

## CLINICAL REPORT

## Generalized Eczema Craquele as a Presenting Feature of Systemic Lymphoma: Report of Seven Cases

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**Eczema craquele, or asteatotic eczema, has been associated with malignant lymphoma although this is rare. Since 1986, we have observed seven patients, six men and one woman, mean age 71.5 years (range 43–86 years), with systemic lymphoma and concurrent eczema craquele. Five patients had T-cell lymphoma, one had a B-cell lymphoma and one had Hodgkin's disease. All patients shared several characteristics: (1) a synchronous onset of eczema craquele and lymphoma, (2) generalized eczema, (3) absence of alternative disease or conditions that could favour the onset of eczema craquele, and (4) eczema refractory to topical corticosteroids and emollients, but which resolved upon lymphoma remission and invariably recurred with the lymphoma relapse. All the patients except one died within 1 year, most with active lymphoma. The finding of recalcitrant generalized eczema craquele should prompt a search for lymphoma, particularly in older men. Lymphoma-associated eczema craquele has most characteristics of paraneoplastic syndromes and may be a hallmark of aggressive lymphoma. Key words: eczema craquele, lymphoma.**

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Eczema craquele (EC), or asteatotic eczema, is a well-described, dermatological disease characterized by a dry, cracked skin due to loss of epidermal lubrication (1–5). It occurs primarily on the legs, especially the shins, less commonly on the trunk and arms (1, 2). Older persons are particularly prone to develop EC (6), because sebum excretion and sweat gland activity in aging skin is reduced, particularly on the limbs. Low humidity contributes as EC is common during the winter and in patients who stay in overheated rooms. Other conditions associated with EC include frequent and prolonged bathing in hot water, overuse of soaps and infrequent use of emollients (7, 8), zinc deficiency and essential fatty acid nutritional deficiency or malabsorption (3, 9–11), diabetes mellitus, myxoedema (2), drug-induced reaction (1, 12), topical corticosteroids (13), acute limb oedema (14) and traumatic denervation (5). EC may

also be a presenting feature of internal malignancy (15). We present seven patients with recalcitrant, widespread EC acting as a harbinger of malignant lymphoma or Hodgkin's disease (HD), a circumstance very rarely reported in the literature (16, 17).

### MATERIALS AND METHODS

We conducted a retrospective study of disseminated EC in adult patients with systemic lymphoma or HD seen between 1986 and 2002 at the Departments of Hematology, Dermatology and Internal Medicine. Seven such patients were drawn from the Dermatology Department database among patients with EC and their charts were thoroughly reviewed. None of the patients had a prior history of skin disorders. All patients had a skin biopsy, and all patients but one were regularly followed until death.

### RESULTS

We found seven patients with EC and lymphoma, six men and one woman. The age range was from 43 to 86 years. Clinical and histological examples of the eczema are given in Figs 1–3. A summary of clinical symptoms, response to topical treatment and type of lymphoma is given in Tables I and II (17, 18). The EC appeared totally or partially recalcitrant to topical steroids and emollients. When the patients received chemotherapy of their lymphoma, the skin symptoms

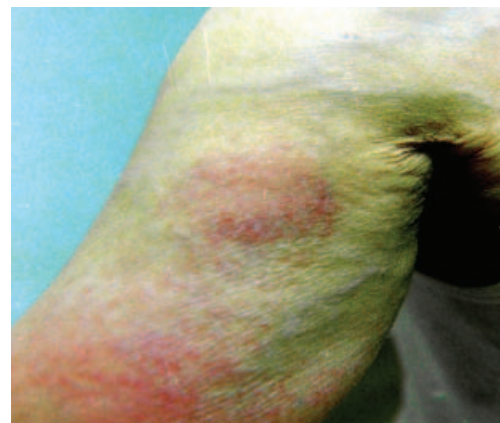


Fig. 1. Case 1: eczema craquele limited to the anterior aspect of the right arm, facing a subcutaneous nodule, then spreading to the whole limb (Hodgkin's disease relapse).

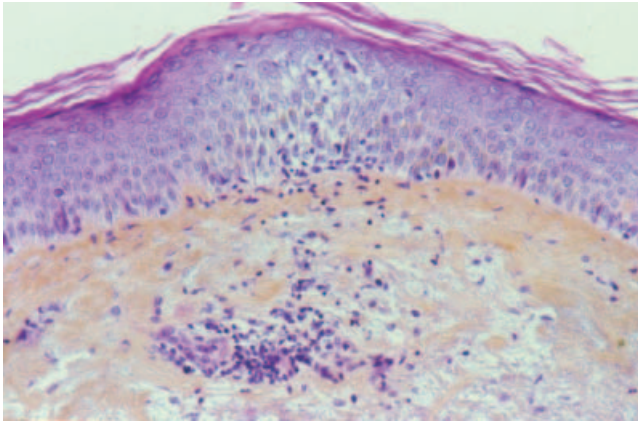


Fig. 2. Case 3: cutaneous biopsy showing spongiosis and exocytosis with an eosinophilic/lymphocytic infiltrate in the superficial dermis and around the vessels (HES  $\times$ 40).



Fig. 3. Case 7: typical eczema craquele on the leg, with linear haemorrhage within the fissures.

improved, but relapsed parallel to lymphoma progression. All but one died within 1 year of the diagnosis. Thus, the EC seems to carry a rather grave prognosis for the lymphoma disease.

## DISCUSSION

Our patients shared the clinical picture of a generalized EC and constitutional symptoms of lymphoma. The EC was remarkable for its widespread distribution, particularly to the limb girdles and trunk, its florid and inflammatory appearance and its unresponsiveness to topical corticosteroid treatment and emollients. Such widespread, treatment-resistant forms of EC are seemingly uncommon. The literature from 1970 to 2003 contains less than 20 cases of widespread resistant EC associated with endocrine disorders, nutritional deficiency including zinc deficiency, and malignancy (15, 18). EC unresponsive to local treatments is uncommon in benign conditions, but is regularly reported to be associated with malignancy (15–17, 19–22).

The diagnosis of EC is usually clinical (23), even though ichthyosis and nummular eczema may be considered. All patients underwent a skin biopsy, which revealed changes compatible with eczema (Fig. 2). Previous studies on EC (24) point to the overlapping characteristics of EC and other forms of eczema. Thus paraneoplastic ichthyosis has long been recognized as associated with HD (23).

The EC was always diagnosed concomitantly with the malignant lymphoma without a past history of EC or other skin disorders. Furthermore, none had hypothyroidism, zinc deficiency, excessive washing with soaps, or a drug-induced rash (2, 9–12).

We found in the literature another three patients with lymphoma and recalcitrant widespread EC (16, 17). The main characteristics of the 10 patients with EC, including our patients, are summarized in Table II. Most are males. The type of lymphoma did not appear to be distributed randomly, but was almost limited to T-cell lymphoma, HD and anaplastic large cell lymphoma. Moreover, the activity of EC closely paralleled the lymphoma in almost all patients. These characteristics, which also applied to three patients with lymphoma and recalcitrant eczema with prurigo nodularis-like lesions described by Callen et al. (25), suggest that generalized EC could represent a true paraneoplastic syndrome (26–31) in patients with lymphoma.

The pathophysiology of EC is not known, although decreased lipids in the skin, decreased humidity, nutritional causes and hormonal disturbances have been implicated (9, 10). The origin of paraneoplastic EC is unclear as well, but a secretion of cytokines by malignant lymphoid cells might be postulated. These cytokines are able to divert the lipid metabolism toward an increased triglyceride synthesis and a decreased cholesterol synthesis (18), which may lead to the disruption of the epidermal lipid barrier, thereby worsening skin dehydration. Quite consistent with the cytokine hypothesis is the observation of transiently localized EC facing a single node relapse of lymphoma in one of our patients with HD.

In conclusion, dermatologists should be aware of the possible association of recalcitrant generalized EC and lymphoma or HD, especially in older men. In agreement with Callen et al. (25), we suggest that such patients undergo a careful physical examination, complete blood cell counts with peripheral blood smears, automated chemistry analysis and serum protein electrophoresis, and a biopsy of any enlarged node. However, routine exams and tests alone may be inadequate in detecting extra-nodal malignant lymphoma in otherwise non-symptomatic patients with widespread EC. Based on our experience, we recommend at least a chest X-ray film and a chest and abdominal-pelvic CT scan. Regular follow-up is suggested.

Table I. Characteristics of the skin eruption in seven patients with haemorrhagic eczema craquele and lymphoma (see also Table II)

Case	Clinical appearance	Topography	Result of skin biopsy	Effect of topical treatment
1	Asteatotic eczema, pruritus	Trunk, shins, arms, face and thighs	Parakeratotic epidermis, lymphocytic and eosinophilic infiltrate of superficial dermis	Unresponsive to steroids and oral antihistamines
2	Asteatotic eczema, pruritus, xerosis, fissured palmo-plantar keratoderma	Abdomen, back, legs and arms	Normal epidermis, perivascular infiltrate in the dermis	Little benefit with steroids
3	Pruritus, eczema craquele	Abdomen, back, thigh and local form (epitrochlean)	Mild hyperkeratosis of the epidermis with exocytosis and spongiosis, lymphocytic infiltrate of the dermis	Unresponsive to steroids
4	Asteatotic eczema, pruritus	Thighs at onset, widespread at relapse	Eczema with exocytosis and spongiosis	Little benefit with steroids and emollients
5	Asteatotic eczema, pruritus	Trunk, arms, legs	Eczema with exocytosis and spongiosis	Unresponsive to daily steroids for 2 months
6	Asteatotic eczema, pruritus	Abdomen, back, legs and arms	Eczema with exocytosis and spongiosis	Unresponsive to daily steroids and emollients
7	Asteatotic eczema, pruritus	Abdomen, back, legs and arms	Eczema with exocytosis and spongiosis	Unresponsive to steroids and oil-in-water emulsion

Table II. Characteristics of 10 patients with adult-onset recalcitrant eczema craquele and systemic lymphoma: 7 patients of this study and 3 patients from the literature

Case no. /ref no.	Age /sex	Type of lymphoma	Course of both conditions	Final outcome
1	75/M	BCL	Parallel	DOL (1 year)
2	43/M	ALCL	Parallel	DOL (1 year)
3	63/M	HD	Parallel	Died of cancer
4	70/M	TCL	Parallel	DOL (14 months)
5	84/F	TCL	Parallel	DOL (4 months)
6	80/M	TCL	NA	DOL (1 year)
7	86/M	ALCL	Parallel	Died (6 months)
Ref. 17	69/M	HD	Refractory	DOL (a few months)
	65/M	HD	NA	DOL (a few weeks)
Ref. 18	29/M	AIL	Refractory	DOL (6 months)

AIL, angioimmunoblastic lymphadenopathy; HD, Hodgkin's disease; ALCL, anaplastic large-cell (Ki-1) lymphoma; NA, not assessable; DOL, died of lymphoma; BCL, B-cell lymphoma; TCL, T-cell lymphoma.

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