milann
The Fertility Specialists

FROM THE EDITOR'S DESK!

Greetings!!!

Dr Kamini A Rao

Medical Director,
Milann

Greetings and best wishes for a healthy and happy new year!

In our first issue of Life +ve for the year 2021, we bring you two articles and two case reports. The first article "Adolescent PCOS" by Dr Aiman and Dr Suchindra gives us a complete insight into the pathophysiology, diagnosis and management of PCOS in adolescents. The second is an article on "Polymorphism and PCOS" by Dr Akhila and Dr Arveen Vohra. Extensive evidence indicates that PCOS is a genetic disease and identification of candidate genes can help to assign predisposition factors and establish genetic makeup of affected women.

We also bring you two case reports – The first by Dr Rupali Khurana and Dr Vyshnavi Rao, entitled "Galloping levels of HCG does not always indicate Molar" which illustrates the importance of thorough monitoring and follow up by serial serum beta HCG and scans in a case with early USG scans showing abnormal cystic spaces in trophoblastic tissue. The extensive monitoring helped avoid unnecessary termination of pregnancy and ensure a positive outcome. The second case report is on "Caesarean Scar Pregnancy" that was identified early in a patient with a prior caesarean delivery and its successful management.

On a different note, the year 2020 was a challenging one for all of us but 2021 seems full of possibilities and we look forward to better times and newer opportunities ahead.

milann
The Fertility Specialists

ADOLESCENT PCOS

Dr S. Aiman Akram
Jr Consultant, Milann,
Indiranagar, Bangalore

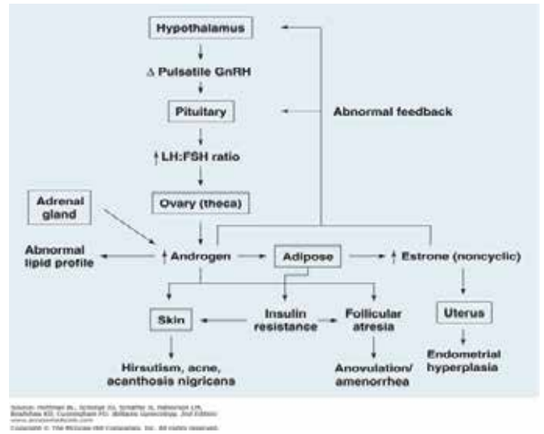
Dr Suchindra R
Sr Consultant, Milann,
Indiranagar, Bangalore

INTRODUCTION:

- Adolescence, as defined by the WHO, is the period between 10 and 19 years of age that includes significant and critical changes in growth, development and puberty. A gynaecological age of 8 or fewer years post menarche is identified within this terminology.
- Polycystic ovary syndrome (PCOS) is the most common endocrinopathy affecting 6–18% of adolescent girls. The major clinical features constituting the syndrome are menstrual irregularities, hyperandrogenism and polycystic ovaries, which could accompany obesity, insulin resistance and infertility in adulthood.
- Diagnosis of adolescent PCOS is both controversial and challenging due to the overlap of normal pubertal physiological changes with the diagnostic criteria.

PATHOPHYSIOLOGY:

- PCOS is a complex interaction of disordered neuroendocrine gonadotropin secretion, hyperandrogenism, insulin resistance, and hyperinsulinemia.
- Ovarian hyperandrogenism is the primary dysfunction with features of hyperinsulinaemia, insulin resistance, elevated luteinizing hormone (LH) and obesity.
- Certain metabolic changes in PCOS are also physiological during puberty. However, both insulin resistance and hyperinsulinemia, present severely in adolescents with PCOS compared to their non-PCOS counterparts. Insulin stimulates ovarian theca cell synthesis of androgens and inhibits hepatic production of sex hormone-binding globulin(SHBG).



CLINICAL FEATURES:

- Menstrual Irregularities:
  Increased levels of LH and low levels of FSH attribute to inadequate gonadal function. Menstrual irregularity is often the earliest clinical manifestation in the adolescent, which can be difficult to distinguish from anovulation associated with puberty because the hypothalamic-pituitary-ovarian axis matures progressively over several years post menarche

- **Hyperandrogenism**
  a. Clinical: Mild comedonal acne is common in adolescent girls, but moderate or severe comedonal acne (i.e. 10 or more facial lesions) or inflammatory acne is uncommon (less than 5%) and is affiliated to clinical hyperandrogenism. Hirsutism is a reliable marker of hyperandrogenism in adolescents, occurring in approximately 60% of girls with PCOS

  b. Biochemical:
  An increased bioavailability of free testosterone and androstenedeione is noted, due to lowered SHBG, increased sensitivity of theca cells to LH, hyperinsulinaemia, and insulin resistance.

- **Pelvic Ultrasound for the diagnosis:**
  Pelvic ultrasound should not be used for the diagnosis of PCOS in those with a gynaecological age of < 8 years (< 8 years post menarche) due to the high incidence of multi-follicular ovaries. A gynaecological age of < 8 years as the cut-off was selected, suggesting that the maximum ovarian volume is reached at age of 20.

ASRM-ESHRE GUIDELINES FOR ADOLESCENT PCOS:

Diagnostic Assessment :

A. Irregular cycles and Ovulatory dysfunction :

Irregular menstrual cycles are defined as:

- Normal in the first year post menarche as part of the pubertal transition.
- 1 to < 3 years post menarche: < 21 or > 45 days.
- 3 years post menarche to perimenopause: < 21 or > 35 days or < 8 cycles per year.
- 1-year post menarche > 90 days for any one cycle.
- Primary amenorrhea by age 15 or > 3 years post thelarche.

- The optimal timing of assessment and diagnosis of PCOS should be discussed, taking into account the psychosocial and cultural factors.

- For adolescents who have features of PCOS but do not meet diagnostic criteria, an "increased risk" could be considered and reassessment advised at or before full reproductive maturity, 8 years post menarche.

- This includes those with PCOS features before combined oral contraceptive pill (COCP) commencement, those with persisting features and significant weight gain.

B. Biochemical hyperandrogenism:

- Free testosterone, free androgen index, or calculated bioavailable testosterone should be used to assess biochemical hyperandrogenism.

- Androstenedione and dehydroepiandrosterone sulfate (DHEAS) could be considered if testosterone levels are normal; however, these provide limited aide in the diagnosis

C. Clinical hyperandrogenism:

- A comprehensive history and physical examination should be completed for symptoms and signs of clinical hyperandrogenism, as severe acne and hirsutism.

D. Ultrasound and Polycystic Ovarian Morphology (PCOM)

- Ultrasound should not be used for the diagnosis of PCOS in adolescents.

MANAGEMENT:

- Lifestyle modifications remain first-line management of overweight and obese adolescents with PCOS. Improved menstrual regularity, decreased cardiometabolic risks, and improved androgen excess can all be achieved with weight loss.

- Combined oral contraceptive pills (COCP) alone should be considered with a clear diagnosis of PCOS for management of clinical hyperandrogenism and/or irregular menstrual cycles.

When prescribing COCPs in adolescents with PCOS:

- Various COCP preparations have similar efficacy in treating hirsutism

- 20-30 micrograms of ethinyloestradiol or equivalent and natural estrogen preparations are preferred

- The relative and absolute contraindications and side effects of COCPs need to be considered.

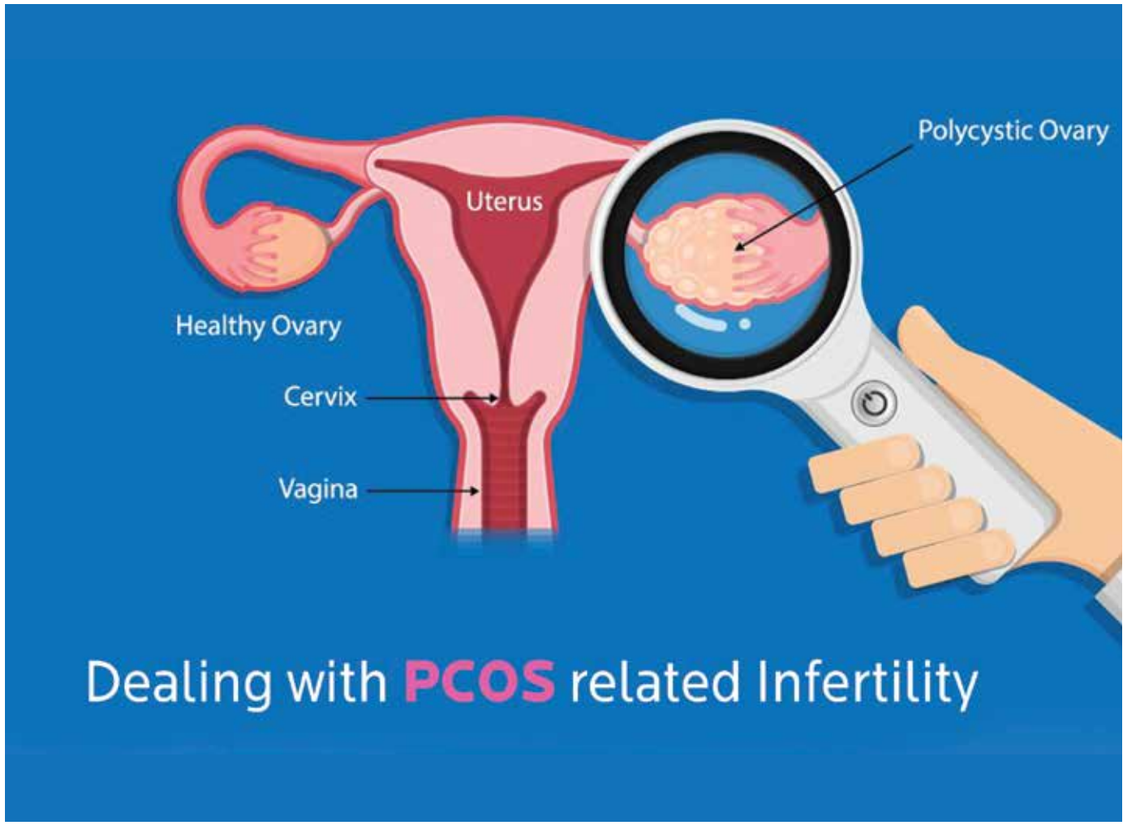
- The risk factors such as high BMI, hyperlipidemia and hypertension need to be evaluated.

- In combination with the COCP, metformin could be considered if BMI >=25 kg/m2 where COCP and lifestyle changes do not achieve desired goals.

- The use of the COCP alone with cosmetic therapy for at least 6 months is recommended prior to considering antiandrogens.

CONCLUSION:

- The diagnosis of PCOS in adolescent girls can be difficult and given its strong association with metabolic syndrome, a complete evaluation is indicated.
- Hyperandrogenemia is often the most reliable finding in the adolescent group, therefore a metabolic workup should be performed.
- Since, PCOS is a complex genetic disorder with familial clustering, the family history for both PCOS and metabolic disease should be ascertained.
- Recognizing adolescents at risk for PCOS and taking measures to reduce androgen levels by COCPs, progestins, antiandrogens or insulin sensitizers is critical in stalling the development of adulthood infertility, diabetes, metabolic syndrome, and endometrial carcinoma.
- In the adolescent where the diagnosis is not clear, it is preferable to follow the symptoms and repeat the evaluation in 6 to 12 months.

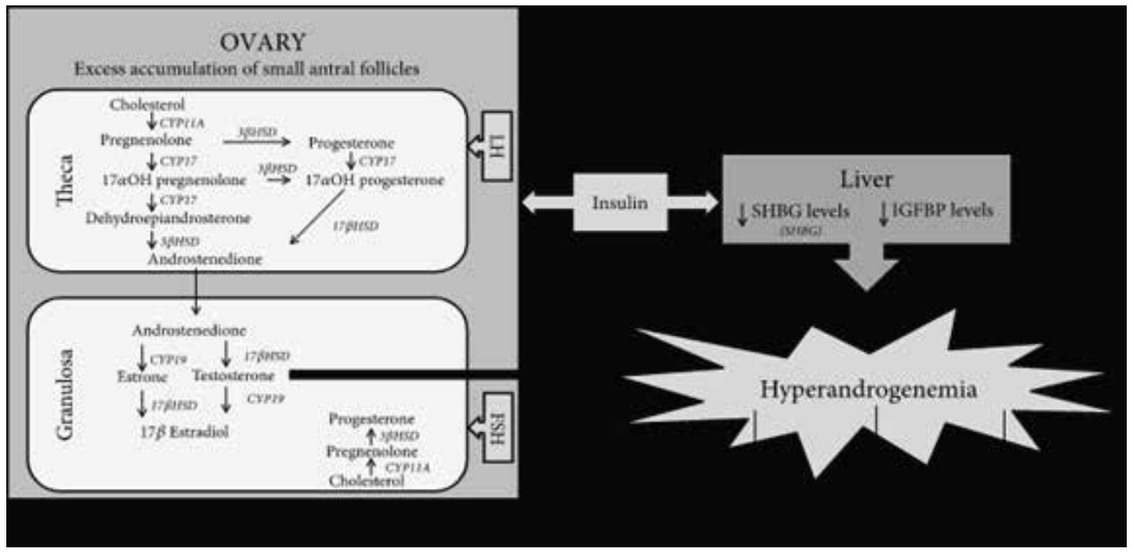


POLYMORPHISM AND POLYCYSTIC OVARY SYNDROME

Dr B Akila Preeti
Jr Consultant, Milann, Indiranagar, Bangalore

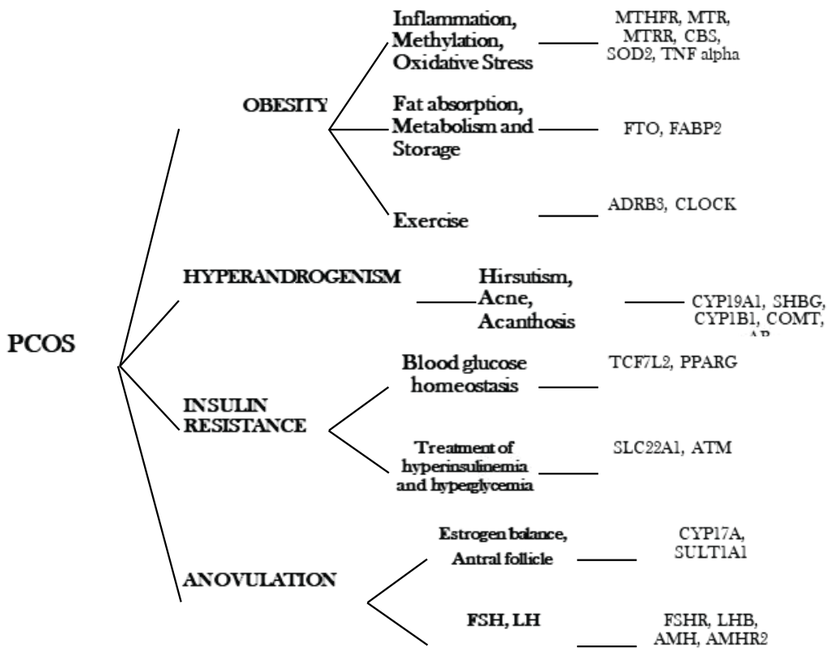
Dr Arveen Vohra
Sr Consultant, Milann, Indiranagar, Bangalore

- PCOS is a heterogeneous hormonal disorder that affects 4% to 12% of women of reproductive age.
- The cause of PCOS is considered to be multifactorial and includes genetic, endocrine, and environmental factors. Unhealthy lifestyle, diet or any infectious mediators increase the risk of PCOS.
- Apart from the environmental factors, there are genetic factors that are responsible for the aetiology of PCOS.
- According to databases, PCOS aetiology involves 241 gene variations.
- Polymorphism or any nucleotide change causes a defect in the transcriptional activity of a gene that leads to PCOS.
- Gene defect perturbs the biochemical pathway and leads to dysfunction of an ovary.



PCOS progression and severity increases with the increase in insulin levels and androgens.

Most commonly associated genes are as follows



OBESITY PCOS ASSOCIATED GENES AND THEIR CLINICAL APPLICATION

1) INSULIN SENSITIVITY

- **TCF7L2(Transcription Factor 7-Like 2 gene):** This gene is involved in insulin sensitivity and energy regulation. Polymorphism increases susceptibility to diabetes and insulin resistance.
- **PPARG (Peroxisome Proliferator -Activated Receptor Gamma):** Responsible for insulin sensitivity and lipid metabolism. Variation results in weight gain and obesity.

2) FAT ABSORPTION AND METABOLISM

- **FTO (Fat Mass and Obesity):** Correlated with dietary fats and satiety. Polymorphism causes high body mass index, high body fat percentage and waist circumference.
- **FABP2 (Fatty Acid Binding Protein 2):** Associated with intestinal absorption of fats and obesity. Variation in this gene affects fat absorption leading to weight gain and shows slower weight loss.
- **ADRB2 (Adrenoceptor Beta 2):** Responsible for fat mobilization in response to exercise. Variation can cause slow weight loss, higher weight re gain and less mobilization of fats through exercises.

5) METHYLATION

Variation in MTHFR, MTR, MTRR and CBS genes help in identifying risk of hyper homocysteinemia and associated conditions

- **MTHFR (Methylene tetrahydrofolate Reductase):** This enzyme is responsible for conversion of folic acid to folate.
- **MTR:** Responsible for conversion of homocysteine to methionine
- **MTRR:** Responsible for conversion of homocysteine to cysteine

All these enzymes help in maintaining the level of homocysteine.

2) INFLAMMATION

- **Tumor Necrosis Factor- alpha:** Inflammatory responses induces obesity and insulin resistance leading to further hormonal imbalance.

Management of inflammation is significant for achievement of weight loss.
Anti-inflammatory dietary support is required.
Intensity of exercises is required to reduce inflammation.

5) METHYLATION

GSTM1 (Glutathione S-Transferase Mu 1): It leads to Phase II detoxification and also removes carcinogens, xenobiotics. Polymorphism may lead to ineffective detox metabolism.

GSTT1 (Glutathione S-Transferase theta 1): It leads to detoxification of environmental and endogenous carcinogens. Variation may lead to increased risk of generation of toxic chemicals.

CYP1A1: Involved in Phase I detoxification and estrogen metabolism. Variation leads to generation of toxic chemicals.

SOD2 (Superoxide Dismutase 2): It encodes a mitochondrial protein that binds to superoxide byproducts of oxidative phosphorylation and converts them to hydrogen peroxide and diatomic oxygen. Polymorphism leads to increased risk to generate toxic chemicals. Requirement of antioxidants in polymorphism

PCOS ASSOCIATED GENES CAUSING INSULIN RESISTANCE

1) INSULIN SENSITIVITY: TCF7L2, PPARG
2) TREATING HYPERINSULINEMIA:

- **SLC22A1, SLC47A1, SLC22A2:** Metformin transportation in different organs gets affected due to these mutations.
- **ATM:** It is responsible for activation of Adenosine monophosphate kinase.

Drug dosage can be optimized based on the variation of these 4 genes.

3) HIRSUTISM, ACNE, ACANTHOSIS:

- **Androgen receptor gene:** Variation leads to increased androgen sensitivity.
- **CYP19A1:** It is responsible for testosterone to estradiol conversion. Polymorphism leads to an increase in testosterone levels.
- **SHBG(Sex Hormone Binding Globulin)** Polymorphism of this gene leads to abnormal SHBG and androgen levels.

4) ESTROGEN BALANCE:

- **CYP1B1:** This gene is responsible for the production of estrogen metabolites and procarcinogens thereby minimizing the risk of cancer.
- **COMT (Catechol -O- Methyl Transferase):** Involved in methylation and inactivation of catechol estrogen. Polymorphism leads to increased risk of breast cancer.

PCOS ASSOCIATED GENES CAUSING INSULIN RESISTANCE

1) ESTROGEN BALANCE:

- **SULT1A1 (Sulfotransferase 1A1):** It is involved in inactivation and elimination of estrogens and its metabolites thus preventing estrogen-mediated mitosis and mutagenesis.

2) ESTROGEN BIOSYNTHESIS:

- **CYP17A1:** This gene is involved in estrogen biosynthesis. Polymorphism leads to high estrogen-progesterone levels, PCOS and breast cancer risk.

3) FSH QUALITY:

- **FSHR:** Mutation in follicle-stimulating hormone receptor gene is responsible for the low quality of body FSH. The requirement of exogenous FSH and its dosage can be decided.

4) FSH ACTION AND OOCYTE NUMBER:

- **LHB:** Polymorphism in Luteinizing Hormone Beta gene decides whether exogenous LH supplement is necessary or not. Polymorphism affects oocyte number.

5) AMH/AMHR2:

- The mutation has an impact on follicular development. FSH dosage can be recommended.

CLINICAL SIGNIFICANCE

- PCOS clusters within families and having a first-degree relative suffering from PCOS conveys a 25% risk of either developing the full-blown clinical picture or having a 25% risk of sharing characteristics of the syndrome amongst siblings.

- The disorder has also been reported to be associated with metabolic syndromes, such as Type II Diabetes, dyslipidemia, and hypertension.
- The increased risk of T2DM and cardiovascular disease in women with PCOS suggests that those affected might share the same etiologic determinants, thus prompting an investigation between PCOS and T2DM-related genes.
- By screening of genes for Obesity, Insulin Resistance, Anovulation, Hyperandrogenism, it provides insight into the conditions which might be due to genetic variations, which are unknown otherwise.
- However, the genetic significance and the exact pathophysiological relevance of most of the genes with PCOS are still unclear and need to be confirmed.
- Polymorphic variants of genes have been garnered mainly by genome-wide analysis and epigenetic regulation such as DNA methylation and non-coding RNAs have been more recently linked with PCOS.

CONCLUSION:

- Polycystic Ovary Syndrome (PCOS) is a heterogeneous endocrine disorder with typical symptoms of oligomenorrhea, hyperandrogenism, hirsutism, obesity, insulin resistance and increased risk of type 2 diabetes mellitus.
- Extensive evidence indicates that PCOS is a genetic disease and numerous biochemical pathways have been linked with its pathogenesis.
- Several genes from these pathways have been investigated, which include those involved with steroid hormone biosynthesis and metabolism, the action of gonadotropin and gonadal hormones, folliculogenesis, obesity and energy regulation, insulin secretion and action and many others.
- Identification of candidate genes can help to assign predisposition factors and establish genetic makeup of affected women.
- This would further help to understand complex phenotypes of PCOS and advance the design of therapeutic approaches which would ameliorate major comorbidities like T2DM, metabolic syndrome, CVD, endometrial cancer, and so forth in later life.
- The severity can only be reduced when proper precautionary measures i.e. weight loss, healthy diet and recommended medications are followed

GALLOPING LEVELS OF HCG DOES NOT ALWAYS INDICATE MOLAR! A CASE REPORT

Dr. Rupali Khurana
Jr Consultant, Milann, JP, Nagar Bangalore

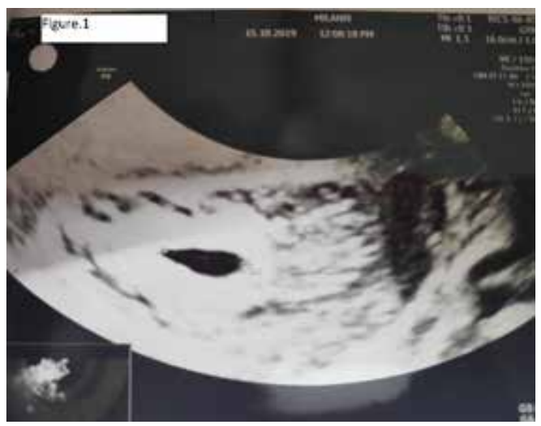
Dr. Vyshnavi Rao
Sr Consultant, Milann, JP, Nagar Bangalore

INTRODUCTION:

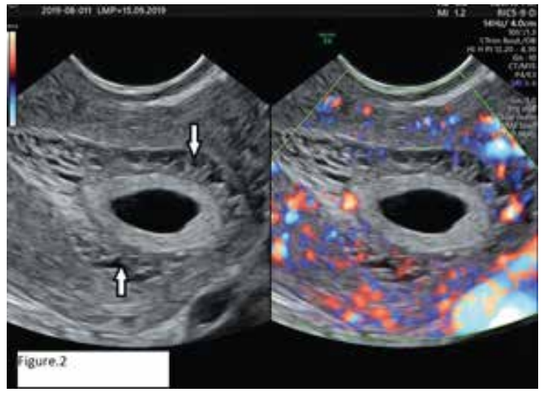
Multiple cystic spaces in trophoblastic tissue can be seen in many conditions. The causes of cystic spaces within the placenta are venous lakes, true placental cysts, hydropic degeneration of placenta & placental mesenchymal dysplasia. The other causes of cystic spaces adjacent to the placenta are subchorionic/retroplacental hematoma and vanishing twin. It is important to differentiate among them because management and outcomes differ. This case report highlights the importance of close follow up in a patient with presence of cystic spaces in trophoblastic tissue in early USG

CASE REPORT

Mrs. B, aged 24 years and Mr. A, aged 28 years presented to our hospital in June 2019 with primary infertility. They were married for 5 years. Mr. A was a case of azoospermia and on further workup was diagnosed as a case of congenital ejaculatory duct obstruction. Open fine needle aspiration of testes was done and an ample number of sperms were obtained which were frozen. After a thorough review of their history and clinical examination the couple was counselled and they decided to go ahead with one cycle of IVF and embryo transfer. Three 8 cell grade A embryos were transferred and proper luteal phase support was given. The patient conceived and she followed up with serum beta HCG. After two weeks of transfer, the values were 1604 mIU/ml and the early pregnancy scan showed a single intrauterine gestational sac corresponding to 4.2 weeks according to the mean sac diameter (Fig 1).



Mrs B was again followed up after one week with serum beta HCG of 4196 mIU/ml but this time her scan showed a single live intrauterine pregnancy corresponding to 5.2 weeks with the periphery of the gestational sac showing multiple small cystic spaces within the trophoblastic tissue. No vascularity was seen within (Fig 2).



The patient was counselled regarding the same. One week later serum beta HCG values were 48875 mIU/ml and the scan showed a single live intrauterine pregnancy corresponding to 6.5 week and multiple small cystic spaces persisting as the previous scan (Fig 3).

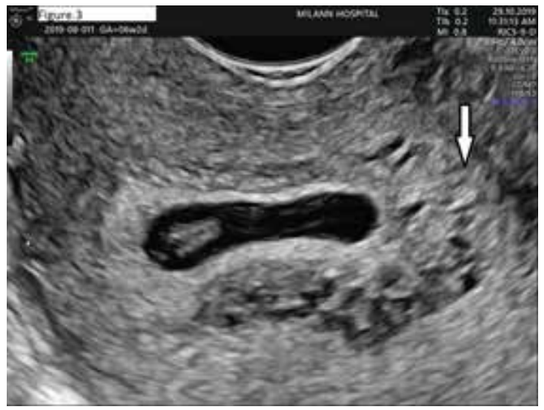
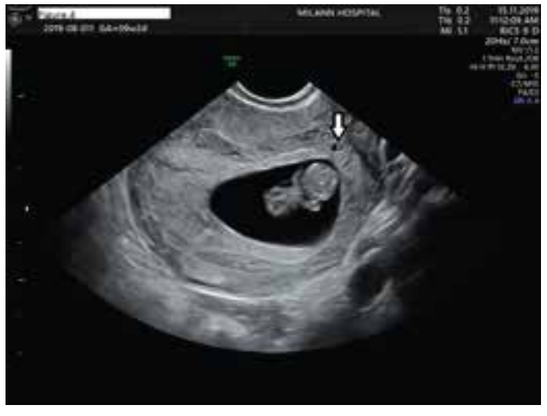


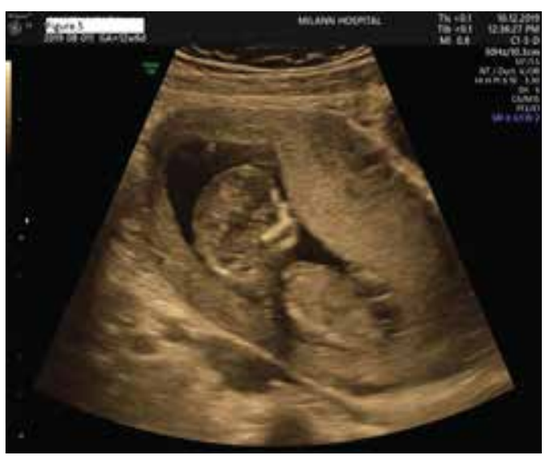
Table 1

Weeks of gestation in scan	Serum beta HCG (mIU/ml)
4.4	1604
5.6	4196
6.0	12210
6.3	20688
6.5	48875

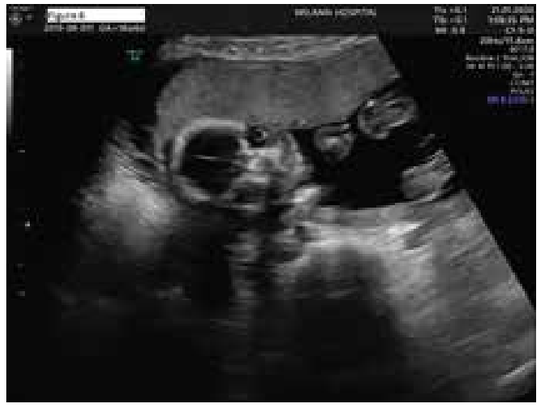
A scan was repeated two weeks later of the second scan and it showed a single live intrauterine pregnancy corresponding to 9.2 weeks and small cystic spaces within the trophoblast were significantly reduced as compared to previous two scans (Fig 4).



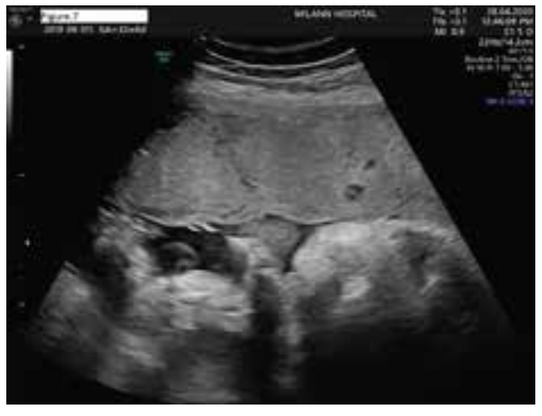
Mrs B was then referred to a maternal and fetal medicine consultant. Her first-trimester scan which included NT for assessment of risk for aneuploidy (low risk), and fetal morphology was normal and gestational age was corresponding to 12.6 weeks with subjective reduction in cystic spaces in comparison with earlier scans (Fig 5).



Her anomaly scan was done at 18.6 weeks which showed no anomaly and the cystic spaces in trophoblastic tissue were further reduced (Fig 6).



Mrs B had an uneventful antenatal period. Her growth scan at 32 weeks was normal (Fig 7).



She delivered a healthy male baby of 2.5kg by C-section at 39 weeks of gestation in a government hospital with an uneventful intraoperative and postoperative period.

DISCUSSION

The presence of cystic areas in trophoblastic tissue during early USG exam A differential diagnosis for the same is PMD. It is important to distinguish PMD from a mole pregnancy because of the unfavourable outcome associated with molar pregnancy.

Placental mesenchymal dysplasia (PMD) is a rare benign entity characterized by placentomegaly and grape-like vesicles resembling molar pregnancy on ultrasonography. The cause of this clinical entity is currently still unknown. All the reports are episodic and no systemic research has been done. The true incidence is not known but it has been estimated at 0.02%. Approximately 23% of the cases of PMD are associated with Beck-with-Wiedermann syndrome, which is characterized by macrosomia, exomphalos, macroglossia, omphalocele, internal visceromegaly, placentomegaly, and increased childhood tumour but the fetuses are normal in the majority of cases. Human chorionic gonadotrophin is useful for differential diagnosis. When there is the combination of a molar appearance to the placenta and a sonographically normal fetus, suspicion for PMD may be particularly increased. In PMD, a blood test reveals elevated AFP while β-hCG slightly increases. The diagnosis of PMD is only confirmed after evaluation of placental pathology. Grossly, it is characterized by placentomegaly, dilated or aneurysmal chorionic vessels, and fibromuscular hyperplasia or cystic villi. Microscopic findings include mesenchymal hyperplasia fibromuscular hyperplasia or cystic villi. Microscopic findings include mesenchymal hyperplasia

In this case, since the serum beta HCG values were constantly within the normal range the diagnosis of molar pregnancy was ruled out. Given the presence of normal fetus on ultrasound and low-velocity colour flow within the cystic placental mass on colour Doppler, the possibility of PMD was considered. The final diagnosis can only be confirmed after the histopathological examination of placenta post-delivery. Mrs B's placenta was reported as normal on gross examination but no microscopic examination was done.

CONCLUSION

This case illustrates the importance of a thorough monitoring and follow up by serial serum beta HCG and scans in a case with early USG scans showing abnormal cystic spaces in trophoblastic tissue. The rare clinical entity, PMD, should be kept in mind in such cases to avoid unnecessary termination of pregnancy.

CAESAREAN SCAR PREGNANCY – A CASE REPORT

Dr.T.Shilpa Reddy
Jr Consultant, Milann, JP, Nagar Bangalore

Dr. Sunitha M
Sr Consultant, Milann, JP, Nagar Bangalore

ABSTRACT:

Cesarean scar ectopic pregnancies are a rare form of extrauterine pregnancies, yet their incidence is increasing, given the rise in caesarean deliveries. Similar to other ectopic pregnancies, cesarean scar ectopic pregnancies pose a great risk for maternal haemorrhage and ultimately maternal mortality. Diagnosis is often delayed and most of the women present with rupture uterus leading to maternal shock. We hereby report a case of a cesarean scar ectopic pregnancy that was identified early in a patient with a prior caesarean delivery and its successful management.

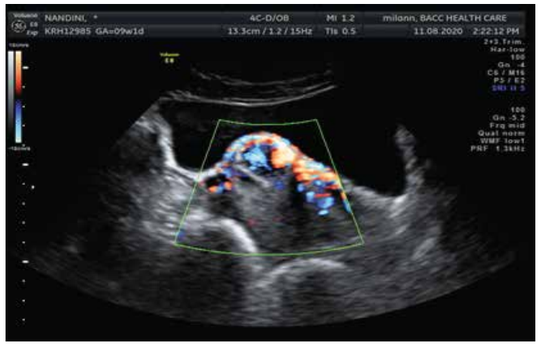
CASE REPORT:

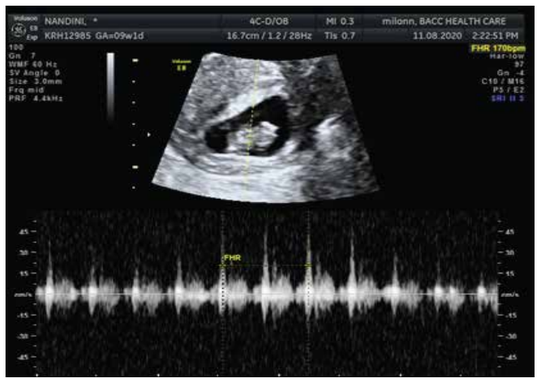
A 33-year-old woman P1L1 presented to Milann with secondary subfertility of 1 1/2 years duration. She was a known case of PCOS with irregular menstrual cycles. Her past obstetric history revealed that she had conceived naturally after evaluation for primary infertility. An elective lower segment caesarean section was performed at 37 weeks of gestational age because of gestational diabetes mellitus and macrosomia. She delivered a 3.9 kg female baby who is currently 5 years old and is alive & healthy. Postoperative period was uneventful. Medical history was nonsignificant except for hypothyroidism for which she was on T.Thyronorm 25 mcg. Physical examination was unremarkable with a BMI of 24. In view of secondary subfertility, the couple were investigated.

Investigations- Female partner: FSH-6.4 mIU/ml, LH-10.2 mIU/ml, AMH-5.2ng/ml, TVS–PCO Morphology. Male partner: Semen Analysis revealed Oligoasthenoteratozoospermia. Because of severe male factor infertility couple were counselled for IVF. OPU was done in November 2019 and 21 oocytes were retrieved. OHSS preventive measures were taken. 15 M2/10 F/8C/6-8CG1 embryos were obtained. A “freeze all” policy was initiated. During her first FET in December 2019, 1-2AA was transferred and she failed to conceive. A second FET was performed in June 2020 during which 3-8CG1 embryos were transferred. She conceived during that cycle. Beta HCG 2 weeks following the embryo transfer was 1570 mIU/ml.

Ultrasonography was done at 5 weeks of gestational age – Gestational sac was seen in the lower uterine cavity near the previous caesarean scar site with evidence of minimal subchorionic haemorrhage 0.7 cms X 0.31 cms. She was clinically stable and was monitored closely. The patient and her attenders were counselled at every visit about the warning symptoms as well as the pregnancy outcome. The patient decided to wait under close surveillance with serial scans.

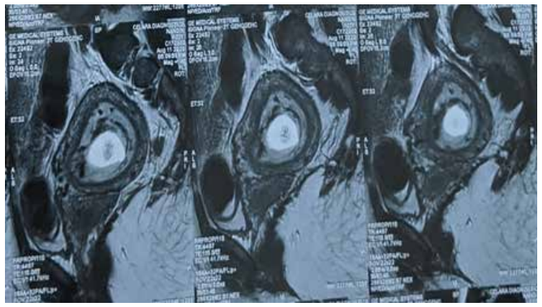
Ultrasonography was done at 9 weeks of gestational age - The gestational sac was seen in the lower uterine segment invading the myometrium at the previous scar area measuring 2.6 x 3 cms. Evidence of fetal cardiac activity was noted. Myometrial mantle - 3 mm. Increased vascularity was noted on Doppler. Serosa was intact.



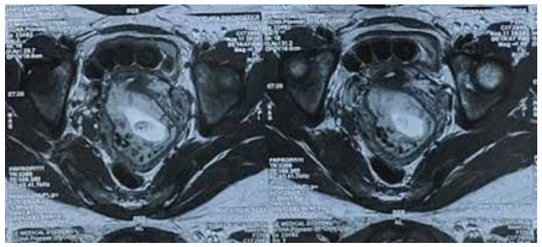


MRI pelvis on 12th August 2020 confirmed the presence of caesarean scar ectopic pregnancy.

SAGITTAL VIEW:

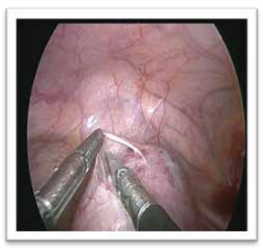


SAGITTAL VIEW:

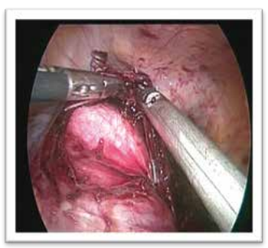


Patient had no complaints of pain/bleeding PV and was asymptomatic. The patient was counselled regarding management options. Surgical management of the scar ectopic pregnancy hysteroscopically under ultrasound and laparoscopic guidance was planned. Patient and attenders were counselled in detail regarding the possibility of torrential haemorrhage and the need for hysterectomy if need be, as a life-saving measure. Informed high-risk consent was taken after explaining the clinical situation.

T.Misoprostol 200 mcg was inserted vaginally 2 hrs prior to the procedure. Suction evacuation was done under ultrasound guidance. The patient had profuse vaginal bleeding; was noted to have an evolving haematoma visible on ultrasound at the region of the caesarean scar area Laparoscopy was performed and the site of the haematoma was identified by a bluish discolouration noted on the lower uterine body. UV Fold of peritoneum was opened, bladder pushed down. There was a bleeder noted near the right uterine artery at the area of the scar defect. There was significant myometrial thinning at the area of the defect suggestive of Imminent scar rupture. Myometrium was reinforced with endo suturing. Hemostasis secured. A check hysteroscopy done showed intact endometrial cavity



BLUISH BULGE NOTED IN THE LUS

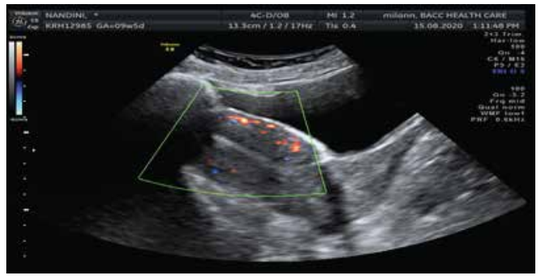


DISSECTION OF UV FOLD OF PERITONEUM

BLEEDER LOCALISED AT THE AREA OF RIGHT UTERINE.

THINNED MYOMETRIUM REINFORCED WITH ENDOSUTURES

She was transfused with 1 unit of PRBC postoperatively. She was given IV Antibiotics and other supportive measures. A repeat Beta HCG 2 weeks following the procedure was 14 mIU. Scan done showed intact myometrium with evidence of healing.



DISCUSSION:

Caesarean scar pregnancy (CSP) is a rare form of ectopic pregnancy whereby the gestational sac is fully or partially implanted within the scar caused by a previous caesarean section (CS). The first case was reported in 1978. Estimates of CSP incidence range from 1/1800 to 1/2500 of all pregnancies. It has been estimated that 6.1% of pregnancies in women with at least one previous CS and a diagnosis of ectopic pregnancy will be CSP.

PATHOPHYSIOLOGY:

Little is known about the mechanism and etiopathogenesis of CSP. Endometrial and myometrial disruption or scarring could be predisposing factors in abnormal pregnancy implantation. The most probable mechanism explaining scar implantation is invasion by the implanting blastocyst through a microscopic tract that develops from the trauma of an earlier CS. The presence of a CS scar in the uterus may also inhibit implantation of the gestational sac secondary to the more global effect of prior surgery on the endometrium, rather than just the physical presence of a scar. The risk of scar implantation might be proportional to the size of the anterior uterine wall defect, possibly caused by a larger surface area induced by the scar.

RECURRENCE:

Most women have a normal pregnancy following a CSP. The risk of recurrence has been reported as 3.2–5.0% in women with one previous CSP treated by dilatation and curettage with or without uterine artery embolisation. Factors associated with increased risk of recurrence include a uterine segment thickness measuring less than 5 mm, gestational sac bulging into the utero-vesical fold, caesarean delivery in a rural community hospital and history of irregular vaginal bleeding and abdominal pain during previous CSP.

DIAGNOSIS:

Box 1. Ultrasound criteria for diagnosis of caesarean scar pregnancy (CSP)

- Empty uterine cavity and closed and empty cervical canal
- Placenta and/or a gestational sac embedded in the scar of a previous caesarean section
- A triangular/round or oval-shaped gestational sac that fills the niche of the scar
- A thin or absent myometrial layer between the gestational sac and the bladder
- Yolk sac, embryo and cardiac activity may or may not be present
- Evidence of functional trophoblastic/placental circulation on colour flow Doppler examination, characterised by high velocity and low impedance blood flow
- Negative 'sliding organs' sign

SAGITTAL VIEW:

CSP can be classified into two types based on imaging findings and pregnancy progression. Type 1 or Endogenic CSP is where implantation occurs on the scar and the gestational sac grows towards the cervico-isthmic or uterine cavity. Type 2, or Exogenic CSP occurs when the gestational sac is deeply embedded in the scar and the surrounding myometrium and grows towards the bladder. In exogenic types, a layer of myometrium may be seen between the gestational sac and the bladder at an earlier stage. This becomes thin and eventually disappears with bulging of the gestational sac through the gap as the pregnancy progresses, thus carrying a greater risk of earlier rupture. In two-thirds of cases, the thickness of the scar may be less than 5 mm. Our case belonged to type 2 exogenic variety

DIFFERENTIAL DIAGNOSIS:

Published literature reveals that 13.6% of CSP are misdiagnosed either as inevitable miscarriages, cervical ectopic or an intrauterine sac implanted in the lower corpus. Sliding sign on the TVS helps to differentiate between an inevitable miscarriage and cervical/CSP.

MANAGEMENT:

There is no consensus on the preferred mode of treatment for CSP; cases and series have reported different treatment modalities (Box 2). There are several variables to consider before recommending a treatment option (Box 3).

All treatment options carry a risk of haemorrhage and subsequent hysterectomy. Treatment should be individualized based on full pre-treatment evaluation. In principle, pregnancy should be ended as soon as possible after confirming the diagnosis, with the aim of removing the gestational sac and the CSP mass to retain future fertility.

Box 3. Factors influencing management choices

Patient factors	• Symptoms • Fertility wishes • Acceptability of prolonged follow up • Associated lesions • Surgical risk factors • Response to initial treatment
Caesarean scar pregnancy (CSP)	• Gestational age • Human chorionic gonadotropin (hCG) levels • Size of CSP mass • Type of CSP • Myometrial thickness • Viability
Facilities	• Interventional radiology • Surgical expertise/facilities • Monitoring facilities

CONCLUSION:

Diagnosis and management of Caesarean scar pregnancy needs considerable expertise and a multidisciplinary approach to prevent complications. Increasing Caesarean section rates indicate that clinicians will encounter CSP from time to time. A primary preventive strategy is to focus on reducing the number of primary CS performed without medical indications. The risk of long-term complications such as CSP and placenta accreta should be specifically emphasized when counselling women requesting CS for nonmedical reasons. Prompt and accurate diagnosis of CSP and individualized treatment and follow up are required to reduce overall morbidity.