Case Report

Pregnancy in an Infertile Woman with Polycystic Ovary Syndrome

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Abstract

Introduction: *The most common cause of anovulatory infertility is polycystic ovary syndrome (PCOS). It is a syndrome of ovarian dysfunction associated with hyperandrogenism and polycystic ovary morphology. Several treatment options are available for women with infertility related to PCOS including weight reduction, clomiphene citrate, gonadotropins, laparoscopic ovarian diathermy, metformin and letrozole.*

Case Presentation: *This is a case report of 32-year-old infertile female who was married for 12 years and tried ovulation induction drugs several times but failed to conceive. She was overweight, hirsute, oligomenorrheic and lastly amenorrheic. Investigations revealed altered ratio of FSH and LH, and polycystic ovaries on ultrasound. Patient was adviced to do regular physical exercise and prescribed metformin and combined oral contraceptive pill. After treatment restoration of regular menstruation occurred, weight reduced and patient became pregnant.*

Conclusion: *Before choosing any treatment option for an infertile woman with PCOS proper control of abnormal metabolic conditions are necessary for a successful treatment outcome.*

Key words: *Polycystic ovary syndrome (PCOS), infertility, metformin.*

Introduction

Polycystic ovary syndrome (PCOS), also called hyperandrogenic anovulation (HA)[1], or Stein-Leventhal syndrome[2], is a set of symptoms due to a hormone imbalance in women[3]. Symptoms include: irregular or no menstrual period, heavy periods, excess body and facial hair, acne, pelvic pain, trouble getting pregnant, and patches of thick darker, velvety skin[4]. Associated conditions include: type 2 diabetes, obesity, obstructive sleep apnea, heart disease, mood disorders, and endometrial cancer[3]. PCOS occurs due to a combination of genetic and environmental factors[5]. Risk factors include obesity, not enough physical exercise and a family history of someone with the condition[6]. Diagnosis is based on two of the following three findings: oligo/amenorrhoea, hyperandrogenism (clinical or biochemical), polycystic ovaries on ultrasound (Rotterdam criteria). Other conditions that produce similar symptoms include adrenal hyperplasia, hypothyroidism, Cushing's syndrome and hyperprolactinemia[7]. The condition was first described in 1935 by American gynecologist Irving F. Stein, Sr. and Michael L, Leventhal, from whom name of Stein-Leventhal syndrome is taken[2]. Infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse"[8]. About 35% of the issues involved with infertility are due to women. A major cause of infertility in women is the inability to ovulate. PCOS accounts for 75% of cases of anovulatory infertility[9-10].

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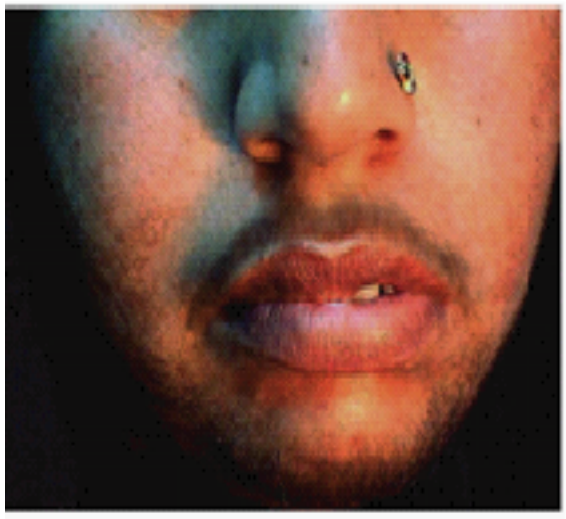
Case Presentation

In January 2014, a 32-year-old Bangladeshi female presented to KYAMCH, Sirajgonj for evaluation of infertility and menstrual irregularity. She was married for 12 years and had a history of abortion 11 years back. She was oligomenorrheic for last 8 years with a period of amenorrhoea for last 6 months. She also complained about excessive facial hair for last 2 years. She took ovulation induction drugs several times with different physicians' advice but failed to conceive. On examination her height was 155 cm, weight 69 kg, BMI-28.72 kg/m², pulse-72/min and BP-120/70 mm of hg. She was hirsute (Ferriman-Gallway 8) and had no acanthosis nigricans. Other systemic examination revealed no abnormality.

Figure -1: Hirsutism



1-A

1-B

Investigations revealed that her pregnancy test was negative and semen analysis of her husband was normal. Then the following investigations were done: Serum LH- 9.88 IU/L, FSH- 2.51 IU/L, TSH- 0.96 mU/L, prolactin- 5.55 ng/L, oestradiol- 210 pmol/L, testosterone-3.23 nmol/L, cortisol (9 am)- 14.30 ng/dl, 17 OH progesterone-1.30 nmol/L, OGTT- fasting-5.2mmol/L, 2 hours after 75 gm anhydrous glucose- 7.1 mmol/L. CBC, renal function, liver function tests, lipid profile reports were normal. USG of whole abdomen showed: mild fatty liver, adenexae - right ovary measures- 5.75×2.01×3.12 cm in size, about 18.92 cc in volume, left ovary measures - 5.60×1.99×3.13 cm in size, about 18.22 cc in volume, tiny follicles were seen in the periphery of the ovaries, suggestive of polycystic ovary. Secondary amenorrhoea with hirsutism together with the appearance of polycystic ovaries on ultrasound established the diagnosis PCOS.

Patient was prescribed Metformin 1 gram twice daily (starting from 500 mg OD dose and gradually increasing the dose)- continued, COCP (combined oral contraceptive pill)- 3 months. Patient was adviced to do regular physical exercise and to have a low glycaemic diet. Patient was on regular follow up. After 4 months regular menstruation was established and 6 kg weight was reduced. After 9 months the patient became pregnant.

Figure 2: USG - Polycystic ovaries

Discussion

PCOS is the most common endocrine disorders among women between the ages 18 and 44 years[10]. It affects approximately 5% to 10% of this age group[6].

The mechanism of anovulation in PCOS is uncertain, but there is evidence of arrested antral follicle development, which in turn may be caused by abnormal interaction of insulin and luteinizing hormone (LH) on granulosa cells[11]. Endocrine disruption such as changed levels of gonadotropin releasing hormone[12], gonadotropins (especially an increase in luteinizing hormone)[12,13], hyperandrogenemia & hyperinsulinemia[14] may also directly decrease fertility. Gonadotropins are released by gonadotroph cells of pituitary gland, these cells appear to harbor insulin receptors, which are affected by elevated insulin levels[12]. A reason that insulin sensitizers work in increasing fertility is that they lower total insulin levels in body as metabolic tissues regain sensitivity to the hormone. This reduces the overstimulation of gonadotroph cells in pituitary[12]. Menstruation can be regulated with COCP to minimize the risk of endometrial hyperplasia. The progestogen component inhibits LH secretion and thus ovarian androgen production & oestrogen component increases SHBG levels thus reduces free androgen concentration[9]. Weight loss, exercise & life style modifications have been proven effective in restoring ovulatory cycle and achieving pregnancy in overweight women with PCOS and should be the 1st line option for these women[15]. Studies also show that overweight women are less likely to respond to pharmacologic ovulation induction method[16]. Reducing insulin resistance by improving insulin sensitivity through medications such as metformin, have been an obvious approach and initial studies seemed to show effectiveness[17,18]. A review in 2014 concluded that there is no evidence that metformin could cause any increased risk of major birth defects in women affected by PCOS and treated during the 1st trimester[19].

Conclusion

The optimal treatment for infertile women with PCOS has not yet been defined. But before any intervention is initiated, preconceptional counseling should be provided emphasizing the importance of life style, especially weight reduction and exercise in overweight women. After controlling the metabolic condition of the disease, patient may be free from infertility.

References

1. Kollmann M, Martins WP and Raine-Fenning N. Terms and thresholds for the ultrasound evaluation of ovaries in women with hyperandrogenic anovulation. Hum. Repord. Update. 2014; 20(3): 463-4.
2. "USMLE-Rx". MedIQ Learning, LLC. 2014. Stein-Leventhal syndrome, also known as polycystic ovary syndrome (PCOS), is a disorder characterized by hirsutism, obesity, and amenorrhea because of luteinizing hormone-resistant cystic ovaries.
3. Polycystic ovary syndrome (PCOS): condition information [Internet]. 2013 May 23 [Retrieved 13 March 2015]. Available from: http;//www.nichd.nih.gov/.2013-05-23.
4. What are the symptoms of PCOS? [Internet]. 2013 May 23 [Retrieved 13 March 2015]. Available from: http;//www.nichd.nih.gov/.2013-05-23.
5. Diamanti-Kandarakis E, Kandarakis H and Legro RS. The role of genes and environment in the etiology of PCOS. Endocrine. 2006; 30 (1): 19-26.
6. How many people are affected or at risk for PCOS? [Internet]. 2013 May 23 [Retrieved 13 March 2015]. Available from: http;//www.nichd.nih.gov/.2013-05-23.
7. How do health care providers diagnose PCOS?" [Internet]. 2013 May 23 [Retrieved 13 March 2015]. Available from: http;//www.nichd.nih.gov/.2013-05-23.
8. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, Sullivan E, and Vanderpoel S, for ICMART and WHO. International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology. Fertility and Sterility. 2009; 92(5): 1522.
9. Turner HE and Wass JAH editors. Oxford Handbook of Endocrinology and Diabetes. 2nd ed. Oxford: Oxford University press; 2009:pp. 288-300.
10. Teede H, Deeks A and Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. BMC Med. 2010; 8(1): 41.
11. Gorry A, White DM and Franks S. Infertility in polycystic ovary syndrome: focus on low-dose gonadotropin treatment. Endocrine. 2006 August; 30 (1): 27-33.
12. Brothers KJ, Wu S, Divall SA, Messmer MR, Kahn CR, Miller RS et al. Rescue of Obesity-induced Infertility in Female Mice due to Pituitary-Specific Knockout of the Insulin Receptor(IR). Cell -

Metabolism. 2010; 12(3): 295-305.

13. Deepak A, Rao Le, Tao B and Vikas. First Aid for the USMLE Step1 2008. McGraw-Hill Medical. 2007. ISBN 0-07-149868-0.

14. Qiao J and Feng HL. Extra-and intra-ovarian factors in polycystic ovary syndrome:impact on oocyte maturation and embryo developmental competence. Human Reproduction Update. 2010; 17 (1): 17-33.

15. Vause TD, Cheung AP, Sierra S, Claman P, Graham J, Guillemin JA et al.; Society of Obstetricians and Gynecologists of Canada. Ovulation induction in polycystic ovary syndrome. J Obstet Gynaecol Can. 2010 May; 32 (5): 495-502.

16. Norman RJ, Noakes M, Wu R, Davies MJ, Moran L and Wang JX. Improving reproductive performance in overweight/obese women with effective weight management. Hum. Repord. Update. 2014; 10 (3): 267-280.

17. Mayo clinic Staff (4 April 2011). "Polycystic Ovary Syndrome-All". Mayoclinic.com. Mayo Clinic. Retrieved 15 November 2011.

18. Lord JM, Flight IH and Norman RJ. Metformin in polycystic ovary syndrome: systematic review and meta-analysis. BMJ. 2003; 327 (7421): 951-3.

19. Cassina M, Donà M, Di Gianantonio E, Litta P and Clementi M. First-trimester exposure to metformin and risk of birth defects: a systematic review and meta-analysis. Hum. Repord. Update. 2014; 20 (5): 656.