# Langerhans cell histiocytosis presenting as fingernail changes

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## INTRODUCTION

Langerhans cell histiocytosis (LCH) identifies a spectrum of disorders that are classified according to the organs involved (single- or multi-organ disease) and the presence or absence of organ failure. Patients younger than 2 years with a multisystem disease have a significantly higher mortality rate than older children.[1]

Nail involvement in LCH is extremely uncommon and rarely reported. To our knowledge, 18 cases have been documented in the literature to date. According to most cases reported, it is thought to indicate a poor prognosis.[2-6] We report the case of a child with nail lesions, which led to a diagnosis of LCH.

## CASE REPORT

A 10-year-old white boy presented in September 2012 with an 11-month history of changes in most of his fingernails. In November 2011 a pediatrician was consulted for the appearance of subungual purpuric lesions in some of his fingernails. Some weeks later, he had a yellowish discharge from the left thumbnail, which was attributed to a bacterial infection and was treated with antibiotics. He showed a partial improvement, and a physician was not consulted again until some months later when he was remitted to our center for recurrence and worsening of the previous lesion. Cutaneous examination found a friable tumor with purulent discharge under the nail plate of the left thumb and subungual haemorrhages in most of the fingernails (Figs 1 and 2). The rest of the physical examination showed erythematous scaly papules with crusts on the scalp, previously diagnosed as seborrheic dermatitis. A biopsy from the tumor in the nail bed and from the scalp showed a diffuse infiltrate in the upper dermis composed of median-large mononuclear cells with abundant eosinophilic cytoplasm and reniform nuclei, admixed with abundant inflammatory cells (Fig 3). Immunohistochemical studies found positivity for CD1a and S100 protein and negativity for CD68. V600E mutation of the *BRAF* oncogene was negative.

*Abbreviation used:*
LCH: Langerhans cell histiocytosis

Further studies, which included laboratory studies, skeletal survey, brain magnetic resonance imaging, abdominal ultrasound scan, and a bone scan, found no alterations. A chest computed tomography scan found multiple cavitated nodules, cysts, and some solid nodules in the lungs. Nonetheless, results of pulmonary function tests were otherwise normal.

These results were consistent with the diagnosis of multisystem LCH without involvement of risk organs. The patient initiated treatment with weekly bolus of intravenous vinblastine (6 mg/m$^2$) and oral prednisone (40 mg/m$^2$/d) according to the Histiocyte Society treatment guidelines.[1]

After 2 cycles of treatment, the patient achieved a partial response with minimal residual lesions on the nails plus an important reduction of the nodules and cysts and disappearance of the subcutaneous

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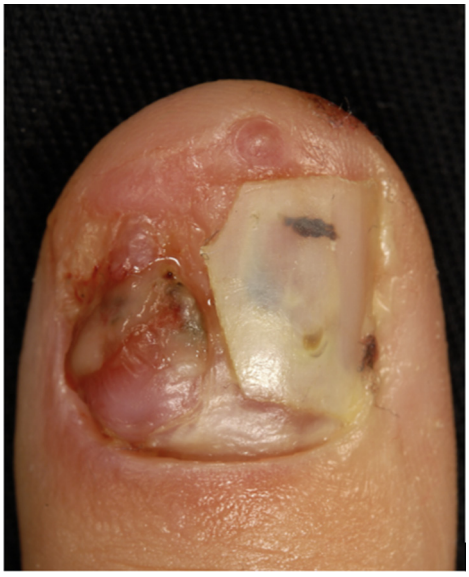

**Fig 1.** LCH left thumbnail involvement shows a friable tumor under the nail plate (nail plate surgically avulsed).

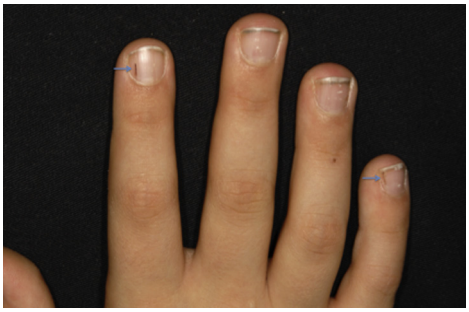

**Fig 2.** LCH with multiple nail involvement. Arrows show purpuric lesion of some fingernails, which resemble splinter haemorrhages.

emphysema on the computed tomography scan. However, after 4 months, the infection on his skin and lungs relapsed. Then he started on the STRATUM II protocol (vinblastine, cytosine arabinoside, and prednisone) achieving a complete remission within 7 cycles. For the last 5 months, the patient has been on a maintenance therapy with mercaptopurine and methotrexate with no evidence of relapse.

## DISCUSSION

LCH is a proliferative disorder in which atypical Langerhans cells infiltrate and accumulate within tissues. The main organs affected are bone, skin, and pituitary followed by lungs, bone marrow, liver, central nervous system, and lymph nodes.[1,7] Skin is involved in 30% to 60% of the cases, presenting as small, erythematous papules in the scalp that may resemble seborrheic dermatitis and yellow-brown scaly papules on the trunk, flexural areas of the neck, axilla, and perineum. The development of purpura and petechiae is common.[1,4,5]

Nail involvement in LCH is distinctly uncommon. The literature focusing on the nail aspects is limited to a few individual cases and a small series. Among the largest pediatric series, no case of nail changes were identified.[8,9]

Some investigators suggest that the real prevalence of these changes is underestimated, as it can be mistakenly attributed to the habit of nail biting. The clinical features comprise hemorrhagic and pustular lesions in the nail plate, longitudinal grooving, hyperkeratosis, subungual thickening, striate nail dystrophy, onycholysis, paronychia, and loss of nail plate.[2-6]

As described in the literature, the histologic findings of the lesions in the nail unit of our patient are similar to those described in the cutaneous lesions, which comprise atypical Langerhans cells.[5,6]

The differential diagnosis includes numerous skin diseases, such as psoriasis, lichen planus, alopecia areata, bacterial and fungal infections, Darier's disease, and Reiter syndrome. Conditions that cause subungual hemorrhages or erytronichia should also be discarded. Bearing in mind that our patient presented with a solitary tumor in the nail, we should also consider diagnosis like verruca vulgaris and pyogenic granuloma and many other tumors.

Several prognostic factors are accepted as poor prognosis predictors: the age of onset, the number of organs involved, and the presence of organ dysfunction. Children younger than 2 years with a multisystem disease have an estimated mortality risk ranging from 37% to 66%.[1,7] Those patients in whom the hematopoietic system, liver, or spleen are affected (high-risk organs) tend have a higher mortality. Although the lung was previously considered a high-risk organ, Haupt et al[7] state that it is no longer considered high risk.

The value of nail changes as a prognostic factor is controversial. Several investigators have postulated that nail involvement would represent an unfavourable sign, as it mostly occurs in patients with multisystem disease with involvement of high-risk organs.[4-6] Timpatanapong et al[5] reported a series of 15 cases, among which 3 had nail involvement resulting in fatal outcome in all. Nevertheless, some other reported cases remitted spontaneously or successfully responded to treatment with chemotherapy.[3]

There is not enough evidence to state that nail changes constitute an independent prognostic factor

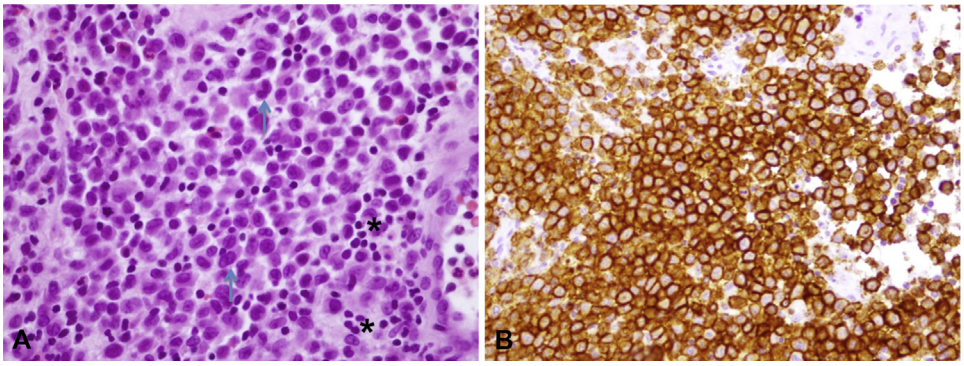


**Fig 3.** Histopathologic features of LCH—left thumbnail bed biopsy. **A,** Mononuclear cells with abundant eosinophilic cytoplasm and reniform nuclei (arrows) and inflammatory cells (asterisk). **B,** Positive immunohistochemical staining for CD1a. (**A,** Hematoxylin-eosin stain; original magnification: x100. **B,** CD1a stain; original magnification: x100.)

of poor outcome. However, nail explorations is of vital importance in some entities, such as histiocytosis, as it can give rise to an early diagnosis and improve the prognosis. Finally, because of its high association with a multisystem disease, nail involvement could be an indicator to perform high-resolution computed tomography in the study of extension.

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