Original Article

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Role of Ultrasonography in Molar Pregnancy Coexisting with Viable Fetus: A Prospective Study

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Abstract

Introduction: Mole with coexisting viable fetus (MCF) is a rare condition, and the diagnosis is important because of the risk of developing severe complications in pregnancy and beyond.

Aim: The aim of this study was to report the sonographic features of molar pregnancy with coexisting viable fetus in singleton and twins.

Materials and Methods: A prospective and randomized study of 12, 350 patients those who were referred for a routine antenatal ultrasound scan in the Department of Radiology, MGM Hospital, Warangal was conducted. The duration of study was 2 years (November 2013-October 2015).

Results: In the present study, 40 patients were diagnosed with a gestational trophoblastic disease on ultrasound. In that, 8 patients were suspected as MCF. Four cases, on follow-up, confirmed the initial diagnosis of molar pregnancy with coexisting viable fetus.

Conclusion: Ultrasonography is useful in diagnosis and follow-up of molar pregnancy with a viable fetus and in detecting further complications. As a continuation of pregnancy with molar changes and the coexisting normal viable fetus is an acceptable option, close surveillance is necessary to detect early signs of complications in such cases.

Key words: Fetus, Molar pregnancy, Ultrasonography

INTRODUCTION

Molar pregnancy with viable fetus has been divided In to three types. The first type is a twin pregnancy with one normal fetus having normal placenta and another complete mole (CHMCF). The second type is a twin pregnancy with a normal fetus, placenta, and another partial mole. The third and most uncommon occurrence is singleton normal fetus with the partial molar placenta (PMCF), where the fetus should have a normal karyotype to survive. The cases with molar pregnancies concurrent with normal intrauterine pregnancies (MCF) have been reported as 2.5-5% of molar pregnancies[1,2] or 1 in 20,000-1,00,000 pregnancies.[3] The clinical entity has aptly been described as sad fetus syndrome[4] and should be reviewed time to time.[5,6] (Twin MCF resulting in a viable live born infant mostly having (a) less discrepantly grown uterine size, (b) lower frequency of preeclampsia, (c) significantly lower serum beta-human chorionic gonadotropin (hCG) values, (d) diagnosed later in gestation - All indicating growth of molar changes are slow or even molar degeneration and subsequently a more benign clinical course. Most of the CHMCF will be terminated prematurely either because of persisting hemorrhage or severe preeclampsia. Nearly, 40% of the patients with gestational trophoblastic disease (GTD) with a viable fetus who opted for continuation of their pregnancies have Lived babies, delivered beyond 32 weeks gestation. Twin pregnancies including a mole and a healthy fetus Give rise to complex clinical considerations, especially in a strongly desired pregnancy. Sebire *et al.*, reported the largest series so far comprising 77 CHMCF, with approximately 27% of the pregnancies achieving live birth and 19% developed persistent GTD (pGTD), without significant differences between those who choose

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to electively terminate pregnancy and those who did not. Recently, Massardier *et al.*,[7] published a series of 14 cases with similar percentages of live birth and a 50% pGTD. Single case reports were also published[8-10] which shows the importance of the role of ultrasound in diagnosing the disease. Pregnancies complicated by CHMCF may result in a viable live-born infant in approximately 40% of the cases. Continuation of such Pregnancies may be an option but, close surveillance is needed to detect complications, most of these pregnancies were electively terminated due to this potential risk. The results of these studies emphasize the value of ultrasound as a screening technique.

MATERIALS AND METHODS

Between November 2013 and October 2015, 12350 patients were referred for routine antenatal scans were included in this study. Ethics Committee Approval was taken to conduct the study. Written informed consent was obtained from patient who participated in this study. 40 patients were diagnosed as molar pregnancies, out of which 8 cases were suspected with molar pregnancy concurrent with live fetus. A chart to document complete mole with a viable fetus and partial mole with viable fetus was performed. All the scans are done on Esoate my Lab 40, Voluson E8 BT 10 Version, and Voluson 730 Pro Machines. Beta-hCG levels were determined by AxSYM total hCG assay. Standard normal ranges were provided by the manufacturer.

RESULTS

In this descriptive study between November 2013 and October 2015, 12350 pregnant women who referred for antenatal scan were included, and 40 cases of hydatidi form mole were diagnosed (0.3% or 3/1000 pregnancy). In that, 8 patients were suspected as molar pregnancy with coexisting viable fetus. Four of them in early gestation suspected as MCF (Figure 1), with advanced gestation three of them showed regression of the suspected molar tissue. One patient aborted spontaneously, and histopathology showed no evidence of molar changes. Four cases, on follow-up, confirmed the initial diagnosis of molar pregnancy with coexisting viable fetus. so It is conventional to wait until the diagnosis becomes clear on ultrasound to avoid the risk of evacuating a healthy pregnancy. The typical ultrasonographic findings of a molar pregnancy consist of a complex cystic pattern with a "snowstorm" appearance, but it should be differentiated from a missed abortion with its degenerated gestational sac, especially during the early pregnancy, or even a partially necrotic leiomyoma which can produce a similar appearance.[11] Twin complete MCF is 2/40 (5%). In 2 cases, ages of the patients were 20-25 years. No H/o infertility/previous molar pregnancy/malnutrition/smoking. Blood group was o+ in both the cases. Partial mole with live fetus is diagnosed in 2 cases out of 40 cases (5%). Ages of the patients were 20-21 years. No h/o infertility/previous molar pregnancy/malnutrition/smoking. Blood group B+ in 1 case, O+ in another one.

Two patients of PMCF (Figure 2) both cases are gravida 2, para 1. The first patient unbooked came with spotting at 33 weeks for ultrasonography which showed single live fetus corresponding to 33 weeks with well-defined multicystic snowstorm like appearing mass approximately measuring 10 cm × 8 cm in the posterior upper uterine cavity and is connected to normal placenta. No evidence of anomalies detected. Oligohydramnios noted. Beta-hCG levels are >10,000 Miu/ml. Follow-up scan done at 35-36 weeks showed severe oligohydramnios and increased the size of lesion noted. Lower segment caesarean section performed at 35-36 weeks, delivered a male baby of 2 kg. Newborn did not show any abnormalities. The second patient came for a routine antenatal scan which revealed singleton normal live fetus

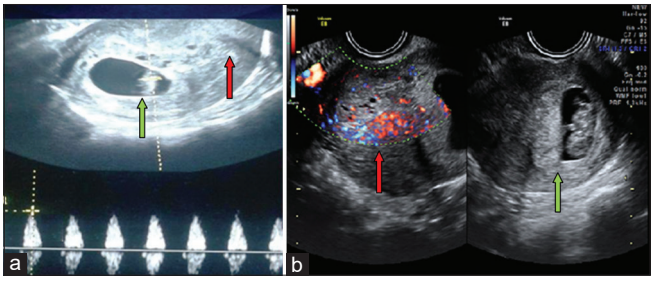

Figure 1: (a and b) Normal gestational sac with live fetus. Adjacent to sac heterogeneous lesion suspected as molar tissue. Spontaneously regressed with advanced gestational age. Green arrow indicates normal placenta; red arrow represents suspected molar tissue

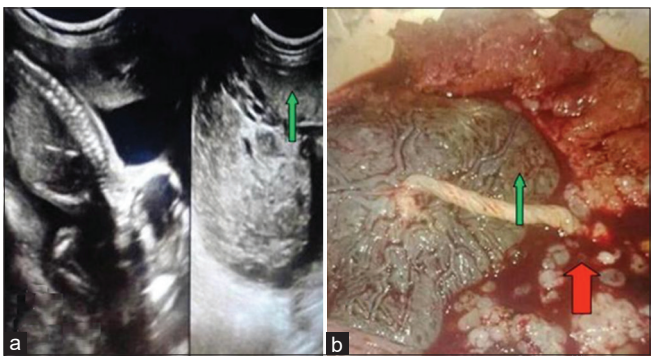

Figure 2: (a) Snowstorm like mass connecting to normal placenta and live 35 to 36 weeks fetus, (b) Macroscopic image of placenta shows molar tissue and normal placenta. Green arrow indicates normal placenta; Red arrow represents molar tissue

of 20 weeks gestation with heterogeneous echogenic mass showing a cluster of cystic spaces of size 15 cm × 7 cm, connected with the small normal placenta. The liquor was less. Serum beta-hCG levels are 44,000 mlU/ml. The patient was advised for amniocentesis and counseling was done. The patient opted termination of pregnancy. Histopathology confirmed the molar changes. Microscopic examination of the placenta in both cases revealed normal villi co-existing with villi showing hydropic changes, cistern formation, and diffuse circumferential trophoblastic hyperplasia consistent with partial molar changes. Comparing our cases to literature reported cases in Table 1.

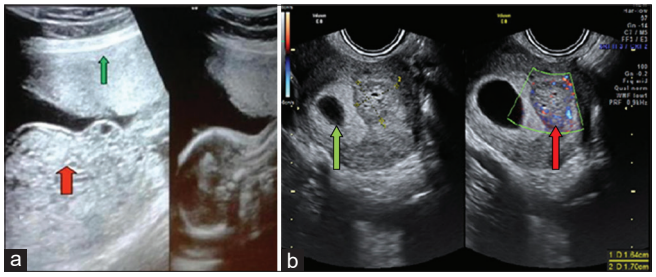

Figure 3: (a) Multi cystic Snowstorm like mass noted at upper posterior uterine cavity with out any connection to normal placenta. Normal placenta noted at upper anterior segment and coexisting live fetus, (b) dichorianic - diamniotic twin with normal gestational sac with adjacent molar tissue in early pregnancy. Arrow indicates normal placenta; red arrow represents molar tissue.

CHMCF (Figure 3) both cases are prime. First patient came for nuchal translucency scan which revealed single live fetus of 11 weeks with the normal placenta and an additional intrauterine echogenic mass with features of hydatidiform mole. We counseled the patient about the continuation of pregnancy and its Outcome need for amniocentesis, possible complications, and postnatal management. With close monitoring patient continued the pregnancy. At 17-18 weeks, patient developed hypertension ultrasound scan revealed increased lesion size and theca lutein cysts. Doppler study showed raised RI values, and persistent early diastolic notch in the uterine artery, and we referred the patient to higher center for further management. Later she developed severe hypertension and pregnancy was terminated at 20-22 weeks of gestation at higher center. The second patient of CHMCF came with spotting for evaluation. Serum beta-hCG levels are 86,878 mIU/ml scan revealed dichorionic diamniotic twins with co-existing complete molar pregnancy in sac B and live fetus of 7 weeks gestational age (GA) in sac A, ended up in medical termination of pregnancy due to vaginal bleeding. Histopathology confirmed the diagnosis. Comparing our cases to literature reported cases given in Table 2.

In contrary to the existing literature; we observed that in all the above cases, the patients age was around 20-25 years with no history of previous molar pregnancies or infertility

Table 1: Clinical variables in 7 patients with a partial hydatidiform mole and a coexisting live term singleton fetus with diploid karyotype

Authors	Maternal age	Gravida/ para	Presenting symptoms	Gestational age at diagnosis/ delivery	Ultrasound features	Outcome	Persistence of disease and treatment
Jones and Lauersen[19]	Not specified	Not specified	Not specified	40/40	Focal HM with normal karyotyping	Normal fetus 46 XX	Not specified
Wunderlich[28]	Not specified	Not specified	Vaginal bleeding	40/40	Focal HM with normal karyotyping	Normal fetus	Not specified
Hartfield[29]	Not specified	1/0	Vaginal bleeding	38/38	Focal HM with normal karyotyping	Normal fetus XY	No
Pool *et al.*[30]	20	1/0	Detected after delivery	38/38	Molar degeneration represented 25% of placenta. No chromosomal analysis	3450 g healthy male baby	No
Parveen *et al.*[31]	NS	NS	Vaginal bleeding	38/38	Large placenta with focal molar changes. 46 XX	2100 healthy female baby	No
Dhingra *et al.*[32]	28	1/0	Vaginal bleeding	38/38	Large placenta, focal molar changes, 46, XX	2100 g, healthy female	No
Our presented cases (2)	21 and 20 years	2/1 2/1	Vaginal bleeding Routine ultrasound	33 and 35/36 20 weeks	Large multicystic Snowstorm like appearing mass (of placenta) connecting to normal placenta Echogenic mass with cystic spaces connecting to small normal placenta Both cases presented with oligohydramnios. No chromosomal analysis	2 kg healthy male baby Aborted	No

NS: Not specified, GA: Gestational age, HM: Hydatidiform mole age (weeks), G/P: Gravidity/parity

treatment. This indicates the change in the presentation pattern of the GTD with viable fetus.

DISCUSSION

Cytogenetically, partial moles usually have triploid karyotype with the extra haploid set of chromosomes of androgenic derivation may be due to dispermic fertilization or with an unreduced diploid sperm. Most of them will have 46 XX and less number with 46 XY karyotype. Whereas complete moles have a diploid karyotype that is entirely of paternal origin. Complete mole consists of multiple vesicles without any e/o fetal parts. Cystic changes are less in partial mole compared to the complete mole. In partial mole usually fetus and large placenta noted, and the fetus usually dies within few weeks of conception (Figure 4). Complete and partial moles have distinct fetal and maternal complications. In partial mole with coexistent live fetus, the fetus is almost always triploid, and the indication for a termination of pregnancy is evident. In contrast, the fetus may be normal in CHMCF and continuation of pregnancy is frequently associated with severe maternal and fetal complications. Differences between the partial and complete molar pregnancy is described in Table 3. There have been so

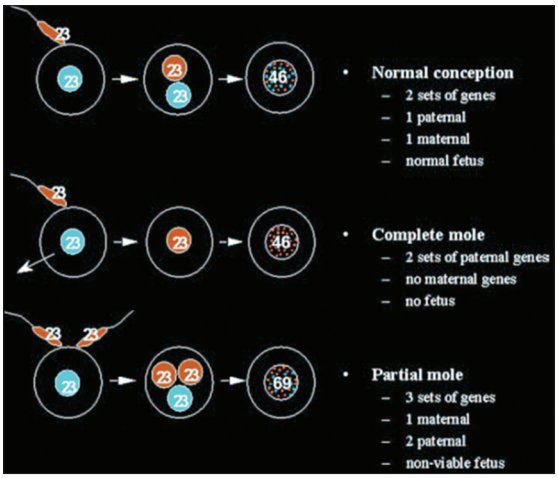

Figure 4: Genetic events occurring in normal conceptions and complete and partial molar pregnancies

far, about 200 cases of twin pregnancy with CHMCF fully documented in literature, while only 56 cases resulted in a live birth.[12] Ultrasonography has made it possible to diagnose hydatidiform mole and co-existent fetus in the first trimester.[13] Prenatal testing of fetal karyotype is essential in deciding continuation and prognosis of the pregnancy. A triploid karyotype indicates a triploid fetus which is severely malformed and, in such cases, termination of pregnancy is recommended. A diploid fetal karyotype (46 chromosomes, 46 XX or 46 XY, 23 maternal and 23 paternal) indicates a viable fetus with a normal placenta co-existing alongside a twin molar placenta. In such a case, the pregnancy can be allowed to continue since it has a considerable chance to result in a normal live baby. Nevertheless, parents who choose to continue a twin pregnancy with complete hydatidiform mole should agree to take the risk of possible maternal complications associated with molar pregnancy such as early-onset pre-eclampsia, hyperemesis gravidarum, hyperthyroidism, vaginal bleeding, anemia, development of theca lutein ovarian cysts, respiratory distress because of trophoblastic embolization to the lungs, and persistent trophoblastic disease (PTD). Parents must be counseled that maternal complications may lead to fetal intrauterine growth retardation, fetal distress, and premature delivery.[14-16] A "wait-and-see" approach should be considered rather than immediate termination of pregnancy because the risk does not increase with advancing GA. Diagnosis should also include molar placental karyotype. Although, not available for our patients, as in most documented case. Marcorelles *et al.*,[17] had suggested that in the case of a normal fetal karyotype, it is justifiable to await developments in the absence of maternal complications.

In cases of singleton normal fetus with the partial molar placenta, fetal survival depends upon several factors.

1. Normal karyotype of the fetus[18]
2. Smaller molar placenta compared to normal placenta[18-20]
3. The onset of molar degeneration and its speed of degeneration
4. Absence of anemia in the fetus[21]
5. Absence of maternal complications such as pre eclampsia.[22]

Table 2: Clinical variables in CHMCF

References	*n*	Intended previable TOP	TOP due to SA, Maternal complications or IUFD	Live neonate (%)	Pre-eclampsia	Persistent GTT (%)	Matastatic GTT
Bristow *et al.*[5]	26	19	NA	7 (27)	7 (27)	15 (57)	5/22 (lung, vagina)
Fishman *et al.*[33]	7	5	NA	2 (28)	NA	4 (57)	0
Matsui *et al.*[3]	18	5	10	3 (17)	5 (28)	9 (50)	6 (lung)
Sebire[16]	77	24	32	20 (26)	NA	15 (93)	NA
Total	128	53		32 (25)		43 (34)	
Our presented cases	2	1	1	0	1	0	0

TOP: Termination of pregnancy, IUFD: Intra uterine fetal death, GTT: Gestational trophoblastic tumor, NA: Not available

Table 3: Difference between complete mole and partial mole

Feature	Partial mole	Complete mole
Karyotype	Most commonly 69, XXX or XXY	Most commonly 46 XX, XY
Pathology		
Fetus	Often present	Absent
Amnion, fetal RBC	Usually present	Absent
Villous oedema	Variable, focal	Diffuse
Trophoblastic proliferation	Focal, slight-moderate	Diffuse, slight-severe
Clinical presentation		
Diagnosis	Missed abortion	Molar gestation
Uterine size	Smaller for dates	50% large for dates
Theca lutein cyst	Rare	25-30%
Medical complications	Rare	10-25%
Post molar GTN	2.5-7.5%	6.8-20%

GTN: Gestational trophoblastic neoplasia, RBC: Red blood cells

Szulman and Surti[23] reported 8 cases of partial mole coexisting with live fetus with normal karyotype after 15 weeks of gestation, but only 2 of the neonates survived. Agarwal *et al*.,[24] from AIIMS, New Delhi reported partial molar pregnancy with a diploid live fetus which was terminated at 28 weeks with good neonatal outcome. In a large study by Vaisbuch *et al*.,[25] they reported 130 cases of twins with CHMCF pregnancy of which 41% were terminated because of the positive probability of serious maternal complications. The recent study by Niemann[26] in 2007 revealed that the risk of PTD after a diploid mole with a viable fetus is similar to that after a singleton molar pregnancy and risk does not change with GA. Elective early termination of such pregnancy because of the risk of PTD alone should not be recommended.[13] Another study in 2009 which evaluated the registered data of patients from 1999 to 2006 showed the 50% (7 cases in 14) rate of gestational trophoblastic neoplasia (GTN) after CHMCF. A high level of beta-hCG at the time of admission may be an indication of poor prognosis of the disease. Partial and complete molar pregnancies have obvious fetal and maternal risks.[27] Thus such pregnant women should be followed more carefully in specialized centers.

CONCLUSION

Ultrasonography plays a key role in diagnosing GTD with coexisting live fetus, guiding disease management, and early detection of its complications. Although detection rate of GTD in the second trimester by ultrasound is 100% whereas it is less in early trimester so, it needs correlation with repeat scans, beta-hCG levels, and histopathological findings. However, beta-hCG is a useful biochemical marker; it is not diagnostic when considered in isolation. We strongly suggest that with a normal karyotype and no gross abnormalities on sonography, pregnancy may be continued as long as maternal complications are absent or, if present, controllable. As a continuation of pregnancy in MCF is an acceptable option, close surveillance is necessary to detect early signs of complications in such cases. An early diagnosis of CMF by high-resolution ultrasound is important for clinical management and helps the patient in making a decision whether to terminate the pregnancy or continue with close fetomaternal monitoring.

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