A new pediatric case of cutaneous pre-B lymphoblastic lymphoma

Cutaneous lesions are observed in children as the initial signs of several neoplasia such as neuroblastoma, histiocytosis, leukemia and lymphoma. Primary cutaneous lymphoma of pre-B phenotype is very rare. We describe a case of an infant affected by this tumor and emphasize its rarity considering the patient's age and the exclusive skin involvement.

A 14-month old girl was referred to our hospital for multiple skin nodules. The first lesions appeared on the right gluteus at the age of 7 months and grew progressively, spreading to glutei and to the right arm and leg. On admission, the child who was in good general condition, had at least 10 cutaneous purplish nodules with a light blue shade, deeply infiltrated, and without superficial ulcerations. Further physical examination was normal. Laboratory blood tests were within normal ranges, except for high lactate dehydrogenase (695 UI/L, nv: <375 UI/L). Chest radiography, abdomen ultrasonography, and a bone scan were normal.

Histologic examination of a skin nodule showed the presence of a dense, diffuse monomorphic infiltrate of medium-sized lymphoid cells in the dermis and in the subcutaneous tissue (Figure 1). Cells exhibited scarce cytoplasm, finely dispersed nuclear chromatin, and inconspicuous nucleoli. Many mitotic and apoptotic figures were observed. Large, pale macrophages containing pyknotic nuclear debris, cell fragments and tumor cells conferred a starry-sky pattern to the histological picture (Figure 2). Immunohistochemically malignant cells were positive for TdT, HLA-DR, CD10, CD43, and CD79a. CD3 and CD5 were expressed by the small proportion of reactive T-lymphocytes. Flow cytometric analysis yielded the following results: 97% $CD45^+$; 80% $CD19^+$; 82% $HLA\text{-}DR^+$; 80% $CD10^+$; 23% TdT; 4% $CD20^+$; 13% $CD7^+$; 13% $CD5^+$; 12% $CD3^+$; 8% $CD4^+$; 4% $CD8^+$; and < 1% Ig λ $light\text{-}chain^+$ cells. These results indicate the presence in the skin of an expanded population of pre-B cells with the following immunophenotype: $CD19^+$, $HLA\text{-}DR^+$, $CD10^+$, $TdT^{+/}$,$CD20^-$, and surface Ig^-.

Polymerase chain reaction (PCR) analysis of the complementary determining region 3 (CDR3) length of immunoglobulin (Ig) heavy-chain genes showed a clonal B-cell population in the skin biopsy. DNA index analysis showed that tumor cells were diploid.

Morphologic analysis of 2 bone marrow biopsies and 4 bone marrow aspirates revealed the presence of few blast cells, immunophenotypically identified as immature myeloid cells. No clonal rearrangement of Ig genes was detected by PCR in bone marrow samples. Cerebrospinal fluid was normal.

Diagnosis of primary pre-B lymphoblastic lymphoma of the skin was made. Our patient was treated according to non-B NHL 97 protocol, ($LSA\text{-}L_2$ modified),[1] proposed by the *Italian Association for Pediatric Hematology and Oncology*. Clinical response was rapid and complete and persists 18 months after diagnosis.

Fewer than 20% of patients with NHL have skin involvement at presentation and most cases are anaplastic large cell lymphomas. Primary cutaneous lymphoblastic lymphoma (LBL) are rare and most are characterised by an immature T-cell immunophenotype, whereas precursor-B LBL with exclusive cutaneous presentation are exceptionally rare.[2]

Approximately 3.5 to 7% of primary skin B-cell lymphomas belong to the lymphoblastic type, suggesting that pre-B LBL may have a tropism for cutaneous sites. The clinical findings are multiple papular and nodular lesions most frequently located on the head, neck, cheek, scalp, and forehead.[3]

There are few reports of primary cutaneous LBL in childhood, and most cases presented bone marrow infiltration or nodal disease.[4,5] In 1984 Meyers *et al.*[6] reported a case of a 5-month old -male with multiple skin lesions and bone marrow with 70% blast cells of lymphoid morphology. Skin lesions and hematologic disease regressed within 2 weeks with chemotherapy but skin lesions recurred followed by central nervous system, bone marrow, and testicular involvement and the child died 8 months after diagnosis. Schimitt *et al.*[3] reported a 19-month old girl who presented a single reddish tumor on the upper arm with diffuse bone marrow infiltration of neoplastic cells. She underwent polychemotherapy according to the $LSA_2\text{-}L_2$ modified protocol and was in complete remission 26 months after diagnosis. Link *et al.*[7] reported two children with pre-B lymphoma of the skin. The first was a 3.5-year old girl with scalp nodules. Bone marrow aspirate and biopsy revealed no lymphoma involvement. She was treated with the Stanford Regimen for Pediatric Non-Hodgkin Lymphoma but eleven months after diagnosis she suffered bone marrow relapse and died. The second patient was a 6-year old girl with a mass on the scalp and cervical adenopathy. Bone marrow was infiltrated by lymphoblasts. This patient

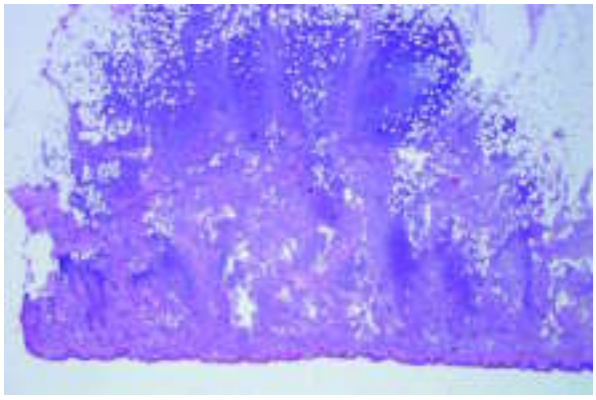

Figure 1. Low power examination: H&E, 1×. Histologic section of the skin biopsy: dense diffuse infiltrate which spares the epidermis and involves the dermis and the subcutaneous fat.

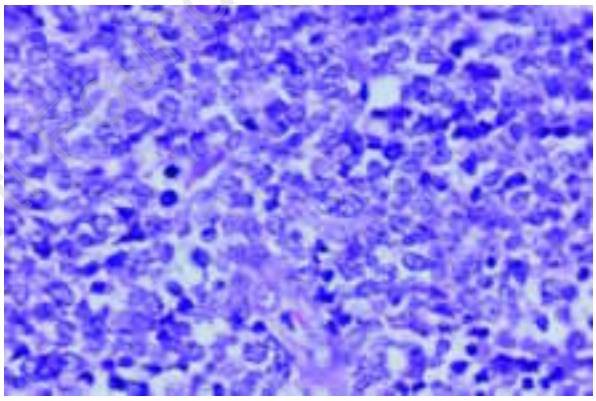

Figure 2. Detail: H&E, 40×. Monomorphous infiltrate of lymphoid cells. These are medium sized and show scarce cytoplasm and large nucleous with fine chromatin and small nucleolus. Mixed with the lymphoid cells are large macrophages containing cellular debris. Numerous pyknotic cells.

was also treated on an LSA_2-L_2 modified regimen and she died of congestive heart failure without recurrent disease 34 months after diagnosis. Millot *et al.*,[8] reported the cases of two children aged 9 years and 6 months respectively, suffering from pre-B lymphoblastic lymphoma with diffuse disease at diagnosis. The first died of central nervous system involvement 24 months after the initial diagnosis, the second child was in complete remission after one year of follow-up.

The case reported here is peculiar because of its clinical presentation and age of the patient at onset. These features highlight the need for rapid and appropriate study of cutaneous lesions in childhood. In the literature we found no reports of spontaneous regression in similar cases but in most cases diffuse disease was present at diagnosis or occurred during follow-up and had a grim prognosis. Therefore, an aggressive chemotherapeutic approach should be adopted.

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