# Leukemia Cutis Presenting with Fingertip Hypertrophy

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## Abstract

*Background*: Patients with leukemia often manifest cutaneous findings, which include nonspecific lesions and specific leukemic infiltrates termed leukemia cutis.

*Objective*: A case of leukemia cutis involving distal finger pads is reported and literature describing hand involvement of specific leukemic infiltrates is reviewed.

*Methods and Results*: An 80-year-old woman with a 10-year history of chronic lymphocytic leukemia developed painful symmetric tumors of her distal finger pads. Histopathological examination of the biopsy specimen revealed infiltration by neoplastic lymphocytes. Only a few cases of leukemia cutis involving the hands have been reported in the literature, none with this particular presentation. The clinical and histopathologic features of leukemia cutis are reviewed.

*Conclusion*: This case emphasizes the importance of obtaining a biopsy specimen for histopathological examination of any suspicious skin lesion in a patient with leukemia.

## Sommaire

*Antécédents*: Des patients leucemiques presentent souvent des manifestations cutanees comportant des lesions non-specifiques et des infiltrats leucemiques specifiques appeles leucemides.

*Objectif*: Un cas de leucemide impliquant les pulpes distales des doigts est reporte et la bibliographic decrivant l'implication d'infiltrats leucemiques specifiques au niveau de la main est revue.

*Methodes et Resultats*: Une femme de 80 ans avec une histoire de leucemie lymphocytaire chronique depuis dix ans developpa des tumeurs symetriques douleureuses de la pulpe distale de ses doigts. L'examen histopathologique de l'echantillon biopsique revela une infiltration de lymphocytes neoplasiques. Seuls quelques cas de leucemide impliquant les mains ont ete reportes dans la litterature et aucun avec cette presentation. Les aspects cliniques et histopathologique des leucemides sont passes en revue.

*Conclusion*: Ce cas souligne l'importance d'obtenir un specimen biopsique pour l'examen histopathologique de toute lesion douteuse cutanee chez un malade leucemique.

Cutaneous eruptions frequently occur in patients with leukemia, and are usually classified into specific and nonspecific lesions. The latter, which are much more common, can be further subdivided into lesions arising from bone marrow failure and reactive or paraneoplastic lesions.[1] The specific eruptions, termed leukemia cutis, result from skin infiltration by neoplastic cells or their precursors. Clinical appearance of leukemia cutis is quite varied, ranging from macules, papules, nodules, or tumors to generalized erythroderma or exfoliative dermatitis. It also manifests in an array of colors from erythematous-pinkish and reddish-brown to dark purple.[2] We present a patient with a long-standing history of asymptomatic chronic lymphocytic leukemia, who, late in the course of her disease, developed painful symmetric tumors of her distal finger pads. The biopsy confirmed diagnosis of leukemia cutis. There are only a few cases in the literature describing patients with specific leukemic infiltrates involving hands. None report the particular fingertip hypertrophy presentation seen in our patient.

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## Case Report

Our patient is an 80-year-old white woman with a 10-year history of chronic lymphocytic leukemia (CLL). Diagnosis of B-cell-type CLL was made based on lymphocytosis with characteristic immunophenotype (dim surface immunoglobulin with light chain restriction, CD20 positivity with coexpression of CD5; CD23 positivity). The patient had remained remarkably asymptomatic since her diagnosis and required no specific therapy. Over the four years leading to presentation, however, she began noticing swelling of her distal finger pads, which progressed to the point that she was no longer able to wear rings. The growths became quite painful. She denied any history of trauma or other precipitating events. Oral antifungal (Lamisil) treatment was prescribed by her primary care physician for suspected tinea infection, but there was only slight improvement. The patient was subsequently referred for dermatologic assessment.

Physical examination in our clinic revealed an elderly woman in no distress. She had marked symmetric distal acral hypertrophy of all ten fingers, with indurated, firm, skin-colored nodules and tumors infiltrating the fingertips (Figs. 1 and 2). No other suspicious skin lesions were observed on total body examination. One of the lymph nodes at the left side of her neck was enlarged; no other lymphadenopathy or hepato-splenomegaly were detected.

The patient's hematological profile showed the following: Her hemoglobin was normal at 135 g/L; her leukocyte count was 94,600/mm$^3$, with 9% neutrophils, 80% lymphocytes, 2% monocytes. The platelet count was 166,000. Polychromatophilia, Burr cells, ovalocytes, and smudge cells were present on the peripheral smear.

A 4-mm punch biopsy specimen was taken from the hypertrophic tissue of the third digit of the right hand. A heavy infiltrate of small lymphoid cells was found in the dermis and subcutis, sparing the epidermis. Cytologically, the lymphocytes were relatively monomorphous and contained hyperchromatic nuclei with round to slightly irregular contours. The process dissected between dermal collagen fibers and surrounded adnexal structures, including blood vessels (Figs. 3 and 4). Morphologic features of marginal zone lymphoma, such as cellular heterogeneity, monocytoid cells, and "colonized" follicular structures, were not identified. Immunohistochemistry demonstrated positivity for CD45, CD20, CD23, and CD43, with variable reactivity for CD5—a profile similar to the phenotype determined by flow cytometry of the original diagnosis of CLL; there was significant immunostaining for cyclin D1.

The combined morphological and phenotypic pathological examination confirmed the diagnosis of chronic lymphocytic leukemia involving the skin. The presence of CD23 weighed against the possibility of Mantle cell neoplasm.

**FIGURE 1** Symmetric fingertip hypertrophy.

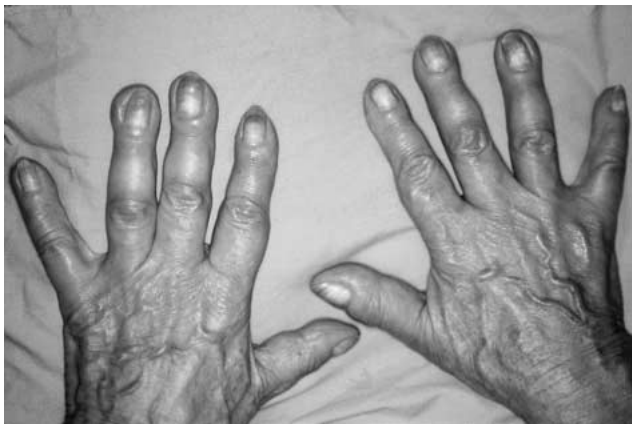
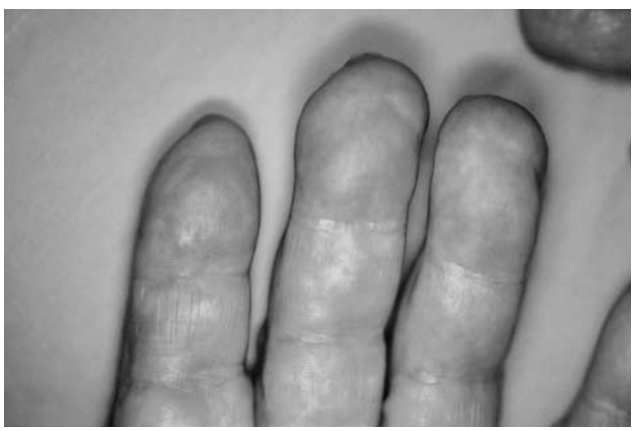


**FIGURE 2** Firm nodules infiltrating the fingertips.



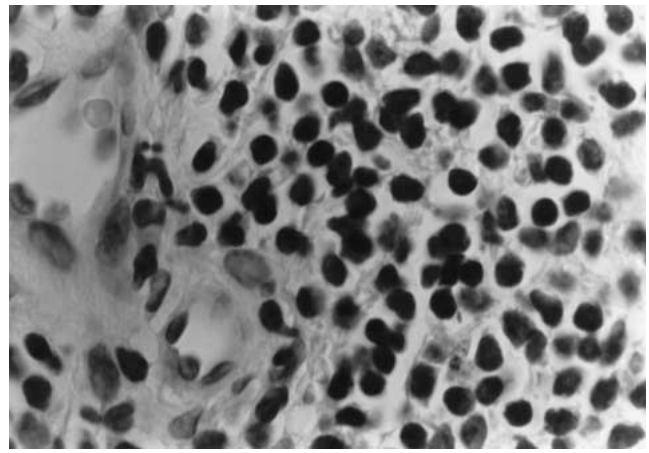
## Discussion

Patients with leukemia often present with specific or nonspecific cutaneous manifestations, including the pallor of anemia, purpura, vasculitis, exfoliative erythroderma, pyoderma gangrenosum, prurigo-like papules, erythema multiforme, urticaria, panniculitis, and acute febrile neutrophilic dermatosis.[3–6] Leukemia cutis, which is much less common than nonspecific manifestations, represents dissemination of systemic disease to the skin and is confirmed by histopathological analysis of the tissue biopsy specimen. The distinction between the two groups is important from the therapeutic and the prognostic standpoints. The presence of leukemic infiltrates of the skin has been associated with a high likelihood of systemic and dermal relapse after standard induction chemotherapy in patients with leukemia.[7,8]

The incidence of leukemia cutis varies greatly according to the type of leukemia. In analysis of 322 cases,

**FIGURE 3** Heavy infiltrate of lymphocytes throughout papillary and reticular dermis, with dissection of dermal collagen (H+E, 400×).

**FIGURE 4** Dermal infiltrate of cytologically monomorphous neoplastic small lymphocytes with hyperchromatic nuclei, adjacent to dermal microvasculature (H+E, 1000×).



Boggs et al.[9] reported a 20% incidence of leukemia cutis in CLL and 3% in acute lymphocytic leukemia. Su et al.[4] presented a clinicopathologic correlation review of 42 leukemia cutis cases. Multiple papules and nodules were the most frequently noted clinical lesions, occurring in 60% of cases. Leukemia cutis usually developed several months after the diagnosis of systemic leukemia, although it occasionally preceded it (aleukemic form). The prognosis of patients with leukemia with skin infiltrates was generally grave: 88% of patients in the series died, most within one year of diagnosis. The greatest interval between histopathologic diagnosis of leukemia cutis and death was found in patients with CLL—a mean of 16 months. In another series, Desch and Smoller[10] retrospectively analyzed 123 skin biopsies from 102 patients with diagnosis of leukemia and identified leukemia cutis in 37 of 123 specimens. Chronic myelogenous leukemia (6/10) and CLL (4/8) were most commonly associated with leukemia cutis. The greatest variety of nonspecific lesions (drug eruptions, infectious lesions, purpura) was seen in patients with acute myelogenous leukemia, suggesting that the index of suspicion for lesions other than leukemia cutis should be higher when these patients present with cutaneous findings.

CLL is known to give rise to both specific and nonspecific cutaneous manifestations, with nodules, tumors, infiltrated plaques, and papular lesions being the most frequently reported clinical presentations.[11] The increased association of CLL and leukemia cutis may result from greater relative frequency of this type of leukemia in Western society, combined with increased longevity of patients with CLL. The histopathology of cutaneous B-cell CLL is generally variable. As in this case, the infiltrate is nonepidermotropic and is diffuse within the dermis or patchy with perivascular and periadnexal involvement. Expression of mature B-cell antigens (CD19, CD20, CD79a) with coexpression of CD5, dim surface immunoglobulin with light chain restriction, CD23, and CD43 is characteristic. This profile helps distinguish CLL from mantle cell lymphoma (CD23 negative) and marginal zone lymphoma of skin-associated lymphoid tissue (CD5 negative).

Different types of leukemia may have relatively distinct distributions of specific lesions. The face and extremities are primarily involved in acute and chronic lymphocytic leukemias. The trunk is mostly affected in acute myelogenous leukemia, whereas in monocytic leukemia the entire skin surface may be involved, along with mucosal surfaces.[1,2,12,13] Leukemic infiltrates can arise in scars from recent surgery, trauma, burns, herpes zoster, herpex simplex, as well as in sites of intramuscular injections.[2] Leukemia cutis presenting as a scrotal ulcer has been reported.[14] There is also a case on record of leukemia cutis arising at the cutaneous larva migrans site.[15] Koebner-like trauma-related etiology is thought to play a role in localization of the lesions.

Our patient presented with distal finger pad hypertrophy, and histopathological examination of the biopsy

specimen was consistent with leukemia cutis. Hand and digit involvement of leukemia cutis is rare. Only several unusual cases have been reported, none with this particular presentation. High et al.[16] described a case of a 72-year-old woman with CLL who, one year after her diagnosis, developed leukemic infiltrates in the form of erythematous smooth nodules over the proximal nail folds of her fingers. Simon et al.[17] presented a case of a 79-year-old male with a several-year history of "humping" of the nails and subungal nodules, involving several fingers and the left big toe. The biopsy of the tissue revealed massive leukemic infiltration, and subsequent peripheral smear confirmed the diagnosis of chronic lymphocytic leukemia. Ausubel et al.[18] described a case of a 63-year-old female in whom reddish-purple plaques on the palms and fingers were the initial clinical expression of systemic leukemia. Calvert and Smith[19] reported a patient with CLL who had clubbing of the fingers and periosteal bone destruction of the distal digits due to leukemic involvement of the distal phalanges and soft tissues of the dorsal and lateral aspects of the fingers. Recently, Yagci et al.[20] documented the case of a 68-year-old man with erythematous swollen nail folds and nail deformity, which were presenting findings of chronic lymphocytic leukemia.

The patient presented here is of interest because of the rare cutaneous manifestation of her leukemia, the symmetric fingertip hypertrophy. This case reemphasizes importance of obtaining a biopsy specimen for histopathological examination of any suspicious skin lesion in patients with lymphoproliferative disorders. Moreover, interestingly, while the diagnosis of leukemia cutis is usually associated with a grave prognosis linked to aggressive systemic disease, our patient has had a remarkable four-year history of skin infiltrates without clinical deterioration of her condition. Because of the increasing pain experienced by the patient, she was referred for local electron-beam radiotherapy, which has been reported to result in rapid symptomatic relief and regression of specific deposits.[1,8] Generally, the treatment of cutaneous lesions involves systemic chemotherapy for underlying leukemia. In a case reported by Yagci et al.,[20] fludarabine therapy induced complete remission of the skin infiltrates.

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