

Severe aplastic anemia and pregnancy: case report

Summary

Introduction: Aplastic anemia is a hematological disorder often aggravated by pregnancy. The pathophysiology of the occurrence of this disease during pregnancy remains unknown. There is no consensus on optimal care. The interest of the question lies in the rarity of occurrence of aplastic anemia during pregnancy.

Observation: We report the case of a 29-year-old woman at 31 weeks of amenorrhea, with no particular medical history. Our patient had an anemic syndrome 10 days before her admission; associated with a fever at 39°C. Clinical and para-clinical investigations confirmed the diagnosis of aplastic anemia. The pregnancy has been completed thanks to supportive care and multidisciplinary interventions, with a good maternal and fetal evolution. Our patient was treated by Cyclosporine after delivery; the breastfeeding was stopped during treatment. The maternal outcome was good. We noted a decrease in transfusion needs within 4 months after delivery.

Conclusion: The morbidity and mortality associated with aplastic anemia at pregnancy is high. Management is multidisciplinary (obstetrician, hematologist, and resuscitator).

Keywords: aplastic anemia, pregnancy, prognosis, treatment, delivery, amenorrhea, abnormal cell proliferation, fibrosis, normochromic normocytic anemia, leukopenia, thrombocytopenia

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Introduction

Medullary aplasia (AM) is a serious and rare disease characterized by quantitative bone marrow failure secondary to the complete or partial disappearance of hematopoietic tissue, without abnormal cell proliferation or fibrosis. It results in a rarefaction of the bone marrow responsible for pancytopenia (normochromic normocytic anemia, leukopenia and thrombocytopenia).¹ There are moderate and more severe forms of AM, which may be genetic (AM constitutional), environmental (AM acquired) or idiopathic (origin unknown: 70%).² The incidence of bone marrow suppression is 2 cases per million inhabitants per year in Europe.¹ Its occurrence during pregnancy is rarely described in the literature.³ The severity of this disease is due to the risk of life-threatening maternal-fetal complications (20 to 30% maternal mortality).³ The pathophysiology of medullary aplasia is complex. Its appearance during pregnancy is poorly explained.⁴ It poses a problem of care, of which there is no consensus and must be multidisciplinary.

Case report

Our patient was 29 years old, with no particular pathological history of 1geste /1 parity pregnant at 31 weeks of amenorrhea (pregnancy not regularly followed), who had an anemic syndrome (asthenia with palmar mucocutaneous paleness) evolving for 10 days, associated with a fever at 39°C. The clinical examination showed a syndrome of marrow failure made of anemic, haemorrhagic, and infectious syndrome with fever at 39°C. The rest of the somatic examination was normal, with no tumor syndrome. The haemogram showed a normochromic normocytic arterogenic anemia, with 6g/dl (average blood volume: 85 fl., Hemoglobin content hemoglobin: 28pg), leukopenia $1.5 \times 10^3/\text{mm}^3$, (with neutrophils at: $0.35 \times 10^3/\text{mm}^3$ and Lymphocytes at: $1.1 \times 10^3/\text{mm}^3$), thrombocytopenia at $15 \times 10^3/\text{mm}^3$. The reticulocyte level was $20000/\text{mm}^3$. The myelogram was poor. A bone marrow biopsy confirmed the diagnosis of aplastic anemia. The etiological assessment was also normal (HCV viral serologies, HBV, HIV, immune status, HPN clone: nocturnal paroxysmal haemoglobinuria). The radiological assessment did not show any

particularities (chest X-ray and abdominal ultrasound), the rest of the biological assessment was negative (in particular the renal balance and liver assessment). The patient was transfused with phenotypic red blood cells and platelet units (hemoglobin was maintained at a level above 90 g/L, platelet count $>20 \times 10^3/\text{mm}^3$, to prevent the serious consequences of thrombocytopenia and anemia on the mother and fetus). Third-generation cephalosporin antibiotic therapy was initiated during infectious episodes.

Fetal monitoring was based on obstetrical ultrasound and fetal doppler, and prevention of fetal immaturity with corticosteroids was instituted. At the 37th week of amenorrhea, the patient was hospitalized for delivery. Her hemoglobin concentration was maintained above 100 g/L and her platelet concentration was greater than $50 \times 10^3/\text{mm}^3$ by transfusion. She gave birth vaginally to a female child of normal weight and Apgar score at 10/10. During immediate postpartum, there was no haemorrhage of delivery or infection. The patient received intensive care monitoring and was discharged after one week. Specific cyclosporin-based treatment was initiated postpartum, breastfeeding was discontinued. The evolution was marked by the reduction of transfusion needs in the 4 months following the delivery.

Discussion

According to the epidemiological data of the literature, nearly 134 cases of medullary aplasia associated with pregnancy are reported, the first was described in 1888 by Ehlich whose evolution was marked by maternal death. Etiologically speaking, and in parallel with our observation, more than 70% of cases of bone marrow suppression are idiopathic. Only one case following Fanconi disease has been reported by Flavia et al⁵ A pregnancy on AM complicated by nocturnal paroxysmal hemoglobinuria PN has also been described in the literature. Pathophysiologically, medullary aplasia involves intrinsic factors (genetic alterations of hematopoietic stem cells), and extrinsic (immunological disorders T-dependent lymphocytes, cytotoxic agents, radiation ...).^{6,7} Her relationship with pregnancy is poorly understood: several authors claim that there is an obvious link. However, some support the hypothesis of its association with

AM, given the regression of some cases after delivery, and relapse in subsequent pregnancies.⁸ Hormonal factors seem to be implicated in this context, including an imbalance between the action of estrogen (inhibiting erythropoiesis), erythropoietin (stimulating erythropoiesis) and placental lactogen.⁸ In addition, several studies have described the role of sex hormones in triggering immune responses. Several evolutionary profiles are reported in the literature.³ As is the case with our observation, the progress of a pregnancy associated with AM may be normal, provided a good multidisciplinary follow-up involving the obstetrician, the hematologist and the resuscitator.³

However, the evolution can be marked by complications including maternal death. Mortality often occurs in a septic or hemorrhagic shock table that is refractory to treatment.⁹ In a 25-year retrospective study, Kuan-ju et al. found that the main obstetric complications caused by AM include prematurity, intrauterine growth retardation, premature rupture of membranes, and pre-eclampsia. They also described poor prognosis factors: severe anemia, platelet count below 20 G/L, bone marrow hypocellularity <25%, and late diagnosis. Some authors propose the medical termination of pregnancy in the early diagnosis of AM, in order to avoid these complications.^{10,11} There are two components to AM management: symptomatic treatment based on transfusion of red blood cells and platelet pellets, and management of infectious episodes; and curative treatment (immunosuppressants, hematopoietic stem cell allograft, hematopoietic and androgenic FDCs). Supportive care remains the first-line treatment for pregnant women. Evolution is conditioned by good monitoring. The transfusion objectives are: hemoglobinemia greater than 80g/L; a platelet count higher than 20 G/L, in order to ensure normal fetal growth, and to prevent hemorrhagic accidents. Globular pellets must be phenotyped, leukored and compatible in the rhesus and kell system. For platelet pellets, HLA compatibility is required.

The management of infectious episodes by broad-spectrum ATBs is also crucial.¹⁰ Immunosuppressive agents and hematopoietic stem cell transplantation (HSC) provide survival in more than 75% of spinal aplasia cases. Their place in curative treatment during pregnancy is controversial. Most authors insist on their formal contraindication given the risk of fetal toxicity,^{10,11} others indicate their use in cases of failure of support measures.¹² Androgen is an alternative to immunosuppressive therapy, it improves the platelet count in 37% of cases. However, its use during pregnancy exposes to the risk of virilization of the female fetus.¹³ The efficacy of corticosteroids or granulocyte growth factors (G-CSF) is also discussed.^{3,10} In parallel with our observation, Geier et al demonstrated that vaginal delivery is often devoid of complications. The indication for cesarean section is guided by obstetric reasons. It is also discussed according to platelet count and the severity of anemia.³ Corticosteroid therapy can be maintained in combination with transfusion. Doses should be increased near term, at the beginning of work and in the immediate post partum.

Conclusion

The association of aplastic anemia with pregnancy is a rare and serious situation. The risk of commitment of maternal-fetal prognosis is the fear of practitioners. The reference treatment is based on well codified support measures.

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Conflicts of interest

The author declares there is no conflict of interest.

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