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Commentary

The Diagnosis of Congenital Mixed Phenotype Acute Leukemia

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DESCRIPTION

Congenital leukemia is a rare disease the majority of cases are Acute Myelogenous Leukemia (AML). Congenital Acute Lymphoblastic Leukemia (ALL) is rare and often of a B cell lineage. Some cases with biphenotypic or Mixed Phenotype Acute Leukemia have been identified (MPAL). We discuss the case of a preterm newborn that was referred to us due to the appearance of blue-violaceous cutaneous nodules on her body at birth. She was a twin produced thru *In Vitro* Fertilization (IVF). In addition to dermal nodules, a physical exam revealed jaundice, hepatosplenomegaly, and peripheral facial nerve palsy. Skin biopsy and immunohistochemistry revealed myeloblastic infiltration of the dermis; bone marrow aspiration revealed 40% blasts of lymphoid lineage. Cytogenetic analysis (46,XX), Fluorescence *In Situ* Hybridization (FISH), and cranial magnetic resonance were all normal. Congenital MPAL was diagnosed in the patient, and an association between IVF and congenital leukemia was suggested.

Congenital leukemia has an unknown cause. Several factors, however, may be associated with the onset of leukemia in the newborn period. These include maternal radiation exposure, high birth weight (>4000 g), high levels of insulin-like growth factors, and exposure to topoisomerase-II inhibitors such as coffee, tea, cocoa, wine, and soy products. The maternal consumption of tiny amounts of tea, coffee, and cacao during pregnancy, there were no leukemia-associated variables in this research. Congenital leukemia is characterized by nodular skin infiltrates, hepatosplenomegaly, lethargy, poor feeding, pallor, purpura/petechiae, and respiratory distress. The nodular skin infiltrates and hepatosplenomegaly were present in the patient. Congenital leukemia is differentiated by the proliferation of immature leucocytes, their infiltration into extra hematopoietic tissue, the absence of disease that can cause leukemoid or leucoerythroblastic reactions, such as congenital infection, ABO incompatibility, and the absence of chromosomal disorders associated with unstable hematopoiesis, such as trisomy 21. Three all of these criteria were met by the patient.

Leukemia cutis may be the first sign of congenital leukemia. As a result of infiltrating leukemic cells in the skin, it manifests as firm firm erythematous or blue-violaceous macules, papules, and nodules. It is estimated that 25-30% of patients may acquire leukemia cutis. These lesions are most commonly seen in AML; however they can also be seen in ALL. Lesions are typically many and distributed in a different pattern. Oral and ocular mucosa involvement is quite rare. Except for the oral/ocular mucosa, palms, and soles, our patient's body was covered in blue-violaceous skin nodules. Although there have been a few cases of spontaneous remission, congenital leukemia has a poor prognosis. Clinical characteristics and overall survival were not found to be significantly different when congenital AML and ALL were compared. Only after a few days of chemotherapy, our patient died.

Acute leukemia's are classified to use a combination of morphology and cytochemical staining. The cells are usually myeloid or lymphoid in origin. In about 5% of cases, however, a single blast population coexpresses myeloid and lymphoid antigens. Acute biphenotypic leukemia, hybrid or mixed lineage leukemia are the terms used to refer to these cases. Bi-lineage leukemia is defined as the occurrence of two distinct lineages of leukemic cells in the same patient at the same time. This type of leukemia, formerly designated as "bi-lineal acute leukemia" and "biphenotypic acute leukemia", is now collectively considered to be "mixed phenotype acute leukemia". The present study discovered CD3 positive for T-lymphoid lineage by bone marrow flow cytometry and MPO positive for myeloid lineage by immunohistochemistry of skin biopsy specimen in patient.

According to the WHO 2008 classification, the present patient has MPAL. To the knowledge of this is the first case of congenital MPAL in the literature. Congenital leukemia is characterized by chromosomal instability. MLL, which encodes a 431-kDa protein, is the most commonly involved gene in infant leukemia. The most common MLL translocations are t(4;11) and t(11;19) in ALL, and t(9;11), t(6;11), and t(11;19) in AML. There were no deletions or translocations (LSI/MLL/DC/BAR-Vysis) or monozomy 7 and 7q deletions (LSI/D7S522/CEP7-Vysis) in our patient. Although IVF is not thought to be associated with an increased risk of juvenile malignancies, some cases of neuro ectodermal tumors (neuroblastoma and medulloblastoma), embryonal cancers, and

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others have been recorded (hepatoblastoma and renal clear cell sarcoma),and retinoblastoma resulting from IVF have been reported. Enhanced ovulation and spermatogenesis caused by various hormonal treatments, manipulations of germ cells and the produced ovum, and pregnancy preservation by progestational hormones are all carcinogenic in these pregnancies. In the presented patient, who had no environmental, prenatal, or familial risk factors, a possible link between IVF and congenital cancer may be suggested. To conclude, skin nodules in a newborn may be a presenting sign of malignancy, and these newborns should be evaluated as soon as possible using laboratory studies, peripheral blood smear, bone marrow aspiration, serologies, cytogenetics, and skin biopsy.