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Pregnancy and Severe Bone Marrow Aplasia Diagnosed at Age 17: A Case Report and Literature Review

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Abstract **Case Report**

Aplastic anemia is a rare and potentially fetal hematological disorder characterized by bone marrow failure leading to peripheral pancytopenia and hypocellular bone marrow. Pregnancy in a woman with severe aplastic anemia is an exceptional clinical situation, exposing the mother to hemorrhagic, infectious, and anemic complications, and the fetus to an increased risk of intrauterine growth restriction, prematurity, premature rupture of membranes, and fetal death. We report the case of a 21-year-old woman, followed for severe bone marrow aplasia diagnosed at the age of 17, and pregnant at 37 weeks and 6 days, and discuss the diagnostic, therapeutic and obstetrical difficulties in light of recent data from the literature.

Keywords: Severe bone marrow aplasia; high-risk pregnancy; pancytopenia; thrombocytopenia; anemia; neutropenia; obstetric complications; multidisciplinary management; immunosuppression; eltrombopag; transfusion; maternal -fetal prognosis.

INTRODUCTION

Bone marrow aplasia is a bone marrow failure characterized by marked bone marrow hypocellularity and altered production of erythroid, myeloid and megakaryocytic cell lineages. It therefore manifests clinically as anemia, neutropenia and thrombocytopenia of varying severity [1].

Acquired bone marrow aplasia is rare, with an estimated incidence of approximately 1 to 2 cases per million inhabitants per year in Western countries. Its pathogenesis is most often of immune origin and involves the destruction or suppression of hematopoietic stem and progenitor cells by abnormal T lymphocyte responses [1,2].

Bone marrow aplasia associated with pregnancy is rare. The causal link between pregnancy and the onset or worsening of bone marrow aplasia remains controversial. However, pregnancy can be associated with worsening cytopenias in some women with pre-existing disease [3,4]. Pregnancy in a woman with bone marrow aplasia is particularly complex because maternal health and fetal development must be managed simultaneously. The main maternal risks include severe anemia, bleeding related to thrombocytopenia, and infections related to neutropenia, while fetal risks include intrauterine growth restriction, prematurity, premature rupture of membranes, and fetal death [3-5].

Recent literature highlights the importance of individualized care and close multidisciplinary monitoring. Supportive transfusion therapy, infection prevention, careful obstetric monitoring, and coordination between hematology, obstetrics, anesthesiology, transfusion medicine, and neonatology teams are essential [3-5].

The objective of this report is to present a case of pregnancy in a 21-year-old woman followed since the age of 17 for severe bone marrow aplasia and to discuss the diagnostic, therapeutic and obstetric considerations associated with this rare condition.

CLINICAL OBSERVATION

This is a 21-year-old patient, G1P1, followed since the age of 17 for severe bone marrow aplasia,

diagnosed due to persistent pancytopenia associated with bone marrow hypoplasia.

The initial diagnosis was made at age 17 due to anemic symptoms. The complete blood count showed a hemoglobin level of 4 g/ dL, a white blood cell count of 1600/µL, a neutrophil count of 740/µL, and a platelet count of 19×10^9/L. Bone marrow aspiration and biopsy revealed severe bone marrow hypoplasia, without tumor infiltration or myelofibrosis, consistent with the diagnosis of severe bone marrow aplasia.

An etiological investigation had been carried out in search of an acquired or constitutional cause, without evidence of an associated etiology.

The patient had received treatment combining transfusion support, antilymphocyte serum (ALS), cyclosporine (Neoral), and eltrombopag (Revolade), with a favorable clinical and hematological outcome. Regular hematological monitoring had been ensured.

The current pregnancy was spontaneous and was diagnosed at 12 weeks of amenorrhea. Given the context of severe bone marrow aplasia, the pregnancy was managed by a multidisciplinary team involving obstetricians, hematologists, anesthesiologists, and the transfusion medicine team.

On admission, the patient was conscious and hemodynamically stable. Her blood pressure was 115/75 mmHg and her heart rate was 90 beats per minute. Clinical examination revealed conjunctival and palmar pallor. The remainder of the physical examination was unremarkable.

The laboratory tests carried out on admission revealed severe anemia with a hemoglobin level of 6 g/ dL, leukopenia at 1750/µL, neutropenia with a neutrophil count of 764/µL and severe thrombocytopenia at 20.5×10^9/L. The hemostasis assessment as well as renal and hepatic functions were normal.

The obstetric assessment performed at 32 weeks of amenorrhea revealed a viable pregnancy, with fetal biometry consistent with gestational age. The amount of amniotic fluid was normal, and Doppler ultrasound of the umbilical and middle cerebral arteries showed no abnormalities.

maternal -fetal monitoring had been initiated, including regular checks of complete blood count, clinical monitoring for infectious and hemorrhagic complications, as well as serial ultrasound monitoring of fetal growth.

The pregnancy had progressed favorably until 37 weeks and 6 days of amenorrhea. Labor began spontaneously, and delivery was vaginal. A transfusion preparation had been arranged in advance, with compatible red blood cell and platelet concentrates made available.

The mother's condition had been favorable, with no hemorrhagic, infectious, or thromboembolic complications. The male newborn weighed 2,987 g at birth and had an Apgar score of 10/10 at 1, 5, and 10 minutes. The postpartum period was uneventful, with no maternal or neonatal complications reported.

DISCUSSION

This case illustrates the complexity of pregnancy in a patient with severe bone marrow aplasia in adolescence. This association remains rare and exposes the patient to an increased risk of maternal and fetal complications, primarily due to anemia, thrombocytopenia, neutropenia, and their hemorrhagic and infectious consequences. The evolution of the aplasia during pregnancy is one of the main challenges in managing this condition.

Pregnancy-associated bone marrow aplasia is a rare condition whose pathophysiological relationship with gestation remains uncertain. Physiological hematological changes related to pregnancy can further complicate the interpretation of laboratory results and delay the diagnosis of severe cytopenias. Jaime-Pérez et al. analyzed published cases of pregnancy-associated aplastic anemia and highlighted the diagnostic and therapeutic difficulties inherent in this condition [4].

Early data in the literature reported a poor maternal prognosis, with hemorrhage and infection being the main causes of morbidity and mortality [3,4]. More recent data, however, reveal an improvement in prognosis, probably linked to advances in supportive care, transfusion strategies, anti-infective management, and the organization of multidisciplinary obstetric care [3-5]. Nevertheless, a recent systematic review and meta-analysis confirm that pregnancy complicated by aplastic anemia remains associated with significant maternal and fetal morbidity [5].

From a diagnostic standpoint, the physiological hematological changes of pregnancy can mask or delay the recognition of severe cytopenia. Jaime-Pérez et al. have highlighted the particular diagnostic and therapeutic difficulties of aplastic anemia associated with pregnancy [4]. From an obstetric and anesthetic point of view, severe thrombocytopenia, profound anemia, the risk of infection and especially the risk of hemorrhage require rigorous preparation for delivery and close coordination between the obstetrics, hematology, anesthesia and transfusion medicine teams [3].

The distinction between pre-existing aplasia and pregnancy-specific aplasia is also important. A recent retrospective study of 54 women and 65 pregnancies reported a live birth rate of 88% in patients

with pre-existing aplasia, but severe maternal or fetal complications in 47% of pregnancies [6]. Active disease before delivery, as well as lower hemoglobin and platelet levels, were associated with adverse outcomes. These findings support the importance of clinical and hematological stabilization of the disease before conception whenever possible.

In adolescents and young adults with aplastic anemia, the search for an underlying constitutional syndrome of bone marrow failure is of particular importance. Current guidelines emphasize the need for appropriate evaluation for hereditary bone marrow failure, especially in young patients, before any definitive treatment decision is made [2,7]. This approach not only helps to clarify the etiology of the bone marrow failure, but also to guide the treatment strategy and anticipate long-term implications, particularly regarding genetic counseling.

The treatment of severe aplastic anemia must be individualized according to the severity of the disease, the patient's age, the availability of a compatible donor, and the response to previous treatments. In selected young patients, allogeneic hematopoietic stem cell transplantation is a potentially curative option, particularly when a compatible donor is available [2,7]. However, this procedure cannot generally be performed during pregnancy, necessitating careful evaluation of the optimal timing. The case reported by Abdel-Azim et al. illustrates this issue: a young woman with severe aplastic anemia during pregnancy was subsequently able to undergo a bone marrow transplant with a favorable outcome, demonstrating that definitive hematopoietic treatment may remain a viable option after pregnancy for some patients [8].

The fundamental principle of managing a pregnancy complicated by severe bone marrow aplasia rests on anticipation and multidisciplinary coordination. This must include regular monitoring of the three hematopoietic lineages, prevention and early management of infectious complications, regular assessment of fetal growth and well-being, and meticulous preparation for delivery. Particular attention must be paid to the risk of hemorrhage, with anticipation of transfusion needs and, when possible, limitation of alloimmunization. The choice of the mode and timing of delivery must be individualized according to the patient's hematological status and obstetric indications, in a center with the necessary expertise in hematology, obstetrics, anesthesia, transfusion, and neonatology [2,3,7].

Maternal and fetal prognosis depends primarily on the severity of aplasia, including the degree of anemia, thrombocytopenia, and neutropenia, as well as the response to treatment and the occurrence of hemorrhagic or infectious complications. In the retrospective study by Wu *et al.,* active aplastic anemia before delivery was strongly associated with the occurrence of maternal and fetal complications. However, no maternal mortality or neonatal hematological abnormalities were recorded in their cohort, suggesting that improved care and appropriate multidisciplinary management could contribute to improving the prognosis [6].

Ultimately, pregnancy in a patient with aplastic anemia remains a high-risk situation requiring individualized assessment and close monitoring. Whenever possible, pregnancy should be considered when the disease is clinically and hematologically stable, following a complete hematological workup and a multidisciplinary discussion to evaluate maternal and fetal risks, therapeutic options, and the obstetric plan. Such an approach, based on anticipating complications and coordinating between different specialties, is essential for optimizing maternal and neonatal outcomes.

CONCLUSION

Pregnancy in a patient with severe aplastic anemia is a rare and likely high-risk situation requiring individualized and multidisciplinary management. Our case highlights the importance of early collaboration between obstetricians, hematologists, anesthesiologists, transfusion medicine specialists, and neonatologists. Close clinical and laboratory monitoring is essential, particularly of the three hematopoietic cell lines, with special attention to hemorrhagic and infectious risks, while fetal growth and well-being must be regularly assessed. In the absence of obstetric contraindications, vaginal delivery can be considered, but the method and timing of delivery must be tailored to each patient based on her hematological status and obstetric indications. Rigorous transfusion preparation is essential given the risk of postpartum hemorrhage and potential peripartum complications. In young patients with severe aplastic anemia, it is also important to investigate for any underlying constitutional syndrome of bone marrow failure and to plan definitive treatment strategies, including allogeneic hematopoietic stem cell transplantation when indicated. Ideally, pregnancy should be considered after stabilization of the hematological malignancy and after specialist hematology consultation. Despite advances in symptomatic and curative treatments, severe aplastic anemia during pregnancy remains associated with significant maternal and fetal morbidity and should therefore be managed in a center with specialized expertise in hematology and obstetrics.

Conflicts of interest

The authors declare no conflict of interest.

Author contributions

All authors contributed to the writing of this manuscript. All authors have read and approved the final version of the manuscript.

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