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Cutaneous T-Cell Lymphoma at a Young Age

Jadwiga Roszkiewicz, MD, Gdansk, Poland
Andrzej Roszkiewicz, MD, Gdansk, Poland
Malgorzata Wojdylo, MD, Gdansk, Poland
Waldemar Placek, MD, Gdansk, Poland
Elzbieta Jasiel-Walikowska, MD, Gdansk, Poland

A case of cutaneous T-cell lymphoma (CTCL) in a 22-month-old patient is discussed, emphasizing the importance of screening for CTCL even in very young patients with atypical symptoms of eczema, atopic dermatitis, or parapsoriasis.

The clinical, histologic, and immunologic diagnostics can now be supported by molecular methods; therefore, patients at the earlier stages of CTCL can be diagnosed and treated with good results.

Cutaneous T-cell lymphoma (CTCL) is classified as a malignant disease with primary T-cell skin infiltration.[1-7] CTCLs represent a heterogeneous group of lymphomas with considerable variation in clinical presentation, histology, immunophenotype, and prognosis. A long-lasting and indolent disease, CTCL usually affects the lymph nodes or causes visceral involvement.[2,4,6,8-13]

The incidence of CTCL has increased from 0.2 cases per 100,000 in 1974 to 0.5 cases per 100,000 in 1988.[14] Mycosis fungoides (MF), one variant of CTCL, develops in approximately 1000 new patients per year in the United States and has estimated 2:1 ratios of men to women and of African Americans to Caucasians.

With more than 75% of patients diagnosed after 50 years of age, CTCL was initially thought to affect mainly middle-aged and older people.[14] However, there are several cases of younger patients with CTCL whose conditions reportedly developed in childhood[15-24] and adolescence.[18,19] The youngest patient with histologically documented MF was a 22-month-old child. The retrospective verification has shown that the first symptoms of MF manifested when he was 6 months old.[22] This report focuses on 2 cases of young boys with CTCL in which the disease developed before 20 years of age.

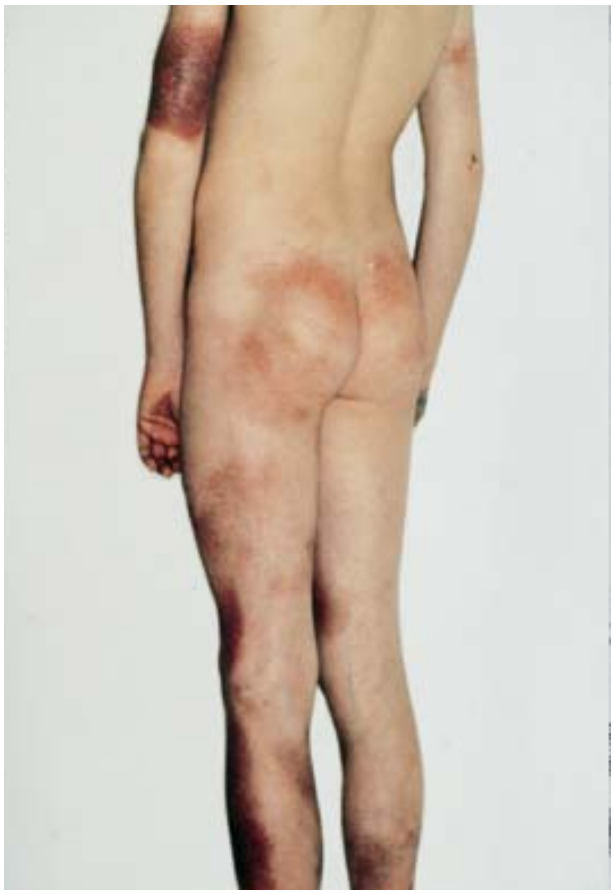

Figure 1. Patient 1 at age 13 years. Poikilodermatous changes on the left arm, buttock, and legs.

Drs. J. Roszkiewicz, A. Roszkiewicz, Wojdylo, Placek, and Jasiel-Walikowska are from the Departments of Dermatology and Pathomorphology, Medical University of Gdansk, Poland. Reprints: Jadwiga Roszkiewicz, MD, Akademia Medyczna, Katedra i Klinika Chorób, Skórnych i Weneryeznych, 80-211 Gdansk, ul. Debinki 7, Poland.

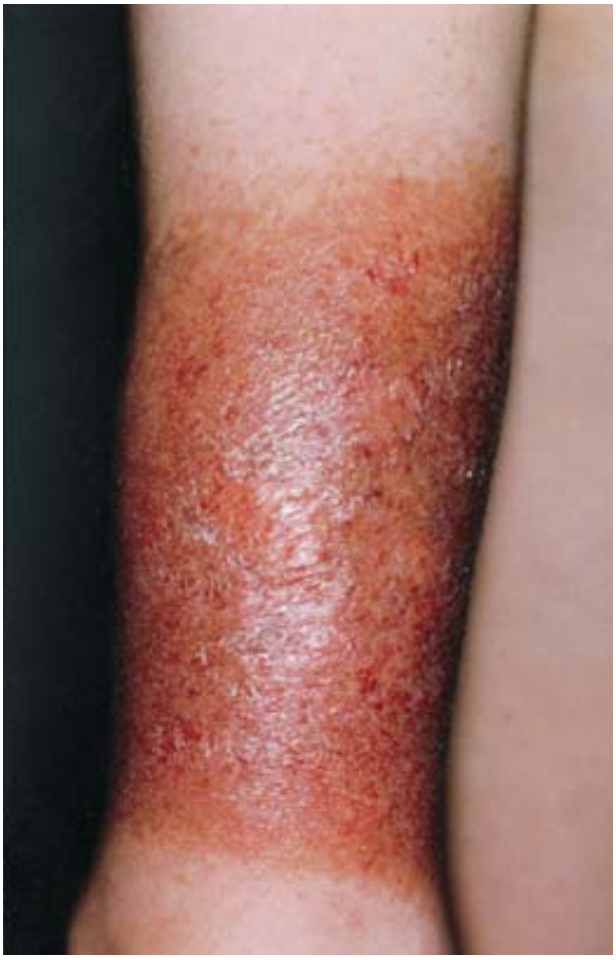

Figure 2. Patient 1 at age 15 years. The patch on the left arm shows a poikilodermatous form of mycosis fungoides.

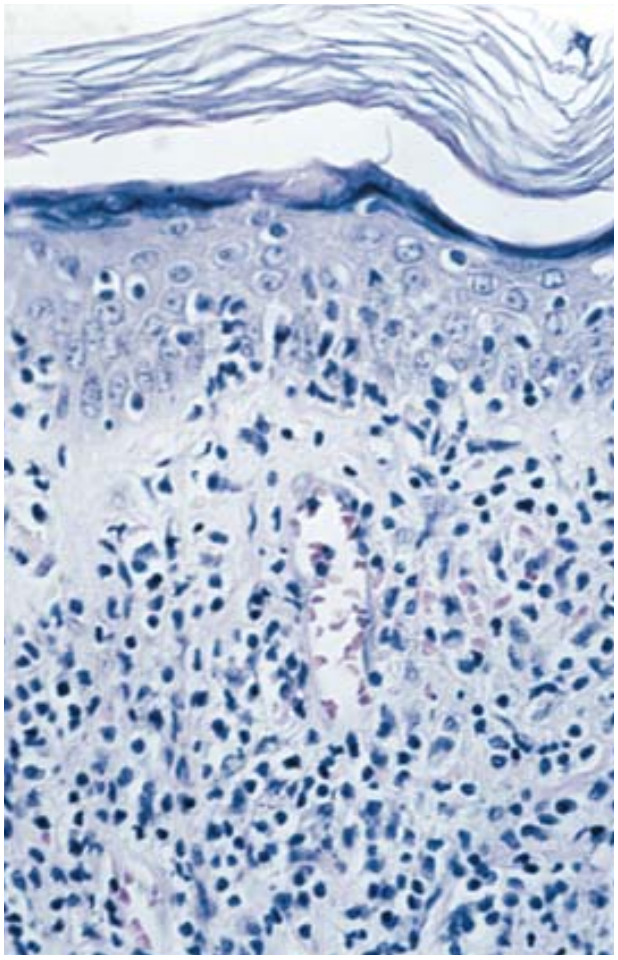

Figure 3. Lesional biopsy specimen from patient 1 showing a dense upper-dermal atypical polymorphous infiltrate with epidermotropism of lymphoid cells (H&E, original magnification ×400).

Case Reports

Patient 1—A 15-year-old boy first had symptoms of CTCL at 7 years of age, including erythematous patches with desquamation and itching of a few months duration on the left arm. Subsequently, the lesions became more brownish and disseminated to his buttocks and legs. At approximately 8 years of age, the patient was hospitalized a few times throughout the year for atopic dermatitis. He was treated with topical glucocorticoids and emollients with good results. At 13 years of age, clinical symptoms and histological examination revealed parapsoriasis en plaque. The clinical presentation included brownish erythematous lesions that were scaling, wrinkled, and up to several centimeters in diameter (Figure 1). The largest lesion was on the left arm, and atrophoderma was present. The histological picture indicated nonspecific chronic dermatitis, but epidermotropism of small lymphoid cells from the upper dermis into the epidermis also was seen. The treatment was oral methoxsalen followed by ultraviolet-A phototherapy (PUVA), with a total dose of 41.5 J/cm^2. After PUVA therapy, the lesions became paler, and topical emollients continued to be applied. After 3 months, the patch on the left arm continued to scale and became denser and darker with an inflammatory edge. Furthermore, a few small nodules, which were tender, appeared on the site. A skin biopsy specimen revealed a diagnosis that could correspond with parapsoriasis, but it was not possible to rule out transformation into MF. The treatment included Re-PUVA photoradiation, ie, the combination of oral isotretinoin 1 mg/kg and PUVA (oral methoxsalen 0.5 mg/kg, followed by ultraviolet-A phototherapy for a total dose of 160 J/cm^2). Re-PUVA caused a partial clinical remission (ie, the inflammatory edge vanished, and the nodules flattened), but the patches had a poikilodermatous character. After 3 months, the nodules reappeared,

the lesions were more infiltrated, and the plaque on the left arm became bigger and painful (Figure 2).

Histological examination showed atypical polymorphous infiltrate in the upper dermis with epidermotropism of lymphoid cells (Figure 3). Many of these cells presented irregularly shaped nuclei and dense chromatin. The results of immunohistochemical staining confirmed MF with most infiltrating mononuclear cells positive for CD3, CD4, and the human leukocyte antigen HLA-DR but nonreactive for CD8 and CD20.

Biomolecular methods confirmed the diagnosis of MF. The monoclonal way of rearrangement of V and J fragments of the T-cell receptor γ-chain was found by polymerase chain reaction and temperature gradient gel electrophoresis. The results of routine hematologic and chemical laboratory testing, bone marrow aspirate, chest roentgenography, and abdominal computed tomography were normal.

The combined Re-PUVA therapy was repeated to a total dose of 206 J/cm^2 UVA, but there was no clinical or histological improvement. The patient was transferred to the Warsaw Oncological Center in Poland in June 1999 for total body electron beam therapy, but technical support was unavailable, so the patient was treated with radioactive cobalt 60 irradiation for a total dose of 33 Gy. The condition went into remission and remained so at the patient's last visit in February 2000.

Patient 2—A 25-year-old man first had symptoms at the age of 14 years. Lesions resembling nummular eczema were present on the buttocks, legs, and axillas. Parapsoriasis also was suspected, and the patient was treated with topical glucocorticoids and emollients. The disease was clinically stable until the patient was 19 years of age when physical examination revealed that the lesions were spreading. The patches became more inflammatory, well circumscribed, and slightly brownish with scaling up to 15 cm in diameter.

Routine histological examination showed light microscopy findings similar to parapsoriasis, but as in the case above, it was associated with the onset of CTCL.

PUVA photoradiation was applied for a total dose of 367.5 J/cm^2 of ultraviolet-A phototherapy. Initially, a good response was observed as the patches became flat. However, there was relapse in less than a year. Examination revealed an erythematous, indurated scaly plaque in a polycyclic configuration with a sharply demarcated edge on the buttock and legs (Figure 4).

Histologic features of the lesional skin of the buttocks, legs, and axillas were virtually identical. In the acanthotic epidermis, there was a dense infiltrate of small-to-medium atypical mononuclear cells that had a small amount of pale cytoplasm and hyperchromatic nuclei. Some of these cells infiltrated in groups, forming a pagetoid appearance. In the papillary dermis, there was a perivascular lymphohistiocytic infiltrate, which consisted of small lymphoid cells that were not atypical (Figure 5, A and B). The results suggested pagetoid reticulosis. The polymerase chain reaction and temperature gradient gel electrophoresis examination of the V and J fragments of the T-cell receptor γ-chain revealed a monoclonal way of rearrangement, which confirmed a diagnosis of CTCL.

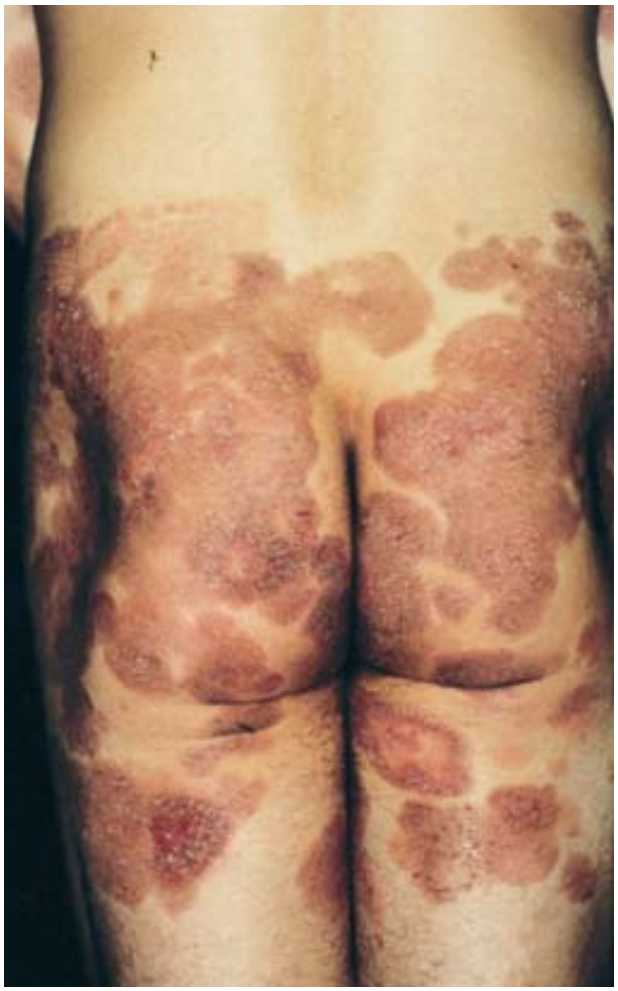

Figure 4. Patient 2 at age 20 years. Erythematous scaly patches and plaques in a polycyclic configuration on buttock and both thighs.

The immunophenotypic results were positive for CD3$^+$ and CD45RO$^+$ (clone UCHL, DAKO). Otherwise, the patient was in good health with no enlargement of the spleen, liver, or lymph nodes.

The patient was treated for 4 months with 6.5 mg/m^2 per day of Targretin capsules (LGD 1069), a retinoid currently in clinical trials in Poland. The

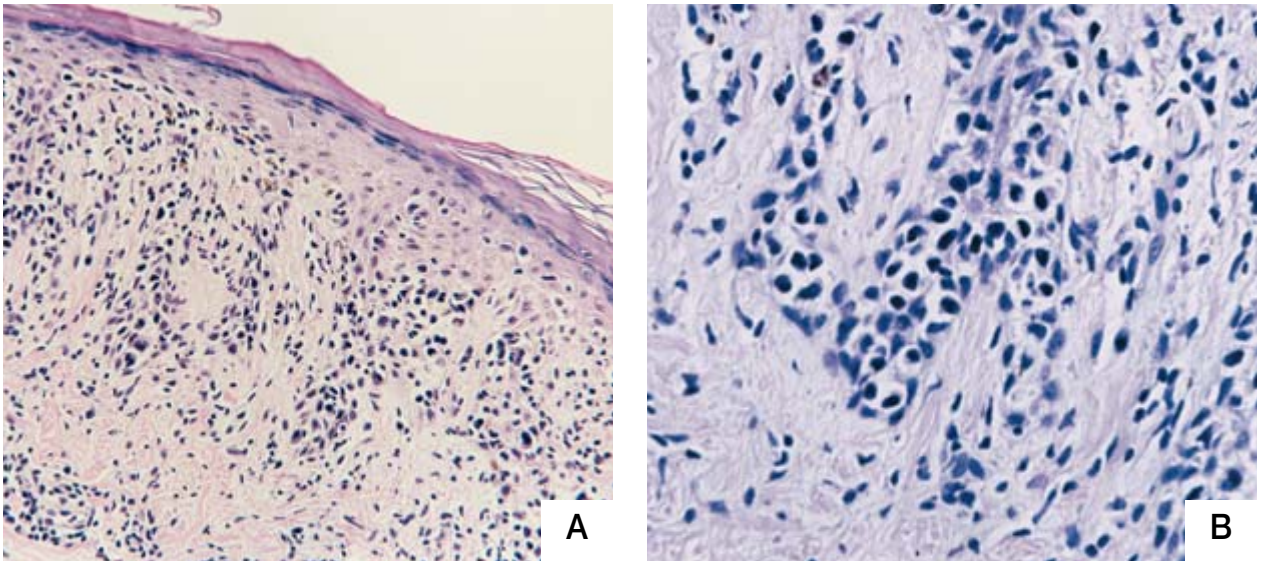

Figure 5. (A) Disseminated pagetoid reticulosis in patient 2. A pagetoid intraepidermal and a small subepidermal infiltrate (H&E, original magnification ×200). (B) Spongelike disaggregation caused by atypical lymphocytic infiltrate in a pagetoid fashion within the epidermis (H&E, original magnification ×400).

therapy had good results with skin lesions becoming flat and pale and some even disappearing. The patient received follow-up after the Targretin treatment and has been stable for 6 months.

Comment

Our findings support previous reports of CTCL manifesting at a young age. Epstein et al[12] and Koch et al[16] found 4% to 5% of patients, respectively, had a case history of MF during the first 2 decades of life. In addition, Woringer-Kolopp disease, a localized cutaneous form of T-cell lymphoma, also has been reported in patients younger than 20 years,[24] and it is possible that the incidence is higher.[15] We suggest that every child or teenager with parapsoriasis or atypical symptoms of atopic dermatitis or eczema be observed carefully for an insidious onset of CTCL.[17,25] CTCL began at age 7 years in our 15-year-old patient, but he was treated for atopic dermatitis until age 13 years, when parapsoriasis en plaque was diagnosed. Two years later, MF developed within the patch on the left arm despite combined Re-PUVA therapy.

In our second patient, skin symptoms first appeared on his legs at age 14 years and resembled nummular eczema or parapsoriasis en plaque. At age 20 years, the diagnosis of patch stage MF, and then pagetoid reticulosis was established by clinical symptoms and by light microscopic examination of skin biopsy.

Pagetoid reticulosis is a rare lymphoproliferative skin disorder characterized by the presence of localized patches or plaques with an intraepidermal proliferation of neoplastic T cells that produce a pagetoid appearance. Extracutaneous dissemination has not been reported.[26-37] Tumor cells have either a phenotype of $CD3^+$, $CD4^+$, and $CD8^-$ or $CD3^+$, $CD4^-$, and $CD8^+$.[2,26,33-37] CD30 can be expressed,[33,34] and clonal T-cell receptor gene rearrangement has been demonstrated.[27,35,38-40]

Two types of pagetoid reticulosis have been described: a localized type (Woringer-Kolopp disease) and a disseminated type (Ketron-Goodman type).[3,26-38,41] There is no significant difference between the 2 types histologically or in the cell surface markers of lymphocytes that infiltrate the epidermis.[3,34] However, the clinical courses are distinctive. The localized form has been regarded as a benign T-cell proliferative disorder.[3,26,28,33,34,41] In contrast, the disseminated type usually has a fatal outcome characterized by progressive cutaneous and extracutaneous involvement.[27,30,36,41] Therefore, some authors[29,32-34,36,42] have defined the disseminated form as a variant of MF with prominent epidermotropism.

Some observations suggest that CTCL symptoms at a young age can indicate a more aggressive variant of CTCL than symptoms revealed in adulthood. There were reported cases involving a 17-year-old boy with MF, whose bone marrow and brain were affected,[13] and a 12-year-old girl who developed a tumoral stage of MF.[20] Meister et al[17] described an 11-year-old African American girl with Sezary syndrome, and Paller et al[23] reported an aggressive, nodular, primary CTCL in an 11-year-old girl.

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However, Zackheim et al[22] and Burns et al[25] concluded that their patients with MF who had onset before the age of 30 years had a prognosis and natural history similar to that of unselected patients with MF and CTCL. Survival time is probably the same in younger and older patients, starting from the time of diagnosis. An important risk factor is the stage and dissemination of the disease at CTCL diagnosis.[12]

Disease progression in both our patients is temporarily under control at this time, but the prognosis for survival is doubtful. Despite treatment and current remission in the first case, there is a possibility that the disease will progress. The prognosis in the second case is similar because the disseminated type of pagetoid reticulosis behaves the same as classic MF.[29,32-34,36,42]

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