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Successful therapy for acute myeloid leukemia in pregnancy

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Case report

A 27-year-old female at 19 weeks of gestation was admitted to the hematology department in July 2015 with suspicion of acute leukemia. The patient was free of any symptoms. The course of pregnancy thus far was normal. On examination, thrombocytopenia (59 G/L), mild anemia (10.2 g/dL) and leukocytosis (14.6 G/L) with 76% of myeloblasts were demonstrated. Bone marrow aspirate showed 50% of myeloblasts. Molecular analysis did not detect *FLT3*-ITD, *FLT3*-TKD, *MLL-MLLT3*, *CBFB-MYH11* and *RUNX1-RUNX1T1*. Cytogenetic examination showed normal diploid karyotype. She was initiated an induction with standard doses of cytarabine (total dose: 2,380 mg) and daunorubicin (total dose: 300 mg). In gynecological examination, the fetus presented no abnormalities, proper length and weight, and a normal amount of amniotic fluid. A partial remission was achieved after the first induction, and she received another course of cytarabine and daunorubicin at the same dosage. No complications were observed during induction treatments. As a result, she achieved complete remission (CR) with measurable residual disease (MRD) at 0.182%. Consolidation with high dose cytarabine (total dose 7,500 mg) was complicated by fever (39.8°C) and *Escherichia coli* bacteremia. The fetus on weekly ultrasound examination remained normal.

Planned C-section delivery was performed at 35 weeks of gestation. C-section was undergone with no complications and resulted in delivery of a 2,490 g and 49 cm child, given 10 points in Apgar score. No developmental abnormalities or organ changes were found in the child.

19 days after C-section, she started second high-dose cytosine arabonoside (HD-Ara-C) at the doses mentioned above and then proceeded to allogeneic hematopoietic stem cell transplantation (allo-HSCT) from an unrelated donor, who was a 21-year-old male, 10/10 human lekocyte antigen (HLA)-matched. Conditioning regimen consisted of busulfan (total dose: 900 mg) and cyclophosphamide (total dose: 8,400 mg). Graft-versus-host disease (GvHD) prophylaxis included anti-thymocyte globulin (ATG), methotrexate and cyclosporine. The patient was transplanted with 5.93 × 10^6/kg CD34(+) cells. Post-transplant aplasia was complicated by severe oral mucositis. No signs of acute GvHD were demonstrated. Bone marrow aspirate on day +28 showed features of regeneration with MRD at 0.210% and full donor chimerism. On day +100 after allo-HSCT, the patient was at complete remission (CR) with MRD negativity. No complaints were reported at follow-up visits in February 2022. Laboratory tests and bone marrow aspirate showed no features of leukemia. Prospective observation revealed normal child development with some more frequent infections in its early years, but no other significant health problems have been reported so far.

Discussion

Myeloid leukemia in pregnant women is uncommon, with an incidence of 1 in 75,000 to 100,000 pregnancies [1]. Appropriate dosing of chemotherapy, continuous fetal monitoring, and timing of the delivery all pose enormous challenges for the medical staff in charge. To date, no formal guidelines have been developed as to how to manage acute myeloid leukemia (AML) in pregnancy [2]. The treatment of a pregnant AML

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patient is especially difficult and challenging because most agents have been found to be contraindicated [3]. Moreover, as there are as yet no randomized controlled trials, the only sources of guidance as to how to treat AML in pregnancy come from published case reports and a few case series.

Our report highlights the complexity of peri-treatment care and the effectiveness of the therapeutic process. Nowadays, a combination of daunorubicin and cytarabine remains the backbone of AML induction, and the same treatment is also recommended for pregnancy [4]. It has been demonstrated that daunorubicin tends to be associated with a relatively lower incidence of reported birth defects, and it possesses at least equal efficacy compared to other anthracyclines [5]. Most fetal defects develop in the first trimester of pregnancy, a phase when the infant is especially prone to the detrimental effects of chemotherapy. It has been demonstrated that chemotherapy in pregnancy can result in as many as 60% of fetal deaths in the first trimester and 43% in the second. The outcomes for babies in the third trimester have been more favorable [6]. On the other hand, chemotherapy administered in the second and third trimesters of pregnancy increases the risk of late miscarriage, prematurity, fetal growth restriction, neonatal neutropenia, and sepsis [7]. It is crucial to report on long-term follow-up of children born of mothers receiving chemotherapy during pregnancy. Otherwise, this could lead to misleading finding of infants healthy at initial presentation, while the consequences of chemotherapy could be demonstrated years after birth [8].

The presented case report shows that chemotherapy can be safely administered during the second trimester of pregnancy and to date this treatment has not been associated with any harm to the child after a 7-year follow-up. Infants born to mothers with hematological malignancies are commonly found to be small for their gestational age. It is not known yet whether this is a result of the disease or of the treatment [9]. None of these have occurred in the presented patient. Available studies show that pregnancy does not have a significant impact on the course of AML compared to non-pregnant patients [10], and this was also the case in our patient.

Authors' contributions

MR, PR — idea, literature search and writing manuscript; AK, KB, MD, AWK — critical review, patient care; GH — critical review

Conflict of interest

None.

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None.

Informed consent

Informed consent was obtained from all patients participated in the study.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; uniform requirements for manuscripts submitted to biomedical journals.

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