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Acute Myeloblastic Leukaemia and Pregnancy: Case Report

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1. Abstract

1.1. Introduction And Importance: Acute Leukaemias (AL) are a group of haematological malignancies characterised by the clonal expansion in the bone marrow of blocked blood cell precursors at an early stage of differentiation, the blasts. AL may be discovered during pregnancy, and some of the early features of AL, such as fatigue and shortness of breath, or changes in the blood count, such as anaemia and thrombocytopenia, may be interpreted as pregnancy-related symptoms, resulting in delayed diagnosis and inappropriate treatment. If not treated immediately, the disease is life-threatening for both mother and fetus.

1.2. Case Presentation: Our objective is to report a case of acute myeloblastic leukaemia during pregnancy and to analyse the clinical and biological characteristics and to evaluate the management modalities in order to improve the maternal-fetal prognosis. The patient had been presenting with a complete medullary insufficiency syndrome for a fortnight on biological examination

1.3. Clinical Discussion: Two thirds are acute myeloblastic leukaemia and diagnosis is usually made in the second and third trimester, however, it may be delayed due to non-specific symptoms and signs of leukaemia.

AML requires treatment as soon as possible as it is life threatening in the short term. Pregnancy does not seem to have an influence on the course 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 leukaemia. In AML, the most commonly used protocol for patients diagnosed during pregnancy is a combination of Cytarabine and Antracyclines.

1.4. Conclusion: The association AL and pregnancy is a rare event. It requires multidisciplinary care. The use of chemotherapy during pregnancy is possible after 20 weeks of gestation. Termination of pregnancy is compulsory before this date. The results of treatment of AML during pregnancy are closer to those obtained in other situations.

2. Introduction

Acute Leukaemia (AL) is a group of haematological malignancies characterised by clonal expansion in the bone marrow of blocked blood cell precursors at an early stage of differentiation, the blasts. There are two main types: Acute Myeloid Leukaemia (AML) and Acute Lymphoblastic Leukaemia (ALL). The incidence of leukaemia increases dramatically with age and peaks at 80-85 years [1]. Although elderly patients are at high risk of AML, the disease can also be seen in women of childbearing age. The incidence of leukaemia in pregnancy is 1 in 75,000 to 100,000 pregnancies [5]. During pregnancy, some of the early features of AL, such as fatigue and shortness of breath, or changes in the blood count, such as anaemia and thrombocytopenia, may be interpreted as pregnancy-related symptoms, leading to delayed diagnosis and inappropriate treatment. If not treated immediately, the disease is prognostic for both mother and fetus. In addition, delaying induction chemotherapy reduces the likelihood of remission [5]. We report below the observation of an AML occurring during a pregnancy admitted to the IBN ROCHD University Hospital of Casablanca. The aim of this article is to report a case of acute myeloblastic leukaemia in a patient of 35 weeks of amenorrhoea and to analyse the clinical and biological characteristics as well as the management. We ensure that the work was reported in accordance with the SCARE 2020 criteria [6].

3. Presentation of Case

This is a 25-year-old patient, 2nd gesture, 2nd pare, with no particular pathological history, pregnant at 35 weeks of amenorrhea

and one day, and had been presenting with a complete medullary insufficiency syndrome for a fortnight on biological examination. Patient was referred from a peripheral hospital accompanied by a midwife. The clinical examination revealed a pale skin and mucous membranes, a blood pressure of 120/60 mmHg, a negative urine dipstick and a patient out of labour with a long posterior closed cervix. There was no bleeding or infectious syndrome. The hemogram showed a haemoglobin 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 on the blood smear. A myelogram was performed confirming the diagnosis of acute myeloid leukaemia with a normal karyotype. The rest of the biological work-up was unremarkable, particularly the haemostasis work-up.

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

The course of action was to ensure biological monitoring every three days, to administer prenatal corticosteroids and to plan a c-section at 36 weeks of gestation after transfusion of red blood cells and platelets. The c-section was performed by an experienced surgeon and gave birth to a healthy male infant in good health, with a birth weight of 3000g, 10/10 Apgar score. The postoperative follow-up of the patient was simple, the patient and her newborn remained hospitalized for three days without complications.

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

4. Discussion

Acute leukemia in pregnancy is an entity described for many years. Two-thirds are acute myeloblastic leukaemias and diagnosis is usually made in the second and third trimester, however, it may be delayed due to non-specific symptoms and signs of leukaemia, such as weakness, fatigue, pallor and difficulty breathing, which may be attributed to pregnancy [7]. AML requires treatment to be started as soon as possible, as it is life-threatening in the short term and any delay or change in treatment for fetal rescue may increase the maternal mortality rate. Pregnancy does not appear to influence the course 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 leukaemia [8].

The timing of chemotherapy initiation is still controversial. It is essential that 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 [9]. 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 delay as in the non-pregnant population, as the risks of malformation are minimal and delay in treatment may compromise the remission rate without improving the 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 who are relatively stable. Furthermore, Barnes et al. confirmed that chemotherapy cannot be delayed in aggressive haematological malignancies 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 [13].

In AML, the most commonly used protocol for patients diagnosed during pregnancy is a combination of Cytarabine and Antracyclines [Idarubicin, Doxorubicin].

Antracyclines are essential in the treatment of AL. They could be cardiotoxic to the fetus. Idarubicin is not recommended during pregnancy as it has a high placental passage due to its lipophilic nature and affinity for DNA [5]. Doxorubicin appears to be the most widely used, relatively risk-free drug and is rarely associated with severe congenital malformations [15]. Experience with Cytarabine in pregnancy is limited. It is an anti-metabolite known to be teratogenic in animal trials [5].

Acute Promyelocytic Leukaemia (AML M3) 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 All-Transretinoic Acid [ATRA] combined 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, 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 complications [19]. Arsenic trioxide (ATO) is another effective drug for the treatment of AML3, 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 due to the increased risk of fetal malformations, intrauterine growth retardation, stillbirth and spontaneous abortion [21,22]. Although the combination of ARTA and OAT is recommended for patients after pregnancy termination or delivery, it should be noted that breastfeeding is contraindicated in this case.

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 weeks of gestation)[4]. However, in patients in good general condition, with stable disease, chemotherapy can be delayed by transfusion therapy until 30 weeks of 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 2nd and 3rd trimester of pregnancy, pregnancy monitoring should be increased. At the end of the pregnancy, an induction can be organised if maternal management requires it. Antenatal corticosteroid therapy for fetal lung maturation may be prescribed. Careful coordination and good communication between the gynaecologist-obstetrician and the haematologist is essential in planning delivery between cycles of chemotherapy to avoid neutropenic phases [25].

5. Conclusion

The association of AL and pregnancy is a rare event. It requires multidisciplinary management taking into account the requirements of the disease and its treatment, the woman and her desire for pregnancy. The use of chemotherapy during pregnancy is possible after 20 weeks of gestation. Termination of pregnancy is required before this date. Pregnancy does not appear to influence the course 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 leukaemia. There are still doubts about the future of children born in these pregnancies due to the small amount of data, which would justify the creation of a register for long-term follow-up, which would make it possible to propose more appropriate therapies.

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