

## Case Report

# Adult cutaneous Langerhans' cell histiocytosis: a rare presentation, successful treatment with thalidomide

P.L. Chandravathi\*, Praneet Awake\*, Anil Fonseca\*\*

\* Department of Dermatology, Venereology and Leprosy, Care Institute of Medical Sciences, Hyderabad, Telangana, India

\*\* Department of Pathology, Care Institute of Medical Sciences, Hyderabad, Telangana, India

### Abstract

Langerhans' cell histiocytosis (LCH) is a rare clonal disorder of proliferating histiocytic cells expressing phenotypic markers of the epidermal Langerhans' cells. LCH generally affects children. Adult LCH with single system disease limited to skin is uncommon and difficult to diagnose. The management of LCH is difficult as these disorders respond inconsistently to immunosuppressive and chemotherapeutic strategies. We report a case of 48 year female, diabetic and hypertensive presented as single system LCH limited to skin with history of recurrent painful erythematous ulcerated lesions in right axilla and both groins since 4 years with and limiting mobility of limbs. She was successfully treated with thalidomide. Thalidomide monotherapy represents an effective, safe and well-tolerated treatment option that should be considered as first-line therapy for single system LCH limited to skin which is rare and difficult to treat.

### Key words

Langerhans' cell histiocytosis, cutaneous, adult, thalidomide.

### Introduction

Langerhans cell histiocytosis (LCH) is an orphan disease of clonal dendritic cells which may involve any organ in the body. LCH being more common in children, the dermatologist may often miss the diagnosis in adults. Its estimated incidence is 1 in 2,00,000 and is rarely seen in adults.<sup>1</sup> Men are more affected than women and it tends to be more aggressive in women.<sup>2</sup> The management of LCH is difficult as the disease responds inconsistently to immunosuppressive and chemotherapeutic drugs.

Thalidomide (N-phthalimido-glutarimide) initially used as tranquilizer, has recently been used for several inflammatory skin diseases.<sup>3</sup> We would like to share our experience

of a pure cutaneous adult LCH case responding to thalidomide.

### Case Report

A 48-year-old female patient presented with recurrent painful erythematous ulcerated lesions in right axilla and both groins since 4 years. Cutaneous examination revealed erythematous ulcer draining purulent secretion alongwith fibrosis and adhesions in her right axilla, and severe ulcers in both groins areas disabling the mobility of limbs (**Figure 1**). The patient had medical history of diabetes and hypertension. She was treated previously with several medications including oral steroids but without any significant improvements. A biopsy was done and sent to the histopathology department.

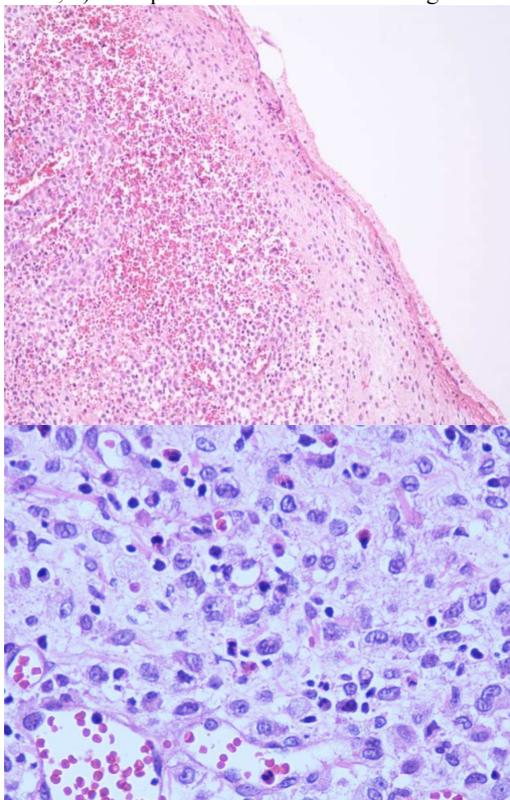
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### Address for correspondence

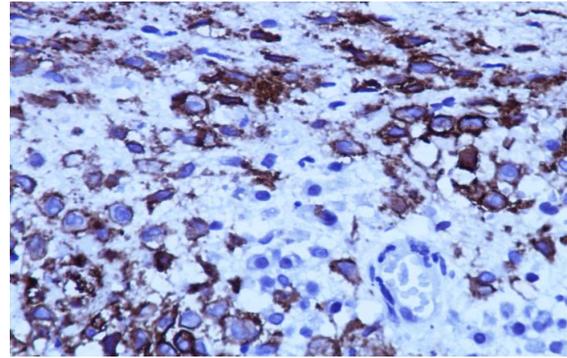
Dr. P. L. Chandravathi,  
Department of Dermatology,  
Care Hospital,  
Road No.10, Banjara Hills,  
Hyderabad - 500 034, Telangana, India  
Email: plchandra@gmail.com



**Figure 1** a) Erythematous ulcers with adhesions in right axilla; b) Multiple severe ulcers in both the groins.



**Figure 2** a) Nodular infiltrate in dermis with ulcerated overlying epidermis (H and E, X10); (b) ovoid cells with moderate amounts of eosinophilic cytoplasm and an indented reniform nucleus with an admixed cellular inflammatory infiltrate of neutrophils, eosinophils and mast cells (H and E, X40).



**Figure 3** Photomicrograph showing immunohistochemical staining positive for CD1a (Immunostain CD1a X100).



**Figure 4** Follow-up post 6 months of thalidomide showing healed lesions.

Histopathological examination revealed a nodular infiltrate in dermis, the epidermis over which was ulcerated. The dermal infiltrate was composed of ovoid cells with moderate amounts of eosinophilic cytoplasm and an indented reniform nucleus with an admixed inflammatory infiltrate of neutrophils, eosinophils and mast cells is noted (**Figure 2**).

**Table 1** Diagnostic work-up of adult LCH.

<i>Diagnostic work-up</i>	<i>Investigations</i>
Baseline evaluation	Routine laboratory tests (CBC, ESR, C-reactive protein, liver and renal function tests, electrolytes), chest X-ray, abdominal ultrasound
Additional diagnostic procedures	
Skin involvement	Skin biopsy, CD 1a immunostain
Bone marrow involvement	Bone marrow biopsy
Pulmonary involvement	High-resolution CT scan, pulmonary function tests, DLCO
Bone involvement	Skeletal X-ray, bone scan, CT scan and MRI imaging
Pituitary involvement	Hormone analysis, cranial CT and MRI brain
Gastrointestinal involvement	Endoscopy
Visceral organ involvement	CT scan

On immunohistochemical study, the tumoral cells showed strong cytoplasmic positivity for CD1a and S100 and negative for CD68, confirming the diagnosis of LCH (**Figure 3**).

She underwent evaluation for detection of any other systemic involvement (**Table 1**). The laboratory reports such as CBC, peripheral blood smear, kidney and liver function tests, serum electrolytes, ANA serology, and tuberculin test were all within normal limits. Bone marrow biopsy report showed no evidence of infiltration. Imaging studies including skull and bone X-ray and CT scan of brain, chest, abdomen, and pelvis were performed to rule out any bone, lymph node, pituitary, or visceral involvement. USG abdomen was normal. Urine osmolality was normal. Thus confirming a diagnosis of adult onset LCH with single system disease localized to skin.

After literature review on management, the patient being diabetic and hypertensive, we started her on thalidomide at a dose of 100 mg in two divided doses. Two months after starting thalidomide, partial improvement was noted. Complete resolution of cutaneous lesions was noted after 6 months of treatment. [Figure 4] When thalidomide was stopped by the patient there was recurrence of the disease. We reinitiated thalidomide in 100 mg dose and her lesions subsided and later on she was kept on maintenance treatment with 50 mg daily with good tolerance.

## Discussion

LCH usually is a multisystem disease mostly seen in children. Patients with focal lesions are usually older than those with multisystem involvement.<sup>4</sup> The association of LCH with malignant conditions has been seen in greater frequency in adult onset LCH like leukemia, myelodysplastic syndrome, Hodgkin's disease, solid tumors.<sup>5</sup> The present LCH case was an unusual single system skin involvement at presentation in a 48-year-old female without any systemic involvement.

The ideal therapy for LCH has not yet been established and varies between cytotoxic or immunomodulatory drugs.<sup>5</sup> Majority of available treatment options are based on small case reports. More recently some studies have shown a good response to thalidomide.<sup>6,7</sup> The drug has anti-inflammatory, anti-neoplastic and immunomodulatory effects and acts through inhibition of TNF- $\alpha$  and IL-6 which have enhanced expression in LCH.<sup>6</sup> The remission of the disease usually starts after 2-3 months of treatment of thalidomide.<sup>7</sup> Recurrence is common once the drug is stopped. Thalidomide seems to be effective in cutaneous type of LCH but is less effective in extracutaneous type.<sup>6</sup> The main side effects are teratogenicity and peripheral neuropathy.<sup>6,7</sup> In our case who was suffering from diabetes and hypertension where steroids could not be used and also less effective, thalidomide was a good option. The advantages of thalidomide are the quick effect, ease of oral use for long term.<sup>7</sup>

Pure cutaneous LCH in an adult is rare and treatment options are few especially if the patient suffering from other medical diseases like DM and HTN. This case is reported for its rarity and dramatic response to thalidomide. Therefore, early diagnosis with prompt treatment is extremely important in avoiding scarring defects and definitive sequelae.

## References

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