Open Journal of
Clinical & Medical
Case Reports

Volume 2 (2016)
Issue 2

ISSN 2379-1039

Fetal Distress as a Presenting Symptom of Acute Leukemia During Pregnancy

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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-inflammatory 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

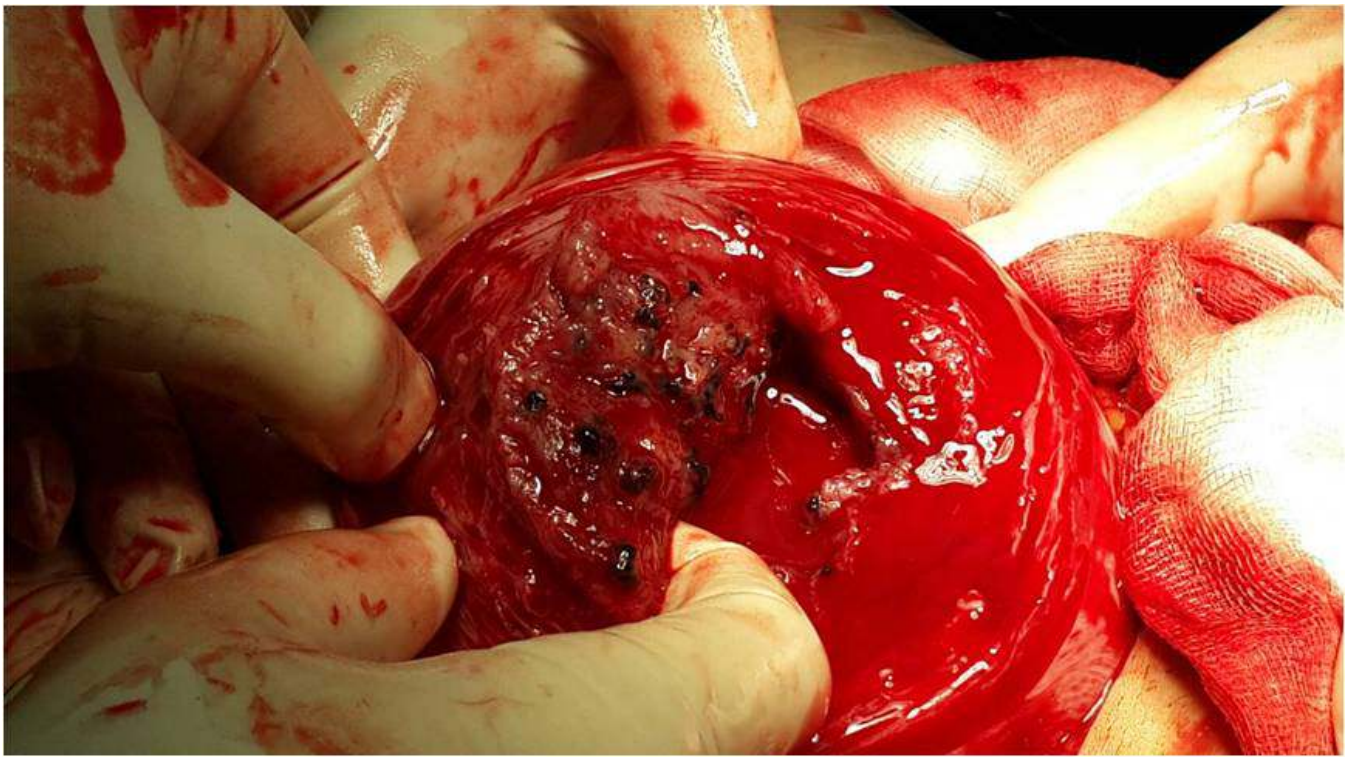

Figure 1: The uterine wall at the placental bed site

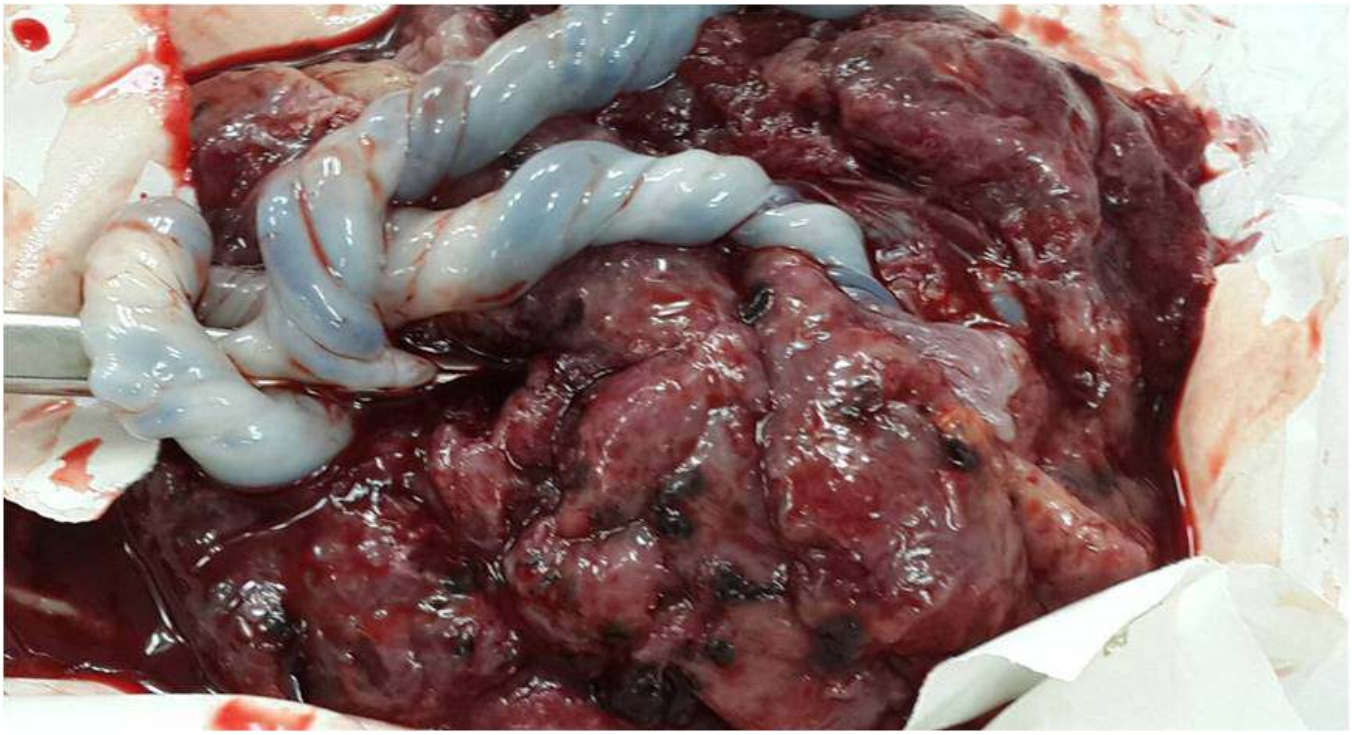

Figure 2: The placenta – Maternal surface

References

1. Shapira T, Pereg D, Lishner M. How I treat acute and chronic leukemia in pregnancy. Blood Rev. 2008;22(5):247-59.

2. Brenner B, Avivi I, Lishner M. Haematological cancers in pregnancy. Lancet 2012;11;379(9815):580-7.

3. Pavlidis NA. Coexistence of pregnancy and malignancy. Oncologist 2002; 7: 279–87.

4. Nakajima Y, Hattori Y, Ito S, Ohshima R, Kuwabara H, Machida S, et al. Acute leukemia during pregnancy: an investigative survey of the past 11years. Int J Lab Hematol. 2014 May 21. doi: 10.1111/ijlh.12256. [Epub ahead of print]

5. Davis SM, Branch DW. Thromboprophylaxis in pregnancy: who and how? Obstet Gynecol Clin North Am 2010; 37: 333–43.

6. Chelghoum Y, Vey N, Raff oux E. Acute leukemia during pregnancy: a report on 37 patients and a review of the literature. Cancer 2005; 104: 110–17.

7. Rizack T1, Mega A, Legare R, Castillo J. Management of hematological malignancies during pregnancy. Am J Hematol. 2009;84(12):830-41.

8. El-Hemaidi I1, Robinson SE. Management of haematological malignancy in pregnancy. Best Pract Res Clin Obstet Gynaecol 2012;26(1):149-60.

9. Milojkovic D, Apperley JF. How I treat leukemia during pregnancy. Blood 2014;123(7) 974-84.

10. Terek, M., Ozkinay, E., Zekioglu, O., Erhan, Y.,Cagirgan, S., Pehlivan, M. et al. (2003) Acute leukemia in pregnancy with ovarian metastasis: acase report and review of the literature. Int J Gynecol Cancer 13: 904–908.

11. Schamberger S, Weber M, Backsch C, Sonnemann J, Markert UR. Establishment of a one-sided *ex vivo* human placenta perfusion model to assess adhesion and invasion behavior of T cell leukemia cell lines. Leuk Lymphoma 2013;54:1811–3.

12. Yagasaki H, Ohashi H, Ito M, Kobayashi S, Kato M, Shichino H et al.. A novel mechanism of transplacental cancer transmission: natural killer/T-cell lymphoma in the paratesticular region is of maternal origin. Blood 2011;117:6046–7.

13. Isoda T, Ford AM, Tomizawa D, Delft FW, Castro DG, Mitsuiki N, et al. Immunologically silent cancer clone transmission from mother to offspring. Proc Natl Acad Sci USA 2009;106:17882–5.

14. Patni S Roberts S, Ashraf M, Wright AM. Acute leukaemia in pregnancy-an unusual presentation. J Obstet Gynecol. 2004 Nov;24(8):930.

15. Lee WL, Wang PH. Major postpartum hemorrhage as an initial presentation of acute myeloid leukemia.Int J Gynaecol Obstet. 1999;66(2):173-4.

16. Vadher BD, Machin SJ, Patterson KG, Sukhu C, Walker H. Life-threatening thrombotic and haemorrhagic problems associated with silent myeloproliferative disorders. Br J Haematol. 1993;85(1):213-6.

17. Bhardwaj A, Nagandla K. Musculoskeletal symptoms and orthopaedic complications in pregnancy: pathophysiology, diagnostic approaches and modern management. Postgrad Med J. 2014 Jun 5.

18. Lenihan M, Krawczyk A, Canavan C. Shoulder-tip pain as an indicator of uterine rupture with a functioning epidural. Int J Obstet Anesth. 2012 Apr;21(2):200-1.

Manuscript Information: Received: December 07, 2015; Accepted: January 22, 2016; Published: January 23, 2016

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Citation: Shechter-Maor G, Ellis M, Sukenik-Halevy R, Inbar S, Sharvit M, Biron-Shental T. Fetal distress as a presenting symptom of acute leukemia during pregnancy. Open J Clin Med Case Rep. 2016; 1070