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Case Report

Adult-onset Langerhans cell histiocytosis: a case report and literature review

成人朗格漢斯細胞組織細胞增生症的一宗病例報告和文獻回顧

PY Leung 梁沛怡 and SC Ng 吳順展

Langerhans cell histiocytosis (LCH) is a haematolymphoid condition that is predominantly seen in the paediatric population. Occurrence in adult population is relatively rare. The disease has various clinical features and is easy to be misdiagnosed. Histopathology and immunohistochemical staining of skin biopsy are very important for the diagnosis of LCH. Treatment protocols remain controversial. Herein, we present a rare case of adult-onset Langerhans cell histiocytosis which was finally diagnosed after 2 years history of skin rash.

朗格漢斯細胞組織細胞增生症是一種增殖性疾病，通常見於兒童，在成人實屬罕見。其臨床特點多樣化，極易被誤診。組織病理學和免疫組織化學檢查對於朗格漢斯細胞組織細胞增生症的診斷非常重要。治療方案仍有爭議。在此，我們介紹一例成人朗格漢斯細胞組織細胞增生症的罕見病例，該病例在 2 年皮疹病史後最終被診斷出來。

Keywords: Adult-onset, Painful erythematous plaque, Langerhans cell histiocytosis

關鍵詞：成人發病的、 疼痛性紅色斑塊、朗格漢斯細胞組織細胞增生症

Case report

An 81-year-old female patient presented with a 2-year history of recurrent painful erythematous papules and plaques predominantly on her abdomen, which progressed to involve her axillae, back and face.

She had history of diabetes, hypertension, gallbladder tubular adenoma with open cholecystectomy done in 2006. She also had anaemia but refused further workup. She initially presented to Surgery Clinic in 2019 with painful erythematous papules and plaques on her abdomen. Multiple wound swabs had been taken from abdomen and lower chest wall lesions, which showed yielded methicillin-resistant *Staphylococcus aureus* on culture.

Social Hygiene Service, Department of Health, Hong Kong
PY Leung, MbChB(CUHK), MRCP(UK)
SC Ng, FHKCP(Dermatology & Venereology), FHKAM(Med)

Correspondence to: Dr. PY Leung

Cheung Sha Wan Dermatological Clinic, 3/F, West Kowloon Health Centre, Cheung Sha Wan Government Offices, 303 Cheung Sha Wan Road, Sham Shui Po, Kowloon

There was no clinical improvement despite repeated hospitalisations administrating multiple courses of antibiotics including intravenous vancomycin. She was then referred to dermatology clinic in the summer of 2021.

On examination, extensively macerated, beefy red and erosive plaques and papules were found on her abdomen, chest (Figure 1a), bilateral axillae (Figure 1b), and back (Figure 1c). Multiple erythematous papules without erosion were found on nose and cheeks.

Punch biopsies were done on the skin lesions over the lower chest wall and back. Histopathology showed sheets of Langerhans cells beneath the epidermis. Abundant eosinophils and sheets of lymphocytes and histiocytes were seen. The Langerhans cells were strongly and diffusely positive for CD1a and S-100. The final diagnosis was Langerhans cell histiocytosis (LCH).

She was then referred to haematology clinic of Princess Margret Hospital for further workup and investigation. Positron Emission Tomography-Computed Tomography (PET-CT) was done, in which no lymphadenopathy or solid organ tumour was found. She and her relatives refused bone marrow biopsy. Whether there was systemic involvement by LCH remained uncertain. She was treated with prednisolone 10 mg daily and topical 0.05% clobetasol propionate ointment for truncal lesions. After few months of treatment, her axillary and abdominal lesions were much improved (Figure 3).

Discussion

The true incidence of LCH is not known because most published studies are not population based. A survey from Germany reported that 66% of the patients with adult-onset LCH were women, with an average age at diagnosis of 43.5 years for all patients.[1]

When evaluating a patient with adult-onset LCH, it is important to consider other conditions which may mimic LCH at clinical or histological levels. These include other types of non-Langerhans cells histiocytosis, such as Erdheim-Chester disease, and Rosai-Dorfman disease, as well as inflammatory dermatoses such as pityriasis lichenoides et varioliformis acuta (PLEVA), pemphigus foliaceus, inverse psoriasis and intertrigo. The diagnosis of LCH is confirmed by histopathological examination, whereby the

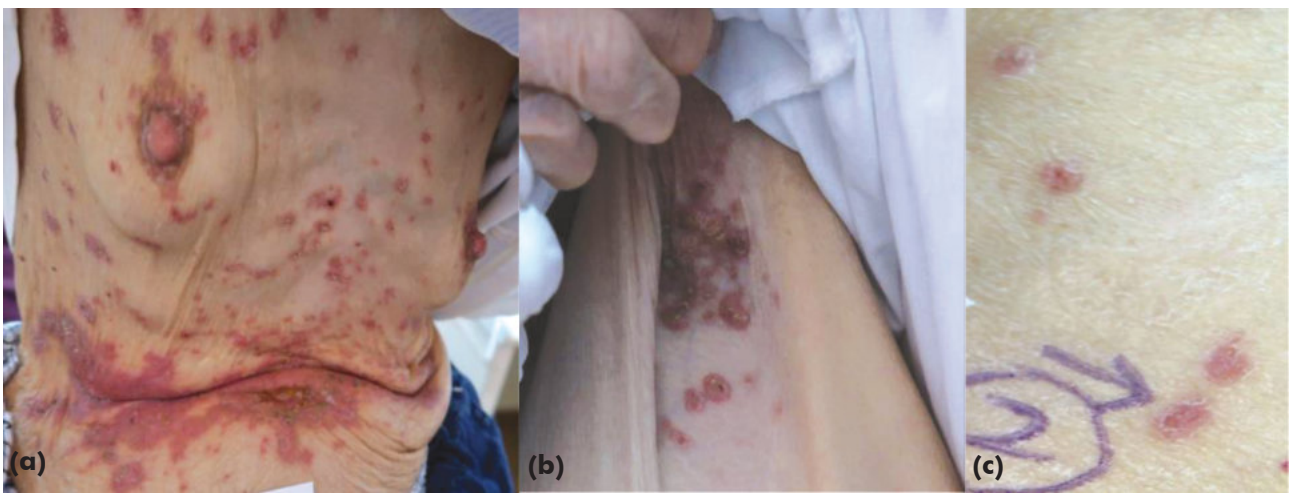

Figure 1. (a) Painful extensive beefy red plaques and papules with erosions on chest and abdomen. (b) Painful erythematous papules on axilla. (c) Discrete painful eroded erythematous papules on back.

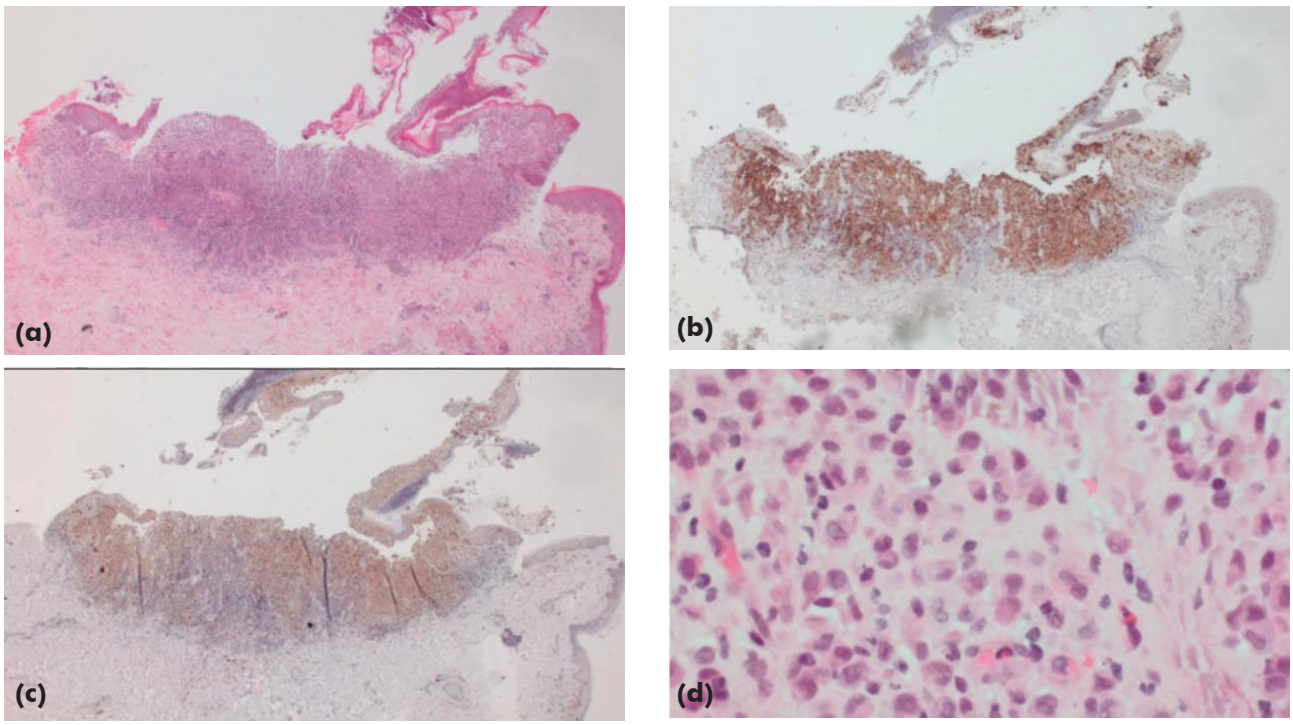

Figure 2 (a) Sheets of Langerhans cell infiltration in the superficial dermis (H&E stain, x25). (b) Langerhans cells with CD1a cytoplasmic and membranous positivity (immunohistochemistry with CD1a, x25). (c) Langerhans cells with S100 nuclear positivity (immunohistochemistry with S100, x25). (d) Langerhans cell with abundant eosinophilic cytoplasm, coffee bean-shaped / lobulated / grooved nuclei. Admixed eosinophils and small lymphocytes are present (H&E, x400).

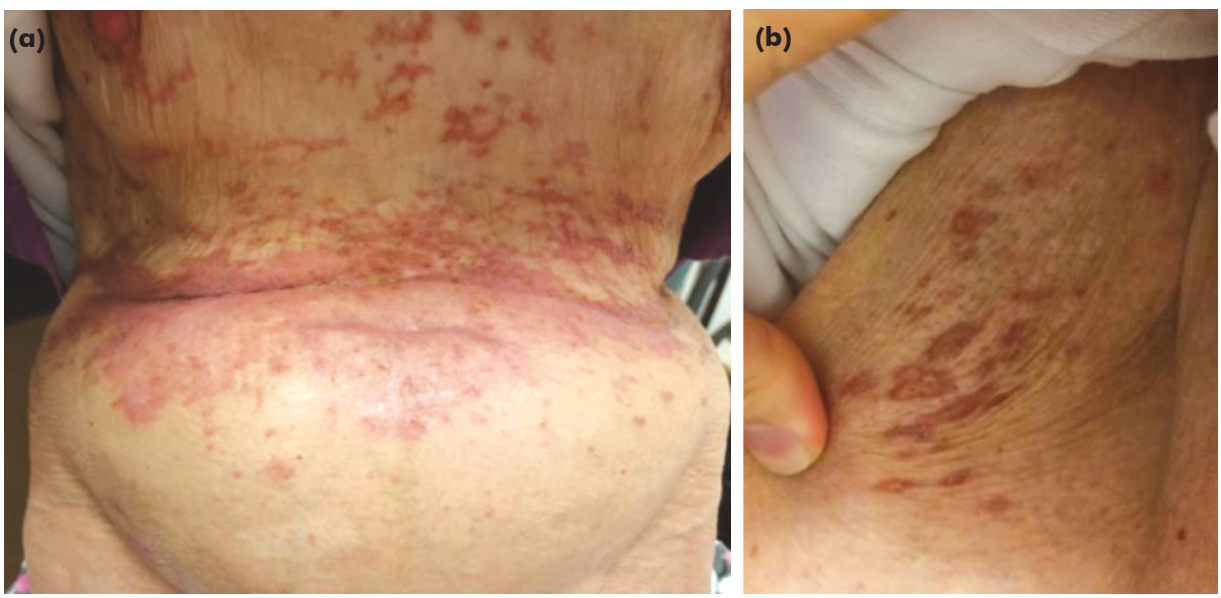

Figure 3. (a) Erythematous plaques, papules, and erosions on abdomen and (b) axillae have been improved after few months of treatment with oral prednisolone and 0.05% clobetasol propionate ointment.

presence of CD1a- and S100-positive neoplastic histiocytes are demonstrated.

LCH may be limited to single organ, for example, skin.[2] It may also involve multiple organ and/or systems. Cutaneous eruptions may appear as small reddish to violaceous solid papules, indurated plaques, with overlying scaling, ulceration or pustule. Bones, bone marrow, lungs, endocrine system, female genital or reproductive tracts, liver, spleen, lymph nodes, gastrointestinal system, or central nervous system may be involved in systemic disease. In LCH, involvement of the calvaria, skull base, maxillofacial bones, and hypothalamic–pituitary axis is common.[3] Diabetes insipidus arises from depletion of vasopressin due to an involvement of pituitary gland or hypothalamus. Other neurological complications are mainly a result of direct tumour cell infiltration causing inflammation and resultant cellular damage, or mass effect from tissue oedema. These may lead to a wide range of neurological symptoms, including but not limited to headaches, seizures, motor or sensory deficits, and cognitive changes.

The workup for adult-onset LCH involves a comprehensive evaluation. This is to assess for the extent of organ involvement and identify if there are any associated malignancies. These may include imaging studies such as X-rays, CT scans, Magnetic Resonance Imaging, and PET-CT scans, as well as bone marrow biopsy, hormone testing, and other laboratory investigations according to clinical symptoms and signs. A multidisciplinary approach involving dermatologists, haematologists/oncologists, endocrinologists, radiologists, and pathologists is crucial in the management.

Several factors have been identified as potential prognostic indicators in LCH. These include age, presence of lymph node involvement,[4] sites of involved organs,[5] and the presence of certain mutations, such as BRAF V600E mutation.[6] Skin-limited LCH seldom requires therapeutic intervention, as it has a lower risk of progression when compared to multisystem LCH with cutaneous presentations.[7]

A study in 2018 showed that LCH in adults is associated with a high prevalence of haematologic and solid organ malignancies.[8] This study was conducted from 1990 to 2015, which identified 132 consecutive adult patients with histologically confirmed LCH. Forty-two (32%) of these patients had at least one malignancy, including 39 solid tumours (74%), 9 lymphomas (17%) and 5 haematologic malignancies (9%). Based on their findings, the authors advocated a search for underlying malignancy in adult-onset LCH.

Options of first line therapy include prednisone, vinblastine, cytarabine or cladribine.[9] Early results of targeted therapy are encouraging but many questions remain, particularly the optimal duration of therapy and the relapse rate after discontinuation of therapy. A BRAF inhibitor in combination with a MEK inhibitor have been shown to be effective in patients with melanoma who have BRAF mutations, and this combination may be effective in patients with LCH.[10] A number of clinical trials of BRAF and other RAS pathway inhibitors in adults and children with LCH are ongoing.

Conclusion

We reported a case of elderly woman with biopsy-proven Langerhans cell histiocytosis, which demonstrated a satisfactory therapeutic response to combined topical and systemic corticosteroid. Systemic involvements and secondary malignancy may take place in patients with adult onset LCH, so it is important to arrange relevant work up for these patients. Individualised treatment strategies for skin-limited or multi-organ disease with a multidisciplinary approach are crucial in the management of adult-onset LCH. Targeted therapies have emerged as potential treatment options, while ongoing research is expected to

provide further insights into their efficacy and safety profile.

References

1. Götz G, Fichter J. Langerhans'-cell histiocytosis in 58 adults. Eur J Med Res 2004;9:510-4.
2. Gurung I, Gao Y, Han K, Peng XB. Adult Onset Langerhans Cell Histiocytosis Limited to the Skin. Indian J Dermatol 2019;64:414-6.
3. D'Ambrosio N, Soohoo S, Warshall C, Johnson A, Karimi S. Craniofacial and intracranial manifestations of langerhans cell histiocytosis: report of findings in 100 patients. Am J Roentgenol 2008;191:589-97.
4. Sato A, Kobayashi M, Yusa N, Ogawa M, Shimizu E, Kawamata T, et al. Clinical and prognostic features of Langerhans cell histiocytosis in adults. Cancer Sci 2023;114:3687-97.
5. Cao XX, Duan MH, Zhao AL, Cai H, Chen J, Gao XM, et al. Treatment outcomes and prognostic factors of patients with adult Langerhans cell histiocytosis. Am J Hematol 2022;97:203-8.
6. Bhatia P, Singh M, Sharma M, Sharma A, Kakkar N, Radhika S, et al. BRAF V600E mutation in childhood Langerhans cell histiocytosis correlates with multisystem disease and poor survival. Blood Cells Mol Dis 2020;82:102356.
7. Simko SJ, Garmezy B, Abhyankar H, Lupo PJ, Chakraborty R, Lim KP, et al. Differentiating skin-limited and multisystem Langerhans cell Histiocytosis. J Pediatr 2014;165:990-6.
8. Ma J, Laird JH, Chau KW, Chelius MR, Lok BH, Yahalom J. Langerhans cell histiocytosis in adults is associated with a high prevalence of hematologic and solid malignancies. Cancer Med 2019;8:58-66.
9. Goyal G, Abeykoon JP, Hu M, Young JR, Shah MV, Bennani NN, et al. Histiocytosis Working Group Single-agent cladribine as an effective front-line therapy for adults with Langerhans cell histiocytosis. Am J Hematol 2021; 96:146-50.
10. Haroche J, Cohen-Aubart F, Emile JF, Arnaud L, Maksud P, Charlotte F, et al. Dramatic efficacy of vemurafenib in both multisystemic and refractory Erdheim-Chester disease and Langerhans cell histiocytosis harboring the BRAF V600E mutation. Blood 2013;121:1495-500.