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CASE REPORT

A Newborn with Congenital Mixed Phenotype Acute Leukemia After *In Vitro* Fertilization

Hacer Ergin [a], Özmert M.A. Özdemir [a,*], Abdullah Karaca [a], Nilay Şen Türk [b], Füsun Düzcan [c], Şeniz Ergin [d], Elif Kazancı [e], Canan Vergin [e], Ayşe Erbay [e]

[a] *Department of Pediatrics, Faculty of Medicine, Pamukkale University, Denizli, Turkey*
[b] *Department of Pathology, Faculty of Medicine, Pamukkale University, Denizli, Turkey*
[c] *Department of Clinical Genetics, Faculty of Medicine, Pamukkale University, Denizli, Turkey*
[d] *Department of Dermatology, Faculty of Medicine, Pamukkale University, Denizli, Turkey*
[e] *Department of Pediatric Hematology-Oncology, Behçet Uz Pediatric Hospital, İzmir, Turkey*

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mixed phenotype acute leukemia (MPAL)

Congenital leukemia is a rare disease. The majority of cases of this disease are acute myelogenous leukemia (AML). Congenital acute lymphoblastic leukemia (ALL) is rare and most often is of B cell lineage. Rarely, some cases have been designated biphenotypic or mixed phenotype acute leukemia (MPAL). Herein, we report a preterm newborn referred to us as a result of the appearance of blue-violaceous dermal nodules on her body at birth. She was a twin and the product of an *in vitro* fertilization (IVF) pregnancy. Physical examination showed jaundice, hepatosplenomegaly, and peripheral facial nerve palsy in addition to dermal nodules. Bone marrow aspiration showed 40% blasts of lymphoid lineage; skin biopsy and its immunohistochemistry revealed myeloblastic infiltration of the dermis. Cytogenetic analysis (46,XX), fluorescence *in situ* hybridization (FISH) analysis, and cranial magnetic resonance were normal. The patient was diagnosed with congenital MPAL, and an association between IVF and congenital leukemia was suggested.

* Corresponding author. Department of Pediatrics, School of Medicine, Pamukkale University, Çocuk Poliklinik Binası, Kat 2, Kınıklı, 20070 Denizli, Turkey.
E-mail address: drozmert@gmail.com (Ö.M.A. Özdemir).

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1. Introduction

Leukemia diagnosed from birth to 6 weeks of age is defined as congenital leukemia.[1] Congenital leukemia cases are fewer than five per 1 million live births, and 80% of cases are nonlymphoblastic.[2] The majority of congenital leukemia cases are acute myelogenous leukemia (AML).[3] Congenital acute lymphoblastic leukemia (ALL) is rare and most often of B cell lineage (B-ALL).[3] Rarely, some cases (around 5%) of leukemias have been designated biphenotypic or mixed phenotype acute leukemia (MPAL).[4,5] Twenty-five to thirty percent of newborns with leukemia have leukemia cutis, which is a direct infiltration of skin and subcutaneous tissue by malignant cells. Leukemia cutis usually occurs in patients with AML but may also be seen in ALL.[4] Herein, a newborn with congenital MPAL is reported and an association between *in vitro* fertilization (IVF) and congenital leukemia is suggested.

2. Case Report

A 10-day-old female newborn was referred to our hospital owing to the appearance of blue-violaceous dermal nodules on her body at birth. The patient was the product of an uneventful pregnancy induced by IVF because of primary infertility. She was born by cesarean section following a 35-week pregnancy as a twin pair to a 24-year-old healthy mother and her unrelated 29-year-old healthy husband. Birth weight, length, and head circumference of the patient were between the 25th and 50th percentiles. Her brother was healthy. There was no history of maternal illness, malignancy, smoking, drug and alcohol use, exposure to X-rays or other known teratogens. It was learned that the mother had consumed just a small amount of tea, coffee, and cacao during pregnancy. Physical examination showed jaundice and multiple nonblanchable, firm, blue-violaceous dermal nodules, 3—10 mm in diameter, on her scalp, face, neck, chest, abdomen, back, buttocks, and extremities (Figure 1). The oral and ocular mucosa, palms, and soles were not affected. Petechiae/ecchymoses were absent. Liver and spleen were palpable 4 cm and 2 cm under the midclavicular line of the costa, respectively. No dysmorphic features were noted. Bilateral fundoscopic examination was normal. On the 6th day of hospitalization, peripheral facial nerve palsy was determined.

The initial complete blood count showed a white blood cell count of 10.200/mm^3, hemoglobin 12.2 g/dL, and a platelet count of 51.000/mm^3. A peripheral blood smear demonstrated circulating blasts (19%), while a bone marrow aspiration showed approximately 40% blasts of lymphoid lineage (Figure 2). Periodic acid Schiff and myeloperoxidase (MPO) stains were negative. Bone marrow flow cytometry showed surface cluster of differentiation 45 (CD45) 85.4%, CD3 62.8%, CD5 63.7%, and CD7 68.3%, while other markers [CD10, CD13, CD15, CD19, CD20, CD22, CD33, CD34, CD79a, CD117, terminal deoxynucleotidyl transferase (Tdt), and human leucocyte antigen-DR (HLA-DR)] were negative. A skin biopsy specimen demonstrated a dense papillary dermis and perivascular infiltrate composed of relatively uniform large neoplastic cells with round to oval nuclei, distinct nucleoli, and little basophilic cytoplasm. The epidermis was intact and a grenz zone was present under the epidermis. Dermal adnexes and subcutis were not involved. Immunohistochemistry of the skin biopsy specimen revealed myeloblastic infiltration with CD34 and MPO positive (Figure 3), whereas TdT/CD117/S-100 and CD1a were negative. The present patient was diagnosed with congenital mixed phenotype acute leukemia according to the World Health Organization (WHO) 2008 classification because CD3 was shown positive (by bone marrow flow cytometry, T-lymphoid lineage) and MPO was shown positive (by immunohistochemistry, myeloid lineage).[5] Cytogenetic analysis performed from a peripheral blood sample showed a normal female karyotype. There were no abnormalities in chromosome 21 or 11q23 region on 20 cells and five cells karyotyped, respectively. Fluorescence *in situ* hybridization (FISH) analysis was performed with an 11q23 region probe (LSI/MLL/DC/BAR-Vysis) and chromosome 7 (LSI/D7S522/CEP7-Vysis). The FISH results for translocations or deletions involving the *MLL* gene and for monosomy 7 or 7q deletions were negative. Serum transaminases and cranial magnetic resonance imaging were normal. Examination of cerebrospinal fluid cytology was free of malignant cells. Blood cultures and serum antibody titers against TORCH infections were negative. Total

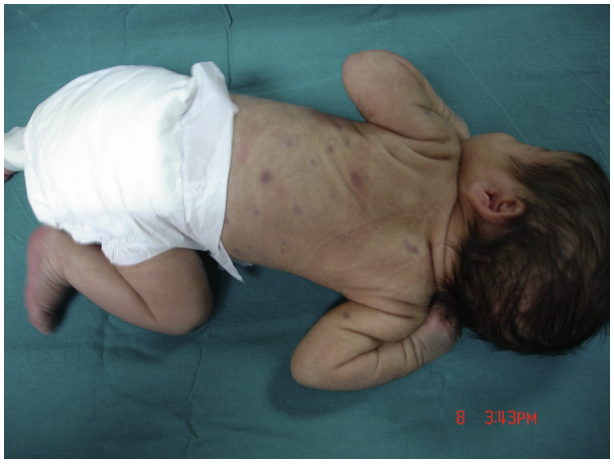

Figure 1 The appearance of dermal nodules.

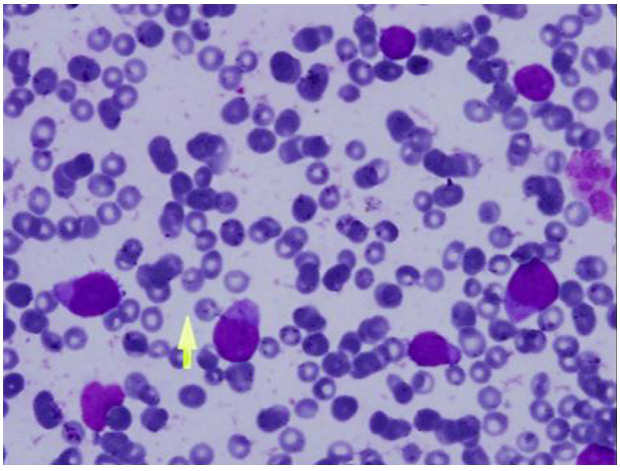

Figure 2 The bone marrow smear showing lymphoblastic cells (Wright's stain, 100×).