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Diginyc partial hydatidiform mole with increased fetal nuchal translucency and ovarian hyperstimulation syndrome

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Summary

Purpose of investigation: Hydatidiform mole (HM) is an abnormal pregnancy characterized by proliferation of cytotrophoblast and syncytiotrophoblast and vesicular swelling of placental villi. The fetus or embryo can be absent or abnormal. HMs can be complete or partial. *Case Report:* A case of diginyc partial HM at 12 weeks of gestational age was referred to the present center of prenatal diagnosis. The patient showed ovarian hyperstimulation syndrome. At ultrasonography, increased fetal nuchal translucency (NT) with fetal anomaly was evident, without sonographic signs of placental mole. Pregnancy was terminated with legal abortion. *Results:* Partial HM (PHM) was suspected by ultrasonographic fetal markers with ovarian hyperstimulation syndrome, but the diagnosis was performed only with fluorescent in situ hybridization. In particular fetal NT appeared increased also in diginyc mole. *Conclusion:* In order to improve the detection rate of PHM, routine histological examinations may be associated to fluorescent in situ hybridization in all cases of fetal anomalies.

Key words: Partial hydatidiform mole; Fetal nuchal translucency; Ovarian hyperstimulation syndrome; Diginyc mole.

Introduction

Hydatidiform mole (HM) is an abnormal pregnancy characterized by proliferation of cytotrophoblast and syncytiotrophoblast and vesicular swelling of placental villi [1]. The fetus or embryo can be absent or abnormal. HMs can be complete or partial. About 90% of complete hydatidiform moles (CHM) are 46, XX for the chromosomes duplication of an haploid sperm after fertilization of an egg in which the maternal chromosomes are either inactive or absent. The other 10% are 46, XY, or 46, XX for fertilization of an empty ovum by two sperm. Practically always partial hydatidiform moles (PHM) have a triploid karyotype [1].

Most triploidy are diandric origin (type I), caused by the fertilization of a haploid ovum by two single sperm or a single diploid sperm; a minority part of triploidy are digynic (type II), caused by a double maternal haploid contribution in the egg. Also the fetal phenotype of PHM is different: in type I fetuses with normal growth and the placenta present molar changes; type II fetuses have an asymmetrical growth restriction and the placenta is normal. Type I is associated with a higher rate of poor outcome [2]. Exceptionally hydatidiform molar pregnancy may be present at diagnosis with an ovarian hyperstimulation syndrome [3].

Median fetal nuchal translucency (NT) and maternal serum markers are different in two phenotypes of triploidy, fetal NT generally is increased in type I [4,5].

The authors have recently observed a case of PHM at 12 weeks of gestational age with ovarian hyperstimulation syndrome, increased fetal NT and other fetal anomaly, but without sonographic and histological placental signs of molar pregnancy; the definitive diagnosis was obtained with fluorescent in situ hybridization.

Case Report

A 31-year-old woman, gravida 2 para 1, was referred to Center for Prenatal Diagnosis of G. Gaslini Institute for an hyperstimulation syndrome in spontaneous pregnancy. The anamnestic gestational age was 12 + 0 weeks.

Her medical and obstetrical history was unremarkable. The first obstetrical consultation was taken at eight weeks of pregnancy with dating ultrasound and there was not evidence of gestational anomaly.

At the present authors' observation the patient presented nausea and cramping abdominal pain since 12 hours. The physical examination showed a decreased lung sound, tachycardia, and abdominal distension. No abnormal vaginal secretions or bleeding were evident. At gynaecological examination, diffuse abdominal pain was evocated and ovaries appear increased in thickness and enlarged with superior ovarian margin extending to umbilical transverse line bilaterally.

A transabdominal ultrasound showed a normal uterus with live fetus, with inappropriate biometry [crown rump length (CRL) 46.4 mm, below the 5th centile] and with a nuchal oedema of 4.5 mm (MoM 3.14) (Figure 1).

The uterine adnexa were enlarged on both sides measuring 11.8 ×8.3×8.1 mm [right ovary] and 11×7.6×8.4 mm [left ovary] with

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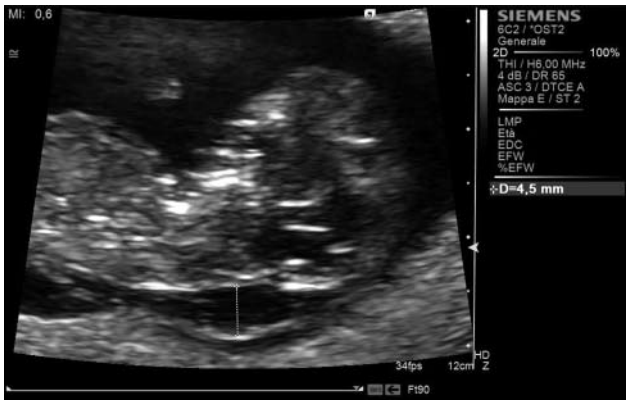

Figure 1. — Nuchal edema of 4.5 mm.

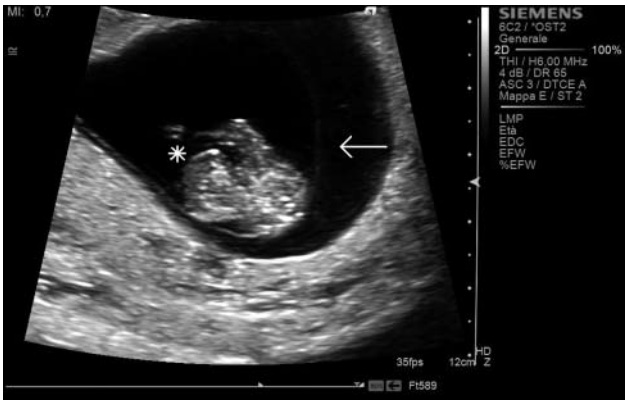

Figure 2. — Bowel herniation and a complete chorioamniotic separation.

multiple bilateral theca lutein cysts, and liquid effusion was present in Douglas pouch measuring six cm in diameter.

Although the fetal anatomy study was limited since the early gestational age, a very large bowel herniation was found for gestational age, possibly an omphalocele, and a complete chorioamniotic separation with amniotic membranes not fused to all uterine wall (Figure 2). The placenta was regular without the aspect of molar pregnancy: the classical "snowstorm" appearance or cystic changes were not evident. The ß-hCG was 653,000 mIU/ml. A combined test of screening showed an elevated risk for trisomy 21 (risk >1:5 with free beta hCG 9.45 MoM, PAPP-A 1.86 MoM and nuchal translucency of 3.14 MoM). For Trisomy 13 and 18 the risk was low. On the basis of the highly elevated ß-HCG and sonographic fetal findings, a molar pregnancy was suspected.

Patient was hospitalized at Center for Human Reproduction for the management of ovarian hyperstimulation syndrome. Patient treatment consisted of intravenous fluid, deep vein thrombosis prophylaxis, monitoring of vital signs, fluid balance, and daily monitoring of electrolytes and hematocrit. The pregnancy was then terminated with legal abortion using dilatation and curettage; chorionic villous sampling was not performed for the patient choice. The histological examination of abortive material showed normal placental tissue without the classical aspect of a partial mole. No signs of chorioncarcinoma were observed. Only the fluorescent in situ hybridization identified the karyotype of villous: chromosomes analysis showed a digynic triploidy, with sexual chromosomes XXY. The serum ß-hCG levels declined to 56,000 mIU/ml at the end of hospitalisation, 96 hours after surgery. A weekly follow up of serum ß-hCG level revealed that the hCG level declined to zero at ten weeks after the abortion.

Discussion

The ultrasonographic diagnosis of PHM is difficult. Indeed, some cases of PHM may present only an enlarged, placenta without obvious vesicular changes [2]. In the first trimester of pregnancy, ultrasonographic detection rate of molar pregnancy is generally low. The detection rate is higher for CHM compared to PHM (95% and lower at 20%, respectively), and in all types of HM the ultrasonographic detection rate was 44% [6]. The sensitivity of ultrasound diagnosis of PHM risk increases with gestational age, therefore the detection rate improves after 14 weeks' gestation [6].

In ultrasonographic diagnosis of PHM, two criteria have been found to be significant: (1) a ratio of transverse to anteroposterior dimension of a gestational sac greater than 1.5 and (2) cystic changes, irregularity, or increased echogenicity in the decidual reaction/placenta or myometrium [7].

In the present case, according to the literature, ultrasound showed a normal placenta, without cystic lesions; the transverse dimension of gestational sac was 90.5 mm, the anteroposterior 47.7 mm; therefore the ratio was 1.89, greater than 1.5.

In PHM also structural fetal abnormalities are frequent. Triploid fetus exhibit malformations of extremities, central nervous system, craniofacial structures, and cardiac anomalies [2]. In the present case a nuchal edema of 4.5 mm and a large incomplete closure of the abdominal wall were evident at ultrasonography (Figures 1 and 2).

Fetal growth restriction is associated with fetal triploidy and it may begin during the first trimester; the CRL is below the 5th centile of the normal range in about two-third of the cases examinated, before 15 weeks, in the study of Jauniaux *et al.* [2]. The growth restriction is due to disproportionate prenatal growth deficiency. A fetus with asymmetrical growth restriction and a normal placental appearance suggest a digynic triploid more than a diandric triploid. In the present case the CRL was under the 5th centile [44.6 mm at 12 weeks and 0 days].

In 2013 Onur E *et al.* reported a persistence of chorioamniotic separation (CAS) and yolk sac still visible in the early second trimester associated with triploidy [8]. When the amnion and chorion are not fused in the second trimester are often are associated with fetal aneuploidy, especially when other sonographic abnormality is found [9]. In the present case, CAS could be due to early gestational age, but it was very evident and it was extended to the entire gestational sac; the yolk sac persistence was not present.

Regarding screening for triploidy by fetal NT and maternal serum, two studies of Spencer *et al.* in 2000 and

Kagan *et al.* in 2008 showed that the combined use of the algorithms for trisomies 21, 18, and 13 can identify about 85% of fetuses with triploidy [4,5]. The identification rate increases to 90% using the fetal heart rate in addiction to fetal NT and maternal serum markers.

Median fetal NT and maternal serum markers are different in two phenotypes of triploidy. In type I there is increased fetal NT and maternal serum total hCG, free ß-hCG, and AFP with mildly decreased PAPP-A. Type II (digynic) is associated with normal or mildly increased fetal NT and markedly decreased maternal serum total hCG, free ß-hCG, and PAPP-A with mildly decreased AFP [4, 5].

The present data's screening appear in contrast with what reported in the literature: the authors' experience of digynic mole showed an increased NT and maternal serum free ß-hCG and a regular PAPP-A.

Conclusion

In conclusion in the present authors' experience, PHD was suspected by different ultrasonographic fetal markers of abnormality associated with ovarian hyperstimulation syndrome, but the diagnosis was made only with fluorescent in situ hybridization.

The ultrasonographic aspect of PHM is not always diagnostic, and in the present authors' experience, it was partially in contrast with that reported in literature [4, 5]. In order to improve the detection rate of PHM, routine histological examinations may be associated to fluorescent in situ hybridization in all cases of fetal anomalies.

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