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A Case Report of Gestational Trophoblastic Disease with Co-Existing Live Pregancies Following In-Vitro Fertilizatio

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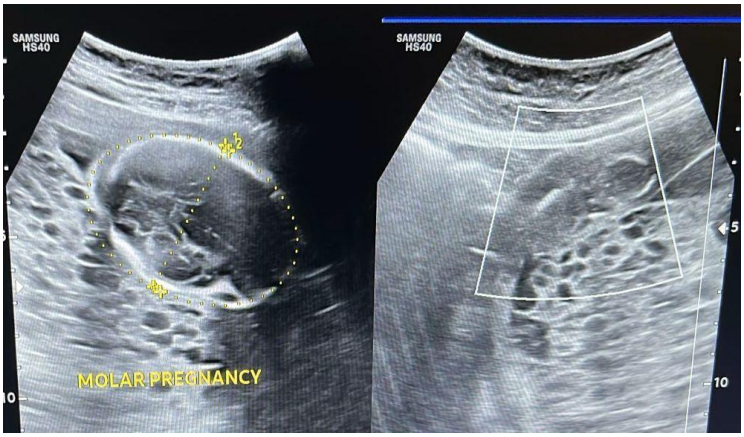
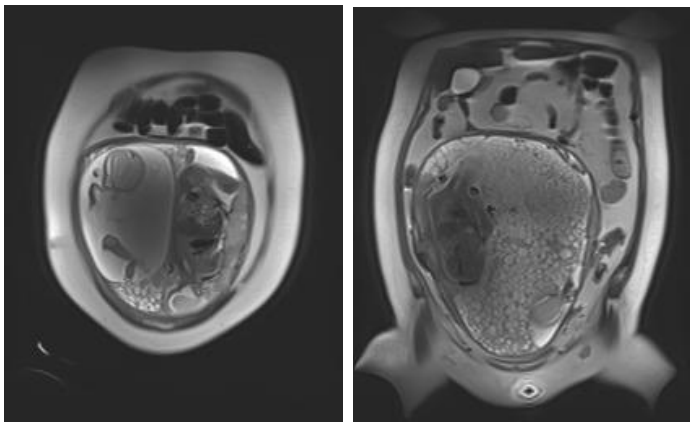
I. INTRODUCTION

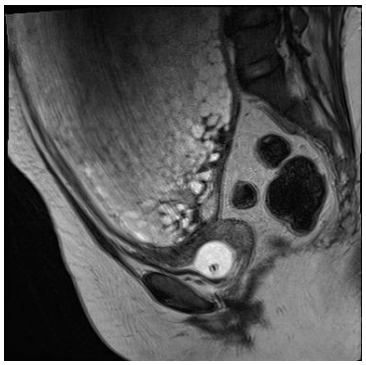
- Hydatidiform Mole with a live fetus is rare with a natural incidence of one in 20,000 to 1,00,000 pregnancies (Jones and lauersen 1975, McDonald and ruffolo 1983).
- IVF has emerged as a boon for infertile couple.
- The occurrence of molar pregnancy along with a precious IVF conception is one of the challenge leading to a multitude of questions regarding the etiology.
- Clinical dilemma to decide regarding continuation of pregnancy or termination could be addressed by prenatal karyotyping of the co-existing fetus and presence and absence of maternal complications or expectant management.

II. CASE PRESENTATION

- A 30 year old women (Husband 33 yrs. old), G_3A_2 , married since 10 years with In-Vitro fertilization (Intra Cyto Plasmic Sperm Injection) conception, 24 week gestation, O +ve blood group (Husband A +ve), unbooked, referred from other hospital, came into the casualty with severe bleeding per vaginum, hypovolemic shock and on inotropic support.
- She had a history of transfer of 2 blastocyst and 1 morula staged embryos with triplet gestation in early USG reports (6 weeks). USG at 11 weeks showed trichorionic triamniotic triplets with one showing molar changes involving placenta.She underwent fetal reduction at 11 weeks and triplets reduced to twins.
- After stabilization of patient, ultrasound and MRI was done.
- Ultrasound showed 2 live fetuses of 23 to 24 weeks with large heterogeneous vesicular lesion approximately measuring 196 mm X 85 mm with small multiple cysts along the posterior wall of the uterus reaching upto the internal os, no internal vasularity was evident finding may suggestive of ? mesenchymal dysplasia of placenta, other differential diagnosis include partial molar pregnancy.







- MRI was done to confirm the diagnosis and to exclude invasion
- MRI showed twin fetus. Evidence of large lesion along the posterior wall of the uterus measuring 12.1X7.2X25 CM. Lesion was completely covering the internal os and their was no radiological sign of uterine wall invasion by the above mentioned lesion.

- While under evaluation the patient had second episode of Severe bleeding per vaginum and was taken up for Emergency Surgery.
- Blood and Blood products arranged.
- Hysterotomy done followed by delivery of two live fetus with one reduced fetus and evacuation of molar tissue done under general anesthesia.
- Post operative period was uneventful and beta HCG levels were followed up and reached negative levels at four weeks post operative.
- The patient was not registered at our center and neither antenatal karyotyping nor pre implantation genetic testing was done for her.

Post Operative Image of Babies Along with Molar Tissue

III. DISCUSSION

- With the current life style and disease patterns the number of infertile couples are on a rise who opt for IVF. IVF has helped many couples to achieve successful pregnancies. These pregnancies are unique as they allow us to analyze embryogenesis and transfer only healthy embryos to ensure a good outcome. The existence of molar pregnancy in IVF conception despite direct evaluation and use of micro manipulation technique is therefore unusual.

- The etiological factors predisposing to molar pregnancies are many and varied. Maternal age, Maternal genetic anomalies, Paternal age, Blood Group, Oral Contraceptives, Environmental factors in particular folate and vitamin A deficiency can pre disposed to molar pregnancy.

- The relationship of molar pregnancy occurring in pregnancies conceived as a result of IVF has not yet been fully explored. The presence of molar tissue with assisted reproduction is scarce with very few cases reported in literature. It was postulated by flam et al that due to increased incidence of aspiration of immature oocytes after ovarian stimulation, it was possible that some immature oocytes with impaired genetic material when subjected to embryo formation may give rise to molar tissue.

- It has been theorized that low quality sperm also might contribute to the phenomenon of irregular cleavage, hence the role of sperm morphology may have a role in the pathogenesis of molar tissue in IVF pregnancies. Tests for genetic evaluation of sperms such as sperm DNA fragmentation may be of value in such cases.

- Partial moles are triploids containing two sets of paternal and one set of maternal chromosomes. The proposed mechanisms for the extra sets of haploid chromosomes in partial moles includes 1. Dispermy 2. Failure of first or second paternal meiotic divisions 3. failure of first or second maternal meiotic divisions. Out of these, the commonest mechanism is Dispermy. Since partial moles arise out of dispermic fertilization, couples undergoing ICSI are actually at reduced risk of the same. While complete moles are possible, partial mole seen with ICSI pregnancy is difficult to explain.

- It is not clear which molecular mechanisms may have contributed to lead to morphologically normal appearing embryos to form molar tissues. However the disruption of the meiotic spindle and loss of maternal chromosome after Oocyte handling or due to fragmentation and degeneration of Oocyte may be a probable cause.

- The transfer of embryos at the blastocyst stage ensures that only the healthiest embryos are transferred.

- There is also the possibility of these cases being diagnosed late. The detection of a fetal heartbeat during early pregnancy can cause the coexistent mole to be over looked as seen in this case. For partial moles, the sensitivity and positive predictive value for the gray scale ultrasound diagnosis of Hydatidiform mole are 20% and 22% respectively.

- These pregnancies are difficult to manage as they are associated with hyper thyroidism, vaginal bleeding, atonicity and risk of embolism and subsequent neoplasia.

- Multiple embryo transfer not only increases chances of multiple pregnancies but also the association of molar tissue. Association of molar tissue along with higher order pregnancies following multiple embryos transfer present a new set of challenges for the clinician.

- American Society for Reproductive Medicine recent guidelines recommend the transfer of one or two embryos in patients less than 35 years of age. However various factors influence the number of embryos actually transferred at ground levels.

- Pre operative workup of such patients presenting with Hydatidiform mole includes careful pelvic ultrasound, MRI, detailed pre anesthetic checkup, complete blood count, blood grouping typing, cross match, thyroid profile, serum electrolytes, LFT, KFT, chest x-ray or ct chest scan, ECG and ECHO.

- During surgery, wide bore cannula and cross matched blood should be available. General Anesthesia is preferred over regional. In advertent fluid overload should be avoided. Post operative surgical challenges are risk of perforation at the time of suction evacuation of the uterus and hemorrhage during an evacuation may be life threatening at times. Detailed counselling of the patient and relative is necessary as the possibility of a life saving hysterectomy following torrential bleeding is a very real possibility. Moreover the release of molar tissue could trigger the coagulation cascade. Thrombo-embolism leading to acute respiratory distress.

- In patient who desire future fertility, decision of doing hysterectomy is very difficult.

- Whether or not to do a repeat Embryo transfer or IVF cycle in such patients is a dilemma for the clinician. Berkowitz el al in a study have reported a higher propensity for a patient with one episode of GTD (Complete or partial mole) to develop a molar disease of either type in an ensuing pregnancy.

- Poor regulation of the polar body and pronucleus formation in fertilized oocytes may be the reason for a recurrent Hydatidiform mole in such patients.

- Pre implantation genetic diagnosis should be offered to such patients to avoid the possibility of recurrent molar pregnancy, if a repeat IVF cycle is desired. Partial Hydatidiform mole is mostly triploid in nature. Abnormal triploid fetus co-existing with partial Hydatidiform mole tends to die in the first trimester while the fetus co-existing with complete Hydatidiform mole does have a chance to survive as has been previously described (Matsu et al.2000).

IV. CONCLUSION

- As most of the women who conceived with assisted reproduction continuation of these pregnancies is desired by them and they are even willing to accept the side effects of the co-existing molar pregnancy. It is hence important to carefully weigh the risks and advantages and draw a line between immediate intervention and expectant management, when health of the pregnant women is not jeopardized as well as the co-existing fetus can be salvaged.

- It is important on treating physician's part to follow standard guidelines for such ART procedures especially with handling of genetic material and timely intervention stays the key in treatment. Although very rare, the possibility of a pregnancy with partial Hydatidiform mole and a co-existing live fetus must be considered for IVF ICSI. Patient who decide to continue with the pregnancy following counselling should be supported and managed by a disciplinary team.

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