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CASE AND RESEARCH LETTERS

## Leukemia Cutis Arising at the Site of Injection of a Tetanus Vaccine Booster

### Leucemia cutis desarrollada en la zona de inoculación de una dosis de recuerdo de la vacuna del tétanos

*To the Editor:*

Leukemia cutis is a rare disorder. Although its prognostic usefulness is known—since it is frequently associated with a poorer prognosis for the underlying disease[1]—the mechanism that leads it to develop in a specific site is unknown. We describe a case of leukemia cutis which developed at the site of injection of a tetanus vaccine booster.

The male patient, aged 64 years, was an exsmoker with a history of hyperuricemia. He had been diagnosed with chronic myelomonocytic leukemia in 2004 during a study of persistent monocytosis in circulating blood. He consulted 3 years later with a lesion that had developed at the injection site of a tetanus vaccine booster. Commencing as a small papule, the lesion progressively grew to become a violaceous mass, friable to the touch, measuring 7 cm by 5 cm (Figure 1). Observed over the following weeks and developing in parallel with the growth of the skin tumor, was a generalized bilateral and symmetric eruption, consisting of macules and papules in confluent plaques, brownish-purple in color, and most evident on the anterior aspect of the trunk (Figure 2). The histopathology study confirmed the presence of a dense infiltrate in the middle and deep dermis, composed of granulocytic cells at different stages of development and with frequent mitoses (Figures 3 and 4). An immunohistochemical study of the cells revealed them to be positive for CD68 and CD43. A predominantly periadnexal and perivascular infiltrate extended between the collagen fibers, but spared the Grenz zone and the epidermis. These findings enabled a diagnosis of skin infiltration by chronic myelomonocytic leukemia to be reached. A computed tomography scan revealed supradiaphragmatic and infradiaphragmatic lymphadenopathies and hepatosplenomegaly, with no changes with respect to previous scans. A bone marrow biopsy showed signs of infiltration by chronic myelomonocytic leukemia, but with no changes with respect to previous studies. In view of the diagnosis of leukemia cutis, intensive chemotherapy was commenced with idarubicin, cytarabine, and etoposide, complemented with radiotherapy for the largest tumor. The patient experienced a complication due to infection caused by extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* and *Staphylococcus haemolyticus*; this was considered to be secondary to the postchemotherapy aplasia. Response to antibiotic

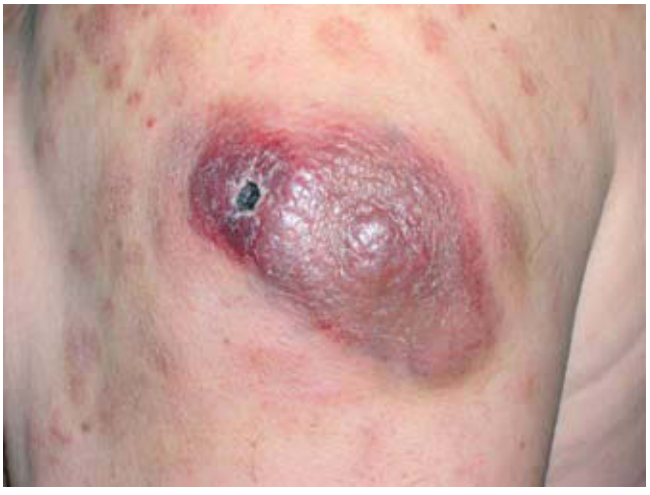

**Figure 1** Violaceous, friable tumor measuring 7 cm by 5 cm.

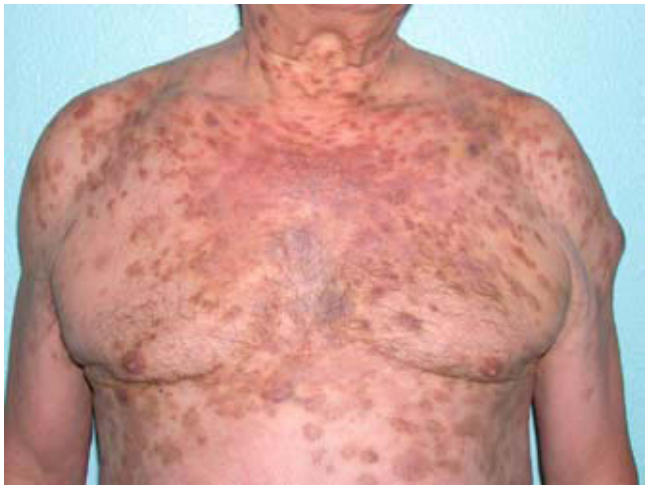

**Figure 2** Generalized bilateral and symmetric eruption.

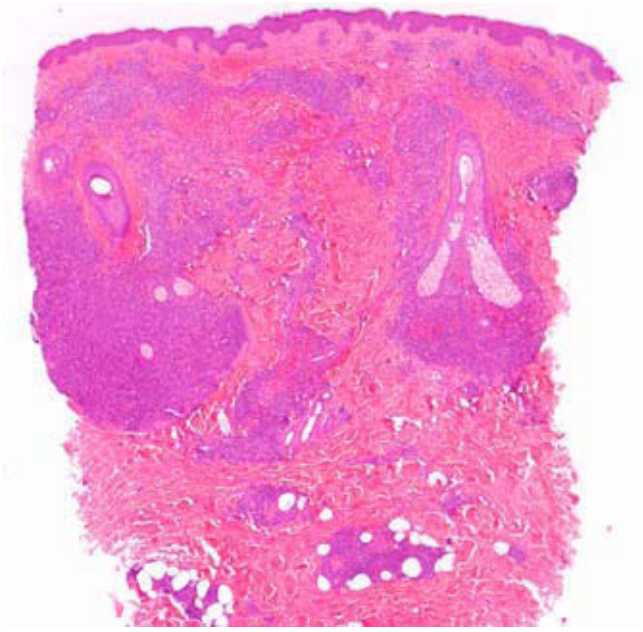

**Figure 3** Predominantly periadnexal and perivascular dense infiltrate in the middle and deep dermis (hematoxylin-eosin, original magnification ×16).

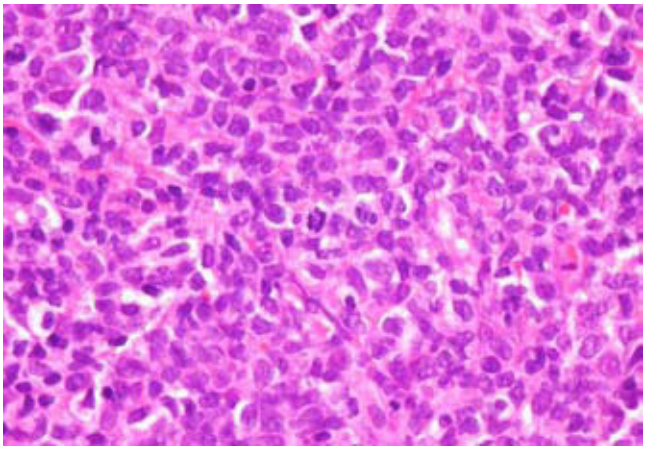

**Figure 4** Granulocytic cells at different stages of development, with frequent mitoses (hematoxylin-eosin, original magnification ×400).

treatment was favorable. In subsequent months, clinical progression was observed, with involvement of the central nervous system in the form of headache and upper motor neuron facial palsy, and treatment was therefore started with azacytidine and cytarabine. During treatment the patient developed septic shock that caused death.

Leukemia cutis, which is defined as a specific manifestation of a malignant hematologic disease, occurs due to dissemination of neoplastic cells to the skin where they proliferate. The condition is rare; incidence is estimated to be 2% to 3% of patients diagnosed with hematologic cancers. As in our patient, it is almost always associated with myeloid leukemia.[2] Although the cutaneous manifestations sometimes precede the hematologic disorder—a condition known as aleukemic leukemia cutis—and may even develop months earlier, in the majority of cases (and as occurred in our patient) they develop in the context of a previously diagnosed hematologic disorder. It is known that specific skin involvement is associated with acute transformation of chronic leukemia,[3] and with a greater likelihood of the neoplastic cells affecting the central nervous system[4]; both these alterations were observed in our patient.

There are no pathognomonic clinical lesions, and lesions can present as plaques, papules, or tumors.[5]

A particular feature of our case was the onset of the cutaneous symptoms at the site of injection of a tetanus vaccine booster. To the best of our knowledge, no such case has previously been reported. There have, however, been reports of other tumors developing at injection sites, namely, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, and Merkel cell carcinoma.[6] From a pathogenic point of view, it seems likely that impaired local immunity in a vaccine injection site,[7] combined with the ease with which myeloid cells migrate to tissues, favors the proliferation of atypical cells. Triggering factors have occasionally been reported for leukemia cutis; for example, the condition has been reported to develop in the area of scars,[8,9] or in cases of herpes simplex virus infection,[10] similar to the Koebner phenomenon in inflammatory diseases. In conclusion, we recommend a histology study of rapidly developing skin lesions with atypical morphologies at sites of vaccine injection, and assessment of the patient to rule out the possibility of leukemia cutis.

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## Randomized Double-Blind Comparative Study of 8-Methoxypsoralen Bath Plus UV-A Treatment Regimens

### Estudio comparativo randomizado a doble ciego de regímenes de tratamiento con 8-metoxypsoraleno en baño-PUVA

*To the Editor:*

Psoralen-UV-A (PUVA) therapy with topical 8-methoxypsoralen (8-MOP) is a widely used treatment for patients with moderate to severe psoriasis.[1,2] The current regimen for bath PUVA involves soaks in a diluted 8-MOP bath followed by UV-A irradiation twice weekly. Bath PUVA has several advantages over oral PUVA as it avoids the adverse effects of oral psoralen administration (gastrointestinal disturbances and the need to use protective eyewear for 24 h after ingestion), produces a more direct psoralen bioavailability to the skin, and requires lower doses of UV-A, resulting in shorter treatment times.

Previous studies investigating the characteristics of PUVA erythema found peak erythemal responses at 96 to 120 hours.[3-5] In addition, we have previously shown that skin remains significantly photosensitive for up to 2 days following trimethylpsoralen (TMP) bath PUVA, possibly due to the presence of psoralen-DNA monoadducts. These findings suggest that in order to achieve the same therapeutic response it may not be necessary to repeat photosensitization prior to the second weekly exposure to UV-A. We have examined this hypothesis.

Approval for the study was obtained from the Tayside Research Ethics Committee, Dundee, Scotland. Patients with symmetrically localized plaque psoriasis on the limbs who were referred for bath PUVA were invited to participate in the study; all participants signed a written informed consent form. The subjects recruited had a minimal phototoxic dose assessment performed by UV-A irradiation immediately after a 15-minute soak in 8-MOP solution (3 mL of 1.2% 8-MOP solution [Crawfords Pharmaceuticals, Milton Keynes, United Kingdom] in 15 L of water). The minimal phototoxic dose was determined at 72 hours.

Patients were randomized to receive 8-MOP soaks twice weekly followed by UV-A irradiation on 1 limb or an 8-MOP soak 1 day of the week and placebo at the time of the second treatment, followed by UV-A irradiation on the other limb.

The random allocation list was generated by computer and allocations were concealed in sequentially numbered opaque envelopes containing the words active (twice-weekly soaks) or inactive (once-weekly soak). Randomization was controlled by the research nurse and carried out after patients had given their written consent to participate in the study.

Sixteen patients (9 women and 7 men) with symmetrically localized plaque psoriasis on the arms or legs participated in the study. Patients less than 18 years of age, on photoactive medication, and those who had received systemic treatment for psoriasis or phototherapy, photochemotherapy, or sunbed therapy in the preceding 3 months were excluded from the study. The treatment was limited to the arms or legs. The majority of patients underwent treatment of the arms (13 patients) and in the remaining 3 patients the treatment was applied to the legs.

During the study, topical steroids and antibiotic or antimycotic preparations were allowed for application only to the flexures and scalp; only emollients were permitted elsewhere. Treatment was performed in accordance with the protocol for stepped incremental UV-A therapy established in this unit. If a patient missed a treatment, the next soak administered was the active soak. Treatment was discontinued at clearance or with 4 exposures after achieving minimal residual activity. The data gathered included total number of treatments and total dose of UV-A to clearance or minimal residual activity, time to relapse, and psoriasis severity score in the plaques.

Patients were followed up at 2, 4, and 6 months and at 1 year.

The scaling, erythema, and induration (SEI) score was recorded for selected plaques at each visit. The nurses who administered the soaks, the patients, and the clinician scoring the plaques were blinded to the treatment allocation. In order to determine psoriasis severity on the study limbs over the course of study, we analyzed the area under the curve of SEI scores over time in all patients. There was a seemingly greater reduction in psoriasis severity on the limbs that received two 8-MOP soaks per week, although the difference between the 2 sides did not reach statistical significance in this small study ($P$=0.29, Wilcoxon signed rank sum test).

Among the 6 patients who attended follow-up, only one showed a difference in time to relapse on the 2 treated limbs; relapse occurred 2 months later on the active (twice-weekly soak) limb.

The aim of this double-blind, intrasubject comparative study was to determine whether omitting one of the 8-MOP baths each week reduced the risk of burning without loss of therapeutic efficacy. A number of difficulties were encountered during the course of the study: patient recruitment was limited by the fact that patients with localized psoriasis are