Case Report

A Case Report of Genetic Cause of Primary Infertility-Xq deletion

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Introduction:

In X-chromosome, the proximal 'p' arm deletions as well as proximal 'q' arm deletions are usually associated with severe abnormalities resulting in primary amenorrhea. With more distal 'q' arm deletions in X-chromosome, menarche may occur normally followed by normal menstrual function but fertility problems do occur¹.

Here is a case report of oligomenorrhea and primary infertility, which ultimately ended in premature ovarian failure and was found to have female karyotype with terminal Xq deletion.

Case report:

Mrs. V. aged 28 years married since nine years presented with a complaint of primary infertility. She attained menarche at the age of 13. Since then her menstrual cyclicity was irregular, once in 2-3 months

with scanty flow and without dysmenorrhea. On examination, her height was 155 cms, and weight 60 kgs. Secondary sexual characters were well developed. Her vital signs were normal. She had abdominal obesity. Bimanual examination revealed a normal sized anteverted uterus. Cervix and vagina were normal and healthy. The couple was thoroughly evaluated for infertility and the male factor was found to be normal.

Her serological investigations at the time of admission were as follows:

Hemoglobin	- 12.5gms%
Serum levels of hormones:	
Prolactin	-15.5ng/ml
Thyroids stimulating hormone	- 2.9mIU/ml
Testosterone	- 0.26 ng/ml
17-hydroxy progesterone	- 2.2 mgs%
FSH	- 19.8mIU/ml
LH	- 7.2 mIU/ml

Ultrasound examination of the pelvis revealed a uterine size of 68X 34X33 mm with endometrial thickness of 5 mm (on the 18th day of LMP), right ovarian size of 22X20 mm, left ovarian size of 20X23 mm with no evidence of mature follicles in both the ovaries.

At diagnostic laparoscopy, pelvic organs were found to be normal along with bilateral positive tubal patency.

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Fig 1 : Sonographic evidence of dominant follicle

Fig 2 : Chromosomal analysis: female karyotype with Xq deletion

She was given a trial of three cycles of clomifene citrate without any success. Clomifene citrate was used for three cycles only at a dose of 50mg daily for five days from day three of the menstrual cycle in the first cycle and 100mg daily for five days in the remaining two cycles. In the fourth cycle she was given clomifene citrate along with gonadotrophins. Clomifene citrate was used at a dose of 100mg per day with FSH at a dose of 75 IU IM for seven days starting from day two of the menstrual cycle and single dose of HCG 5000 IU IM on the 11th day when the dominant follicle reached 18 mm in diameter.

The patient was lost to follow up for nearly six months but later approached us again with a history of eight months of amenorrhea. She was again evaluated for infertility. She was subjected to the estimation of serum gonadotrophins levels. Follicular stimulating hormone was 46.7 mIU/ml, luteinizing hormone level was 17.8 mIU/ml and serum estradiol level (E2) was less than 5pg/ml. All the values were consistent with menopausal range. There was also sonographic evidence of absent ovarian follicles. All these features suggested ovarian failure. The case was diagnosed as premature ovarian failure as her age as only 29 years.

Karyotyping was done. Cytogenetic analysis of peripheral blood lymphocytes showed female karyotype with terminal Xq deletions in all the cells examined (Fig. 2)

Discussion:

X-chromosome contains a short 'p' arm and a long 'q' arm. Most of the women with Xp deletions are short statured, regardless of their ovarian function, indicating the presence of other structural determinant genes within this region¹. The 'q' arm deletions generally result in ovarian failure, if they involve the proposed "critical region" – i.e. Xq13-q26. Proximal deletions like Xq15 are usually more severe, resulting in primary amenorrhea. With more distal 'q' arm deletions, menarche may occur but subsequently premature ovarian failure ensues¹.

Two regions of the X-chromosome were hypothesized to contain putative ovarian determinant genes, the POF1 region at Xq26-28 and another region at Xq13.3-Xp22². A more recently designated region of Xq22 is now termed POF2 and contains the Diaphanous 2 gene (Diaph 2)³. Deleted ovarian determinant genes probably enhance follicular atresia, but not to the extent that is observed in patients with a complete X-chromosomal deletion (45 X O)

Hence it is concluded that not only in primary amenorrhea, but also in women with dysovulatory infertility and repeated failed induction, karyotyping is indicated so that unnecessary treatment overburden can

be prevented and appropriate genetic counseling can be offered to the infertile couple. In selected cases, in which the genetic defect is known, it may be possible to use pre-implantation genetic diagnosis to screen embryos prior to uterine transfer and also, if conception occurs, prenatal diagnosis by chorionic villus sampling or amniocentesis is strongly recommended to rule out chromosomal rearrangements.

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