CASE REPORT

Childhood hypopigmented mycosis fungoides: a commonly delayed diagnosis

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SUMMARY

Primary cutaneous lymphomas (PCLs) are exceedingly rare in children and adolescents, with mycosis fungoides (MF) being the most frequent PCL diagnosed in childhood. There are numerous unusual clinical variants of MF, including the hypopigmented type form (HMF). HMF is exceptional overall, but comparatively common among children. We present an 8-year-old boy with a 3-year history of progressive, generalised, scaly, hypopigmented round patches and few erythematous papules. He was first diagnosed with pityriasis alba (PA), and moisturisers were prescribed with no improvement. Skin biopsy showed typical features of MF, and the patient was successfully treated with narrowband ultraviolet B. HMF may simulate atopic dermatitis, PA, pityriasis lichenoides, tinea versicolour, vitiligo, postinflammatory hypopigmentation or leprosy. Therefore, persistent and unusual hypopigmented lesions should be biopsied to rule out this rare variant of MF.

BACKGROUND

Mycosis fungoides (MF) is the most common primary cutaneous lymphoma in children. Hypopigmented mycosis fungoides (HMF) is an extremely rare variant. HMF is usually observed in dark-skinned individuals, comparatively common among children, and often shows a T-suppressor CD8+phenotype.[1–3] The diagnosis of MF in childhood is commonly delayed, since it can show clinical as well as histological resemblances to benign inflammatory disorders. Few studies have reviewed MF in childhood, however, the hypopigmented variant is probably associated with better prognosis than classic MF.[1 4 5] In the presented case, diagnosis was made 3 years after the onset of the dermatosis. This case illustrates the importance of clinical suspicion for MF in patients with hypopigmented lesions, particularly in children.

CASE PRESENTATION

We present an 8-year-old Caucasian boy with a 3-year history of progressive, generalised, scaly hypopigmented round patches, 2–5 cm in diameter, associated with few erythematous papules, with normal overlying skin (figures 1 and 2). The boy was otherwise healthy, with no signs of atopy (namely xerosis, periorbital darkening or Dennie-Morgan infraorbital fold), and had no family history of atopy, other inflammatory dermatosis or significant environmental exposure. He was skin phototype III. He was initially diagnosed with pityriasis alba and, during the 3 symptomatic years, prescribed moisturisers. However, during this period he showed no improvement and new hypopigmented lesions appeared continuously.

INVESTIGATIONS

A punch biopsy from a hypopigmented patch showed typical features of MF (lymphocytic infiltration in the upper and mid-dermis with mild atypia and epidermotropism of single and clustered lymphocytes; figure 3). Most lymphoid skin cells were CD8+/CD3+(49%), the γδ-T-cell subpopulation was increased (18%) and T-cell receptor rearrangement analysis did not show clonal T-cell population. The patient had no lymphadenopathy or organomegaly; renal, hepatic function and complete blood count with differential were within normal limits; chest X-ray and abdominal ultrasound were likewise normal. The patient was diagnosed with HMF, stage Ib (T2N0M0B0).

DIFFERENTIAL DIAGNOSIS

Pityriasis alba (PA), a very common disease, was considered the most likely diagnosis during the first clinical observations, when the patient presented fewer hypopigmented lesions. However, generalised lesions and poor response to moisturisers, in a patient with no history of atopy, do not support the PA diagnosis. Additionally, in PA, the hypopigmented lesions are generally confined to the face, neck and upper arms.[6]

Other diagnoses considered were vitiligo and pityriasis lichenoides (PL). Vitiligo is characterised by totally amelanotic lesions, with typical convex borders. This patient did not show truly depigmentated lesions, and the lesions spared the face and genitals, which is not a suggestive distribution for vitiligo.

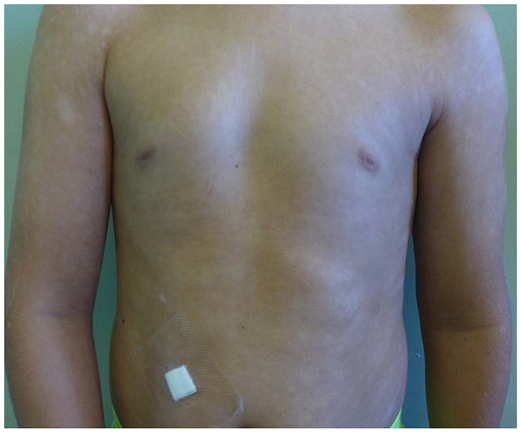

Figure 1 Patient presentation: generalised hypopigmented round patches 2–5 cm in diameter, slightly scaly.

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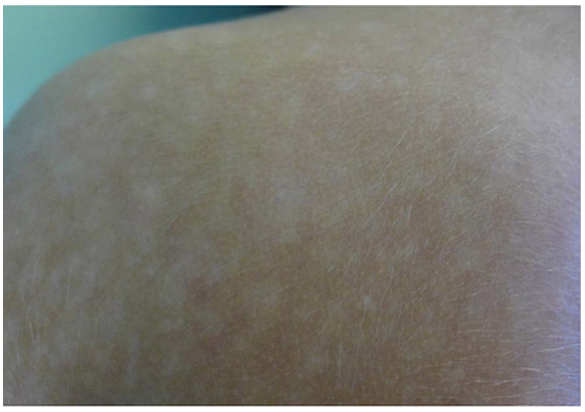

Figure 2 Patient presentation: generalised hypopigmented round patches 2–5 cm in diameter, slightly scaly, with no infiltration.

Pitiryasis lichenoides et varioliformis acuta (PLEVA) and pytiriasis lichenoides chronica (PLC) represent two ends of a disease spectrum that mostly affect young patients. PLEVA generally presents as recurrent crops of ulcerative papulonodules, lasting for weeks and PLC is characterised by recurrent crops of red-brown scaly papules that can persist for months; all forms of PL can result in postinflammatory hypopigmentation or hyperpigmentation. Histologically, the typical features of PL are parakeratosis, lymphocytic infiltrate, exocytosis, spongiosis and red blood cell extravasation. In the presented case, the patient had a continuous progressive course, the progression of erythematous papules to hypopigmented lesions was not observed and there were none of the histological features usually associated with PL or with posthypopigmented inflammation.[3 7] Although not a common feature of MF, erythematous papules were already described particularly in HMF.[8]

TREATMENT

The patient was treated with narrowband ultraviolet B (UVB) phototherapy sessions, 3 times weekly, achieving complete clinical response, after a cumulative dose of 41.7 J/cm^2 in 30 sessions (figure 4).

OUTCOME AND FOLLOW-UP

The patient experienced no recurrence of the disease 10 months after discontinuation of phototherapy.

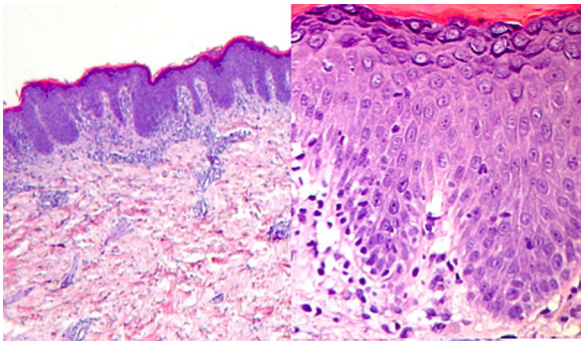

Figure 3 Dermatopathology: parakeratosis and acanthosis, lymphocytic infiltrate in the superficial dermis, lymphocytes presenting moderate atypia and epidermotropism, occasionally resembling Pautrier's microabscesses.

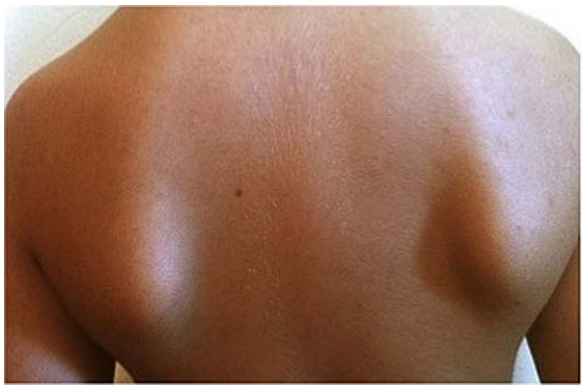

Figure 4 Complete clinical response after 30 sessions of narrowband ultraviolet B phototherapy. The cumulative dose was 41.7 J/cm^2.

DISCUSSION

MF is the most common primary cutaneous lymphoma (PCL). It is mainly a disease of the elderly, generally in the fifth and sixth decades of life, and exhibits a slight male predominance.[9] MF is classified as an indolent lymphoma according to WHO-EORTC PCL classification.[10] The cutaneous expression of MF consists of four basic patterns: an early patch stage with eczematous features; a plaque stage; a tumour stage; and an erythrodermic stage. Progression to tumoural lesions generally occurs several years after onset of the disease.[9]

Zackheim and McCalmont[11] referred to MF as 'the great imitator'—a description previously reserved for syphilis. Diagnosis is frequently difficult, since numerous clinical variants of MF are described, including granulomatous, pustular, bullous, hyperkeratotic and verrucous forms. Moreover, the differential diagnosis includes several benign skin disorders such as eczema, psoriasis and contact dermatitis. The presenting colour varies from pink to orange, to a dusky violet red, brownish and, more rarely, hypopigmented.[4] The latter is mainly observed in Asians and dark-skinned individuals, and is generally diagnosed at a younger age than classic MF.[4 12–14] Our patient showed hypopigmented lesions associated with few erythematous papules. It was previously suggested that this clinical presentation of HMF might be predominantly observed in Caucasian patients; alternatively, erythematous lesions can be difficult to identify in higher phototypes.[8]

MF may seldom arise in children and young adults, and although HMF is an extremely rare variant, it is comparatively common among children diagnosed with MF.[1–3] Clinically, HMF may mimic benign skin diseases for which diagnosis is generally supported only by clinical features, including vitiligo, tinea versicolour, PA, PLC or postinflammatory hypopigmentation.[8] In the presented case, the lesions were initially misinterpreted as PA, and diagnosis was delayed by 3 years. MF in childhood is likely to be underestimated.

Contrary to classic MF in the early patch stage, HMF generally shows prominent epidermotropism and minimal dermal involvement or fibroplasia of the reticular dermis,[1 12] as we observed in our patient. Furthermore, unlike classic MF, which characteristically presents with a CD4+phenotype, HMF often displays a T-suppressor CD8+phenotype.[1 15] In our patient, there was no evidence of a monoclonal gene rearrangement in the lymphocytic population; however, an inverted CD4/CD8 ratio was observed, suggesting that the neoplastic population was CD8+. Although the presence of T-cell clonality supports the diagnosis of MF, the absence of clonality should not be a criterion to rule out the diagnosis.[8]

Treatment modalities for HMF include topical corticosteroids alone or in combination with narrow band UVB, or psoralen and UVA. There are no established protocols for the treatment of MF in children; phototherapy offers an effective option for the treatment of HMF, but recurrences are common.[16 17] In the largest retrospective study on paediatric HMF, 45.7% (16/35) of patients improved with phototherapy; however, 20% of these recurred, and only 7% (5/35) had a complete response. In the same study, one patient progressed to tumour stage.[9] Likewise, in a small cohort of hypopigmented MF (mean age at diagnosis 34.4 years), recurrence was observed in 8 of 9 patients after phototherapy, and none of the patients progressed beyond stage 1 disease.[4] Agar *et al* reported on the overall survival (OS), disease-specific survival (DSS) and risk of disease progression (RDP) of patients with MF and Sézary syndrome from a cohort of 1502 patients. They observed that the hypopigmented variant had an OS and DSS of 98% at 20 years, with RDP of 9% at 20 years, which was significantly better than classic MF.[15] These findings support the hypothesis that HMF may have a better course than classic MF.[1 5] Few studies have reviewed MF in childhood, and we believe that additional data are necessary to better assess prognosis and outcome in this subset of patients.

Early classic MF is characterised by a predominantly Th1-type immune response. Evolution from patches to plaques and tumours accompanies a shift from Th1 to Th2 response. In HMF, the CD8+T-cells participate in the Th1 immune response, and thus may prevent evolution to aggressive stages, even though the cells are malignant. In cases of patients with HMF with a CD4+neoplastic infiltrate, CD8+T cells may also have an important immunoregulatory action.[18] Moreover, CD8+phenotype predominance is consistent with the hypothesis that hypopigmentation results from lymphocyte cytotoxicity against melanocytes and melanogenesis, as observed in vitiligo pathogenesis.[8 18] Therefore, hypopigmentation might represent the clinical translation of the protective immune response, and a marker of good prognosis.

Learning points

- Mycosis fungoides (MF) is the most common primary cutaneous lymphoma in children.
- Hypopigmented mycosis fungoides (HMF) is an extremely rare variant, but relatively common in childhood.
- HMF is more frequently observed in dark-skinned individuals and, contrary to classic MF, usually presents a CD8+phenotype.
- HMF can be efficiently treated with phototherapy, but recurrence rates are high.
- HMF is associated with a better prognosis than classic MF, and hypopigmentation may represent the clinical translation of the protective immune response associated with a CD8+phenotype.

Contributors MG participated in the management of the patient during phototherapy. ÓT is responsible for the dermatopathology in our department. AM is responsible for the paediatric ambulatory unit and also reviewed the manuscript. AG was responsible for the patient during the staging and follow-up and for writing the manuscript.

Competing interests None.

Patient consent Obtained.

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