Fetal Distress as a Presenting Symptom of Acute Leukemia During Pregnancy

Gil Shechter-Maor*; Martin Ellis; Rivka Sukenik-Halevy; Shmuel Inbar; Merav Sharvit; Tal Biron-Shental

*Gil Shechter-Maor
Department of Obstetrics and Gynecology, Meir Medical Center, Kfar Saba, Israel
Tel: 972-5283-62331. Email: gilshec@gmail.com

Abstract
The diagnosis is complicated by overlapping disease and gestation-related symptoms.

Here we describe a 37-year-old patient who was diagnosed at 26 weeks gestation with acute myelocytic leukemia which presented with shoulder and neck pains, elevated liver enzymes, thrombocytopenia and non-reassuring fetal heart rate required an emergency cesarean delivery. The maternal side of the placenta and the placental site on the endometrium were covered with small macroscopic hemorrhages.

Given the lack of data in the literature regarding presenting symptoms of acute leukemia in pregnancy, we believe that this case report provides important clinical information for practitioners.

Keywords
Acute leukemia; Pregnancy

Introduction

Acute leukemia in pregnancy is rare and poses risks to both the mother and the fetus. The incidence of acute leukemia is approximately 1 per 10,000 pregnancies [1, 2] and therefore data regarding presenting features of leukemia during gestation are limited to case reports. Acute myelogenous leukemia is more common than acute lymphoblastic leukemia in pregnancy, mirroring its increased frequency in adults generally [3]. The incidence of acute leukemia is equally distributed between the trimesters [3, 4].

The diagnosis is complicated by overlapping disease and gestation-related symptoms and the limited performance of imaging studies in pregnancy [2]. Acute leukemia may cause leukostasis, thrombosis, and disseminated intravascular coagulation [5, 6].

Given the acute and severe nature of the disease and regardless of the gestational age at the time of the diagnosis, immediate treatment is indicated to improve maternal and fetal outcomes [7].

The management of acute leukemia in pregnancy is complex and requires a multidisciplinary approach in order to provide appropriate obstetric and hematologic care for the mother, and obstetric and neonatal care for the fetus. [8]. Pregnancy does not affect the course of acute leukemia which has the
same prognosis in pregnant women and non-pregnant patients [Jane Blood 2014].

In the first trimester, termination of pregnancy should be discussed because of the potential fetal consequences of chemotherapy. Chemotherapy treatment during the second or third trimester may not require termination of pregnancy, because remission of acute leukemia and delivery of a normal infant are likely to be obtained [6].

There is limited published information regarding the effects of leukemia on the fetus and placenta and the presenting symptoms of acute leukemia in pregnancy.

In this paper we report on a patient with acute myeloblastic leukemia presenting at 26 weeks gestation.

Case Report

A 37 year old pregnant woman presented to our obstetric emergency room with acute musculoskeletal pain in her right shoulder, neck and right lower chest. Her medical history was unremarkable. She was at 26 weeks gestation of her third pregnancy with normal prenatal care. She had previously had two uneventful pregnancies and had spontaneous vaginal deliveries of two healthy children.

She had presented to the emergency room a month earlier with the same complains. Physical examination and fetal examination at that time was normal as was a complete blood count. She was treated with non-steroidal anti-inflammator agents.

On current admission blood pressure was 105/67 mmHg and she was a-febrile. Her $O_2$ saturation was 100%. She had tenderness of her right shoulder and neck. Her uterus was soft and non-tender and she did not have peritoneal signs. She was connected to fetal heart rate was monitor and blood was drawn for complete blood count, creatinine, liver enzymes, amylase and coagulation workup (PT, PTT, Fibrinogen).

The differential diagnosis included: Atypical preeclampsia with pain originating in the liver capsule, intra-abdominal bleeding, cholecystitis and a musculoskeletal origin (a strained muscle).

The monitor did not detect any contractions. The fetal heart rate had a baseline of 140 beats per minute with repeated variable decelerations which were defined as category II. Fetal ultrasound demonstrated an anterior intact placenta, a fetus in a vertex presentation with a normal pulse but with reduced body movements and tone. No free peri-hepatic fluid was detected, ruling out intra-abdominal bleeding or rupture of the liver capsule. Vaginal examination revealed a closed cervix.

Due to the repeated decelerations and the decreased biophysical profile, she was treated with Betamethasone to improve fetal lung maturity in anticipation of delivery.

Laboratory testing revealed: 24 000 leukocytes blasts present on the blood smear, hemoglobin was 10 g/dL and the platelet count was 48 000/µL. The fibrinogen was decreased at 164mg/dL. A diagnosis of attenuated HELLP syndrome was considered but the normal blood pressure and the blasts in the peripheral blood did not support HELLP.

Within an hour, late decelerations appeared with reduced variability. No fetal movements were detected on repeat ultrasound examination. The decision was made to deliver the baby via an emergency
cesarean section.

The surgery was uneventful. A baby boy was delivered, weighed 760gr, corresponded with 19th percentile for the gestational week, with Apgar scores of four at the age of one minute and eight at five minutes. Cord blood pH was 7.05 with base excess -10.4mM/L. Intravascular microthrombi were visible on the maternal side of the placenta and on the placental bed on the uterus (Figure 1, 2).

Placental pathology revealed distal villous hypoplasia, luminal and mural thrombi in chorionic and stem villi vessels and small retro-placental hematomas with signs of organization. The decidual vessels were markedly congested. Some immature hematopoietic cells were found between the placental villi.

The blood smear was diagnostic for acute leukemia and on flow cytometry myeloid markers were present on the blasts, confirming a diagnosis of acute myelogenous leukemia. Molecular examination of a bone marrow aspirate specimen revealed a characteristic mutation in the FLT3 gene and lack of mutation in the NPM gene. Cytogenetic analysis of the bone marrow was normal. This combination of findings confers an adverse prognosis.

Three days post delivery induction chemotherapy for leukemia was begun. Treatment was uneventful and the patient achieved a complete remission. Because of her adverse prognosis she then underwent an allogeneic stem cell transplant from a sibling donor. The procedure was uncomplicated and she remains in complete remission.

The neonate continues to receive supportive care for delayed development in the neonatal intensive care unit three months after birth.

Discussion

Little has been published regarding the presentation of acute leukemia in pregnancy. Most of the available data regarding leukemia in pregnancy focus on chemotherapy and its influence on fetal and maternal outcomes.

About half of the women treated with chemotherapy, usually during the second and third trimester achieved remission and the other half either relapsed or died from progression of the disease. Some of the infants were born with few adverse outcomes including transient pancytopenia and respiratory distress [2, 4, 10].

Since treatment is urgent and mandatory in acute leukemia and outweighs related complications, chemotherapy is not considered a contra-indication and is given to pregnant women with acute leukemia. Treatments' results are similar to those of the non-pregnant population [2, 4, 10].

Although placental metastases are rare, some reports have demonstrated trans-placental cancer transmission [11, 12, 13]. Histological examinations of the placenta and the umbilical cord should be performed to assess leukemic cell infiltration. In our case, immature hematopoietic cells were found between the placental villi. These findings reflect maternal blood transfusion to the placenta and to the fetus and as such it is not surprising that myeloblasts were found in placental villi as well as in the neonatal vessels. The presence of blasts in neonatal vessels has been described [1, 4, 12]. They spontaneously disappear within few days and do not reflect fetal metastases. The placental findings in
the current case reflect similar phenomena and were not consistent with metastases. However, the findings of intravascular micro thrombi on the maternal side of the placenta and on the placental bed in the uterus were unexpected and might explain the presentation of suspected fetal distress by fetal heart rate monitoring as well as by the decreased fetal movements.

Our case highlights the difficulty of the diagnosis of hematological malignancies during pregnancy because the clinical presentation is with symptoms which are common in an otherwise normal pregnancy. The typical presentation of patients with acute leukemia is backache because of lytic lesions in the bones [17]. Our patient’s pain was located in neck, shoulder and chest and suggested a differential diagnosis that is characteristic for pregnancy complications such as atypical HELLP syndrome, but also cholecystitis, a referred pain from the diaphragm that is irritated by intra-abdominal bleeding [18] and musculoskeletal pain.

Post-partum hemorrhage and coagulopathies were previously described as presenting events of acute Leukemia [14, 15, 16]. However in our case, despite the hypofibrinogenemia and thrombocytopenia, there was no major bleeding before the delivery and during the cesarean section.

Our case demonstrates the need for a high index of suspicion. Maternal fetal medicine is characterized by treating both the mother and the fetus. Their interests are not always the same, and therefore decisions sometimes must be taken prior to completing maternal evaluation. For example, as a response to fetal distress that happened in our case. Physicians should always remember to complete maternal evaluation and think of a wide differential diagnosis to avoid missing important conclusions.

**Figures**

![Figure 1](image_url)

**Figure 1:** The uterine wall at the placental bed site
References


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Authors Information: Gil Shechter-Maor1,2; Martin Ellis1,3; Rivka Sukenik-Halevy1,2; Shmuel Inbar1,2; Merav Sharvit1,2; Tal Biron-Shental1,2
1Department of Obstetrics and Gynecology, Meir Medical Center, Kfar Saba, Israel
2Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
3Hematology Institute, Meir Medical Center, Kfar Saba, Israel

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