International Journal of Biomedical Research

ISSN: 0976-9633 (Online)
Journal DOI:10.7439/ijbr
CODEN:IJBRFA

Case Report

Primary ovarian failure in a teenager - A Case Report

V.B. Bangal[*1], N. B. Ghorpade[2], S .P.Gavhane[3], M.Suryawanshi[4]

[1]*Professor, Dept. of Obstetrics and Gynaecology, Rural Medical College of Pravara Institute of Medical Sciences, (Deemed University) Loni, Maharashtra, India*
[2]*Endoscopic Surgeon, Dept. of Obstetrics and Gynaecology, Rural Medical College of Pravara Institute of Medical Sciences, (Deemed University) Loni, Maharashtra, India*
[3]*Assistant Professor, Dept. of Obstetrics and Gynaecology, Rural Medical College of Pravara Institute of Medical Sciences, (Deemed University) Loni, Maharashtra, India*
[4]*Senior Registrar, , Dept. of Obstetrics and Gynaecology (OBGY), Rural Medical College of Pravara Institute of Medical Sciences, (Deemed University) Loni, Maharashtra, India*

***Correspondence Info:**
Dr. Vidyadhar B. Bangal
Professor, Dept. of Obstetrics and Gynaecology (OBGY),
Rural Medical College of Pravara Institute of Medical
Sciences (Deemed University), Loni, Maharashtra, India
E-mail- vbb217@rediffmail.com

Abstract

Primary ovarian failure (POF) is a heterogeneous disorder affecting approximately 1% of women <40 years. The most severe forms present with absent pubertal development and primary amenorrhea.Fifty percent of these cases are due to ovarian dysgenesis.These patients have poor fertility potential and are at risk of development of metabolic and systemic complications due to low levels of oestrogen. The diagnosis of POF may have a deleterious psychological impact and may lead to depression in a young, otherwise healthy woman.A case report of a teenage girl ,who presented with primary amenorrhoea due to ovarian failure is presented .She was investigated to confirm the diagnosis. Parents were counselled about the poor fertility prospects and the risk of other metabolic and systemic complications in long run due to low level of oestrogen.

Keywords: Primary ovarian failure, Primary amenorrhoea, Hypoplastic uterus, Hypoplastic ovaries, Ovum donation, Hypergonadotrophic ovarian failure

1. Introduction

Primary ovarian insufficiency is the loss of function of the ovaries before age 40.[1] A commonly cited triad for the diagnosis is amenorrhoea, hypergonadotropinism, and hypoestrogenism. If it has a genetic cause, it may be called gonadal dysgenesis[2] Fuller Albright *et al*. in 1942 first reported a syndrome in young women characterized by menopausal levels of follicle stimulating hormone (FSH), low estrogen levels and amenorrhoea. They named the condition "primary ovarian insufficiency" to distinguish the condition from secondary ovarian insufficiency, which is the failure of the pituitary to secrete FSH.[3] It has been estimated that POF affects 1% of the population.[4,5] Serum follicle-stimulating hormone (FSH) measurement alone can be used to diagnose the disease. Two FSH measurements with one-month interval have been a common practice. The anterior pituitary secretes FSH and LH at high levels due to the dysfunction of the ovaries and consequent low estrogen levels. Typical FSH in POF patients is over 40 mIU/ml (post-menopausal range).[6]

2. Case report

Sixteen year old girl was brought to gynaecological out patient department by her parents with the complain of

their daughter not having attended menarche. She did not have any other complain suggestive of cause for her primary amenorrhoea. There was nothing significant in the perinatal history of the child. There was no history of any major medical or surgical illness in the past. She was eldest sibling in the family with one younger sister and brother each. She had not been investigated or treated for her complains in the past. There was no significant family history of genetic ,metabolic ,endocrine or autoimmune diseases.

On examination, the girl weighed 45 kgs and her height was 162 centimeters. She did not have any gross features suggestive of any genetic or endocrinal or autoimmune disorder. Her breast development was subnormal. Other secondary sex characters were well developed. Her blood pressure was 110/70 mm of Hg. Her systemic examination did not reveal any abnormality. Her external genitalia were normal and hymen was intact.

Abdominal and pelvic ultrasonography revealed small tubular shaped uterus of size 5.3×1.3×1.9 cms with 3mm of endometrial thickness. The cervix and the body of the uterus were approximately of same size. Both ovaries measured 15mm ×20mm each. The findings were suggestive of Hypoplastic premature (Prepubertal) uterus and ovaries. Magnetic resonance imaging study of abdomen revealed uteus of 4.8×3.0×2.8 cms with small ovaries. There was no renal anamoly associated with this condition.

Her hormonal profile revealed normal Serum TSH value of 2.18 mIU/L. Her S.FSH (161.0 mIU/ml) and S.LH (41.11 mIU/ml) levels were grossly raised. Her S. Estradiol (12.90 pg/ml) level was low.Her S.AMH (<0.50ng/ml)value was very low. Diagnosis of hypogonadotrophic hypogonadism secondary to primary ovarian failure was made.

On further evaluation by laparoscopy the imaging findings were confirmed. Uterus was approximately of 4.5cm×3×2 cms in size and both ovaries were grossly hypoplastic. Vaginoscopy performed through 5mm hysteroscope revealed normal vaginal and cervical development .Patient did not have withdrawal bleeding following progesteron and then Oestrogen plus progesteron challenge test.

Patient's parents were counselled about the clinical condition and its implications on child fertility and possible complications due to hypoestrogenism. They were explained about the possible options available regarding her future childbearing. They were adviced for follow up .

3. Discussion

Premature ovarian failure (POF) causing hypergonadotrophic hypogonadism occurs in 1% of women. The age of onset can be as early as the teenage years, but varies widely. If a girl never begins menstruation, it is called primary ovarian failure. In majority of cases the underlying cause is not identified. The known causes include: (a) Genetic aberrations, which could involve the X chromosome or autosomes. A large number of genes have been screened as candidates for causing POF; however, few clear causal mutations have been identified. (b) Autoimmune ovarian damage, as suggested by the observed association of POF with other autoimmune disorders. Anti-ovarian antibodies are reported in POF by several studies, but their specificity and pathogenic role are questionable. (c) Iatrogenic following surgical, radiotherapeutic or chemotherapeutic interventions as in malignancies. (d) Environmental factors like viral infections and toxins for whom no clear mechanism is known.[1]

POF is biochemically characterized by low levels of gonadal hormones (estrogens and inhibins) and high levels of gonadotropins (luteinizing hormone, LH, and follicle stimulating hormone, FSH) (hypergonadotropic amenorrhoea).[2] The elevation of FSH is usually more marked than that of LH and an FSH value >30 U/L is indicative of ovarian failure. Ultrasound frequently reveals small ovaries without evidence of growing follicles. In the cases with primary amenorrhoea, gonadal dysgenesis is documented by the finding of streak ovaries. Histological examination of biopsies performed during pelvic laparoscopy in the case of hypoplastic ovaries (0.20–0.30 ml on ultrasound) may reveal the presence of primary follicles.[3]

The only features of history which are helpful in determining aetiology of ovarian failure are positive a family history, a concurrent autoimmune disorder or stigmata of one of the inherited conditions. In many instances a formal pedigree enquiry is required to determine other female family members who may be affected, particularly if the inheritance is passed through an unaffected male. Ten to 30% of women with POF already have a concurrent autoimmune disorder the most common of which is hypothyroidism.[1]

Management of POF needs to address the two major medical issues—hormone replacement therapy (HRT) and infertility. It is important to initiate the hormonal replacement therapy after the diagnosis of POF, as untreated patients are at a great risk of bone loss due to increased osteoclast activities, resulting in osteopenia as well as osteoporosis.[7] Furthermore, most of the patients develop symptoms of estrogen deficiency, including vasomotor flushes and vaginal dryness, both of

which respond to estrogen therapy effectively. Most women with primary ovarian failure opt for long term oestrogen replacement therapy in order to prevent symptoms of oestrogen deficiency and osteoporosis. The youngest women may require HRT for nearly 40 years. The degree to which this long term administration of oestrogen prevents cardiovascular disease or increases risk of breast cancer is unknown and we can only extrapolate from studies in older postmenopausal women. The main choice in oral HRT formulations is between conjugated oestrogens and oestradiol valerate which largely interchangeable. For those women are troubled by a side effects from oral oestrogen, a transdermal preparation may be the answer, particularly for those with concurrent hypertension or with additional risk factors for thrombosis. The transdermal estradiol patch (typically 100 mcg) is commonly recommended because of several advantages. It provides the replacement by steady infusion rather than by bolus when taking daily pills. It also avoids the first-pass effect in the liver.[8]

Infertility is the result of this condition, and is the most discussed problem resulting from it. Between 5 and 10 percent of women with POF may spontaneously become pregnant. Currently no fertility treatment has officially been found to effectively increase fertility in women with POF, and the use of donor eggs with *In-Vitro* Fertilization (IVF) and adoption have become more popular as a means of becoming parents for women with POF. Some women with POF choose to live child-free.[9]

There are additional health implications of the problem. Osteoporosis or decreased bone density affects almost all women with POF due to an insufficiency of estrogen. There is also an increased risk of heart disease, hypothyroidism in the form of Hashimoto's thyroiditis, Addison's disease, and other auto-immune disorders.[3]

Women also require personal and emotional support to deal with impact of diagnosis on their health and relationships. In addition, associated pathology needs to be assessed and managed so that long-term follow-up is essential to monitor HRT and for health surveillance.

Genetic counselling is nowadays recommended for several reasons, when a genetic form of POF is suspected or identified. All women who experience POF before the age of 30 years should perform a blood test for chromosomal assessment Genetic investigations may be useful for the early diagnosis of genetic defects underlying POF, when a female is born from a family with other female members affected with POF.[3]

4. Conclusion

The diagnosis of premature ovarian failure in a young women is a devastating event. One of the most neglected aspects of POF is the long-term psychological scar left by the diagnosis. This is especially true of younger women who experience low self-esteem and depression which cannot be accounted for solely by oestrogen deficiency. Counselling and support is essential for all women.

Patients with POF have infertility and hormone deficits. At present, fertility cannot be restored if the diagnosis is made after complete follicular depletion. In some cases, early diagnosis by genetic investigation may instead lead to advice for early conception or oocyte harvesting and preservation. Hormone defect may be substituted by estrogen/progestin preparations. The only solution presently available for the fertility defect in women with absent follicular reserve is represented by ovum donation.

References

1. Santoro N. Mechanisms of premature ovarian failure. *Ann Endocrinol.* 2003; 64:87-92.
2. Timmreck LS, Reindollar RH: Contemporary issues in primary amenorrhea. *Obstet Gynecol Clin North Am* .2003; 30:287-302.
3. Peccoz PB and Persani L Premature ovarian failure *Orphanet Journal of Rare Diseases* 2006, 1:9 doi:10.1186/1750-1172-1-9
4. Eberhard Nieschlag; Hermann M. Behre; Susan Nieschlag (July 2009). *Andrology: Male Reproductive Health and Dysfunction*. Springer. pp.221–. ISBN978-3-540-78354-1. Retrieved 10 November 2010.
5. Hubayter ZR, Popat V, Vanderhoof VH, *et al.*. "A prospective evaluation of antral follicle function in women with 46,XX spontaneous primary ovarian insufficiency". *Fertil. Steril.2010;* 94 (5): 1769–74
6. *Conway GS. Premature ovarian failure. Br Med Bull 2000; 56: 643–649*
7. Anasti JN, Kalantaridou SN, Kimzey LM, Defensor RA, Nelson LM . "Bone loss in young women with karyotypically normal spontaneous premature ovarian failure" *Obstet Gynecol.1998;* 91 (1): 12–5.
8. Kalantaridou SN, Nelson LM . "Premature ovarian failure is not premature menopause". *Ann. N. Y. Acad. Sci.* 2000;900: 393–402.
9. Van Kasteren Y. Treatment concepts for premature ovarian failure. *J Soc Gynecol Investig* 2001;*8*:*58*–59.