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Acute myeloblastic leukemia discovered in the 3rd trimester of pregnancy

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Abstract

Acute leukemia (AL) rarely occurs during pregnancy. Its incidence is estimated at 1/100 000 pregnancies. In 2/3 of the cases, it is acute myeloblastic leukemia (AML). The dilemma is between chemotherapy which should not be delayed for a better therapeutic prognosis and a foetus at risk of malformation or morbidity and mortality by induced prematurity. We report the observation of a 25-year-old patient in whom we diagnosed AML occurring during a pregnancy at 35 weeks of amenorrhea, and who benefited from obstetrical management then chemotherapy.

Keywords: Pregnancy, acute myeloid leukemia, Acute Myeloblastic Leukemia protocol, chemotherapy

Abbreviations: AL: Acute leukemia, AML : Acute Myeloid Leukemia, ALL: Acute Lymphoblastic Leukemia, ATO: Arsenic trioxide, APL: Acute promyelocytic leukemia, DIC: Disseminated Intravascular Coagulopathy

Introduction

Acute leukemia (AL) is a group of a malignant blood disease characterized by clonal expansion in the bone marrow of blood cell precursors blocked at an early stage of their differentiation, the blasts. There are two main types: Acute Myeloid Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL). The incidence of leukemia increases dramatically with age and peaks at 80-85 years of age **[1]**. Although elderly patients are at high risk for AL, the disease can also be seen in women of childbearing age. The incidence of leukemia in pregnancy is 1 in 75,000 to 100,000 pregnancies **[2,3]**. During pregnancy, some of the early features of AL, such as fatigue and shortness of breath, or changes in blood counts, anemi,a and thrombocytopenia, may be interpreted as pregnancy-related symptoms, resulting in delayed diagnosis and inappropriate treatment **[4]**. If not treated immediately, the disease affects both maternal and fetal prognosis. In addition, delaying induction chemotherapy negatively impacts the likelihood of remission **[5]**. We report the observation of a 25-year-old patient in whom we diagnosed AML occurring during a pregnancy listed in our training.

Observation:

This is a 25-year-old patient, G2P2, with no particular pathological history pregnant at 35 weeks of amenorrhea who has presented for two weeks a syndrome of complete bone marrow failure on the biological assessment.

The clinical examination revealed a mucocutaneous pallor, a blood pressure of 120/60 mm Hg, a negative urine dipstick and a patient not in labor. There were no Hemorrhagic or infectious syndromes. A complete blood count showed a hemoglobin of 8.6 g/dL, VGM: 96 fl., CCMH: 35.5 g/dl; platelets: 134,000/mm3, leukocytes: 1700/mm3 with 8% of PNN or 136/mm3 and 74% of lymphocytes or 1258/mm3, with pancytopenia in the blood smear. A myelogram was performed confirming the diagnosis of acute myeloid leukemia with a normal karyotype. **(Figure 1)** The rest of the biological workup was unremarkable, especially the hemostasis workup.

The patient had neither clinical nor biological signs of lysis syndrome.

The course of action was to ensure biological monitoring every three days, to administer prenatal corticosteroid therapy and to plan extraction at 36 days' gestation by cesarean section under cover of transfusion of red blood cells and platelets. This will give birth to a healthy male infant. The cesarean section and the postoperative follow-up were uneventful.

Induction chemotherapy with Aracytine 100mg/m2 for 7 days and Daunorubicin: 12 mg/m2 for 3 days according to protocol AML03 allowed a complete remission of the disease. The patient received 2 consolidation courses followed by a maintenance treatment. After a 6-month follow-up, the patient is still in complete remission.

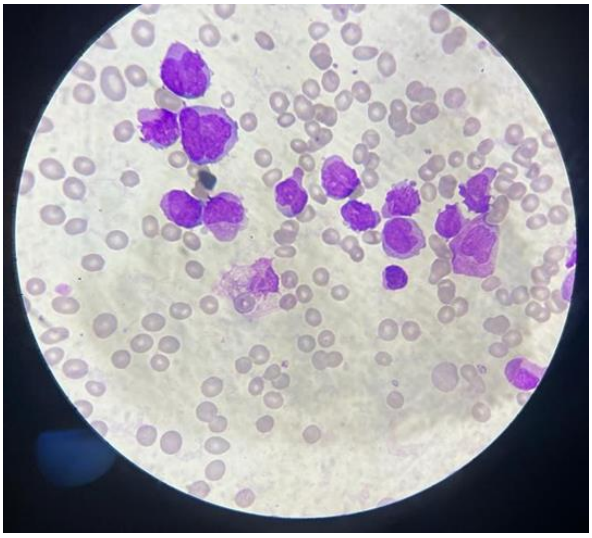

Figure 1: Microscopic aspect of the myelogram

Discussion

Since the first publication by Virchow in 1845 **[6]**, just over 400 cases of acute leukemia in pregnancy have been published. Two-thirds are represented by acute myeloblastic leukemia and the diagnosis is usually made in the second and third trimester, however, it may be delayed due to non-specific symptoms and signs of leukemia, such as weakness, fatigue, pallor, and difficulty breathing, which can be attributed to pregnancy **[7]**. AML requires treatment to be initiated as soon as possible, as the short-term prognosis is life-threatening, so any delay or change in treatment for fetal salvage is likely to increase the maternal mortality rate. Pregnancy does not seem to have an influence on the evolution of AML. Indeed, survival and remission rates are comparable to those of non-pregnant women. There is no evidence that pregnancy worsens the prognosis of leukemia **[8]**.

The timing of chemotherapy initiation is still controversial. It is essential that the treatment is not delayed to allow fetal maturation. If AML occurs in the first trimester, the chances of a successful pregnancy are low; with significant teratogenic risks from chemotherapy, it is therefore generally advisable to consider medical termination of the pregnancy rather than allowing spontaneous abortion during a potentially thrombocytopenic or coagulopathic phase. When AML is diagnosed in the second or third trimester, chemotherapy may not require termination of the pregnancy. It can be successfully administered and should be started without any delay as in the non-pregnant population, since the

risks of malformation are minimal and delay in treatment may compromise the remission rate without improving fetal prognosis **[9]**. Greenlund LJ et al. reported that the mortality rate of patients who chose to delay treatment was significantly higher than those who did not **[10]**. However, a meta-analysis showed no significant difference between chemotherapy during pregnancy and chemotherapy after pregnancy in terms of remission rates **[11]**. In addition, we believe that delayed treatment may be well tolerated in patients with relatively stable disease. In addition, Barnes et al. confirmed that chemotherapy cannot be delayed in aggressive a malignant blood disease because of the fatal risk to the mother and fetus secondary to disease progression **[12]**. Also, Wang et al. demonstrated that receiving low-dose chemotherapy during pregnancy may reduce the efficacy of induction therapy and the survival rate of these patients, but hematopoietic stem cell transplantation may improve the prognosis **[13]**.

In AML, the most commonly used protocol for patients diagnosed during pregnancy is the combination of Cytarabine and Antracyclines (Idarubicin, Doxorubicin). Antracyclines are essential in the treatment of LA. They are cardiotoxic to the fetus. Idarubicin is not recommended during pregnancy because it has a significant placental passage due to its lipophilic nature and affinity for DNA **[14]**. Doxorubicin seems to be the most widely used, and its use is relatively risk-free. It is rarely associated with serious congenital malformations **[15]**. Experience with Cytarabine in pregnancy is limited. It is an anti-metabolite known to be teratogenic according to clinical trials in animals **[7]**.

Acute promyelocytic leukemia (APL) poses the problem of disseminated intravascular coagulopathy (DIC), which may interfere with the management of the pregnancy. Its treatment is based on the administration of trans-retinoic acid (ATRA) associated with chemotherapy. However, ATRA is highly teratogenic and has also been associated with miscarriages in 40% of patients and its administration in the first trimester has resulted in approximately 14% of malformations **[16,17]**. In contrast, its administration in the second or third trimester may result in a high cure rate **[18]** and does not appear to increase the risk of fetal complicationsb**[19]**. Arsenic trioxide (ATO) is another effective drug for the treatment of APL, and its application has significantly improved the management of these patients over the past two decades **[20]**. However, ATO is highly toxic to the embryo and is contraindicated at all stages of pregnancy because of the increased risk of fetal malformations, intrauterine growth retardation, stillbirth, and spontaneous abortions **[21,22]**. Although the combination of ARTA and ATO is recommended for patients after pregnancy termination or delivery, it should be noted that breastfeeding is contraindicated in this setting.

The risk of malformation decreases with advancing pregnancy, so the therapeutic decision should take into consideration the age of the pregnancy and the aggressiveness of the AML. In practice, therapeutic termination of pregnancy can be discussed when AML is diagnosed early in pregnancy **[10]**. When therapeutic termination of pregnancy is not possible, the timing of fetal extraction should be determined in advance and treatment should be started as soon as possible (if possible after 20 days' gestation) **[4]**. However, in patients in good general condition, with stable disease, chemotherapy can be delayed by transfusion therapy until 30 weeks' gestation, allowing extraction of a viable child **[23]**. Chemotherapy can also be delayed, post-delivery, if the diagnosis of AML is made at the end of the third trimester of pregnancy **[24]**. If cytotoxic agents are administered during the second and third trimesters of pregnancy, pregnancy monitoring should be increased. At the end of the pregnancy, an induction can be organized if maternal management requires it. Antenatal corticosteroid therapy for fetal lung maturation may be prescribed. Careful coordination and good communication between the obstetrician-gynecologist and the hematologist are essential in planning delivery between cycles of chemotherapy to avoid neutropenic phases **[25]**.

Conclusion:

The association of AL and pregnancy is a rare event. It requires a multidisciplinary management taking into account the imperatives of the disease and its treatment, the woman and her desire for pregnancy. The use of chemotherapy during pregnancy is possible after 20 days' gestation. Pregnancy must be terminated before this date. The results of AML treatment during pregnancy compare favorably with those obtained in another situation, with the same intensity of treatment. There are still doubts about the future of the

children born from these pregnancies, given the small amount of data, which would justify the creation of a registry for long-term follow-up, which would make it possible to propose more appropriate therapies.

References:

1. Hao T, Li-Talley M, Buck A, Chen W. An emerging trend of rapid increase of leukemia but not all cancers in the aging population in the United States. Sci Rep. 2019;9(1):12070.
2. McGregor AK, Das-Gupta E. Acute myeloid leukaemia in pregnancy. Br J Haematol. 2015 Aug;170(4):441-2.
3. Abadi U, Koren G, Lishner M. Leukemia and Lymphoma in Pregnancy. Hematol Oncol Clin North Am. 2011;25(2):277-91.
4. Ganzitti L, Fachechi G, Driul L, Marchesoni D. Acute promyelocytic leukemia during pregnancy. Fertil Steril. 2010;94(6): 2330.e5-2330.e6.
5. Ali S, Jones GL, Culligan DJ, Marsden PJ, Russell N, Embleton ND, et al. Guidelines for the diagnosis and management of acute myeloid leukaemia in pregnancy. Br J Haematol. 2015;170(4):487-95.
6. Chelghoum Y, Vey N, Raffoux E, Huguet F, Pigneux A, Witz B, et al. Acute leukemia during pregnancy: A report on 37 patients and a review of the literature. Cancer. 2005;104(1):110-7.
7. Shapira T, Pereg D, Lishner M. How I treat acute and chronic leukemia in pregnancy. Blood Rev. 2008;22(5):247-59.
8. Brenner B, Avivi I, Lishner M. Haematological cancers in pregnancy. The Lancet. 2012;379(9815):580-7.
9. Abdel-Hady ES, Hemida RAH, Gamal A, El-Zafarany M, Toson E, El-Bayoumi MA. Cancer during pregnancy: perinatal outcome after in utero exposure to chemotherapy. Arch Gynecol Obstet. 2012;286(2):283-6.
10. Greenlund LJS, Letendre L, Tefferi A. Acute Leukemia during Pregnancy: A Single Institutional Experience with 17 Cases. Leuk Lymphoma. 2001;41(5-6):571-7.
11. Horowitz NA, Henig I, Henig O, Benyamini N, Vidal L, Avivi I. Acute myeloid leukemia during pregnancy: a systematic review and meta-analysis. Leuk Lymphoma. 2018 4;59(3):610-6.
12. Barnes M. Burkitt lymphoma in pregnancy. Obstet Gynecol. 1998;92(4):675-8.
13. Wang P, Yang Z, Shan M, Lu S, Zhang L, Li S, et al. Maternal and Fetal Outcomes of Acute Leukemia in Pregnancy: A Retrospective Study of 52 Patients. Front Oncol. 2021;11:803994.
14. Pereg D, Koren G, Lishner M. The treatment of Hodgkin's and non-Hodgkin's lymphoma in pregnancy. Haematologica. 2007;92(9):1230-7.
15. Avilés A, Neri N, Nambo MJ. Long-term evaluation of cardiac function in children who received anthracyclines during pregnancy. Ann Oncol Off J Eur Soc Med Oncol. 2006;17(2):286-8.
16. Weisz B, Meirow D, Schiff E, Lishner M. Impact and treatment of cancer during pregnancy. Expert Rev Anticancer Ther. 2004;4(5):889-902.
17. Yang D, Hladnik L. Treatment of acute promyelocytic leukemia during pregnancy. Pharmacotherapy. 2009;29(6):709-24.
18. Sanz MA, Montesinos P, Casale MF, Díaz-Mediavilla J, Jiménez S, Fernández I, et al. Maternal and fetal outcomes in pregnant women with acute promyelocytic leukemia. Ann Hematol. 2015;94(8):1357-61.
19. Verma V, Giri S, Manandhar S, Pathak R, Bhatt VR. Acute promyelocytic leukemia during pregnancy: a systematic analysis of outcome. Leuk Lymphoma. 2016;57(3):616-22.
20. Kayser S, Schlenk RF, Platzbecker U. Management of patients with acute promyelocytic leukemia. Leukemia. 2018;32(6):1277-94.
21. Sanz MA, Fenaux P, Tallman MS, Estey EH, Löwenberg B, Naoe T, et al. Management of acute promyelocytic leukemia: updated recommendations from an expert panel of the European LeukemiaNet. Blood. 2019;133(15):1630-43.
22. Naujokas MF, Anderson B, Ahsan H, Aposhian HV, Graziano JH, Thompson C, et al. The broad scope of

health effects from chronic arsenic exposure: update on a worldwide public health problem. Environ Health Perspect. 2013;121(3):295-302.

23. British Committee for Standards in Haematology, Milligan DW, Grimwade D, Cullis JO, Bond L, Swirsky D, et al. Guidelines on the management of acute myeloid leukaemia in adults. Br J Haematol. 2006;135(4):450-74.
24. Ali R, Ozkalemkas F, Kimya Y, Koksal N, Ozkocaman V, Yorulmaz H, et al. Pregnancy in chronic lymphocytic leukemia: experience with fetal exposure to chlorambucil. Leuk Res. 2009;33(4):567-9.
25. Merviel P. Cancer et grossesse: aspects obstétricaux. J Gynécologie Obstétrique Biol Reprod. 2004;33(1):15-22.