result of the rapid increase in the number and size of the skin lesions, we decided to perform total skin electron beam therapy.

TSEB was performed 4 days after the last chemotherapy cycle. The patient was standing in an upright position on a static base while being irradiated using a six-dual-field technique. The electron beam with effective central axis energy of 6 MeV was used to treat three anterior and three posterior stationary treatment fields, each having a superior and an inferior portal with beam angulations; 18.5 degrees above and 18.5 degrees below the horizontal axis. Skin surface distance (SSD) was 347.5 cm from a Varian Truebeam linear accelerator™. As a result of the 0.6 cm Plexiglas scatter plate which was placed 20.5 cm in front of the patient the effective energy was about 1 MeV. Details on the Stanford technique were published by the American Association of Physicists in the Medicine (AAPM) report No. 23 [1].

The entire wide-field skin surface received 1.5 Gy each day cycle. Irradiation was given 5 times a week. Doses of 19.5 Gy were delivered during 4 weeks. Verification of delivering doses was performed routinely as part of the quality

assurance using thermoluminescent dosimeters (TLD) placed at multiple locations on the patient's skin. A boost to medial thigh and plantar surfaces was planned to compensate for underdosing in these regions based on TLD measurements and due to clinical findings in these regions.

During wide-field skin irradiation, external eye shields were used routinely to protect the cornea and lens. Shielding of the digits and lateral surfaces of the hands or feet were necessary to prevent a local skin reaction resulting from overlapping treatment fields in these areas. The shields were usually placed near the patient.

The patient tolerated the radiation treatment well. After 9 Gy the patient's skin lesions appeared smaller in size and were darker in color. After completion of radiation treatment, the lesions were markedly decreased in size and color (Figure 2). The patient had mild nasal mucositis in the form of nasal bleeding during the treatment. No other acute toxicity was noted during or after the TSEB treatment. Two weeks later, 4 Gy TBI in 2 fractions delivered before initiation of allogeneic hematopoietic stem cell transplantation (SCT).

The patient was in remission 4 months post radiation. Local skin recurrence was clinically apparent in the form of a solitary nodule on her lower left leg. The left inguinal lymph nodes were slightly enlarged. Histologic examination of skin lesion showed leukemic infiltration. Therefore three cycles of azacitidine and donor lymphocyte infusions were used as salvage therapy for AML skin relapse. Repeat clinical examination 2 months later showed no residual or new skin lesions. The patient achieved a complete remission over 8 months at regular follow-up visits after azacitidine therapy without recurrence till today.

**Figure 1**

Lesions' appearance on the back before radiotherapy; multiple nodular lesion of leukemia cutis on back of the patient before total skin electron beam therapy



Figure 2

Lesions' appearance after radiotherapy; the lesions as seen one week after completion of total skin electron beam therapy



Table 1

Published Cases of leukemia cutis treated with TSEB.

References	Age of patient	Total dose (Gy)	Dose per fraction (Gy)	Local boost	Acute toxicity	Disease free interval for cutaneous disease	Year of pub.	Follow up
Rubin et al [4]	11 months	19	1.18	12@3 Gy: Perineum	mild erythema, skin desquamation, hyperpigmentation	12 months	1985	n.a.
Kawazoe et al [5]	35 years	12	2.0	unknown	unknown	3.5 months	1991	died due to systemic relapse
Peppek et al [6]	13 years	16	2.0	6@2 Gy: scalp	oral mucositis II, moderate skin desquamation, hyperpigmentation	19.5 months	2008	died due to systemic relapse
Peppek et al [6]	18 years	18	2.0	none	none	4 months	2008	died due to systemic relapse
Majd et al [7]	15 months	planned 16 Gy (only 15Gy received)	2.0	planned: Perineum and plantar surfaces	mild fatigue	resolving of skin nodules after 10 Gy	2012	discontinued the TSEB systemic relapse during Radiotherapy
Hauswald et al [8] *	n.a.	29 Gy mean dose	Mean: 10Gy	n.a.	matigue, mild erythema, dry desquamation, mild edema and alopecia	Mean: 13.5 months	2012	n.a.
Our case report	26 years	19.5 Gy	1.5 Gy	medial thigh and plantar surfaces	mild nasal mucositis	4 months (local recurrence: lower leg)	2013	complete remission till today (8 months after starting azacitidine chemotherapy)

\* The study included four leukemia patients (AML n = 2, CLL n = 1, PDC n = 1).

DISCUSSION

Here we report a case of disseminated LC occurring 7 months after diagnosing AML in which total skin electron beam therapy (TSEB) treatment was a successful treatment for skin infiltration and resulted in complete resolution of the cutaneous nodules, with residual cutaneous pigmentation.

Retrospective studies show that cutaneous involvement of leukemia is associated with poor long-term survival. Despite aggressive therapy, most patients die within a few months [2] Patients with intermediate cytogenetic risk AML without FLT3 ITD mutations but with NPM1 mutations have a significantly better overall survival (OS) and event-free survival (EFS) than those without NPM1 mutations [3].

Literature on Leukemia cutis in an AML patient treated with TSEB is very rare (Table 1). Rubin et al. and Kawazoe et al. concluded that total skin radiation is potentially effective to treat LC [4,5]. Furthermore, Peppek et al. recommended the consideration of TSEB for palliation [6]. Hauswald et al. indicated the feasibility of TSEB in cutaneous manifestations in leukemia, especially in palliative situations. Although there was an early systemic relapse during the course of radiotherapy, Majd et al. concluded that TSEB was successful in eliminating the associated skin

nodules of LC [7,8].

Radiotherapy is considered to be beneficial to treat the widespread skin involvement in LC, as the skin can act as a sanctuary for leukemic cells [9]. In our case, TSEB was initiated before performing TBI and SCT because of the rapid progressive diffuse skin involvement observed after chemotherapy. The use of TSEB before TBI seems to be a valuable option to treat LC. With such a treatment we are able to deliver high radiation doses with limited skin penetration depth, thus avoiding systemic toxicity [10]. Future studies, may analyze different doses and energies that may maximize response duration while minimizing toxicities.

In conclusion, disseminated skin nodules of LC showed significant improvement during TSEB with complete resolution after treatment course. Our case report demonstrates that TSEB is not only a palliative treatment to relieve the skin lesions, but also an effective treatment to control the progression of LC. More case series are necessary to have a greater level of evidence about the proper management of these patients and, especially, the role played by radiotherapy.

#### Abbreviations

LC: Leukemia cutis; AML: Acute myeloid leukemia; TSEB: Total skin electron beam therapy; TBI: Total body irradiation; SCT: Stem cell transplantation; NPM1: Nucleophosmin 1; PML-RARa: Promyelocytic leukemia retinoic protein acid receptor a; FLT3: FMS-like tyrosine kinase-3 gene; ATRA: All-trans retinoic acid; ICE-A regimen: idarubicin, etoposide, cytarabine, ATRA; SSD: Skin surface distance; TLD: Thermoluminescent dosimeters

#### Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

#### Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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