

# Initial cutaneous manifestation of lymphomas in children

## Apresentação cutânea inicial de linfomas na infância

Maria Christina Lopes Araujo de Oliveira<sup>1</sup>  
Priscila Cezarino Rodrigues<sup>3</sup>  
Benigna Maria de Oliveira<sup>5</sup>

Luciana Baptista Pereira<sup>2</sup>  
Keyla Cunha Sampaio<sup>4</sup>  
Marcos Borato Viana<sup>6</sup>

**Abstract:** Cutaneous lymphomas comprise a heterogeneous group of lymphoproliferative disorders with skin involvement and are classified as a subgroup of non-Hodgkin lymphomas. From 1981 to 2007, 100 children with non-Hodgkin lymphomas were admitted to the Hematology Unit of the Federal University of Minas Gerais Teaching Hospital. In nine of these children, the skin was involved at the onset of the disease. Three patients were classified as having primary cutaneous lymphoma, while in six the disease was systemic with cutaneous involvement. In seven patients, the immunophenotype was T-cell, in one it was B-cell, and in the remaining case the immunophenotype was indefinable. No deaths occurred in any of the children with primary cutaneous lymphoma.

**Keywords:** Lymphoma, T-cell, cutaneous; Pediatrics; Prognosis

**Resumo:** Os linfomas cutâneos compreendem um grupo heterogêneo de desordens linfoproliferativas que envolvem a pele e são classificados como um subgrupo dos linfomas não Hodgkin. No período de 1981 a 2007, 100 casos de linfomas em crianças foram admitidos no Serviço de Hematologia, do Hospital das Clínicas da Universidade Federal de Minas Gerais, sendo que nove apresentaram manifestação cutânea inicial. Três pacientes foram classificados como linfoma cutâneo primário e seis como sistêmicos. Sete pacientes apresentaram linfoma de células T, um, linfoma linfoblástico B e um, imunofenótipo indefinido. Nenhum óbito ocorreu nos pacientes com linfoma cutâneo primário.

**Palavras-chave:** Linfoma cutâneo de células T; Pediatria; Prognóstico

Lymphomas involve the skin either primarily or secondarily and are classified as a subgroup of non-Hodgkin lymphomas (NHL). They can only be considered primary cutaneous lymphomas (PCL) when the initial presentation is in the skin and there is no evidence of extracutaneous involvement at diagnosis, following complete staging.<sup>1,2</sup> In children, NHLs represent 6 to 10% of malignant neoplasms. After the gastrointestinal tract, the skin is the extranodal site most affected.<sup>3,4</sup>

The objective of this study was to describe the

clinical course of children with skin manifestations of lymphoma being followed-up at the hematology department of the Teaching Hospital of the Federal University of Minas Gerais. In a retrospective study of 100 children with NHL admitted to the department between 1981 and 2007, nine patients had skin involvement at diagnosis. The study was approved by the Internal Review Board of the Federal University of Minas Gerais.

Of the nine patients, four were boys and five were girls (Figure 1). The median age at diagnosis

Received on 23.05.2010.

Approved by the Advisory Board and accepted for publication on 07.06.10.

\* Study conducted at the Pediatric Hematology Unit, Teaching Hospital of the Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

Conflict of interest: None / *Conflito de interesse: Nenhum*

Financial funding: None / *Suporte financeiro: Nenhum*

<sup>1</sup> PhD. Associate Professor, Department of Pediatrics, Federal University of Minas Gerais (UFMG), Belo Horizonte, Minas Gerais, Brazil.

<sup>2</sup> Master's Degree. Assistant Professor, Department of Clinical Medicine/Dermatology, Federal University of Minas Gerais (UFMG), Belo Horizonte, Minas Gerais, Brazil.

<sup>3</sup> Master's Degree. Physician, Hematology Department, Teaching Hospital of the Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

<sup>4</sup> PhD. Physician, Hematology Department, Teaching Hospital of the Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

<sup>5</sup> PhD. Adjunct Professor, Department of Pediatrics, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

<sup>6</sup> PhD. Full Professor, Department of Pediatrics, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

CHART 1: Classification and clinical characteristics of the patients with cutaneous manifestations of lymphoma

Patient	Classification and immunophenotype	Sex	Age at diagnosis (years)	Cutaneous	Lymph node manifestations	Bone marrow involvement	Other involvement	Clinical course manifestations
1	Precursor cell lymphoblastic lymphoma of undefined immunophenotype.	F	4.9	Nodules on the right leg, left upper and lower eyelids.	Right inguinal	Yes	Hepatomegaly Splenomegaly	Complete remission. Two years of follow-up.
2	Nodal anaplastic large cell lymphoma of T-cell phenotype	F	9.9	Nodules on the inside and back of the left thigh.	Periportal, perisplenic, para-aortic, mesenteric and mediastinal	No	Infiltration in the lumbosacral joint and in the sacroiliac joint; osteolytic lesions in the brain.	Did not achieve remission. Died 9 months after diagnosis.
3	Precursor B-cell lymphoblastic lymphoma.	F	1.5	Nodules on the scalp.	Cervical and axillary	Yes	Infection, septic shock, hepatosplenomegaly	Remission after first cycle of chemotherapy (Protocol GBTL1-LLA 99). Death from septicemia during period of neutropenia.
4	Diffuse lymphocytic non-Hodgkin lymphoma. Poorly differentiated, T-cell phenotype.	F	10	Erythematous, violaceous nodules disseminated on the limbs and face.	Absent	Yes	Splenomegaly	Remission for two months after the first cycle of chemotherapy. Death during second cycle of chemotherapy.
5	Primary cutaneous anaplastic large T-cell lymphoma.	M	12.9	Vegetating tumor with infiltrated borders on the right arm (single lesion).	Absent	No	Absent	Complete remission after chemotherapy (5 months of follow-up).
6	Systemic T-cell lymphoma with cutaneous involvement (unclassified subtype).	M	8.5	Erythematous, hyperchromic nodules disseminated over the buttocks, limbs and face.	Absent	Yes	Absent	Remission after the first cycle of chemotherapy. Recurrence in the central nervous system one year later. Further remission after second cycle of chemotherapy (11 years of follow-up).
7	Systemic T-cell lymphoma with cutaneous involvement (unclassified subtype).	F	3.3	Ulcerated tumor in the vulvar region and infiltrated nodules on the lower limbs.	Absent	No	Infiltration in the central nervous system	Complete remission (3 years and 8 months of follow up).
8	Primary cutaneous lymphoma: Subcutaneous panniculitis-like T-cell lymphoma.	M	2.4	Erythematous, infiltrated nodules disseminated on the backs of the hands and feet and erythematous, infiltrated plaques on the external ears, face, trunk and limbs.	Absent	No	Arterial hypertension	Complete remission. (8 years and 5 months of follow-up).
9	Primary cutaneous T-cell lymphoma	M	2.0	Tumor on the knee.	Absent	No	Absent	Complete remission (unclassified subtype). (17 years of follow-up)

GBTL1-LLA 99: Brazilian Group for the treatment of acute lymphoblastic leukemia, 1999.

was 4.9 years (range 1.5 to 12.8 years). These nine patients all had skin lesions at diagnosis, located principally on the upper and lower limbs, followed by the face and scalp. In seven children, multiple lesions were present, while two children had single lesions (Figures 1A and 1B). In four patients, there was spinal involvement, affecting the central nervous system in one and causing lymphadenomegaly in another. Therefore, the disease was considered systemic with skin involvement in six patients and primary cutaneous in three. All were submitted to systemic chemotherapy, which differed in accordance with the presentation and histological type.

The median time of follow-up was 3.4 years, ranging from 3 months to 17.4 years. The three patients initially diagnosed as PCL (patients 5, 8 and 9) achieved complete remission and remained in remission until the end of the study. Of the six children with the systemic disease, three are still in remission and three have died, two due to complications of the treatment, while the third, who was human immunodeficiency virus (HIV)-positive, died from the primary disease (patient #2). All the deaths occurred during an active phase of the disease.

Unlike systemic NHL in which the most com-

mon cell lineage is B, cases of PCL are generally T-cell related. Cutaneous T-cell lymphomas constitute a heterogeneous group of lymphoproliferative diseases characterized by a clonal expansion of mature post-thymic T-cells that infiltrate the skin. Cutaneous B-cell lymphomas are rare in children except in the uncommon cases of precursor B-cell lymphoblastic lymphoma (B-LBL) in which the initial manifestation of the disease is in the skin.<sup>5</sup> In the present sample, T cell lineage was the most prevalent, occurring in seven patients. Only one case of B lineage was found and in one case the immunophenotype could not be defined (negative for B and T markers).

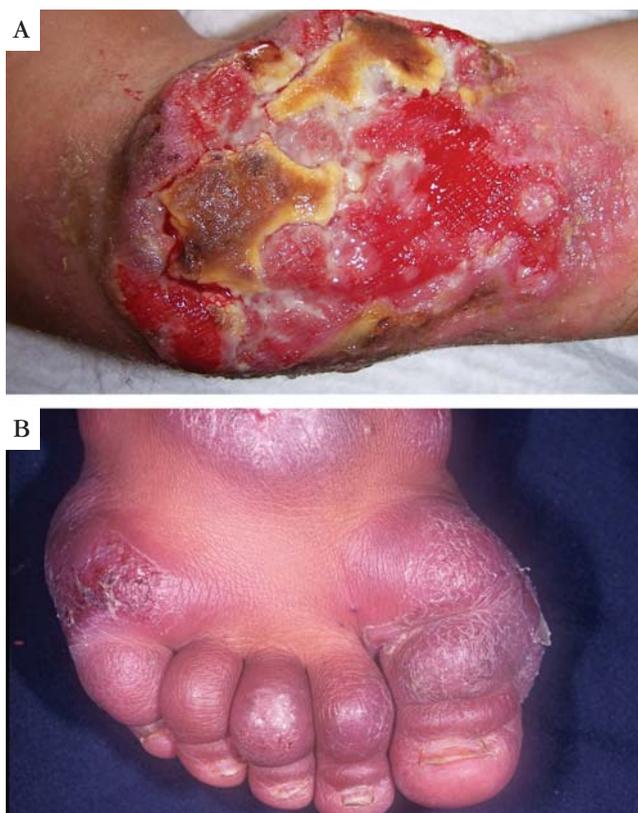
Mycosis fungoides (MF) is the most common form of cutaneous lymphoma in children and adolescents, accounting for 40% of cases. Clinical progression is slow.<sup>1,6,7</sup> In the present sample, no cases of MF were found, which may reflect a true epidemiological variation or, more probably, a variation related to the sample population.

Anaplastic large cell lymphomas (ALCL) may be primary to the skin (patient #5) or may be systemic (patient #2). In children, the systemic form is more common and prognosis is poorer when the skin is also affected.<sup>8,9</sup> Prognosis is better in cases of primary cutaneous ALCL and cytogenetic alterations such as t(2;5)(p23;q35) translocation and the product of the resulting fusion, anaplastic lymphoma kinase (ALK) protein, which occur in the systemic form, are not generally found. Therefore, although the morphological status is identical, the hypothesis has been raised that primary cutaneous CD 30-positive ALCL and systemic ALCL may represent different diseases that differ in their clinical behavior and in their pathogenesis.<sup>10</sup>

One patient was classified as having subcutaneous panniculitis-like T cell lymphoma (Patient #8), since the neoplastic infiltrate was diffusely affecting the subcutaneous tissue. This is a less common subtype of primary cutaneous T-cell lymphoma.<sup>1</sup>

With respect to the patient with the B immunophenotype, the histological type consisted of a precursor B-cell lymphoblastic lymphoma. As reported in the literature, precursor B-cell neoplasias generally present as acute lymphoblastic leukemia. Precursor B-cell lymphoblastic lymphoma is rare. It occurs in young, female patients and tends to affect the skin and long bones.<sup>5</sup> The patient in the present sample was also young and female, with spinal involvement at diagnosis, later developing lymphoblastic leukemia. She died three months after the beginning of treatment.

It is interesting to note that in three patients in the present sample the initial diagnosis was not cutaneous lymphoma but rather several different conditions that clinically resemble lymphoma: bacillary



**FIGURE 1:** Cutaneous manifestation of lymphomas. **A.** Primary anaplastic large cell lymphoma. **B.** Primary cutaneous lymphoma: subcutaneous panniculitis-like T-cell lymphoma

angiomatosis (patient #2), American tegumentary leishmaniasis (patient #5) and mastocytosis (patient #8). This reinforces the need to take a diagnosis of cutaneous lymphoma into consideration even in children despite the fact that it is rare in this age-group.

In relation to prognosis, patients with primary cutaneous lymphoma generally have a greater probability of disease-free survival than patients with secondary cutaneous lymphoma, despite the fact that the histological and immunohistochemical features of the secondary skin lesions are identical to those of the systemic disease.

In conclusion, non-Hodgkin lymphoma (NHL) with primary skin manifestation is a rare disease in childhood, accounting for around 1% of cases of NHL in children and adolescents. It may be confused with other non-neoplastic conditions. Although small, the present sample suggests that in cases of primary cutaneous lymphoma prognosis is indeed favorable; however, this is not the case with the systemic form of the disease, which should probably be considered to belong to the group of NHL in which the risk of recurrence and death is high. □

## REFERENCES

1. Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. 2005;105:3768-85.
2. Kadin ME, Carpenter C. Systemic and primary cutaneous anaplastic large cell lymphomas. *Semin Hematol*. 2003;40:244-56.
3. Fink-Puches R, Chott A, Ardigó M, Simonitsch I, Ferrara G, Kerl H, et al. The spectrum of cutaneous lymphomas in patients less than 20 years of age. *Pediatr Dermatol*. 2004;21:525-33.
4. Sharon V, Mecca PS, Steinhilber PG, Trippett TM, Myskowski PL. Two pediatric cases of primary cutaneous B-cell lymphoma and review of the literature. *Pediatr Dermatol*. 2009;26:34-9.
5. Kahwash SB, Qualman SJ. Cutaneous lymphoblastic lymphoma in children: report of six cases with precursor B-cell lineage. *Pediatr Dev Pathol*. 2002;5:45-53.
6. Vonderheid EC, Bernengo MG, Burg G, Duvic M, Heald P, Laroche L, et al. Update on erythrodermic cutaneous T-cell lymphoma: report of the International Society for Cutaneous Lymphomas. *J Am Acad Dermatol*. 2002;46:95-106.
7. Wain EM, Orchard GE, Whittaker SJ, Spittle MSF, Russell-Jones R. Outcome in 34 patients with juvenile-onset mycosis fungoides: a clinical, immunophenotypic, and molecular study. *Cancer*. 2003;98:2282-90.
8. Hung TY, Lin YC, Sun HL, Liu MC. Primary cutaneous anaplastic large cell lymphoma in a young child. *Eur J Pediatr*. 2008;167:111-3.
9. Le Deley MC, Reiter A, Williams D, Delsol G, Oschlies I, McCarthy K, et al. Prognostic factors in childhood anaplastic large cell lymphoma: results of a large European intergroup study. *Blood*. 2008;111:1560-6.
10. Kempf W. CD30+ lymphoproliferative disorders: histopathology, differential diagnosis, new variants, and simulators. *J Cutan Pathol*. 2006;33(Suppl 1):58-70.

---

**MAILING ADDRESS / ENDEREÇO PARA CORRESPONDÊNCIA:**  
**Maria Christina Lopes A Oliveira**  
**Rua Engenheiro Amaro Lanari, 389 - Apt. 501**  
**CEP: 30.320-580 Belo Horizonte - MG, Brazil**  
**E-mail: chrismariana@gmail.com**

How to cite this article/Como citar este artigo: Oliveira MC, Pereira LB, Rodrigues PC, Sampaio KC, de Oliveira BM, Viana MB. Initial cutaneous manifestation of lymphomas in children. *An Bras Dermatol*. 2010;86(4):799-82.