Photodynamic therapy for multi-resistant cutaneous Langerhans cell histiocytosis

Valérie Failla, Odile Wauters, Marie Caucanas, Nazli Nikkels-Tassoudji, Arjen F. Nikkels

Department of Dermatology, University Hospital of Liège, Liège, Belgium

Abstract

Langerhans cell histiocytosis is a rare group of proliferative disorders. Beside cutaneous involvement, other internal organs can be affected. The treatment of cutaneous lesions is difficult and relies on topical corticosteroids, carmustine, nitrogen mustard, and photopheresis. Systemic steroids and vinblastine are used for recalcitrant skin lesions. However, some cases fail to respond. An 18-month-old boy presented a CD1a+, S100a+ Langerhans cell histiocytosis with cutaneous and severe scalp involvement. Topical corticosteroids and nitrogen mustard failed to improve the skin lesions. Systemic corticosteroids and vinblastine improved the truncal involvement but had no effect on the scalp lesions. Methylaminolevulinate (MAL)-based photodynamic therapy (PDT) resulted in a significant regression of the scalp lesions. Control histology revealed an almost complete clearance of the tumor infiltrate. Clinical follow-up after six months showed no recurrence.

Although spontaneous regression of cutaneous Langerhans cell histiocytosis is observed, the rapid effect of photodynamic therapy after several failures of other treatments suggests that photodynamic therapy was successful. As far as we know this is the first report of photodynamic therapy for refractory skin lesions. Larger series are needed to determine whether photodynamic therapy deserves a place in the treatment of multi-resistant cutaneous Langerhans cell histiocytosis.

Introduction

Langerhans cell histiocytosis (LCH) is a rare group of proliferative disorders. The prevalence is estimated between 1 and 2 per 1,000,000. The male-female ratio is 2:1. Usually LCH affects young children, particularly between the ages of one and three years. LCH affects the skin in 40% of the cases, but almost any other internal organ may be involved. The clinical expression and the prognosis principally depend on the clinical type and the number of organs affected. First-line treatment for the cutaneous lesions relies on topical corticosteroids. Topical chemotherapy (nitrogen mustard, carmustine) or PUVA-therapy are interesting second-line options. Systemic chemotherapy is reserved for severe and refractory cutaneous involvement.

Notwithstanding, some cases fail to respond and require alternative therapy. Photodynamic therapy (PDT) is an FDA-recognized treatment option for superficial basal cell carcinoma, Bowen’s disease and actinic keratosis. The preferential accumulation of the photosensitizing agents in hypermetabolic cells (i.e. precancerous and cancerous cells) explains the selectivity of PDT. The spectrum of other cutaneous oncological conditions effectively treated by PDT is continuously increasing. The presence of an oligoclonal proliferation of LCHs in LCH was the rationale for PDT treatment. This paper reports the first successful PDT treatment of multi-resistant scalp Langerhans cell histiocytosis in a young boy.

Case Report

An 18-month-old boy visited the dermatology department for erythematous and squamous lesions of the trunk and the scalp. The lesions appeared at the age of eight months and progressively spread over the trunk and scalp. A pediatrician proposed a diagnosis of atopic dermatitis. The child was otherwise healthy, did not take any medication and presented a normal development. There were no signs of growth retardation. There was no particular family medical history.

Skin examination revealed infiltrated, sometimes purpuric, papular and slightly squamous, ill-defined lesions on the trunk. These lesions were neither pruritic nor painful. Severe inflammatory and crusting lesions were evidenced on the scalp and behind the ears (Figure 1). These lesions were painful and itchy, and the child used to scratch them. Further clinical examination was unremarkable. No adenopathies were evidenced. A cutaneous biopsy was performed under local anesthesia. Histology suggested LCH. Immunohistochemical staining revealed a CD1a+, S100a+ infiltrate with a proliferative Ki67 fraction of 15%, confirming the diagnosis of LCH. Electron microscopy to ascertain the presence of Birbeck granules was not performed. An extensive internal workup, including ultrasound, blood sampling, chest radiography and chest CT scan, was normal. The final diagnosis was a cutaneous LCH (multifocal single organ disease), according to the current classification of histiocytic disorders. The clinical score for disease activity was 2 (clinical findings: 2, laboratory evaluation: 0, radiological studies: 0).

No regression of the skin lesions was observed following topical applications of very potent corticosteroids (clobetasol propionate 0.05% cream, Dermovate®, GSK), but the itching sensations were partially relieved. Subsequent treatment with topical nitrogen mustard (10 mg/50 mL H2O, 3 times/week, for three weeks (Mustargen©)) also failed to improve the skin lesions. PUVA therapy was not performed, as efficacy on the hairy scalp is limited. Systemic corticosteroids (40 mg/m²/day) also failed. Finally, following systemic vinblastine (Velbe©), a partial regression of the truncal lesions was observed but the aspect of the scalp lesions did not improve. During the second chemotherapy course, fever and neutropenia with a bilateral interstitial pneumopathy suddenly appeared, necessitating interruption of treatment. The pulmonary lesions resolved and four months later, a subsequent treatment combining vinblastine and corticosteroids (once every two weeks for six months) was started. The truncal lesions progressively disappeared but the scalp and ear lesions resisted. A new skin biopsy of the scalp was performed, revealing S-100a+ and CD1a+ Langerhans cell histiocytosis. The Ki67 growth fraction was 5%. Finally, a methylaminolevulinate (MAL)-based photodynamic therapy was

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aspects and quality of life. As the prognosis of disease typically presents as a reticulo-micronodular syndrome with dyspnea, a dry cough involving the scalp. Cranial, mandibular, vertebral, and the pelvic bones are the most frequently affected. Lung disease usually affects one single bone and the young age of the child, prompted us to perform PDT under total anesthesia. As no previous experience is available on PDT in LCH, a standard treatment procedure was chosen. It is clear that specific PDT protocols for LCH should be developed according to future clinical experience. The child did not experience any post-procedure pain and did not ask for pain reducing medication. The time course of the crusting was similar to superficial basal cell carcinoma treatments.

In summary, as far as we know, this case presents the first successful PDT treatment of multiresistant cutaneous LHC. More experience should be gathered to determine the appropriate role of PDT in the management of cutaneous LHC.
References