The Journal of Obstetrics and Gynecology of India (January–February 2021) 71(1):78–81
https://doi.org/10.1007/s13224-019-01296-2

CASE REPORT

Pregnancy and Its Successful Outcome in a Patient with Multiple Myeloma

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Received: 13 August 2019 / Accepted: 4 December 2019 / Published online: 10 January 2020

Abstract
Multiple myeloma is a B-cell neoplastic disorder and represents 1% of all cancers and 13% of hematological malignancies. It is predominantly a disease of elderly, and less than 3% of all cases are below the age of 40 years. We present the case of a 29-year-old lady with multiple myeloma who had spontaneous conception during maintenance therapy and subsequently a successful pregnancy outcome. She gave birth to a healthy female infant through normal vaginal delivery and subsequently could remain off therapy for 5 years. Since the patient had a history of abortions and stillbirth, it was a precious pregnancy and we could successfully salvage both the mother and the baby. Young female patients of myeloma who are in remission can be encouraged to start a family during their reproductive years with the support of a comprehensive care team of hematologists/oncologists and obstetricians.

Keywords Myeloma · Pregnancy · Bad obstetric history

Introduction

Multiple myeloma (MM) is a B-cell neoplastic disorder and represents 13% of hematological malignancies. It is predominantly a disease of elderly, and less than 3% of all cases are below the age of 40 years [1]. The exact incidence of multiple myeloma in women of reproductive age group is not described. The number of patients successfully treated for multiple myeloma and subsequently having a planned normal pregnancy is few [2–4]. We present this case of a 29-year-old lady diagnosed with multiple myeloma who had spontaneous conception during maintenance therapy and subsequently had a successful pregnancy outcome.

Case Summary

A 29-year-old [P1 (twin) A2 L0] woman presented in the April of 2009 with complains of progressive weakness and backache of 9-month duration; she was bedridden for the past 2 months. She had history of voluntary medical termination of pregnancy (MTP) at 10 and 12 weeks of gestations, respectively. The third pregnancy in 2008 was a twin gestation; at 30 weeks of gestation, she had premature rupture of membranes (PROM), subsequently she had spontaneous labor pain and vaginal delivery. The first of the twins was a stillborn male (birth weight 1.02 kg), and the second of the twin (male, birth weight 1.3 kg) succumbed 24 h after birth as a result of respiratory distress syndrome. The fetuses had no congenital malformations.

Her blood investigations raised the suspicion of an underlying multiple myeloma. Laboratory investigation revealed hemoglobin level 8.8 g/dl, total leukocyte count 4.4×10^9/L and platelet count 254×10^9/L. Serum electrophoresis showed an M-band (5.7 g/dl) in the gamma region, which was confirmed to be IgG kappa subtype on serum immunofixation. Bone marrow examination showed the presence of

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60% atypical plasma cells suggestive of multiple myeloma. The patient was treated with systemic chemotherapy (VAD regimen: vincristine at 0.4 mg/day on days 1–4, doxorubicin at 9 mg/m^2 on days 1–4 and dexamethasone 40 mg/day on days 1–4, days 9–12 and days 17–20 of a 28-day cycle × 6 cycles). She achieved complete remission following six cycles of chemotherapy. The family pertaining to financial constraints was not able to go for an autologous stem cell transplant (ASCT) and hence opted for maintenance therapy with thalidomide (100 mg oral days 1–28) and dexamethasone (20 mg oral once weekly). On regular follow up, her disease continued to be in complete hematological remission. She was counseled regarding possible risks to the fetus if she conceived while on chemotherapy. Following counseling, she opted for barrier method of contraception. In January 2012, she presented to us with a history of 3-month amenorrhea. The urine test (β-HCG test) for pregnancy was positive. Ultrasonography (USG) examination showed single live intrauterine fetus of 12 weeks gestational age with no evidence of any developmental defects. In view of the previous pregnancy losses, the patient desired to continue the present pregnancy and she was counseled to undergo regular fetal monitoring to rule out any congenital defects. Her chemotherapy was stopped at 12 weeks of gestation, she had regular antenatal follow-up every 4 weeks with her obstetrician, and repeat USG at 32 weeks gestation showed a single live fetus with cephalic presentation with fetal growth appropriate for gestational age. At 37 weeks of gestation, she had a spontaneous vaginal delivery at a tertiary care hospital and gave birth to a normal healthy female baby (birth weight 2.6 kg). There were no intra-partum complications, and the Apgar score was 8 at 1 min and 10 at 5 min. The postpartum period was uncomplicated. The patient was under obstetric follow-up at her hometown. Since ours is a superspeciality institute and we do not have a separate department of obstetrics and gynecology, we collaborate with other hospitals and medical institutes to provide obstetrics and gynecological care to our patients and they continue to remain under medical supervision for their hematological disorders both physically in out-patient department and via digital communication. This patient continued to remain in disease-free hematological remission for the next 5 years of follow-up. She subsequently had a disease relapse and was treated with second-line chemotherapy (bortezomib, cyclophosphamide and dexamethasone). After achieving remission, she underwent an autologous stem cell transplant (ASCT) and continues to be in remission till date. Her child has followed up with us and the pediatrician, she has had a normal growth and development, and no long-term adverse effects of exposure to maternal chemotherapy have been documented in the past 6 years.

Discussion

Multiple myeloma is a malignant disease characterized by an abnormal proliferation of plasma cells. It predominantly affects the elderly; however, it may be seen infrequently in young females of the reproductive age group. Fertility, reproduction and pregnancy outcome are the major challenges in women in this age group. Immunomodulatory drugs (IMDs) like thalidomide and lenalidomide used in the treatment have known to cause amenorrhea. These drugs are teratogenic and are associated with amelia and phocomelia in fetus [5], patients are hence counseled not to conceive, while on therapy with these drugs. Thalidomide affects the limb development during embryogenesis resulting in phocomelia and amelia. Late adverse effects are not known. We monitored both the mother (for her hematological disease status) and child (because it was a precious and successful pregnancy). We wanted to see if there was an long-term impact of thalidomide on the child during her neonatal and early childhood development. Pre-clinical animal studies in rats and monkeys with proteasome inhibitor bortezomib have shown testicular seminiferous tubule degeneration in males and ovarian luteal necrosis in females but there has been no evidence of teratogenicity [2]. The levels of cytokines such as interleukin-6 (IL-6), insulin-like growth factor (IGF-1) and VEGF have been shown to be elevated during normal pregnancy [6]; therefore, it could be hypothesized that the pregnant state creates a permissive marrow environment for the progression of myeloma. There are only 11 cases reported of known cases of myeloma that had received therapy before pregnancy as summarized in Table 1. We could not find any case where disease was in complete remission and myeloma therapy could be stopped altogether during pregnancy and subsequently with the disease being in remission as seen in our case.

To the best of our knowledge, this is the first case report on successful pregnancy outcome in a young female with a bad obstetric history who was on maintenance therapy with immunomodulatory drugs (IMDs) for multiple myeloma. The pregnancy was uneventful, and her disease did not relapse during the course of the pregnancy. She gave birth to a healthy female infant through normal vaginal delivery and subsequently could remain off therapy for 5 years. Fertility and reproduction in young patients with hematological malignancies are an area of great debate and concern. Management of pregnancy in patients with

Table 1 Pregnancy and outcome in previously treated women with multiple myeloma

Reference	Age at diagnosis	Myeloma subtype	Therapy before pregnancy	Therapy during pregnancy	Duration of remission	Maternal status	Neonatal status
Khot et al. [2]	30 years	IgD lambda	VAD + ASCT	No	5 years	Alive	Healthy
Brisou et al. [4]	26 years	K light chain	VAD	No	10 years	Alive	37 wks healthy
Aviles et al. [7]	32 years	NA	Yes	CMOP + MP	Pregnancy during chemo	Died	36 wks healthy
	37 years	NA	Yes	CMOPD + MP	Pregnancy during chemo	Died	38 wks healthy
	24 years	NA	Yes	CMOPI + MP	Pregnancy during chemo	Alive	33 wks healthy
	35 years	NA	Yes	DAI + MP	Pregnancy during chemo	Alive	34 wks healthy
	39 years	NA	Yes	DAI	Pregnancy during chemo	Alive	38 wks healthy
Sakata et al. [8]	41 years	L light chain	VAD + IFN	No	NA	Alive	Healthy
Rosner et al. [9]	NA	NA	Yes	No	NA	Died	Healthy
Kosova et al. [10]	NA	–	RT + U	No	Yes	Died	Healthy
Lergier et al. [3]	21 years	Ig G	MP + CYC	CYC	Stable disease	Alive	39 wks healthy

hematological malignancies who are undergoing chemotherapy, those who have successfully completed treatment and are in disease-free state is a big challenge for both the hematologist and obstetricians. It is well-known that striking physiologic changes occur during pregnancy and dose and/or drug adjustments are very important in the management of these cases. It is essential to maximize the cure chance and survival of the mother and to minimize the treatment-related toxic effects to the fetus. Priority must be given to health of the mother, and termination of the pregnancy is the most important choice in early trimester in cases requiring urgent treatment. In 2nd and 3rd trimester, antineoplastic chemotherapy is generally reasonable in spite of some risks, and close monitoring is mandatory for mother and fetus [11, 12] (Table 2).

Our experience with this patient shows that with the support of a comprehensive care team of hematologists/oncologists and obstetricians and pediatricians, it is possible for young female patients of multiple myeloma in remission to experience the joy of motherhood.

Table 2 Guidelines for management of reproductive health issues in women with cancer

A. General considerations
Understand the natural history of the disease
Counsel the patient regarding potential risks of chemotherapy on fertility, reproduction and pregnancy
Counsel the patient for contraceptive measures during and post-chemotherapy
Plan for oocyte preservation prior to chemotherapy in non-pregnant women
Understand the social and religious beliefs of the patient
B. During pregnancy
Risk of teratogenicity and fetal malformations due to cytotoxic drugs is highest during 1st trimester
Risk decreases as the pregnancy progresses
In Ist trimester, pregnancy should be terminated before starting or continuing chemotherapy
If cancer is detected during 2nd or 3rd trimester of pregnancy, delay treatment till fetal maturity and delivery
Elective delivery is the preferred choice
Avoid breast feeding during chemotherapy
C. Post-therapy
Assess patient's reproductive function post-therapy
Delay planned pregnancy for at least up to 1 year after completion of therapy
Monitor the patient for disease remission status at regular 3–6-month intervals

Compliance with Ethical Standards

Conflict of interest The authors declare that he has no conflict of interest.

Informed Consent Informed consent was taken for publication of this case report from patient.

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