



PGT-M : A RAY OF HOPE FOR COUPLES WITH GENETIC DISEASE

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INTRODUCTION:

In 1968, Gardner & Edwards succeeded in sexing rabbit embryos at approximately day 5 after fertilization.¹ Since then , the rapid development of the genetic & assisted reproductive techniques permitted the birth of the first baby after in-vitro fertilization in 1978 and the first successful application of PGD A in 1990.²

Here I am going to present a case report of a couple, heterozygous for Xeroderma pigmentosum to show how the successful application of PGD for XP resulting in the transfer of a healthy embryo resulting in an ongoing pregnancy of 18 weeks at present.

XP is a rare autosomal recessive disorder , first described by Hebra & Kaposi in 1874, which is caused by a defective nucleotide excision repair (NER) system which produces mainly skin, ocular & neurological alterations.³

CASE REPORT:

Couple XY, (35 year old female, 38 year old male, MF- 6 years), both heterozygous for XP , came for genetic evaluation. They had a history of consanguineous marriage. Patient P1L1A1 , first pregnancy was spontaneously conceived, outcome was a male baby with FTVD ,I year after birth , baby developed skin pigmentation & photophobia. Now the baby is 5 year old. Second pregnancy was also spontaneously conceived in 2017, it was a twin pregnancy with DCDA twins, prenatal testing was done at Amrita institute, Cochin, & both fetuses were found homozygous for XPC gene, most common gene for XP, Hence MTP was done at 5 months. Couple was also evaluated at the same time , both were detected to be heterozygous variants for XP. Couple came to craft hospital for an opinion. After a thorough discussion with geneticist , plan for ICSI +PGT-M+Frozen ET was made. Pre PGD work up was done. Targeted variant analysis of selected XPC gene was done by PCR using customized primers & by bidirectional Sanger sequencing. Patient herself was a case of Diminished Ovarian Reserve (DOR) hence plan for oocyte accumulation done. COS outcomes (diag).First ICSI was done in June 2019, through which 10 embryos were formed , which included 4 Day 3, 5 Day 5 & 1Day 6 embryo. The embryos were subjected to PGT-M in view of couple history of XP. Out of 10 embryos , 2 came out to be normal, 5 affected, 2 were carriers & 1 undiagnosed.

First FET was done in Dec 2019, FET protocol was HRT, 1 Day 5 (1*2BB) normal embryo was transferred, which ended as a biochemical pregnancy. Second FET was done on 15 July 2020, this time 2 D5 embryos (1*2BA,1*2BC), one normal & other carrier was transferred as the couple insisted for this. Viability scan was done which showed a single alive I/U fetus of 6 weeks 4 days. At 13 weeks NT was done which was low risk, Pt was given option of Amniocentesis but couple refused, hence NIPT was done which was low risk. Presently its an ongoing pregnancy of 18 weeks with anomaly scan booked at 20 weeks.

COS OUTCOMES

COS (1ST)
PROTOCOL: CCC+ANTAG
3M2 & 2M1 aspirated

COS (4TH)
Cancelled due to poor growth

COS (2ND)
Cancelled due to poor growth

COS (5TH)
Cancelled due to poor growth

COS(3RD)
PROTOCOL: CCC+ANTAG
10 M2 aspirated

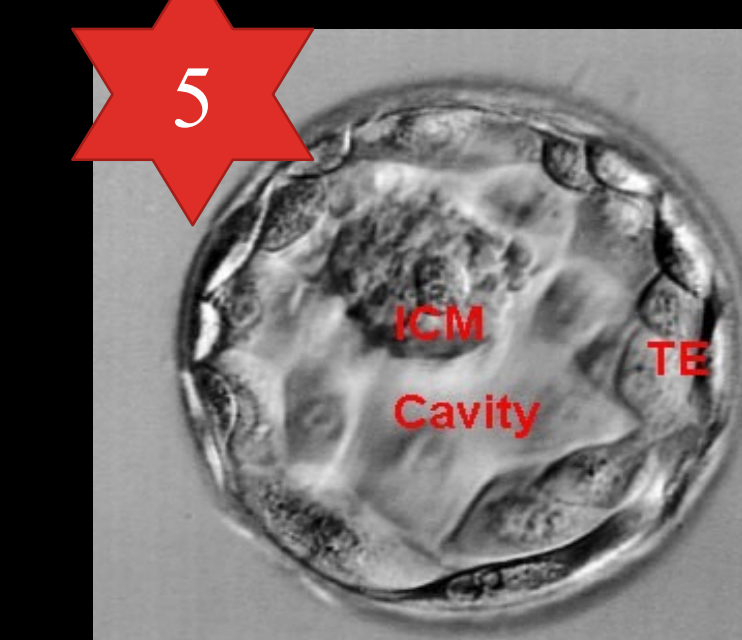
COS(6TH)
PROTOCOL:CCC+ANTAG
5 M2 aspirated



3

1st-4th
embryo
o

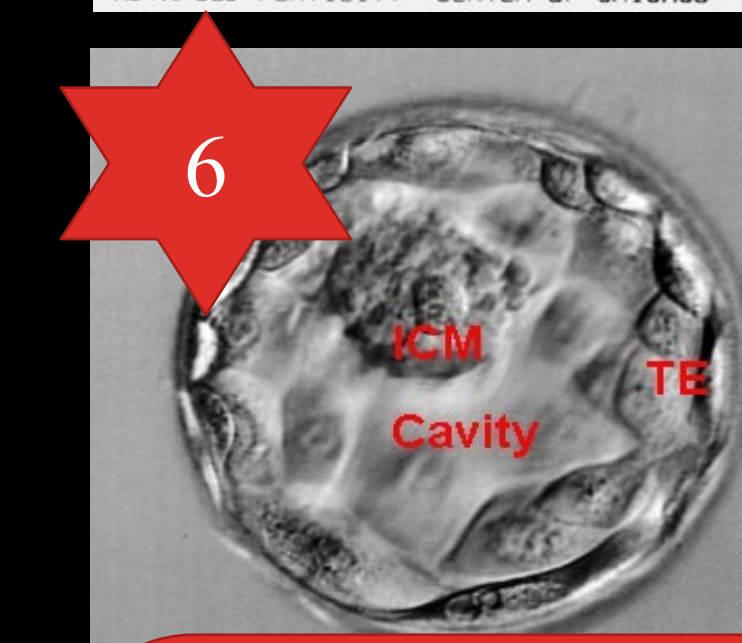
3 were affected &
1 was
undiagnosed



5

5th-9th
embryo
o

2 were normal &
2 were carriers &
1 was affected.



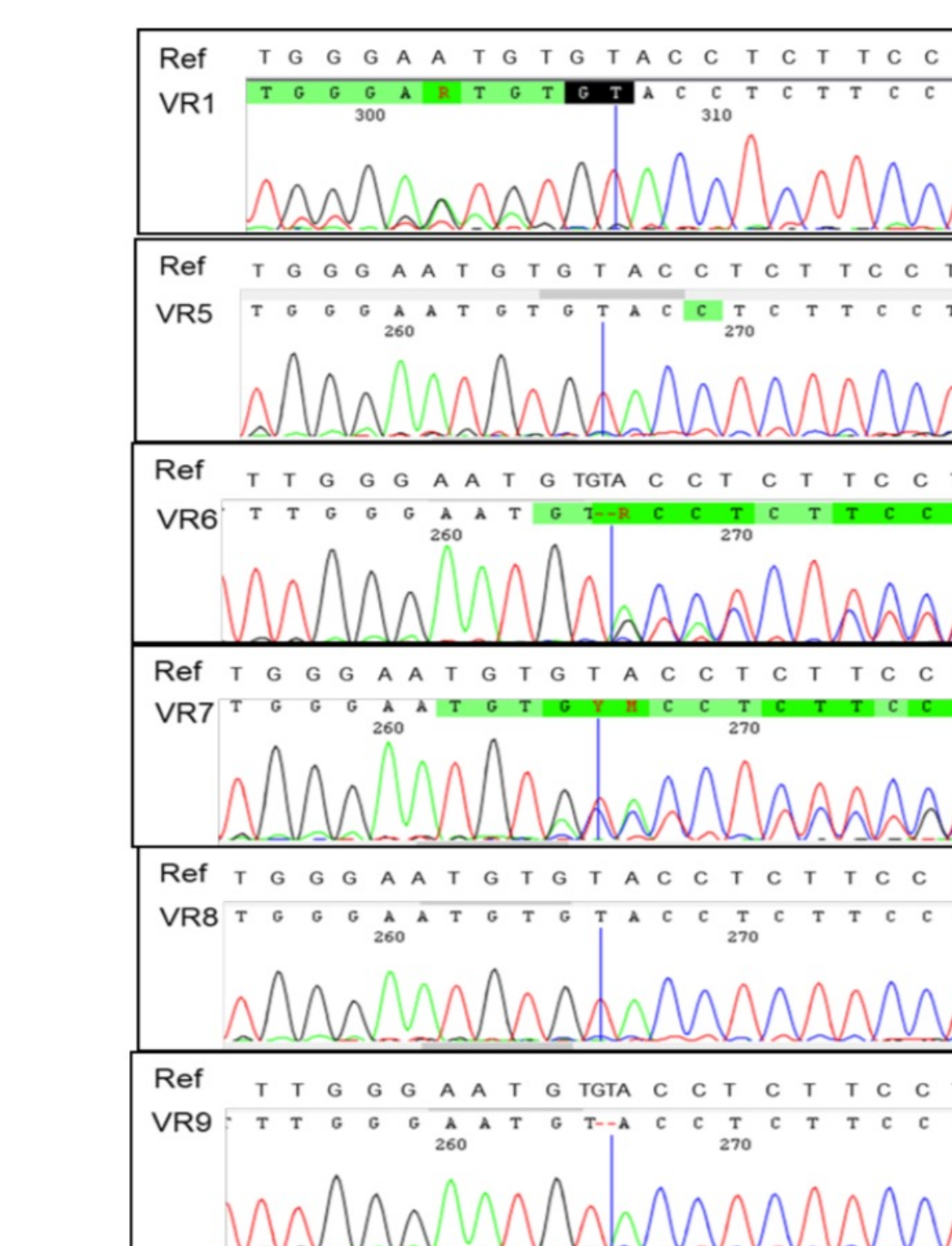
6

10th
embryo
o

Affected

Sanger Evaluation Results:
Snapshot of chromatogram showing variants in XPC gene are given below-

XPC gene (c.2277_2278GT)



Heterozygous Deletion (2-bp deletion)
(Need to Re-sequence)

Homozygous wild (Normal)

Heterozygous Deletion (2-bp deletion)

Heterozygous Deletion (2-bp deletion)

Homozygous wild (Normal)

Homozygous Deletion (2-bp deletion)

CONCLUSION:

In conclusion, PGT-M is a valid reproductive option for couples affected by rare monogenic disorders like XP. In this case report it is well elaborated how this technique helped a couple to have an healthy ongoing pregnancy of 20 weeks, serving as a boon to them. **This is the 1st case of XP in India detected by using novel ad hoc technique of PGT-M, resulting an healthy outcome.**

REFERENCES:

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3. J.E.Cleaver, "Defective repair replicationof DNA in XP," Nature ,vol.218,no.5142,pp.652-656,1968.

THANKS