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*Case Report*

# Juvenile-Onset Non-Poikilodermatous CD8+CD56+ Mycosis Fungoides

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**Abstract:** The most frequent primary cutaneous lymphomas observed in childhood and adolescence are mycosis fungoides (MF) and CD30-positive lymphoproliferative diseases. We report a 22-year-old female who presented with a 6-year history of multiple well-demarcated large roundish-oval scaly and reddish-brownish patches and plaques on the trunk and extremities. Histopathology revealed the focal parakeratosis and prominent epidermotropism of atypical lymphocytes, which were positive for CD8, CD56, and TIA-1 and showed a loss of CD7 and CD5 expression. T-cell receptor (TCR) gene rearrangement analysis (multiplex-PCR, BIOMED-2) of the lesional skin demonstrated the rearrangement of the gamma chain (tube A: 162 nt). Based on clinicopathological findings and a complete work-up, she was diagnosed with juvenile non-poikilodermatous C8+/CD56+ MF in stage IA. Resolution of the skin lesions was achieved by 16-week narrowband UVB phototherapy and clobetasol propionate 0.05% ointment. Juvenile-onset non-poikilodermatous CD8+CD56+ MF represents a very rare MF subtype and is associated with an indolent course. In order to avoid too aggressive diagnostics and treatments, clinicians should be aware of this rare and indolent MF variant in childhood and adolescence.

**Keywords:** CD8+ mycosis fungoides; cutaneous T-cell lymphoma; primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma; parapsoriasis en plaques; subcutaneous panniculitis-like T-cell lymphoma; NK/T-cell lymphoma

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## 1. Introduction

The most frequent primary cutaneous lymphomas observed in childhood and adolescence are mycosis fungoides (MFs) and CD30-positive lymphoproliferative diseases, including lymphomatoid papulosis and primary cutaneous anaplastic large-cell lymphoma. Over the last few decades, more than three hundred cases of juvenile-onset MF have been published by clinicians from dedicated cutaneous lymphoma centres around the globe, providing useful information on the clinicopathological findings, therapies, and prognostic aspects of juvenile MF. Unlike adult-onset MF, paediatric-onset MFs usually do not show up with the classic presentation seen in adults. The majority of children/adolescents with MF present with non-classic variants, whereby the hypopigmented variant is the most frequent form, observed in over 60% of all cases [1–3]. Other forms include hyperpigmented, folliculotropic, poikilodermatous, or unilesional MF and overlapping variants. The most predominant immunophenotype in adult-onset MF is CD3+ and CD4+. However, the immunohistochemistry of previously published cases with juvenile-onset MF very often demonstrated the CD3+, CD4− and CD8+ phenotype. Childhood cases of cytotoxic T-cell lymphoma have rarely been reported and may be of concern because of poor prognosis [1–12]. We report a case of juvenile non-poikilodermatous C8+CD56+ MF.

## 2. Case Report

A 22-year-old female presented with a 6-year history of multiple, slightly itchy, well-demarcated, large, roundish-oval, scaly, and reddish-brownish patches and plaques on the trunk and extremities (Figure 1).

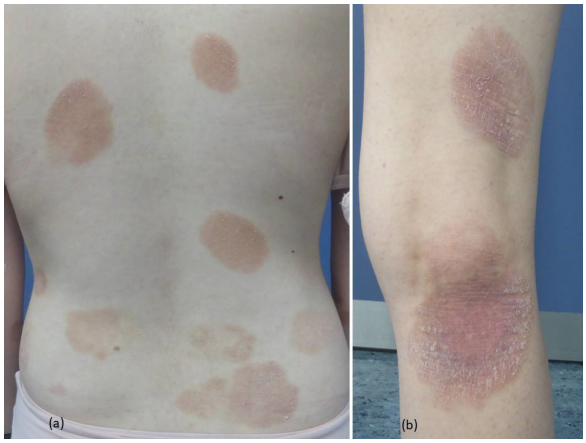


**Figure 1.** A young female with well-demarcated scaly reddish-brownish patches/plaques on the back (**a**) and dorsal leg (**b**).

They developed within about two weeks and remained more or less unchanged since their appearance. Histopathology revealed focal parakeratosis and the prominent epidermotropism of atypical lymphocytes (Figure 2a). In the upper dermis, there were scanty eosinophils and brownish melanophages as well. On immunohistochemistry stains (Figure 2b–d), the infiltrating lymphocytes were mainly positive for CD8, CD56, TIA-1, and granzyme B and showed a loss of CD7 and CD5 expression. CD30 expression was sporadically observed only in non-atypical T-lymphocytes. T-cell receptor (TCR) gene rearrangement analysis (multiplex-PCR, BIOMED-2) of the lesional skin demonstrated the rearrangement of the gamma chain (tube A: 162 nt). The flow cytometry of the peripheral blood revealed a slightly decreased CD4/CD8 ratio with an increase in CD8+ cells and a decrease in CD4+ cells.

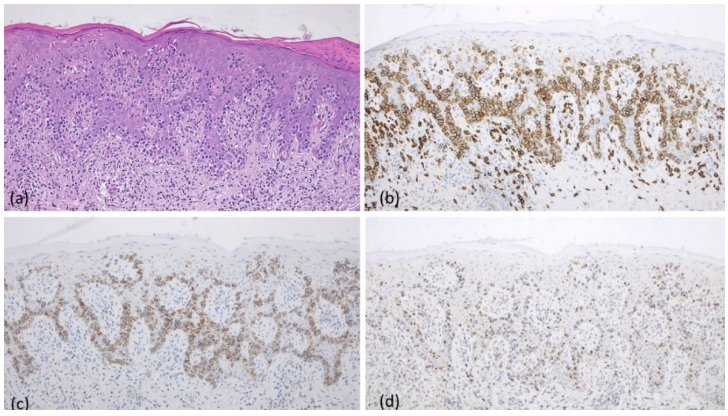


**Figure 2.** Haematoxylin–eosin stain of a skin biopsy obtained from the leg (Figure 1b) revealed the focal parakeratosis and prominent epidermotropism of atypical lymphocytes. Immunohistochemically (**a**), the infiltrating lymphocytes were mainly positive for CD8 (**b**), CD56 (**c**), and TIA-1 (**d**); magnification: 100×.

A small (max. 0.11%) subpopulation of CD3+CD8+CD5− cells was found. However, TCR gene rearrangement was not detectable in the peripheral blood. A complete work-up, including a lymph node and abdomen ultrasound and blood smear, did not reveal evidence for lymphoma spread. With respect to the clinicopathological findings and

complete work-up, the patient was in stage IA (T1b, N0, M0, B0; ISCL/EORTC). The patient was started on a clobetasol propionate 0.05% ointment and three-weekly outpatient whole-body narrowband ultraviolet B phototherapy (311 nm). The initial irradiation dose was 200 mJ/cm$^2$, which was increased by 20% on each subsequent visit. The dose was increased until improvement or erythema was observed. Finally, the skin lesions resolved with hyperpigmented patches after 16 weeks of treatment (Figure 3).

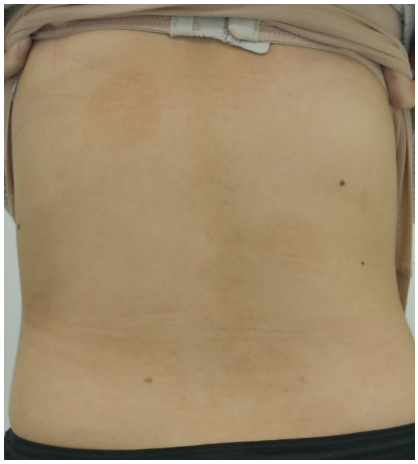

**Figure 3.** Resolution with hyperpigmentation of non-poikilodermatous CD8+CD56+ MF following 16 weeks of narrowband ultraviolet B phototherapy.

## 3. Discussion

Uncommon variants of MF have been reported in children and adolescents, particularly including the hypopigmented variant [2,3]. In the present case, a classic clinical MF plaque type was observed. Immunophenotypically, however, the neoplastic T lymphocytes showed a strong expression of CD8, CD56, and TIA-1—a cytotoxic expression profile that is significantly different from classic MF, which is characterised by a CD4+ immunophenotype. Ben-Amitai et al. [1] reported that CD8+ MF is overrepresented in the paediatric age group with a very good prognosis. However, the CD8+CD56+ immunophenotype is extremely rare in children and adolescents with MF [4–10]. The present case is very similar to the case of a juvenile-onset non-poikilodermatous CD8+CD56+ MF previously reported by Kempf et al. [7], also presenting with non-poikilodermatous lesions. Most of the previously described patients with this phenotypic variant were adults at the time of diagnosis and often manifested with widespread poikilodermatous skin lesions [4–10].

The most important differential diagnosis of juvenile-onset CD8+CD56+ MF is primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma and subcutaneous panniculitis-like T-cell lymphoma, which have a much more rapid and aggressive clinical course including early ulcerating and necrotising tumours and subcutaneous lesions, respectively [3,7,9]. Since juvenile-onset CD8+CD56+ MF, primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma, and subcutaneous panniculitis-like T-cell lymphoma share common immunohistological features, the distinction between these conditions must be made predominantly based on clinical features, disease history, and complete work-up results [3,6–9]. In the present case, the age at disease onset, clinical work-up, and appearance of skin lesions did not suggest a diagnosis of the above-mentioned aggressive T-cell lymphoma subtypes. Another clinical differential diagnosis includes large plaque parapsoriasis, which has been described very rarely in childhood [11]. However, histopathology, immunophenotyping, and genotyping aid in differentiating parapsoriasis from juvenile-onset CD8+ MF. Notably, juvenile-onset CD8+ as well as juvenile-onset CD8+CD56+ MF can be controlled in most patients by skin-directed therapies, including phototherapy and topical corticosteroids [2–10]. Notably, there is often a significant delay until the establishment of a correct diagnosis of childhood MF, which may be detrimental to the prognosis [12].

## 4. Conclusions

Juvenile-onset non-poikilodermatous CD8+CD56+ MF represents a very rare MF subtype and is associated with an indolent course. In order to avoid diagnostics and treatments that are too aggressive, clinicians should be aware of this rare and indolent MF variant in childhood and adolescence.

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**Institutional Review Board Statement:** This non-interventional case study was approved by the Institutional Review Board at the Ruhr-University Bochum (IRB Study ID #16-5985). All procedures performed in studies involving human participants or their data were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

**Informed Consent Statement:** Informed consent was obtained from the patient presented in this study.

**Data Availability Statement:** All crucial data generated or analysed during this case study are included in this published article.

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**Conflicts of Interest:** The authors declare no conflicts of interest.

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