Case Report

Nail involvement in Langerhans cell histiocytosis: Diagnostic and prognostic Clues

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Abstract

Introduction: Despite its rarity, nail involvement in Langerhans cell histiocytosis (LCH) may show various clinical presentations. This study aims to show the roles of nail involvement in LCH patients as the diagnostic and prognostic clues.

Case illustrations: We presented four cases of multisystem LCH in children which were already confirmed by skin biopsy with various nail abnormalities. We were able to perform nail biopsy in two patients and confirmed the nail involvement. Histopathological examination showed the infiltration of Langerhans cells characterized by indented/reiform nuclei and CD1a expressions. All patients had high-risk organ involvements.

Discussion: Langerhans cells may infiltrate the nail bed, proximal nail fold, and nail matrix. Further infiltration may destruct the nail plate. Hypothetically, we suggest that the nail bed as the initial infiltration site of Langerhans cells. The different sites of involvement lead to different clinical presentation. Nail abnormalities may predict a poorer prognosis, as they mostly occur in patients with multisystem disease.

Conclusions: Nails should be routinely inspected in the suspicion of LCH. The presence of nail abnormalities in LCH patients may predict a poorer prognosis.

Keywords: nail, Langerhans cell histiocytosis, diagnosis, prognosis

Background

Langerhans cell histiocytosis (LCH) is a proliferative disorder characterized by the accumulation and infiltration of atypical Langerhans cell within various tissues.¹ It represents a spectrum of disorder that ranges from a mild single organ involvement to a severe multisystem disease.¹² The main organs affected are bone, skin, and pituitary.³ Other organs involved are liver, spleen, hematopoietic system, lungs, lymph nodes, and central nervous system, excluding the pituitary.³ Nail involvement in LCH is considered uncommon and rarely reported.¹² Histopathological examinations from the affected nails, which comprise atypical Langerhans cells, was generally accepted to confirm the diagnosis.⁴ We present four cases of multisystem LCH with nail involvement admitted to the outpatient clinic of Dermatology and Venereology of Dr. Cipto Mangunkusumo National General Hospital Jakarta, for the past two years. We were able to perform nail and skin biopsy for two cases. Whereas, only skin biopsy was done to the other two cases. All biopsies confirmed the diagnosis of LCH. This study aims to emphasize that nail abnormalities may be the diagnostic and prognostic clues in LCH.
Case Illustrations

Case 1

A three-year-old boy was presented with discrete erythematous papules and plaques distributed widely throughout his body for the past two weeks. Purpuric striae affecting four fingernails were found during physical examination (Figure 1A). His parents noticed these nail abnormalities five days before the consultation. There was also abdominal distension due to liver enlargement. Skin and nail bed biopsies were performed and showed infiltration of large mononuclear cells with nuclear grooves within the epidermis and dermis (Figure 1B). We performed immunohistochemistry for the nail specimens (Figure 1C), which yielded positive result for S100 and CD1a.

Figure 1. A. Subtle purpuric striae on the thumbnail. B. The large mononuclear cells with nuclear grooves within the epidermis and dermis (hematoxylin and eosin, 1000x). C. Positive CD1a expression (CD1a, 1000x)

Case 2

A two-year-old boy presented to our outpatient clinic with chronic erythematous and purpuric rash affecting the abdomen, palms, and soles. He was immobilized during the past month. There were purpuric striae affecting all his fingernails and the first digit of his left toenail (Figure 2). There were massive liver and spleen enlargement. Plain radiography showed multiple osteolytic lesions on the cranium, bilateral iliac bones, and femurs, which led to the pathological fracture of the right proximal femoral shaft. Skin biopsy was performed and showed atypical cells with eosinophilic cytoplasm and indented nuclei in the epidermis and superficial dermis.

Figure 2. Purpuric striae on finger- and toenails

Case 3

A two-year-old boy presented with multiple purpuric papules dispersed widely throughout the whole body, some of which were covered by crusted and scales. We also found multiple subungual purpurae on his fingernails, partly were arranged as purpuric striae (Figure 3). Ophthalmologic findings included suspicion of the orbital involvement with lagophthalmos, corneal exposure, and proptosis in
both eyes. There were liver and spleen enlargement. Additionally, osteolytic lesions on multiple areas were shown on plain skull radiography. Skin biopsy was performed and showed the infiltration of large mononuclear cells with indented nuclei in the epidermis and epidermal-dermal interface. There were also perivascular and interstitial lymphocytes and histiocytes infiltration in the upper dermis. Immunohistochemistry was not performed. The patient's parents refused further treatment and examination. He passed away four months later due to pulmonary and central nervous system involvements.

Figure 3. Multiple subungual purpurae on the fingernails and purpuric papules on the palms

Case 4

A 2.5-year-old girl was brought for clinical evaluation of her skin lesions, which appeared three months before presentation. There were multiple purpuric papules, erosions, and excoriations covered with dark red crusts distributed mainly on the face, trunk, and genital. There were severe nail involvement manifesting as nail plate destruction, onychodystrophy, and paronychia that affected all fingernails and both first digits of the toenails (Figure 4A). There were liver and spleen enlargement. Consultation to the Ophthalmology Department revealed eyelid involvement manifested as diffuse palpebral mass, along with lagophthalmos. She underwent skin and nail biopsies. Histopathological examination from the nail unit showed the destruction of the nail plate with hyperplastic squamous epithelial cells and a tumor within the connective tissues (Figure 4B). The tumor comprised of pleiomorphic cells with eosinophilic cytoplasm and reniform nuclei. There were also dense infiltrates consisted of lymphocytes, neutrophils, and eosinophils. Immunohistochemistry revealed positive CD1a on most atypical cells with reniform nuclei (Figure 4C).

Figure 4. A. Nail plate destruction, onychodystrophy, and paronychia on the left thumbnail. B. The pleomorphic cells with eosinophilic cytoplasms and reniform nuclei were shown by black arrows (hematoxylin and eosin, 400x). C. Positive CD1a expression (CD1a, 400x)
Discussion

Bender and Holtzman\textsuperscript{5} in 1958, followed by Kahn\textsuperscript{6} in 1969, were among the first who reported the nail involvement in LCH. It is considered a rare manifestation.\textsuperscript{1,2} Reports focusing on nail involvement to date is limited to few individual cases and small series.\textsuperscript{1} Among two extensive pediatric series by Esterly\textsuperscript{7} in 1985 and Rivera-Luna\textsuperscript{8} in 1988, no case of nail involvement was described. Some experts think that the exact prevalence may be underestimated.\textsuperscript{1} Nail involvement in LCH manifests as onycholysis, subungual hyperkeratosis, nail dystrophy, fragile lamina, paronychia, subungual pustules, nail fold destruction, longitudinal grooving, purpuric striae of the nail bed, and a friable tumor under the nail plate.\textsuperscript{1,4,9,10} Considering the enormous variation of nail involvement in LCH, nail inspection has become a routine procedure applied in our department while examining LCH patients. We present four cases of nail involvement in LCH, which manifested as purpuric striae (case 1 and 2); subungual purpura and purpuric striae (case 3); nail plate destruction, onychodystrophy, and paronychia (case 4).

Langerhans cells appear as large cells (10-15 μm in diameter) with indented/reniform nuclei.\textsuperscript{2} They contain Birbeck granules and express SI100, CD1a, and CD207 (langerin).\textsuperscript{2} The detection of Birbeck granules by electron microscope has been widely replaced by the detection of CD1a expression by immunohistochemistry.\textsuperscript{11} The histopathological findings of the affected nail units of the two cases described above consistently showed infiltration of large mononuclear cells with indented/reniform nuclei, whether interspersed within the epidermal and dermal portion of the nail bed or concentrated and formed a mass under the nail plate. Both also showed positive CD1a expression, which confirmed the diagnosis of LCH. The infiltration and accumulation of Langerhans cells in various parts of the nail unit remain the histopathological hallmark to confirm the nail involvement in LCH. Although we did not perform a nail biopsy for the other two cases, we believe that the nails were similarly involved. The nail abnormalities found in those two cases were consistent with the clinical findings of nail involvement in LCH described above, and their skin biopsies confirmed the diagnosis of cutaneous LCH. Therefore, we suggest performing nail inspection routinely in the suspicion of LCH since the presence of abnormalities may become an important diagnostic clue.

In the first case, the nail involvement was found in the early course of the disease. Whereas, the fourth case showed a more advanced stage. We hypothetically suggest that the nail bed is the initial infiltration site of atypical Langerhans cells. It can explain the histopathological abnormalities found in our patient, which clinically only showed subtle involvement of the nail bed (purpuric striae). Besides the nail bed, Langerhans cells can also be detected in the nail matrix and the proximal nail fold.\textsuperscript{12} These cells may migrate into the epidermis, causing slight spongiosis and intraepithelial accumulations.\textsuperscript{12} Therefore, epidermotropism is often seen.\textsuperscript{13} Further infiltration may destruct the nail plate.\textsuperscript{4} It explains the abnormalities found in another patient, which showed advanced involvement with nail plate destruction, onychodystrophy, and paronychia. The presence of a tumor comprised of pleomorphic cells with reniform nuclei indicates nail bed infiltration. Marked hyperplasia of the squamous cells indicates nail plate abnormality. Although we could only take the biopsy specimen from the nail bed and the nail plate, we believe that the atypical Langerhans cells have already infiltrated other nail units, namely nail matrix and nail fold. We thought that the infiltration to the nail matrix might contribute to the abnormal growth of the nail plate, whereas the infiltration to the nail fold might cause paronychia. Considering those explanations, we suggest performing nail biopsy mainly from the nail bed tissue if the abnormalities were found early within the nail bed, such as purpuric striae. If there is an advanced involvement of the nail, we suggest performing a longitudinal biopsy. This procedure allows us to confirm the abnormality found in the nail matrix, proximal and lateral nail folds, nail bed, and nail plate.\textsuperscript{14}

Conclusion

Finally, some authors believe that nail involvement is correlated with multistystem disease and a poorer prognosis.\textsuperscript{15-17} All of our cases affected young children aged around two years and showed liver and/or spleen involvements, which were considered high-risk organs.\textsuperscript{11} The early onset of the disease and the presence of organ failure are the leading negative prognostic indicators.\textsuperscript{15} All our four cases had purpuric nail lesions with multiple organ involvement. We concluded that the presence of nail abnormalities in LCH might predict an unfavourable outcome.
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