Original Article

SPONTANEOUS TRIPLET PREGNANCY DURING MULTIDRUG THERAPY TREATMENT FOR LEPROSY – A CASE REPORT

Dr. Suhas Gaikwad[1], Dr. Vidya Gaikwad[1], Dr. Mariam Dilshad Shaikh[1], Dr. Rushikesh. A. Phutane[1]

[1]Department of Obstetrics and Gynaecology, Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune 411018, India.
Corresponding author: Dr. Mariam Dilshad Shaikh

DOI: 10.47750/pnr.2023.14.02.220

Abstract

Leprosy is a chronic disease affecting mainly skin, mucous membranes, and peripheral nerves due to Mycobacterium leprae and can be exacerbated during pregnancy. Spontaneous triplet pregnancies are rare; however, these multiple pregnancies are associated with increased risk of maternal and neonatal morbidity and therefore should be prevented. Both leprosy and multiple gestation independently are risk factors for prematurity and low birth weight. This article describes a patient who had both these high-risk factors in her pregnancy undesirably due to spontaneous conception with Triamniotic-Trichorionic triplets while undergoing leprosy treatment with multidrug therapy (MDT) consisting of dapsone, rifampicin and clofazimine.

Introduction

Incidence of spontaneous triplet pregnancy is rare and is determined approximately 1/7000 [1], of which Triamniotic-Trichorionic gestation occurs the least. Also, Leprosy is a chronic infectious disease which can be exacerbated in pregnancy [2]. This case highlights that a woman had spontaneous conception of triplet gestation while undergoing leprosy treatment with multidrug therapy (MDT) consisting of Dapsone, Rifampicin and Clofazimine with no family history of multiple gestation or any treatment for ovulation induction.

Case Report

A 26-year-old female, presented to our outpatient department with complain of amenorrhea since one and a half months. She was a diagnosed case of Borderline Tuberculoid Multibacillary leprosy, on oral MDT as per WHO regimen consisting of Dapsone, Rifampicin and Clofazimine for 8 months. Her obstetric history included one living child 3 years old born via spontaneous vaginal delivery and one medical abortion two and a half years back. Her previous menstrual cycles were regular. There was no history of any contraception or intake of oral contraceptive pills. There was no history of pregnancy with multiple gestation in family. Her urine hCG done in OPD was found to be positive. It was a spontaneous conception. Her physical examination revealed no significant findings other than Bilateral thickening of ulnar nerve. On per speculum examination cervical ulceration was noted and pap smear was collected, which was found to be negative for malignancy. Uterus was 6 weeks size on per vaginal examination. Ultrasonographic evaluation indicated Trichorionic-Triamniotic intrauterine gestation of 6 weeks, with live gestation. It was a spontaneous Triamniotic- Trichorionic Triplet pregnancy during MDT

treatment. The patient then desired for medical termination of pregnancy as she was not willing to take maternal and fetal risks of pregnancy associated with both leprosy and multiple gestation. She then underwent elective dilatation and evacuation to terminate the pregnancy at 7 weeks of gestation. Her post-operative period was uneventful and she was discharged the next day.

DISCUSSION

This is a case of Trichorionic Triamniotic pregnancy which is a spontaneous conception and not due to ovulation induction which is very rare. Maternal physiological changes with multiple foetuses are intensified as compared to singleton gestation [3] therefore increasing the risk of perinatal and postnatal complications both for the mother and her babies [4]. Also, triplet birth has higher risk than singleton in terms of poor birth outcomes like preterm and infant death rate [5, 6]. The risk of aneuploidy in a triplet pregnancy is higher than singleton pregnancy since there are three foetuses each of which is at risk [7]. Thus, based on their frequency of prematurity, low birth weight, IUGR, infant mortality rate, it is relevant to characterise all triplet pregnancies high risk [8].

Leprosy or Hansen's disease is a chronic infectious disease. The causative organism is mycobacterium leprae affecting skin, nerves, and mucous membranes, if untreated causes permanent damage. If cured on time the disability is avoided. The WHO recommends multidrug therapy consisting of Dapsone, Rifampicin and Clofazimine for 12 months in case of MB leprosy. This combination is highly effective and patient is no longer infectious after taking first dose itself. However, pregnancy is an immunocompromised state leading to relative decrease in cellular immunity allowing M. leprae to proliferate [9]. It is most dangerous during third trimester when infection can lead to adverse obstetric and foetal outcomes such as low birth weight, prematurity, exfoliative dermatitis in new-born and erythema nodosum in pregnant mother [2]. Duncan et al., 2007 conducted a study where they found that babies of mothers with leprosy had complications such as low birth weight, smaller placentae, slower growth, increased susceptibility to infections, and greater infant mortality than those of non-leprous mothers [10]. However, leprosy is not a contraindication for pregnancy. Although fewer adverse effects are associated with MDT during leprosy treatment like rifampicin causes post-natal haemorrhages, also efficacy of contraceptive drugs decreases due to rifampicin induction of liver enzymes. Transitory hyper-pigmentation of babies is seen at birth with clofazimine. Dapsone-induced haemolytic anaemia is seen in mother and their babies and methemoglobinemia is seen when it is given in 3rd trimester [2].

Also, dapsone which is a sulfonamide, apart from its anti-bacterial action has anti-inflammatory effects by reducing inflammatory cytokine levels. Shirooie et al., 2021 conducted a study to see the effect of dapsone in testosterone induced PCOS in rats and found that dapsone reversed the effects of testosterone and improved PCOS signs, thereby improving LH and FSH levels; thus, oocyte maturation, progesterone, and estrogen secretion, and also it has beneficial properties like anti-inflammation and anti-oxidant effects [11]. Therefore, further studies and investigations are required to evaluate exact mechanism of its protecting as well as any stimulating properties of dapsone on ovaries of humans.

CONCLUSION

Multi gestational pregnancy with leprosy has implications for the physician, obstetrician, leprosy health worker, neonatologist as well as the family of the pregnant woman all of whom provide support and care to the patient.

This case highlights a rare spontaneous triplet pregnancy during multidrug therapy for leprosy. A multi gestational pregnancy with leprosy is usually more stressful both physically and emotionally as compared to normal singleton pregnancy. Multiple gestation with leprosy influences maternal and foetal outcome in pregnancy, as both together intensifies the risk of preterm, premature, and low birth weight babies, along with worsening of leprosy in pregnancy and hence our patient decided to terminate this pregnancy. Also, the patient did not have any history of pregnancy with multiple gestation in family or ovulation induction treatment. She spontaneously conceived with triplet gestation during treatment with dapsone, rifampicin and clofazimine. So, a question arises whether any of these drugs independently or in combination have any relation in inducing ovulation, whether dapsone

causes stimulation or hyperstimulation of ovaries based on its protective properties on polycystic ovaries in a study conducted on rats or was it just a co-incidence? We think that further studies and investigations are required to assess mechanism of dapsone on ovaries in humans, as well as to evaluate spontaneously conceived Trichorionic-Triamniotic triplet pregnancies.

References:

1. Yıldırım, E. Spontaneous triplet pregnancy and trap sequence, case report. *BMC Pregnancy Childbirth* **19**, 328 (2019). https://doi.org/10.1186/s12884-019-2484-3
2. Fatola, C., Venyo, A., Venyo, L., & Lindsay Maloney, D. (2015). Leprosy in pregnancy; a review of the literature [Review]. *Hamdan Medical Journal*, *8*(1), 83-95. https://doi.org/10.7707/hmj.320
3. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap III L, Wnstorm KD. Williams Obstetrics 22nd ed, USA: McGraw Hill 2005; 912-922.
4. Ziadeh SM. The outcome of triplet versus twin pregnancies. Gynecol Obstet Invest 2000; 50: 96-99.
5. Keith, L. G., & Oleszczuk, J. J. (2002). Triplet births in the United States. An epidemic of high-risk pregnancies. *The Journal of reproductive medicine*, *47*(4), 259–265.
6. Martin, J. A., MacDorman, M. F., & Mathews, T. J. (1997). Triplet births: trends and outcomes, 1971-94. *Vital and health statistics. Series 21, Data on natality, marriage, and divorce*, (55), 1–20.
7. Karakaya, B., Celik, H., Esercan, A., Aktulay, A., Ustun, Y., Eyi, E., & Erkaya, S. (2018). Our results of spontaneously conceived triplet pregnancies. *Medicine Science | International Medical Journal*, 1. https://doi.org/10.5455/medscience.2017.06.8748
8. Multifoetal pregnancy in Cunningam FG, FG Norman, Heveno KJ: Gilstrap LC, Hanth CJ, Wenstrom DK edited Williams obstetrics (21 st edition),USA,MC-GRAW HILL2001
9. Gimovsky, A. C., & Macri, C. J. (2013). Leprosy in pregnant woman, United States. *Emerging infectious diseases*, *19*(10), 1693–1694. https://doi.org/10.3201/eid1910.130463
10. Duncan, M. E., Miko, T., Howe, R., et al. (2007). Growth and development of children of mothers with leprosy and healthy controls. *Ethiopian medical journal*, *45 Suppl 1*, 9–23.
11. Shirooie, S., Khaledi, E., Dehpour, A. R., Noori, T., Khazaei, M., Sadeghi, F., & Sobarzo-Sánchez, E. (2021). The effect of dapsone in testosterone enanthate-induced polycystic ovary syndrome in rat. *The Journal of steroid biochemistry and molecular biology*, *214*, 105977. https://doi.org/10.1016/j.jsbmb.2021.105977
12.