Splenic rupture in a pregnant woman as the debut of chronic myeloid leukemia

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Abstract

Chronic myeloid leukemia (CML) during pregnancy is rare and entails significant maternal and fetal risks. We present an unusual case of chronic phase CML that debuted with massive splenomegaly and splenic rupture in a 30-week pregnant woman. During the debut, the patient developed abdominal pain, hemoperitoneum, and acute fetal distress, requiring an emergency splenectomy and Cesarean section. This challenging picture demanded an interdisciplinary approach involving hematology, obstetrics and surgery. After overcoming the initial emergency, a deep molecular response was achieved with imatinib. This case is unique in illustrating the exceptional presentation of CML during pregnancy, with early splenic rupture. It highlights the therapeutic challenges in balancing the maternal-fetal risks, the usefulness of tyrosine kinase inhibitors during advanced pregnancy and the need for close communication between specialties to optimize the outcomes in complex clinical situations. (Acta Med Colomb 2024; 49. DOI: https://doi.org/10.36104/amc.2024.3063).

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Introduction

Chronic myeloid leukemia (CML) is a chronic myeloproliferative neoplasm characterized by the presence of the Philadelphia chromosome or reciprocal translocation between chromosomes 9 and 22, which produces the BCR-ABL fusion gene. This gene codes for a constitutively active tyrosine kinase that promotes cellular proliferation and inhibits apoptosis, leading to the development of CML (1, 2).

Chronic myeloid leukemia accounts for 15-20% of all leukemias. Its global incidence is estimated at 1 to 2 cases per 100,000 inhabitants per year, being more frequent between the ages of 30 and 40, with a median age at diagnosis of 57 years (3, 4). Chronic myeloid leukemia during pregnancy is rare, with an estimated incidence of one case per 75,000-100,000 pregnancies (5). Although pregnancy does not worsen the course of CML, the disease can affect placental circulation and fetal development, due to leukostasis. Treatment during pregnancy is complicated due to the potentially teratogenic effect of tyrosine kinase inhibitors (TKIs) like imatinib and dasatinib. Interferon alpha would be the safest option, as it does not inhibit DNA synthesis or cross the placenta (6), with leukapheresis being a complementary alternative in the event of symptomatic leukostasis or a very high leukocyte count (7).

Massive splenomegaly, defined as a spleen length of more than 20 cm or weight greater than 1,000 g, is a common complication in patients with CML, with a prevalence of up to 60% (8). During pregnancy, massive splenomegaly poses various risks, both maternal and fetal. In the mother, it increases the possibility of vascular steal syndrome of the pregnant uterus, thrombocytopenia, anemia and splenic infarction, as well as a higher risk of premature birth or abortion. In the fetus, it is associated with intrauterine growth restriction, respiratory distress and fetal death. A serious complication is splenic rupture, with an incidence of up to 1% in the third trimester, that manifests as acute abdominal pain due to hemoperitoneum, with severe hypotension, and has 75% maternal and 95% fetal mortality. Treatment is emergency splenectomy, ideally before total rupture, which is a highly lethal catastrophic complication (9).

This report describes the complexity of treating a pregnant patient in her third trimester who debuted with CML complicated by massive splenomegaly and subsequent splenic rupture. This unusual case tested the interdisciplinary communication capacity of our medical team, demanding delicate deliberations to balance the maternal and fetal risks involved. Resolving this challenging clinical picture displayed our expertise in the comprehensive care of the mother-child dyad, optimizing their wellbeing in the context of a serious hematological disease during advanced pregnancy.

Case report

We present the case of a patient in her thirties from Huaura, Peru. No prior medical history was recorded, but she did have an obstetric history of multiparity (G5 P3 C0 V3 A1 E0 M0). At the time of diagnosis, the patient was in active gestation, with 30 weeks confirmed by a first-trimester ultrasound, having had a total of seven regular prenatal visits, all without complications.

She was admitted to the emergency room with a week-long history of moderate, stabbing left upper quadrant abdominal pain which did not radiate, and was associated with generalized weakness. During the three days prior to admission, the patient had three episodes of nausea and vomiting, with no other warning signs related to her gynecological-obstetric status.

On her admission physical exam, she had mild pain with deep palpation of the left upper quadrant. A palpable spleen was found 10 cm below the left costal margin, with no signs of peritoneal irritation. The fundal height was 27 cm, with fetal movements present. No uterine activity was noted, and vaginal discharge was negative. Laboratory tests showed moderate anemia (hemoglobin: 10.2 g/dL), thrombocytosis (platelets: 853,000/mm^3) and hyperleukocytosis (leukocytes: 256,000/mm^3) with 44% blasts, 13% myelocytes, 4% metamyelocytes and 4% basophils, according to the automated complete blood count. Coagulation, kidney function and liver function profiles were within normal limits. Fetal wellbeing was preserved.

After a detailed evaluation by the hematology service, the possibility of accelerated phase CML was proposed. Preventive measures to avoid leukostasis were suggested, and early pregnancy termination was considered. A bone marrow biopsy showed 90% cellularity, with myeloid precursor hyperplasia, suggesting chronic myeloproliferative syndrome. Flow cytometry confirmed the presence of chronic-phase CML, with expression of CD45+, CD34-, HLA-DR ++, CD38++, CD7-, CD117-, and CD11b-. The diagnosis was confirmed with a molecular panel that identified the presence of the BCR/ABL p210 fusion gene (Sokal Index: 0.9 points, classified as intermediate risk).

The patient began treatment with 400 mg of oral imatinib every 24 hours, along with 100 mg of oral allopurinol every eight hours until her eventual discharge.

During her first days of hospitalization, the patient was clinically stable. However, after the seventh day, her condition worsened. She developed tachycardia, increased stabbing pain in the left upper quadrant, and dyspnea with oxygen saturation (SaO_2) reduced to 88%, which required supplementary oxygen via nasal cannula with an FiO_2 of 32% (SaO_2 93%). At the same time, her hemoglobin progressively decreased. The obstetric evaluation indicated acute fetal distress. In response to this situation, she was taken to surgery, where an estimated hemoperitoneum of 500 cc was found. She required urgent general surgery with an exploratory laparotomy. During the intervention, a hemoperitoneum of approximately 2,000 cc was found along with an approximately 12 cm rupture of the anterior splenic capsule (Figure 1), with active bleeding (Figure 2). The patient underwent a splenectomy, and two laminar drains were placed in the left iliac fossa. A Cesarean resulted in the birth of a healthy male infant at 31 weeks gestation, with no complications. Four units of packed red blood cells were transfused due to an estimated 3,000 cc blood loss during surgery. The patient was then transferred to the special care unit for monitoring.

In the postoperative period, the patient had febrile episodes on day 12, due to a hematoma in the anterior abdominal wall (1,200 cc volume) and persistent intra-abdominal collections (total volume of 100 cc). Broad-spectrum antibiotic treatment was started with 1 g of intravenous imipenem every eight hours and 1 g of intravenous vancomycin every eight hours. The patient's platelet count gradually increased, improving with no need for transfusions. In addition, the total leukocyte count decreased with the oral cytoreduction therapy mentioned previously.

After 12 days of broad-spectrum antibiotic treatment, the volume of the intra-abdominal collections decreased to 40 cc, and the abdominal wall hematoma decreased to 450 cc. The patient progressed favorably and was discharged after 33 days of hospitalization, with clinical and laboratory improvement.

The patient was followed as an outpatient by the hematology service. A complete blood count drawn two months after discharge showed a complete hematological response (Table 1). After 12 months of treatment with 400 mg of oral imatinib every 24 hours and 100 mg of oral allopurinol every eight hours, an adequate molecular response was not achieved (considering 9.54% BCR/ABL p210 detected, corresponding to treatment failure), and therefore she was switched to 70 mg of oral dasatinib every 12 hours. After 30 days on this new treatment regimen, there was a greater molecular response (0.5% BCR/ABL p210 detected). To date, the patient continues to have a good response to treatment and maintains a high quality of life.

Discussion

This study describes an exceptional clinical case of chronic myeloid leukemia (CML) in a pregnant woman, which debuted with acute splenic rupture, a rare and highly challenging clinical scenario.

Chronic myeloid leukemia during pregnancy is an uncommon clinical situation, with an estimated incidence of one case per 75,000-100,000 pregnancies (10). While the course of CML does not appear to worsen with pregnancy, significant rates of obstetric complications, like intrauterine growth restriction (19.3%), premature birth (17.5%), miscarriage (12.3%) and fetal demise (3.5%), have been reported in previous case series (11). Massive splenomegaly occurs in up to 60% of patients with CML,

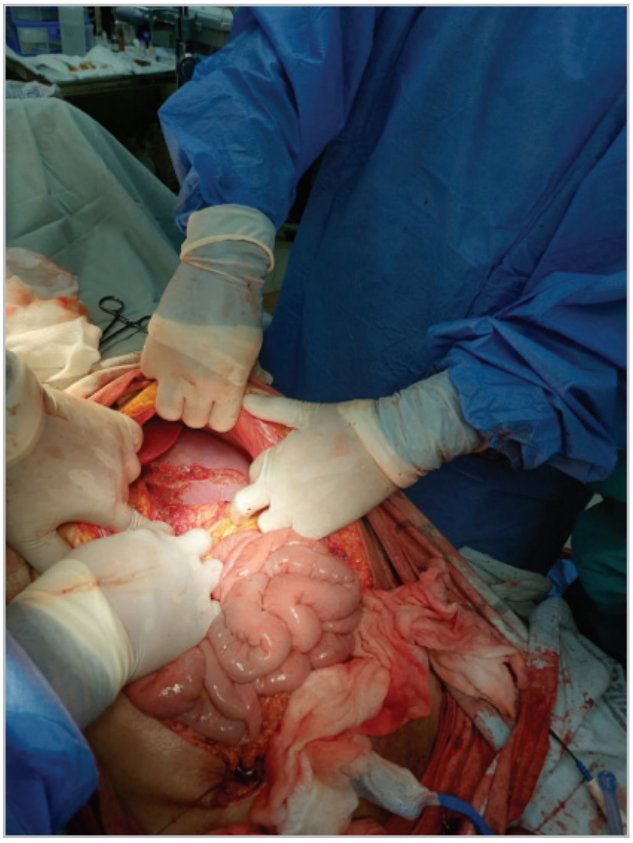

Figure 1. *Intraoperative findings. Figure 1 shows the intra-operative findings during the patient's exploratory laparotomy. The open abdomen can be seen, exposing the left upper quadrant. The lower edge of the spleen is visible, showing an approximately 12 cm laceration involving the entire width of the splenic parenchyma. This complete splenic rupture is associated with moderate hemoperitoneum, secondary to active bleeding from the site of the lesion. The image shows the severe anatomical involvement resulting from splenic rupture in the context of massive splenomegaly associated with chronic myeloid leukemia during advanced pregnancy.*

Figure 2. *Surgical specimen. Figure 2 shows the surgical specimen corresponding to the entire spleen after emergency splenectomy. Marked splenomegaly can be seen, measuring 30 x 20 x 10 cm. The smooth, shiny capsule is intact except at the lower pole, where a 12 cm-long laceration with jagged edges can be seen, extending horizontally from side to side. The splenic parenchyma appears congestive, friable, and darkly purple. This macroscopic finding is consistent with the diagnosis of splenic rupture secondary to massive splenomegaly in the context of advanced chronic myeloid leukemia. The fragility of the splenic parenchyma infiltrated by the leukemic proliferative process explains the occurrence of this rare and potentially fatal complication.*

with the risk of uterine vascular steal, thrombocytopenia, anemia and splenic infarction. However, splenic rupture during pregnancy is extremely rare, with very few cases documented in the literature (12).

This report contributes the first published case, to our knowledge, of acute splenic rupture in the context of early chronic-phase gestational CML. The cause of such an early complication despite initially mild splenomegaly (15 cm) is unclear and merits further research. There may be hormonal and immunological factors associated with the pregnancy which can accelerate disease progression and splenic fragility.

Table 1. *The patient 's benchmarks and main results.*

Date	02/12/22	02/15/22	02/18/22	05/07/22	05/16/22	02/07/23	02/27/23	04/07/23
Benchmarks	**Admission**	**Diagnosis and imatinib initiation**	**Admission to OR**	**Complete hematological response**	**Third month follow up**	**Twelfth month follow up Treatment failure**	**Beginning of dasatinib**	**Greater molecular response**
Hemoglobin	9	8.2	7.6	12.1			11.6	
Leukocytes	319,070	270,200	305,020	4,060			6,460	
Platelets	559,000	580,000	688,000	310,000			279,000	
BCR/ABL p190		Not detected						
BCR/ABL p210		Detected			9.49%	9.54%		0.05%
Karyotype		46,XX (100%)						

The case also highlights the therapeutic complexities of gestational CML, where caution due to possible adverse fetal effects of the tyrosine-kinase inhibitors (TKIs) led to an initially conservative approach, despite marked leukocytosis. This probably contributed to the development of massive splenomegaly which ultimately required emergency splenectomy. Future studies should determine the efficacy and safety of low-dose second or third generation TKIs in advanced pregnancy, to prevent accelerated progression as seen in this case.

One unresolved point is the long-term effect of fetal exposure to hydroxyurea and imatinib during brief periods in the initial stages of pregnancy. It would be useful to conduct long-term pediatric follow-up of these children.

Finally, this case emphasizes the importance of a close interdisciplinary approach between hematology, obstetrics and surgery, to optimize the maternal-fetal results in challenging clinical situations. Effective communication and decision-making, carefully balancing the risks and benefits, were essential in the successful treatment of this patient.

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