

# A case of acute myeloid leukemia during pregnancy presenting as acute appendicitis

Liese Boudry, Sandrina Lambrechts, Françoise Lacquet, Romaric Croes, Kathleen Scharpé

## ABSTRACT

**Introduction:** The incidence of pregnancy associated leukemia is approximately one in 75,000 to 100,000 pregnancies. The majority of leukemias diagnosed during pregnancy are acute. Of these acute leukemias, two-thirds are myeloid. Early and prompt diagnosis is challenging, hence unspecific symptoms such as fatigue, dyspnea or weakness are easily attributed to the physiological changes during pregnancy. **Case Report:** A case of a 33 weeks pregnant female, presenting with abdominal pain. During an emergency cesarean section performed for fetal distress, the appendix presented swollen and an appendectomy was performed. The diagnosis of acute leukemia was made, based on the laboratory findings showing thrombocytopenia, anemia and leukocytosis with a high percentage of circulating blasts in the peripheral blood. Microscopy of the appendix showed inflammation with an

abnormal infiltration of blasts. The patient was referred to a tertiary center and treated for acute myeloid leukemia (AML). She died due to relapse 16 months after the initial diagnosis. **Conclusion:** AML during pregnancy is rare. Appendicitis being its first presentation is very uncommon. After taking care of initial concerns regarding the fetal well-being, chemotherapeutic treatment has to be commenced as soon as possible, in order to obtain the best chances of survival for the mother.

**Keywords:** Leukemia, Pregnancy, Appendicitis, Fetal distress

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Liese Boudry<sup>1</sup>, Sandrina Lambrechts<sup>2</sup>, Françoise Lacquet<sup>3</sup>, Romaric Croes<sup>4</sup>, Kathleen Scharpé<sup>5</sup>

**Affiliations:** <sup>1</sup>Specialty Registrar, Department of Obstetrics and Gynecology, Algemeen Ziekenhuis Sint Blasius, Dendermonde, Belgium; <sup>2</sup>Gynecologist, Department of Oncology, University Hospitals Leuven, Leuven, Belgium; <sup>3</sup>Clinical biologist, Laboratory Medicine, Department of Hematology, Algemeen Ziekenhuis Sint Blasius, Dendermonde, Belgium; <sup>4</sup>Pathologist, Department of Pathology, Algemeen Ziekenhuis Sint Blasius, Dendermonde, Belgium; <sup>5</sup>Gynecologist, Department of Obstetrics and Gynecology, Algemeen Ziekenhuis Sint Blasius, Dendermonde, Belgium.

**Corresponding Author:** Liese Boudry, AZ St. Blasius, Department of Obstetrics and Gynecology, Kroonveldlaan 50, 9200 Dendermonde; Ph: +32 472 65 27 47; E-mail: liese-boudry@gmail.com

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## INTRODUCTION

The association of leukemia and pregnancy is uncommon. Its prevalence is based on estimates and seems to be approximately one in 75,000 to 100,000 pregnancies. The majority of acute leukemias are of myeloid lineage, as lymphoblastic leukemia is more common in childhood and adolescence [1]. Acute myeloid leukemia (AML) is characterized by an excessive proliferation of immature myeloid cells resulting in hematopoietic insufficiency [2]. Most symptoms are

related to complications of the pancytopenia, such as infections or hemorrhagic diathesis. Early diagnosis is challenging, since the initial symptoms of leukemia can be misleading and easily attributed to physiological changes related to the pregnancy. We report a case of acute appendicitis due to involvement by acute leukemia in a pregnant patient. This presentation is extremely rare, though being aware of this possibility is important in the prompt diagnosis and management.

## CASE REPORT

A 23-year-old pregnant female presented at 33 weeks gestation with right sided abdominal pain, reduced fetal movements and vomiting. She was afebrile and there were no signs of active labor - vaginal examination showed no dilation of the cervix. Cardiotocography revealed tachycardia and a reduced variability. Obstetric ultrasound showed a fetus in cephalic position, a right lateral placenta and a normal amount of amniotic fluid.

The clinical presentation was not entirely fitting, but placental abruption carried the highest suspicion, so an emergency cesarean section was performed. A healthy girl of 2078 g was born. There were no signs of abruption, so the exact cause of the acute abdominal pain remained unknown. After exploration of the abdomen, eventually an appendectomy was performed, since the appendix was relatively swollen, though not particularly red or inflamed.

A complete blood count revealed a normochromic normocytic anemia, thrombocytopenia and leukocytosis. By further examination of the peripheral blood smear, a leukoerythroblastic formula was noted and the presence of an important blast population (86%) (Figure 1). A routine blood sample taken six weeks earlier, was perfectly normal. Upon history and morphologic characteristics, the early diagnosis of de novo AML was made (Table 1).

Postoperative, the patient was referred to a tertiary oncologic center. Further analysis confirmed the presence of AML based on bone marrow morphology, flow cytometry and biopsy. Definitive diagnosis of AML M2 (FAB classification) or AML with maturation (WHO 2008) was made. Waiting for stabilization and wound healing, alternative cytotoxic therapy was started (Hydroxyurea). One week later, she underwent standard chemotherapy and an allogeneic bone marrow transplant, but 16 months later she died due to relapse.

The child was admitted to the NICU with respiratory distress and an initial unilateral, but subsequent bilateral pneumothorax. She recovered well and is currently five-year-old and healthy.

Retrospective review of the pathology of the appendix revealed infiltration of the mucosa and submucosa by blasts (CD34 positive on immunohistochemistry). There was no extensive neutrophil infiltration, diagnostic for acute, exudative appendicitis. Thorough retrospective microscopic examination of the placenta showed no evidence of AML.

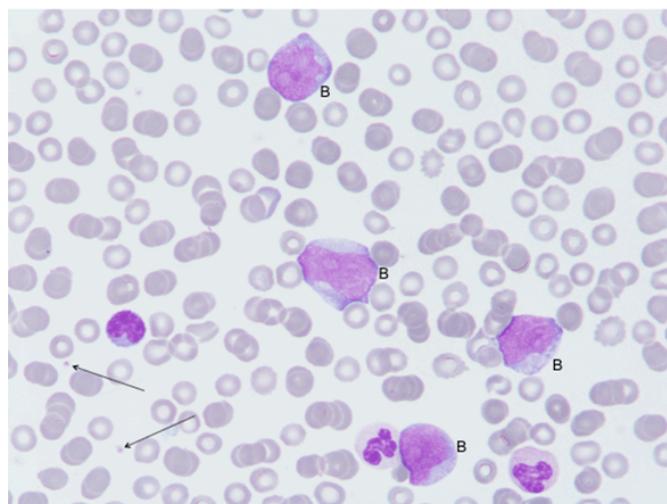


Figure 1: Peripheral blood smear. Blasts (B) are medium to large cells with a large nucleus. The nuclear chromatin pattern shows immature features and 1 or 2 nucleoles can be distinguished. One mature lymphocyte can be seen (left) and 2 mature granulocytes (right under).

Only very few thrombocytes are visible (arrow)

Table 1: Laboratory findings

	Hb (g/dL)	WBC ( $10^3/\mu\text{L}$ )	PLT ( $10^3/\mu\text{L}$ )
03-02-2010	12.2	10.6	264
08-04-2010	11.3	8.2	279
20-05-2010	11.1	46.3	32
21-05-2010	10.0	37.2	33

Abbreviations: Abbreviations: Hb (Hemoglobine), WBC (white blood cells), PLT (platelets)

## DISCUSSION

Acute appendicitis as the initial manifestation of AML is extremely rare and has only been described in three non-pregnant patients [3–5]. Early symptoms of acute leukemia, such as fatigue, pallor, weakness and dyspnea are non-specific and often attributed to the pregnancy. Anemia and thrombocytopenia can be falsely blamed on the pregnancy, thus resulting in a delay of diagnosis. Whilst these are relatively common findings in pregnancy, neutropenia is more rare and merits further investigation. The presence of circulating blasts in a blood film, suggesting a hematological malignancy, is an indication for a bone marrow biopsy. However, as in the presented case, fetal distress can limit the time available for accurate diagnostics. Suspected causes of fetal distress include maternal anemia, disseminated intravascular coagulation and leukemic cells affecting the placental transport and exchange of nutrients and oxygen [6].

Treatment of acute leukemia is urgent and induction therapy should be administered as soon as possible,

considering the aggressive nature of this condition. The main treatment for acute leukemia is chemotherapy. When diagnosed in the first trimester, elective termination of pregnancy is reasonable, regarding the high risk of spontaneous miscarriage, serious fetal malformations and fetal death as a result of the chemotherapeutic treatment. However, current evidence suggests that in utero exposure to anticancer treatments in the second and third trimester does not significantly increase the fetal morbidity or mortality [7]. Therefore, premature delivery to enable adequate treatment is not always necessary, and treatment delays may compromise maternal outcome without favorably influencing the neonatal condition. However, the timing of the administration of chemotherapy is important, in order to avoid induced pancytopenia immediately prior to delivery. Therefore, it should not be given after 35 weeks of gestation, because spontaneous delivery is increasingly likely to occur, before the bone marrow is recovered. The time gap also allows the fetal system to eliminate the drugs before delivery, which is especially important in preterm babies whose abilities to metabolize drugs is limited [6].

The decision on the timing and the mode of delivery in patients with acute leukemia is based primarily on the gestational age and the fetal wellbeing. In any case, planned delivery is easier to manage than spontaneous labor. The goal is a vaginal delivery, because of the lower risks of infection and the faster recovery. Elective cesarean section is only indicated for obstetric reasons. Considering anesthesiology, the cytopenia has to be taken in account for both vaginal delivery and cesarean section. Epidural analgesia should be avoided in women with significant thrombocytopenia or neutropenia, because of the risk of hematoma and infection. Alternatives, such as systemic opioids should be considered. For the same reason, especially after surgery, prophylactic antibiotic treatment is advisable. Following delivery, appropriate AML therapy should be commenced or continued as soon as feasible.

The reported fetal loss for chronic and acute leukemia is 20%, presumably mainly due to the disease, rather than to the associated therapy [8]. The same consideration can be made for the reported fetal distress and prematurity during therapy for acute leukemia.

In the past, pregnancy was thought to have a negative impact on the progress of leukemia, but current data suggest a similar prognosis for women treated during pregnancy and age-matched non-pregnant patients [9].

Appendectomy is the treatment of choice for appendicitis in pregnant patients. Whereas the same applies for leukemic patients, correct diagnosis and management of the leukemia has a greater impact on the overall survival [10]. Both (perforated) appendicitis and appendectomy during pregnancy are associated with a high risk of premature delivery [11].

Compared to the three prior case reports of appendicitis with leukemic cell infiltration, our patient

was the youngest and survived the longest. Being the youngest, she probably was the strongest and therefore survived longer.

Placental metastases are exceedingly rare. Of all maternal malignancies, melanoma is the most common culprit. The risk factors of cancer in the newborn are unknown. In all pregnant women with a history of a malignancy, a thorough histological examination of the placenta is required. Close follow-up of the infant is recommended, especially in cases of proven placental involvement, although specific recommendations are lacking. Anyhow, in every patient with recent diagnosis of a malignancy, a maternal and neonatal blood sample has to be taken, in search of circulating tumor cells [12].

## CONCLUSION

We report a unique case of appendicitis in a pregnant patient as a result of acute myeloid leukemia (AML). Due to fetal distress on initial presentation, delivery could not be postponed in this case. Treatment of acute leukemia during pregnancy ordinarily poses quite a challenge. Each case should be studied individually, weighing the aggressiveness of the disease and the likelihood of a cure. Both mother and unborn child have to be carefully considered and a multidisciplinary approach is required.

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## Author Contributions

Liese Boudry – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published

Sandrina Lambrechts – Analysis and interpretation of data, Critical revision of the article, Final approval of the version to be published

Françoise Lacquet – Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Romarc Croes – Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Kathleen Scharpé – Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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