CASE REPORT

Childhood hypopigmented mycosis fungoides: a commonly delayed diagnosis

Ana Gameiro, Miguel Gouveia, Óscar Tellechea, Ana Moreno

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 versicolor, vitiligo, post-inflammatory 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+/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. 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 depigmented lesions, and the lesions spared the face and genitals, which is not a suggestive distribution for vitiligo.

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).

Figure 1 Patient presentation: generalised hypopigmented round patches 2–5 cm in diameter, slightly scaly.
Pityriasis lichenoides et varioliformis acuta (PLEVA) and pytiriasis lichenoides chronica (PLC) represent two ends of a disease spectrum that mostly affect young patients. PLEV A 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.37 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/cm² in 30 sessions (figure 4).

OUTCOME AND FOLLOW-UP
The patient experienced no recurrence of the disease 10 months after discontinuation of phototherapy.
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.\(^1\) 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 MF 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.\(^16\) Moreover, CD8+phenotype predominance is consistent with the hypothesis that hypopigmentation results from lymphocyte cytotoxicity against melanocytes and melanogenesis, as observed in vitiligo pathogenesis.\(^17\) Therefore, hypopigmentation might represent the clinical translation of the protective immune response, and a marker of good prognosis.

**Contributors** MG participated in the management of the patient during phototherapy. OT 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.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**REFERENCES**

Unusual presentation of more common disease/injury