

Case Report

Recalcitrant scalp and intertriginous rash in a patient with diabetes insipidus: diversity of cutaneous manifestations and pitfalls in diagnosis of adult Langerhans histiocytosis

一名尿崩症患者的頭皮及對磨部位的頑抗性皮疹：成人郎格罕細胞性組織細胞增生症的皮膚表徵之多樣性及診斷之陷阱

H Ranu and SH Pang

Langerhans cell histiocytosis (LCH) is a proliferative histiocytic disorder of unknown cause characterized by the accumulation of Langerhan cells in various tissues. Typically a disorder of childhood, features of this disease have been well documented in children but remain ambiguous and poorly documented in adults leading to many pitfalls in diagnosis. We report a case of Langerhans cell histiocytosis in a young lady who presented with cutaneous involvement of varying morphology and review the various cutaneous manifestations of adult Langerhans cell histiocytosis reported in the literature to date.

郎格罕細胞性組織細胞增生症是一種不明成因的增生性組織細胞疾病，其特徵為郎格罕細胞積聚於多個不同組織。郎格罕細胞性組織細胞增生症為典型的兒童疾病，故兒童的病症特色有著詳盡的記載；但成年患者的記載却相對貧乏及含糊不清，衍生了不少診斷上的困難陷阱。我們報告了一個少女案例，有著多種形態的皮膚影響；繼而就現有文獻中對成年郎格罕細胞性組織細胞增生症患者所報告的種種皮膚表徵進行回顧。

Keywords: Langerhans cell histiocytosis, presentation, treatment

關鍵詞： 郎格罕細胞性組織細胞增生症，表現，治療

Dermatology Unit, Singapore General Hospital, Singapore

H Ranu, MBBS, MRCP, MSc Clin Derm
SM Pang, FRCP, FAMS

Correspondence to: Dr. H Ranu

Block 6 Level 9, Dermatology Unit, Singapore General Hospital, Outram Road, 169608, Singapore

Introduction

Langerhans cell histiocytosis is a rare condition that can occur at any age and commonly affects bones, lung, pituitary gland, skin, liver, bone marrow and the gastrointestinal tract. The cutaneous manifestations are diverse and a high index of suspicion is needed to make the

diagnosis. It is imperative the diagnosis be made as quickly as possible because time from presentation to diagnosis is of prognostic importance in adults with the disease. In this case report, we attempt to highlight the diversity of the cutaneous manifestations of adult Langerhans cell histiocytosis and the need for histological diagnosis early on to avoid delay in intervention and achieve the best outcome.

Report

We report a 33-year-old preschool teacher with a background of hypertension and polycystic ovarian syndrome who presented with a non-healing skin rash. She had been suffering from a scalp rash for 4 years and had recently developed rashes over her axilla, body and groin over the past 6 months. The rash was both painful and pruritic in nature. Examination revealed tender yellowish crusted papules over the scalp (Figure 1). There were erythematous papules and pustules noted over her chest, lower back and suprapubic region. She also had linear erosions and fissuring in the groin creases (Figure 2). She was also found to have a fatty liver on ultrasound with elevated transaminases. Work up for the cause of the fatty liver revealed hypothyroidism which was central in origin and evaluation of the rest of her anterior pituitary hormones revealed growth hormone deficiency, intact cortisol and sex hormone axis and mildly elevated prolactin levels. She was put on thyroxine replacement. Further questioning revealed that she had been having polyuria, polydipsia and nocturia for the same duration as her skin rash. Diabetes insipidus was confirmed via a water deprivation test and she was commenced on desmopressin therapy. An MRI of the pituitary gland revealed nodular thickening and enhancement of the pituitary stalk. Apart from the liver involvement and diabetes insipidus, she had no other systemic

symptoms to suggest Langerhans cell histiocytosis. A musculoskeletal survey was entirely normal. A diagnosis of Langerhans cell histiocytosis was suspected and skin biopsies were performed from the scalp, axilla and groin rash.



Figure 1. Clinical photograph of the patient showing yellowish crusted papules and pustules scattered in a diffuse manner over the scalp.



Figure 2. Clinical photograph of the patient showing sharp-edged linear erosions and fissuring of the groin and erythematous papules and nodules over the suprapubic region.

All 3 specimens showed a dermal infiltrate of histiocytes with pale eosinophilic cytoplasm and reniform nuclei, admixed with variable numbers of neutrophils, eosinophils and lymphocytes. Immunohistochemical studies demonstrated CD1a and S100 positivity in all 3 specimens (Figure 3). In the scalp, the lesion extended perifollicularly deep into the dermis and around adnexal structures. A full skeletal survey and bone scan showed no bony involvement. A computer tomography (CT) scan of her chest, abdomen and pelvis revealed a few vague hypodensities in her liver and incidental nodular hyperplasia of the left adrenal gland but no splenomegaly, intrabdominal lymphadenopathy or pulmonary involvement. A magnetic resonance imaging (MRI) scan of her abdomen confirmed a diffuse nodular involvement of her liver. The staging of disease was done. This patient had Langerhans cell histiocytosis with multisystemic disease and organ dysfunction affecting 3 organs: the skin, pituitary and liver. The patient was commenced on chemotherapy with high dose prednisolone and vinblastine.

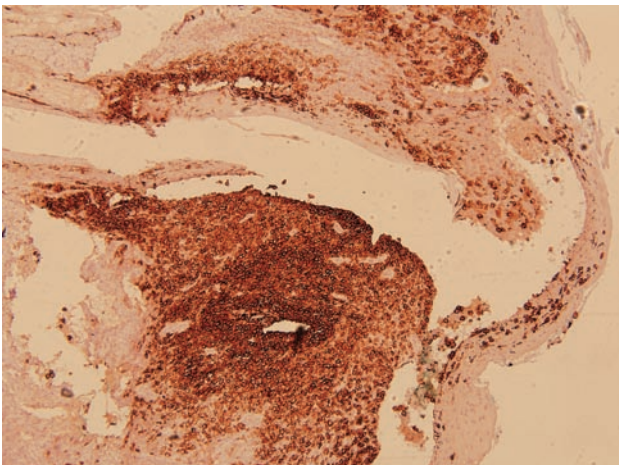


Figure 3. Photomicrograph of the biopsy specimen taken from the groin. Dense infiltrate of Langerhans cells infiltrating the papillary dermis showing immunoreactivity for CD1a surface antigen on inflammatory histiocytic cells of the lesion on the groin.

Discussion

The skin is the physiological habitat of Langerhans cells where they ingest and process proteins, migrate to the lymph nodes and present antigens to lymphocytes. The common feature in LCH lesions regardless of organ involvement, is an immature form of Langerhans cells identifiable by a series of characteristic features, including intracellular Birbeck granules and expression of surface CD1a. The Histiocytic Society has given confidence levels for the diagnosis of LCH. Demonstration of Birbeck granules by electron microscopy remains the gold standard for identifying Langerhans cells. However, the demonstration of CD1a surface antigen on lesional cells in an appropriate clinicopathological setting is considered to be adequate for a definitive diagnosis.¹ The cutaneous manifestations range from perifollicular crusted papules, vesicles and pustules on the scalp, erythematous or purpuric papules plaques and nodules, erosive intertrigo of the folds with a predilection for the axillae, groins and submammary region to fluctuant abscesses and draining sinuses. Nail involvement is not uncommon and is thought to be a marker of multisystem disease.² Among the nail changes described are onycholysis, dystrophy, subungual pustules, subungual hyperkeratosis and hemorrhages. The cutaneous signs of LCH have mimicked various other conditions such as nodular prurigo,³ varicella⁴ and eruptive xanthoma⁵ (Table 1). LCH is a pleomorphic disease entity and can easily be misdiagnosed as keloids, sarcoidosis, intertrigo, eczema, seborrhoeic dermatitis, hidradenitis suppurativa, folliculitis and disseminated granuloma annulare. When confined to the scalp, LCH can be mistaken for lichen planopilaris and folliculitis decalvans.⁶ Our initial impression of the scalp lesions was that of dissecting cellulitis and the follicular occlusion triad of acne conglobata, hidradenitis suppurativa and dissecting cellulitis was high on our list of differential diagnoses. Furthermore, there was considerable involvement of the intertriginous region which is also seen in hidradenitis

Table 1. Table illustrating the common misdiagnoses of Langerhans cell histiocytosis in adults**Pitfalls in diagnosis of Langerhans cell histiocytosis**

Sarcoidosis

Keloids

Nodular Prurigo

Intertrigo

Eczema

Seborrhoeic dermatitis

Hidradenitis suppurativa

Folliculitis

Eruptive xanthoma

Disseminated granuloma annulare

Lymphoma

Folliculitis decalvans

Lichen planopilaris

suppurativa. This misdiagnosis illustrates the need for biopsy early on to avoid missing the diagnosis.

For the treatment of skin-limited LCH, there have been reports of response to topical steroid creams, imiquimod,⁷ nitrogen mustard, intralesional interferon-alpha,⁸ isotretinoin, low dose methotrexate⁹ and narrowband ultraviolet B.¹⁰ PUVA therapy has also been reported to be successful in treating the cutaneous lesions of patients with multisystemic disease as an adjunct to the chemotherapeutic agents for an accelerated recovery of the skin.¹¹

Patients with refractory skin lesions will nearly always need systemic treatment. Among the systemic agents reported to have been used successfully are thalidomide, etoposide, prednisolone, vinblastine and radiotherapy. The use of aggressive therapy such as systemic chemotherapy and radiotherapy in isolated cutaneous LCH remains controversial. The risks of treating a possibly non-malignant and self limited disease with therapies associated with

acute and chronic morbidity needs to be carefully considered.

LCH remains a rare, diverse and somewhat enigmatic collection of clinical syndromes. The prognosis is best when a single system is involved and worst in multisystem disease. The cutaneous manifestations of LCH if recognized and detected early can be invaluable in ensuring early screening and treatment of other organ systems, which when involved can lead to significant morbidity and mortality. Among all the systems involved in LCH, the skin is the most accessible making it the ideal choice for histological confirmation. Hence the need for a high index of suspicion as the cutaneous manifestations of LCH are diverse and perplexing.

References

1. Aricò M, Girschikofsky M, Génereau T, Klersy C, McClain K, Grois N, et al. Langerhans cell histiocytosis in adults. Report from the International Registry of the Histiocyte Society. *Eur J Cancer* 2003;39:2341-8.
2. Mataix J, Betlloch I, Lucas-Costa A, Pérez-Crespo M,

- Moscardó Guilleme C. Nail changes in Langerhans cell histiocytosis: a possible marker of multisystemic disease. *Paediatr Dermatol* 2008;25:247-51.
3. Holme SA, Mills CM. Adult primary cutaneous Langerhans' cell histiocytosis mimicking nodular prurigo. *Clin Exp Dermatol* 2002;27:250-1.
 4. Gönül M, Kiliç A, Cakmak SK, Gül U, Unal T. Pure cutaneous Langerhans cell histiocytosis resembling varicella. *Australas J Dermatol* 2007;48:54-6
 5. Chi HD, Sung KJ, Koh JK. Eruptive xanthoma like cutaneous Langerhans cell histiocytosis in an adult. *J Am Acad Dermatol* 1996;34:688-9.
 6. Hancox JG, James AP, Madden C, Wallace CA, McMichael AJ. Adult onset folliculocentric langerhans cell histiocytosis confined to the scalp. *Am J Dermatopathol* 2004;26:123-6.
 7. Taverna JA, Stefanato CM, Wax FD, Demierre MF. Adult cutaneous Langerhans cell histiocytosis responsive to topical imiquimod. *J Am Acad Dermatol* 2006;54: 911-3.
 8. Chang SE, Koh GJ, Choi JH, Lee KH, Sung KJ, Moon KC, et al. Widespread skin- limited adult Langerhans cell histiocytosis: long-term follow-up with good response to interferon alpha. *Clin Exp Dermatol* 2002; 27:135-7.
 9. Steen AE, Steen KH, Bauer R, Bieber T. Successful treatment of cutaneous Langerhans cell histiocytosis with low dose methotrexate. *Br J Dermatol* 2001;145:137-40.
 10. Imafuku S, Shibata S, Tashiro A, Furue M. Cutaneous Langerhans cell histiocytosis in an elderly man successfully treated with narrowband ultraviolet B. *Br J Dermatol* 2007;157:1277-9.
 11. von Stebut E, Schadmand-Fischer S, Brauninger W, Kreft A, Doberauer C, Steinbrink K. Successful treatment of adult multisystemic Langerhans cell histiocytosis with psoralen-UV-A, prednisolone, mercaptopurine, and vinblastine. *Arch Dermatol* 2008;144:649-53.