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LANGERHANS CELL HISTIOCYTOSIS SUCCESSFULLY TREATED WITH COMBINATION OF THALIDOMIDE AND CORTICOSTEROID

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ABSTRACT

Langerhans cell histiocytosis (LCH) is rare disease characterised by clonal proliferation of Langerhans cells. The effectiveness of the current standard of treatment for LCH has not been proved in prospective trials, and 50% of patients treated with the current standard of treatment were unresponsive. Here we describe a case of a patient with LCH that was unresponsive after treatment with vinblastine and prednisolone but showed improvement after treatment with thalidomide and methylprednisolone.

A 51-year-old woman was admitted to the haematology and medical oncology outpatient clinic due to an ulcerative skin lesion on the left auricular, axilla, inguinal and perineum regions. She was diagnosed with multi-organ LCH and was previously treated with vinblastine and prednisolone, but with a non-complete response. Her PET/ CT F-18 FDG body scan compared with previous one showed no resolution in abdominal nodes. There was interval progression in hypermetabolic skin thickening in the left external auditory canal, bilateral axilla and perineum, and mild interval increase in metabolic activity within the L4 vertebral lesion. She was given ultraviolet light phototherapy and continued with a chemotherapy regimen consisting of etoposide and methylprednisolone. After that she was treated with thalidomide 1 × 100 mg and methylprednisolone, which improved her skin condition.

KEYWORDS

Langerhans cell histiocytosis, thalidomide

LEARNING POINTS

- There is no gold standard of treatment for Langerhans cell histiocytosis (LCH) in adults.
- Around 50% of patients with LCH were unresponsive to the standard therapy and no standard regimen was recommended for patients with refractory LCH.
- A combination of thalidomide and corticosteroid may be a therapeutic option in patients with LCH.

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INTRODUCTION

Langerhans cell histiocytosis (LCH) is rare disease characterised by clonal proliferation of Langerhans cells[1,2]. It commonly affects children, rather than adults[3]. The cause is unknown, and it is regarded as a neoplasm, reactive disorder or aberrant immune response[2].

Available data regarding treatment of LCH in adults is not optimal[4]. Accepted first-line therapy for LCH according to LCH-III protocol is combination of vinblastine and prednisolone in a patient requiring systemic therapy. However, 50% of patients were unresponsive to the standard therapy[1]. Currently there is no standard regimen for patient with refractory LCH[5]. Some reports suggest the effectiveness of thalidomide in treating LCH[6,7].

Here we describe a case of a patient with LCH, which was unresponsive after treatment with vinblastine and prednisolone but showed improvement after treatment with thalidomide and methylprednisolone.

CASE DESCRIPTION

A 51-year-old woman was admitted to the haematology and medical oncology outpatient clinic due to ulcerative skin lesions on the left auricular, axilla, inguinal and perineum regions. She was diagnosed with multi-organ LCH and was previously treated with vinblastine and prednisolone, but with a non-incomplete response. Complete blood count, fasting glucose, urea and creatinine were within normal limits. Serum alanine transaminase (ALT) was normal, serum aspartate transaminase (AST) was slightly raised (AST level: 54 U/l; reference value: 12–42 U/l), and serum alkaline phosphatase (ALP) was elevated (ALP level: 128 U/l; reference value: 39–99 U/l). Her PET/CT F-18 FDG body scan compared with the previous one showed interval resolution of right axillary adenopathy, metabolic resolution in the aortocaval and right paratracheal nodes and no resolution in abdominal nodes. There was interval progression in hypermetabolic skin thickening in the left external auditory canal, bilateral axilla and perineum, and mild interval increase in metabolic activity within the L4 vertebral lesion.

The patient was given ultraviolet light phototherapy and continued with a chemotherapy regimen consisting of etoposide and methylprednisolone, with no significant improvement in clinical appearance. After that she was treated with thalidomide 1 × 100 mg and methylprednisolone, which improved her skin condition.



Figure 1. Comparison of skin lesion in auricular area before (left) and after (right) thalidomide treatment.



Figure 2. Comparison of skin lesion in axillary area before (left) and after (right) thalidomide treatment.



Figure 3. Comparison of skin lesion in inguinal and perineal area before (left) and after (right) thalidomide treatment.

DISCUSSION

LCH is a condition with various clinical manifestations, which are characterised by clonal proliferation of Langerhans cells. It may be present as a mild, self-limiting disease or life-threatening involving multi-organ and disseminated conditions[3]. It can affect multiple organs such as bones, skin, pituitary gland, lymph nodes, liver, spleen, gut, lung, central nervous system and the haematopoietic system[4].

The current standard of choice for the treatment of LCH is chemotherapy with vinblastine and prednisolone[3]. However, although this regimen is a standard for paediatric LCH patients, its effectiveness in adult patients has not been proved in prospective studies[4]. The patient outcome with this regimen generally is poor. Several ongoing trials are still being conducted to determine the optimal first-line therapy[3].

The treatment for patients who are refractory to initial treatment is more difficult. There is also no recommended standard regimen for a patient with refractory LCH.

Combinations of vinca alkaloids, alkylating agents, anthracyclines and platinum drugs have been tried, but have shown no favourable response in improving survival[5]. Etoposide may also be used to treat symptomatic LCH. Monotherapy with etoposide is favoured by some experts considering minimal risk of neurotoxicity and no steroid-related adverse events[4].

In this case, the patient was previously treated with vinblastine and prednisolone but showed no complete response; phototherapy was used to treat the cutaneous lesion. Some case reports showed psoralen plus ultraviolet A and narrow-band ultraviolet (UV) B phototherapy are effective in treatment of cutaneous LCH[4]. UV-A radiation may penetrate the dermis and induce apoptosis of Langerhans cells and regulate the production of cytokines. Meanwhile, mechanism of UV-B in LCH is still unknown. It was hypothesised that UV-B may increase secretion of anti-inflammatory cytokines[8].

Some case series and early trials showed the benefit of thalidomide in treatment of LCH[3], although the mechanism of the action of thalidomide in LCH is uncertain. Thalidomide produces anti-neoplastic and anti-inflammatory activity by inhibiting the production of tumour necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which is expressed extensively in LCH lesions[6]. Thalidomide acts by inhibiting the transcription and secretion of TNF-α and increase the degradation of TNF-α mRNA[9]. It is possible that thalidomide acts by inhibiting over-expression of cytokines in LCH[6].

A combination of thalidomide and corticosteroid may be a therapeutic option in patients with LCH. Further research regarding effectiveness of thalidomide and corticosteroid regimen in LCH is required.

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