



















From the Editor's Desk.....

It is a pleasure to bring you the first issue of Life +ve for the year 2025!

Our first case report is that of a High-Risk Pregnancy with mechanical mitral valve who had a successful outcome despite all challenges. High risk pregnancies always pose a risk to both mother and baby. Careful planning, appropriate treatment and a multidisciplinary approach are essential for best outcomes.

We next bring you a case series on Genital Tuberculosis. In India despite the rampant prevalence of TB, it frequently eludes recognition due to its varied presentation, nonspecific symptoms and overlap with other gynecological disorders. The article is a presentation of a series of 5 cases who came to the OPD and on evaluation for infertility were diagnosed with genital (endometrial) tuberculosis thanks to thorough evaluation, a high degree of suspicion and expertise in ultrasound.

Our third case report is that of a successful pregnancy outcome in an advanced maternal age female, with poor ovarian reserve and single euploid blastocyst obtained from a single oocyte. In this case the use of a frozenthawed single euploid embryo transfer allowed sufficient time for comprehensive genetic evaluation and a multidisciplinary approach involving the infertility specialist, embryologist and geneticist brought maximum benefit to the couple.

Our last case report brings you a rare case of Essential Thrombocytosis (myeloproliferative disorder) and its successful fertility and pregnancy management. This complicated case was handled with the use of Injinterferon alpha and again a multi-disciplinary approach involving a haematologist, geneticist, fertility specialist, obstetrician and neonatologist ensured a positive outcome.

We do hope you find this issue interesting and welcome your feedback and suggestions. Happy reading!

Triumph over challenges High-risk pregnancy- a success story



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INTRODUCTION

Pregnancy in women with mechanical prosthetic heart valve replacement is highly complicated, mainly because of the need for anti-coagulation. Anti-coagulant is required to prevent thromboembolic complications. In addition, pregnancy is a hypercoagulable state. Examples of the types of thromboembolic complications that have occurred during pregnancies associated with mechanical prosthetic valves include stroke, valve thrombosis, and myocardial infarction. Choosing which type of anticoagulation to use during pregnancy is problematic, as there is no perfect form available. Therefore, the major concerns associated with pregnant women with mechanical heart valves are thromboembolic complications (including fatal events), maternal bleeding, and increased fetal events

Here is case of a woman with mechanical mitral valve who had a high risk pregnancy and successful outcome despite all challenges.

CASE REPORT

Mrs. MA, 35 years, married for 10 years, conceived naturally while she was on treatment process for IVF. She was a known case of Rheumatic Heart Disease (RHD) and underwent mitral valve replacement in 2006 after she developed mitral valve regurgitation. She had been on anti-coagulant (Tab. Acitrom 4mg) since then. Prior to the present pregnancy, she had conceived naturally and had a missed miscarriage at 10 weeks. She underwent suction evacuation under GA with antibiotic prophylaxis to prevent endocarditis. Despite following cardiologist's advice strictly, she had blockage of valve and underwent valve replacement.

Three months later, she conceived spontaneously. Soon after pregnancy confirmation (4weeks+5 days), Tab. Acitrom was stopped and she was started on Inj. Clexane 60mg BD. She was also continued on Tab. Inderal 10 mg (Beta-blocker). As she was high risk with mechanical mitral valve

replacement and on anti-coagulant + Beta-blocker, management involved multi-disciplinary approach along with cardiologist. Complications of pregnancy with mechanical valves including thromboembolic events, maternal endocarditis, feto-maternal haemorrhage, miscarriage and premature birth were discussed with the couple and need for compliance with medications and consultations was emphasized. NT scan done at 12 weeks showed normal NT value and double marker test was low risk for Trisomy 21, 13 and 18. She had regular intake of Iron, Calcium and Folic acid supplements. She received 2 doses of tetanus toxoid vaccination in second trimester. Anomaly scan at 20 weeks showed no obvious structural anomalies or soft markers. Fetal ECHO done at 23 weeks showed structurally normal heart. Growth scan at 28 weeks showed normal growth and normal fetal dopplers. USG at 34 weeks showed interval growth lag of 1.5 weeks with estimated fetal weight (EFW) at 11th centile, suggestive of late onset IUGR. Mild feto-placental insufficiency was noted, CP ratio - 1.48 which was normal. She was started on protein supplements and was monitored with fetal dopplers twice weekly. At 35 weeks + 1 day, EFW - 2020 gm, fetal dopplers showed CP ratio - 1.14 which was at 5th centile for gestational age. She was given steroid prophylaxis and continuously monitored with fetal dopplers and NST. She was planned for elective LSCS at 36 weeks. Her delivery was meticulously planned with multidisciplinary approach involving anaesthetist, cardiologist, obstetrician and paediatrician. PT was 38.8 and INR was 1.59 prior to surgery. Inj. Clexane 60mg was stopped 12 hours prior to surgery. As there was high risk for excessive bleeding during surgery, 2 units FFP and 1 unit of PCV were kept ready. She was given prophylactic antibiotics- Inj. Magnex forte 1.5 gm, 1 hour prior to surgery. She underwent Elective Caesarean Section at Milann Hospital, Kumarapark and delivered a healthy male baby weighing 2.14 kg. Baby had good APGAR score at birth and did not require NICU support. Surgery was uneventful with EBL- 400ml. 2 units of FFP transfused intraoperatively. As per Cardiologist's recommendation, bilateral tubectomy was done and lactation was suppressed. Inj. Clexane was restarted 6 hours after surgery. Infective Endocarditis prophylaxis -lnj. Magnex forte 1.5 gm bd for 48 hours and lnj. Gentamycin 80mg bd for 24 hours. Mother was managed in high dependency unit for 24 hours, shifted to ward later. She was started back on Tab. Acitrom 4mg on POD3 with tapering of Inj. Clexane. PT and INR were repeatedly monitored till INR was 2.3. She was discharged on POD4. During her follow-up at 10days, 1 month and 3 months, she was asymptomatic and haemodynamically stable.

DISCUSSION

Pregnancy is associated with a hypercoagulable state. Women requiring anticoagulation need careful attention throughout pregnancy and through the post-partum period. The choice of anticoagulant therapy, the degree of monitoring, and the therapeutic target should be modulated by balancing the risks and the benefits to the mother and fetus (2).

As pregnancy progresses, the risk of hypercoagulability increases, due to increasing levels of thrombogenic factors VII, VIII, and X; von Willebrand factor; and fibrinogen, and decreases in protein S. The risk is highest in the immediate post-partum period and slowly decreases back to pre pregnancy levels by 8 to 12 weeks post-partum. However, in women with mechanical heart valves, valve thrombosis often occurs during the first trimester.

Risk of Thrombosis: Valve thrombosis may occur earlier in pregnancy due to subtherapeutic anticoagulation during transition from Vitamin K Antagonists (VKA) to heparins in the early stages of pregnancy, continuously changing anticoagulant agent pharmacokinetics (particularly Low Molecular Weight Heparin) in pregnancy that lead to underdosing, or other, unidentified homeostatic factors germane to patients with mechanical valves. Mechanical valve thrombosis is the most feared complication, and carries a 20% risk of mortality.

Risk of Bleeding: Delivery poses the greatest risk for bleeding. Women must be transitioned off long acting anticoagulant agents to receive regional anaesthesia or undergo Caesarean delivery. Careful planning of the timing and mode of delivery is critical.

Fetal Loss: LMWH throughout pregnancy is associated with a 12.2% rate of fetal wastage.

Conclusion: High risk pregnancies always pose risk to both mother and baby. Careful planning, appropriate treatment and multidisciplinary approach are essential for best outcome.

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Case Series Of Genital Tuberculosis



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INTRODUCTION

Endometrial tuberculosis presents a significant challenge in the realm of infertility, often manifesting in subtle and enigmatic ways that complicates diagnosis and management. In India despite the rampant prevalence of TB, it frequently eludes recognition due to its varied presentation, nonspecific symptoms and overlap with other gynaecological disorders. Genital tuberculosis is said to be prevalent in 10% of the infertile population. Endometrial TB can lead to chronic inflammation, scarring, and structural changes in the reproductive system, ultimately impairing fertility. Thus a high index of suspicion is always necessary for a reproductive clinician to clinch the diagnosis. This presentation is a case series of 5 cases of endometrial tuberculosis at Milann Fertility Centre Kumarapark, Bangalore that were elusive of diagnosis. Empirical treatment of unexplained infertility with ATT is unacceptable by us, but a high index of suspicion and understanding the varied presentation of the disease will clinch diagnosis and help patients. Understanding the enigmatic nature of endometrial TB is crucial for improving outcomes and guiding appropriate therapeutic interventions in an affected individual.

Case 1: A 35 year old woman Mrs.X, with primary infertility for 8 years, poor ovarian reserve (AMH-0.9), with blocked tubes had one failed IVF cycle due to poor quality embryos had come to the OPD for fertility treatment.

- The patient had 1 IVF cycle and obtained 3-8CGA due for transfer.
- 1st cycle of HRT, ET-8.9mm echogenic day 12, and hence cycle cancelled
- 2nd cycle -DR-HRT, patient had intermittent spotting since day 12 despite high dose HRT and thus cycle was cancelled. ET-9.5 mm
- The patient had intermittent spotting throughout the cycle and the ET remained thick 10 days post that. In view of persistent thick ET therapeutic curettage was planned.

- To our surprise, on HPE: granulomatous inflammation was identified S/O TB AFB stain- no bacilli.
- Gene Xpert- Negative.
- TB culture (BACTEC)-positive
- This is diagnostic of TB
- Now on retrospection the hazy endomyometrial junction, upturned tubes on 3d USG also pointed towards chronic endometritis suggestive of TB.
- •On further evaluation, the Chest Xray of the patient showed an old TB nodule, the patient is on ATT.

PIC: 1a. Upturned tubes



1b. Endometrium with a hazy endomyometrial junction

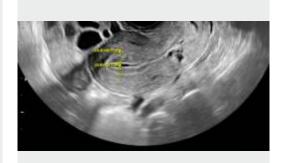


Case 2:

- A 29 year old primary infertility patient for 9 years with bilateral tubal block and severe male factor had come to the OPD for ART.
- She underwent 1 IVF cycle and got 8-8CGA embryos.
- Fresh embryo transfer was done- she failed to conceive.
- She had 2 cycles of HRT both of which were cancelled due to suboptimal ET (6.5mm), fluid in endometrial cavity and hazy endomyometrial junction.
- On 3D ultrasound the patient had a T shaped cavity.
- In view of unhealthy blocked tubes, T shaped uterus, recurrent thin ET and fluid in the endometrial cavity suspicion of TB was aroused; an endometrial biopsy was taken.
- HPE: Granulomatous inflammation
- Gene Xpert-TB positive
- Patient was started on ATT.

PIC: 2a. T shaped Uterus (Satisfying CUMES criteria) 2b. Fluid in endometrial cavity





Case 3:

- A 24 year old woman with primary infertility of 6 years had hydrosalpinx for which B/L clipping of the tubes was done, endometrial biopsy PCR for TB was negative 4 years ago. Patient came for ART for tubal factor.
- IVF cycle, 5 blasts obtained, fresh ET done ET-9 mm,1 blast transferred-failed to conceive.
- 2 cycles of HRT tried, both cycles cancelled due to secretory and thin endometrium (max ET-6.8mm)
- 3rd cycle high dose HRT, 10mm endometrium, 2 blast transferred and failed to conceive.
- 6 months later 4rth cycle HRT-FET, in view of polyp at fundus, diagnostic hysteroscopy +polypectomy + HPE was done
- HPE: Granulomatous endometritis for endometrial sample
- Gene Xpert-TB positive
- Here the polypoidal endometrium, old hydrosalpinx point towards development of TB. Being a paucibacillary and indolent disease it took a lag period to show up in HPE,

PIC: 3a. 3D USG showing polyp



3b. Hysteroscopy image showing polyp



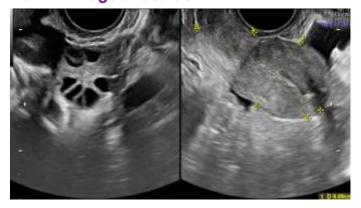
Case 4:

- A 30 year old with secondary infertility, P1L0A4 (biochemical pregnancy losses), developed severe preeclampsia in her first pregnancy and delivered at 28 weeks. She is ANA+ve. The male partner is 33 years old and had asthenoteratozoospermia.
- In view of the biochemical pregnancy losses, evaluation for RPL was done and was found to have a unicornuate uterus on USG.
- Subsequently, hysteroscopy was done-normal
- Endometrial biopsy done
- Gene Expert-TB positive
- HPE- Granulomas+
- Patient on ATT.

PIC: 4a. Unicornuate uterus on USG



4b. 2 D Image of uterus



Case 5:

- A 35 year old woman with primary infertility for 6 years was referred to our Centre for IVF due to tubal factor.
- IVF cycle yielded 12-8CGA embryos, fresh transfer 1-blast, failed to conceive.
- 1st FET cycle, 1-blast transferred-failed to conceive.
- She underwent DHL proceeded to left salpingectomy, Tube HPE-granulomatous salpingitis, hysteroscopy-normal, Endometrial biopsy done –granulomatous inflammation suggestive of TB.
- She underwent ATT for 6 months, repeat EB- negative for TB(HPE-proliferative)
- Gene Xpert- Negative.
- HRT FET cycle-2 blastocysts transferred, she conceived in the first transfer post treatment (DCDA twins). She delivered twin live babies

PIC: 5a. Normal Hysteroscopy



PIC: 5b. Endometrium post IVF cycle, normal pattern



DISCUSSION

The fact that diagnosis of genital tuberculosis is not easy is well known. From this cohort of 5 cases, which had no constitutional or straight forward signs & symptoms pointing towards tuberculosis, a high degree of suspicion and meticulous scanning landed us the diagnosis. The clues mainly were in the ultrasound. Thus advanced knowledge of ultrasound gave us the clues to run the tests and in 2 cases to re run the tests for tuberculosis. Post ATT one patient conceived and had a live term baby while the other 4 cases are still in the ATT period.

From this cohort of endometrial TB patients in infertility we understand the importance of Ultrasound soft markers in diagnosing or suspecting endometrial tuberculosis. India being a highly endemic zone for tuberculosis, more emphasis cannot be made on the need to evaluate for TB in patients presenting with infertility.

Successful pregnancy outcome in advanced maternal age female with Poor ovarian reserve and single euploid blastocyst obtained from a single oocyte



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INTRODUCTION

Advanced maternal age (AMA) has been seen to be associated with lower implantation rates, increased miscarriage rates, and more risk of fetal chromosomal abnormalities. The primary factor affecting the success of assisted reproductive technology (ART) is the presence of aneuploid embryos, which is dependent on maternal age. Preimplantation genetic screening (PGS) offers a viable option that can reduce abortion rates and shorten the time to achieve live birth in AMA patients undergoing ART. At present, trophectoderm (TE) biopsy at the blastocyst stage has the potential to become the gold-standard technique for PGS.

We report the case of a 41-year-old lady with secondary infertility, recurrent pregnancy losses and poor ovarian reserve who underwent multiple cycles of ovulation inductions, intrauterine inseminations and IVF-ICSI, and finally conceived with single euploid blast transfer (with PGT-A).

CASE REPORT

Mrs. S, 41 years old, married for 15 years to Mr. R, 48 years old, with regularly occurring short cycles of 24 days duration and no dysmenorrhea. There was no significant past or medical history noted. She presented as a known case of secondary infertility with recurrent pregnancy losses along with male factor in form of teratozoospermia.

Patient started with her fertility treatment journey in 2012 with ovulation induction and intrauterine insemination and failed to conceive. She underwent her first IVF cycle in 2012, 12 oocytes were retrieved, fresh embryo transfer was done with 2 blasts, resulting in dichorionic diamniotic twin conception. LSCS was done at 27 weeks due to preterm premature rupture of amniotic membranes and both babies didn't survive due to complications of prematurity.

Patient underwent her 2nd IVF cycle in 2014, 5 oocytes were obtained, fresh embryo transfer (single blast) was done and failed to conceive. This was followed by an IUI conception and a healthy girl baby by LSCS in 2017.

After this, desirous for a second child, the couple further underwent 2 cycles of OI+IUI between 2019-20 leading to first trimester losses, managed medically. Further 4 cycles of IUI were done between 2020-21 with failure to conceive. The 3rd cycle of IVF was started for the patient in January 2022 (Antagonist protocol) with 2-8CGA embryos frozen. FET cycle was cancelled twice due to a drop in the endometrial lining. Patient underwent diagnostic hystero-laparoscopy with bilateral tubal clipping (bilateral tubes sacculated and dilated) with endometrial ploughing in July 2022. Uterine cavity was normal and found adequate for implantation with presence of bald areas in endometrium. HRT-Frozen embryo transfer protocol cycle was started in September 2022 and embryo transfer was done with failure to conceive.

After extensive counselling and prognostication—the couple was advised to undergo IVF-ICSI stimulation followed by PGT-A (Pre implantation Genetic Testing) in view of recurrent IVF failures with advanced maternal age. 4th IVF cycle was started for the patient in February 2024 with antagonist protocol with recombinant LH and FSH. Patient had 4 small follicles on the baseline scan, out of which only one responded to stimulation (A FOI of 25%). Single oocyte was retrieved, ICSI was done, and single Day 5 blast (1-4AB) was obtained, biopsied for pre-implantation genetic testing (PGT-A) and frozen, further reported as euploid blast.

Downregulated Frozen Embryo Transfer protocol was started, and finally, frozen embryo transfer was done in July 2024 and she conceived with successful ongoing pregnancy.

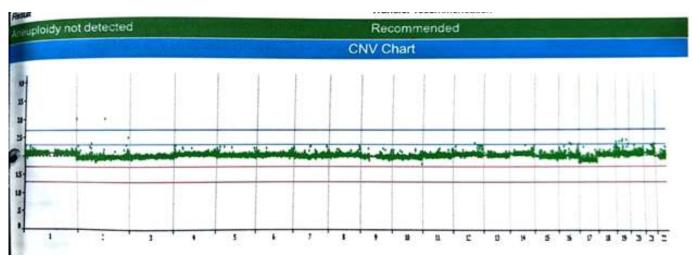


Fig 1: NGS Report of biopsied embryo revealing Euploid status

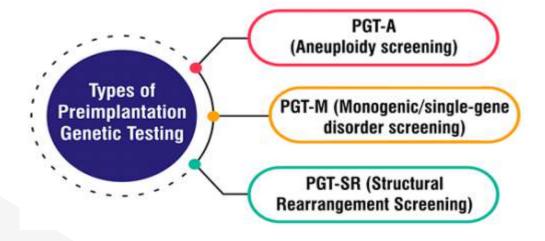
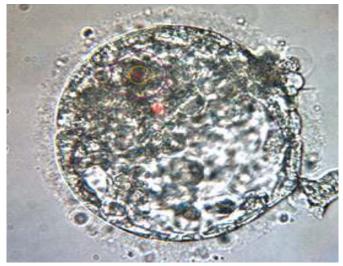


Fig 2: Types of Preimplantation
Genetic Testing







DISCUSSION

PGS is the key strategy promoting the clinical success of ART cycles in AMA patients specially with a euploid embryo resulting in increased pregnancy rate. This was substantiated by the **STAR Study** which showed no overall improvement in Ongoing pregnancy rate and Live birth rate in women aged 25-40 years, but does support the use of PGT-A for women aged 35-40 years to improve outcomes per frozen-thawed embryo transfer. Furthermore, a SET (Single embryo transfer) reduced the likelihood of multiple pregnancies, which are associated with higher abortion rates and premature deliveries with new born complications. Another study by Ariel et. al concluded that as an euploidy increases with age, beyond the age of 37, PGT-A becomes cost effective as well.

CONCLUSION /

The use of frozen-thawed single euploid embryo transfer allows sufficient time for comprehensive genetic evaluation, while also enhancing implantation and pregnancy rates in advanced maternal age patients undergoing PGS. Therefore, this group of patients may benefit from PGT-A. At the same time, a multidisciplinary approach is required involving the infertility specialist, embryologist and geneticist to reach a collaborative decision for maximum benefit to the couple.

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A Rare Case Of Essential Thrombocytosis (Myeloproliferative Disorder) Tips And Tricks In Fertility And Pregnancy Management With Interferons



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INTRODUCTION /

Essential thrombocythemia (ET), polycythaemia vera (PV), and myelofibrosis (MF) comprise the heterogenous group of BCR-ABL1-negative myeloproliferative neoplasms (MPN) and manifest with a wide spectrum of clinical presentations ranging from asymptomatic to limiting constitutional symptoms as well as an increased risk of thromboembolic events and transformation to acute myeloid leukaemia (AML). MPDs are blood cancers caused by changes in the stem cells inside bone marrow, the tissue that makes blood cells. These changes cause the body to make too many blood cells. This excess can be any type of blood cell — white, red, or platelets.

MPDs are a group of blood diseases that can be caused by inherited genetic mutations. Possible cause is due to mutation in JAK2 and TET2 genes. MPDs usually affect only one type of blood cell. Rarely do they affect more than one. Essential thrombocythemia - too many platelets, the blood's clotting cells, can lead to blood clots, increasing the risk of heart attack or stroke. This is the type of MPD which our patient had.

CASE REPORT

Mrs X 31 years old & Mr Y 33, years old came to Milann Fertility Centre, Whitefield, Bangalore in 2022 with H/O secondary infertility having been trying to conceive for the past 4 years. They were married since 5 years (2017). Patient had a history of spontaneous miscarriage of approximately 10 weeks' gestation in year 2018.

Incidentally she was detected with thrombocytosis in June 2020 with platelet count 13,37,000/cumm, when complete blood count was done for viral infection. She was referred to a Hematologist and underwent further investigations like:

▶PT-12.7 ▶INR-1 ▶APTT-34.5 (High)

Molecular Genetic testing in Myeloproliferative Neoplasms

- ▶ JAK 2 (EXON 14 & 12) NEGATIVE
- ► CALR (EXON 9) NEGATIVE
- VWF ANTIGEN 100 (60-150)

- ▶ MPL (EXON 10) NEGATIVE
- Factor VIII Assay 130% (50-150)
- BCR-ABL 1 transcript by breakpoint analysis -Not detected.

Flow Cytometry was done

- T cell marker- CD3 Count- 810 cells/ microL (Normal)
- B cell marker- CD19 Count 172 cells/ microL (94-378 cells / microL)
- NK CELL marker CD 56 25 cells/ microL (120-490 cells/microL)
- CD3 Lymphocyte-79.6 % (60.5-76.9%)
- CD 19 lymphocytes 16.88 % (5.5 15%)
- » CD 56 lymphocytes- 2.49 % (6.5- 15%)

APLA Test

- ANTI CARDIOLIPIN ANTIBODY Ig G & Ig M & Ig A- NEGATIVE
- Anti-Nuclear Antibody NEGATIVE
- ➤ ANTI TPO 7.1 IU/mL (< 5.6 IU/mL)</p>
- ▶ B 2 Glycoprotein Ig G & Ig M NEGATIVE
- ▶ ANTI TG- <3 (< 4.11 IU/mL)</p>

Treatment- She was started on Tab Hydroxyurea 500 mg BD. She was also a known case of hypothyroidism and was on Tab Thyronorm 50 mcg.

At Milann hospital, she was started on Tab Ecospirin 150 mg OD, Tab Dexona 0.5 mg BD and husband was advised for Semen analysis, DFI & Culture Sensitivity. Ovulation Induction, SSG and IUI was the treatment plan. Ovulation induction was done with step up letrozole 2.5 mg.

INVESTIGATIONS

HSA-Teratozoospermia (morphology - 1%)

DFI-34%

Culture Sensitivity-No growth

Husband was prescribed antioxidants.

SSG was done-Bilateral tubes patent.

IUI was done, and patient conceived with Beta HCG 164. She was started on Inj Clexane 40 mg OD. However the repeat Beta HCG was 44 after 48 hours and it was termed a biochemical pregnancy.

Later karyotyping for the couple was advised and they were referred to a hematologist. IVF was planned with PGT-A (in view of 2 abortions and Teratozoospermia). Karyotyping was normal for both, so further Whole Exome Sequencing(WES) was advised to rule out gene mutation in the couple (MPDs can be caused by inherited genetic mutations).

WES-Normal for husband

WES-Wife was carrier of Thalassemia Alpha - Autosomal Recessive.

Hematologist's opinion was taken, and she was started with Inj. Peg Interferon alpha-2B 80 mcg s/c once a week for 16 doses for thrombocytosis. Patient was also advised to stop taking Tab Hydroxyurea keeping in mind plan for pregnancy.

In the next cycle, stimulation for IVF was started with random start protocol and mild stimulation (to prevent high E2). Based on her TSH reports, she was started on Tab Thyronorm 62.5 mcg. Ovum Pick Up was done in Nov 2023 and 7 oocytes retrieved. Two Day 5 Blastocysts were obtained and sent for PGTA.

She was started on HRT for FET after 1 cycle and FET was done in Feb 2024, 1-3-BB (Euploid) embryo was transferred. She conceived with twin gestation, but by 8 weeks, it reduced to single gestation (vanishing twin). She was continued on LPS with Tab Ecospirin 75 mg OD, Tab HCQ 200 mg OD, Inj Peg Interferon alpha-2B 80 mcg s/c and Tab Thyronorm 100 mcg.

NT Scan and Double Markers were normal but she was diagnosed with Placenta Previa during Anomaly scan. She had episodes of spotting, hence was advised for coagulation profile and was advised to stop Tab Ecospirin and to continue Inj Clexane with Tab Pause 500 mg 1-1-1 and to maintain oral hydration.

Given the potential teratogenicity and the concerns about potential leukemogenic effects of hydroxyurea, interferon- α (IFN), is considered an alternative treatment for cytoreduction, mitigation of thrombosis risk and symptom management in essential thrombocythemia.





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Thus in this case Hydroxyurea was stopped and Inj interferon alpha was started with a multidisciplinary approach involving a haematologist, geneticist, fertility specialist, obstetrician and neonatologist to handle such a complicated case.

She continued pregnancy till 37 weeks and was on Arg 9 sachets BD, Tab HCQ 200 MG OD, Inj Clexane 40 mg s/c, Tab Iron and Calcium. She had elective Caesarean section in Oct 2024 in view of IUGR with on and off bleeding P/V. She delivered a healthy baby boy of 2.3kg. She continued with Inj Clexane and Peg Interferon alpha post-delivery.

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