TRIPLOIDY

In triploidy each chromosome occurs 3 times for a total chromosome number of 69. Approximately 1% of clinical conceptions are triploidy with the majority miscarrying in the early part of the 1st trimester[1]. The reported prevalence of triploidy decreases from 1/1,500 at 10-14 weeks gestation[2] to 1/10,000 at term[3].
Triploidy may be from either paternal or maternal origin. The 3 possible karyotypes are: 69, XXX; 69, XXY; and 69, XYY. Approximately 75% of cases are of paternal origin, usually from the fertilization of an ovum by two haploid sperm (dispermy). The production of sperm and eggs requires meiosis, a specific type of cell division. Before meiosis I, a diploid cell replicates its DNA. In meiosis I the DNA divides so that each daughter cell receives 2 identical strands of DNA. During meiosis II the chromosome separates into single strands before division into 4 cells, each haploid, with one chromosome of each pair. Hence, triploidy can also result from a failure of division of either meiosis I or II in the father[3].
Triploidy of maternal origin (digyny) is due to a failure of division during meiosis I or II[3]. Digynic triploidy is more commonly identified in the fetal period than diandric triploidy[4]. The documentation of a few livebirths of digynic triploidy suggests that they have a survival advantage over diandric triploidy[5].
The prevalence of 69XYY in pre-implantation genetic studies (8.7%) is 12 times higher than in clinical pregnancies (0.74%). This suggests that an excess paternal contribution to the embryo adversely affects development[6].
Since the formation of a triploid embryo is a random event, the couple's future reproductive potential would not be affected.
First trimester growth restriction has been described with triploidy[7]. Asymmetry between the head and abdomen may also be apparent during the 1st trimester. The deficit in triploidy 1st trimester trunk and head volume is 45%, in contrast to a 15% reduction in the crown-rump length. Hence, the trunk and head are decreased even after correcting for the crown-rump length[8]. Congenital anomalies have been detected on 1st trimester ultrasound examinations of triploidy fetuses[9].
With 1st trimester diandric triploidy there may be a large cystic appearing placenta (Fig. 1). The 1st trimester nuchal translucency (NT) is increased (Fig. 2). Maternal serum ?-hCG is significantly increased and PAPP-A is slightly decreased. Digynic triploidy has a small placenta, a normal NT and significantly lower ?-hCG and PAPP-A.

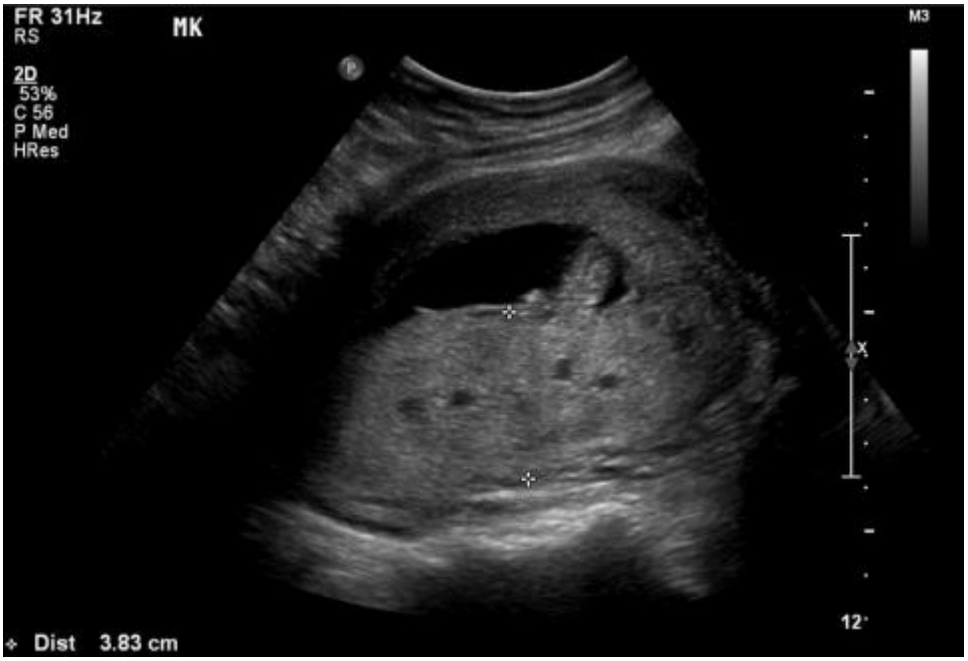

Figure 1. Triploidy. Thickened cystic 1st trimester placenta (graticules). Click for bigger image.

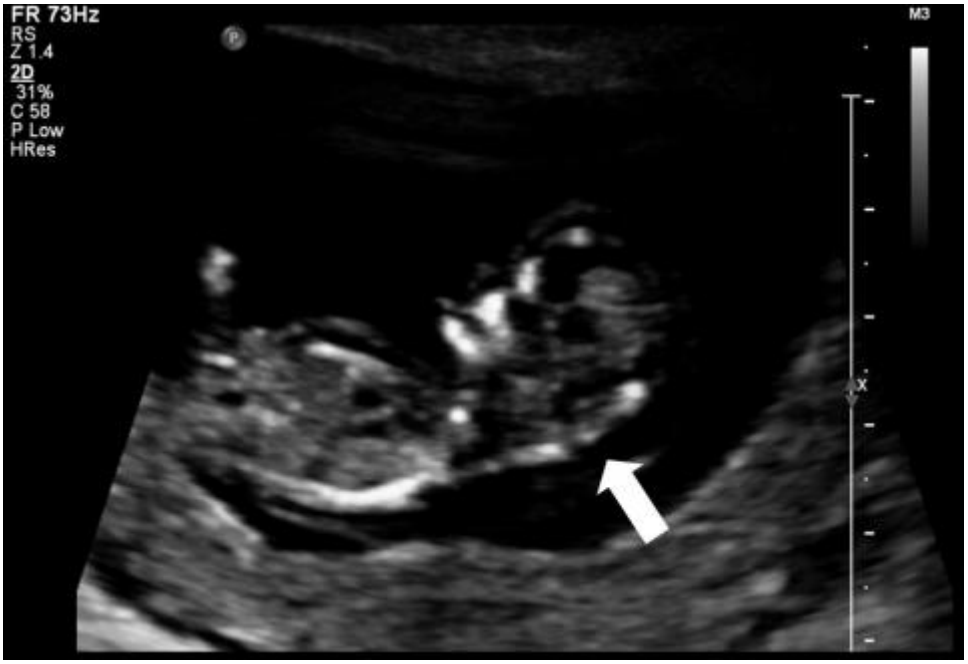

Figure 2. 1st trimester triploidy with a thickened nuchal translucency (arrow) and anascara. Click for bigger image.

The differences in triploidy phenotype are due to genomic imprinting with the extra paternal set of chromosomes leading to an over-expression of hCG[2]. Hence, the characteristic biochemistry is what permits identification of triploidy with a 1st trimester genetic screen. The use of the combined algorithms for trisomy 21, 18, and 13, detects approximately 85% of 1st trimester triploidy fetuses with a 3% false positive rate[10].

The first trimester biochemical markers are not applicable to twin pregnancies. However, 1st trimester growth restriction and a small placental volume can be used to suggest chorionic villus sampling of one fetus in a twin gestation[11].

McFadden et al[4] have reported that the 2nd trimester triple screen results with digynic triploidy (low levels of hCG and unconjugated estriol) is interpreted by the established computer programs as an increased risk for trisomy 18. The elevated hCG and AFP in diandric triploid fetuses may be due to the presence of a partial hydatidiform mole, or the generally increased placental mass with diandric triploid fetuses who do

not have a mole.
71.4% of 2nd trimester fetuses with triploidy present with asymmetric intrauterine growth restriction[10]. Characteristically, there is a marked discrepancy in the head to abdomen ratio that results from a more severe lag in abdominal circumference, in contrast to the head circumference (relative macrocephaly) (Fig. 3).

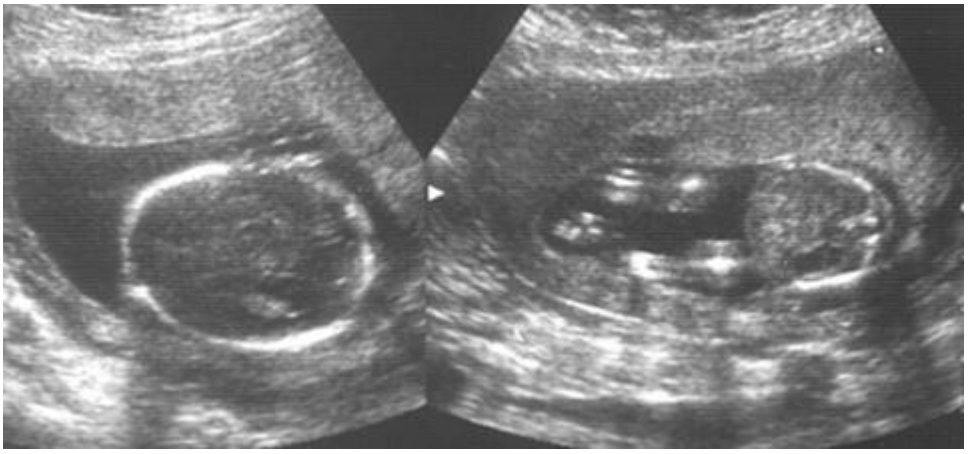

Figure 3. Asymmetry between the head and abdomen in 2nd trimester triploidy. Click for bigger image.

Triploidy fetuses have a plethora of fetal anomalies that have been described involving almost every organ system (Table I). This list illustrates the breadth of the triploidy spectrum. However, there is not a single anomaly that would be considered pathognomonic for triploidy.

TABLE I. CONGENITAL ANOMALIES ASSOCIATED WITH TRIPLOIDY[12,13,20,21,22,23]

CENTRAL NERVOUS SYSTEM

- Ventriculomegaly
- Holoprosencephaly
- Hydranencephaly
- Dandy-Walker malformation
- Agenesis of the corpus callosum
- Encephalocele
- Neural tube defect
- Interhemispheric cyst

FACIAL/HEAD

- Micrognathia
- Microphthalmia
- Hypertelorism
- Cataracts
- Mid-face hypoplasia
- Low-set ears
- Cyclopia/proboscis

- Cleft lip/palate

CARDIAC

- Ventricular septal defects
- Atrial septal defects
- Truncus arteriosis
- Pulmonary atresia

RESPIRATORY

- Bilateral pleural effusions
- Pulmonary hypoplasia

GASTROINTESTINAL

- Omphalocele
- Gastroschisis
- Duodenal atresia
- Diaphragmatic hernia
- Hyperechogenic bowel
- Ascities

GENITOURINARY

- Renal cystic dysplasia
- Renal agenesis
- Renal hypoplasia
- Ambiguous genitalia

SKELETAL/LIMBS

- Syndactyly (3rd & 4th digits)
- Clubbed feet
- Hitchhiker's toe
- Kyphoscoliosis

2 VESSEL UMBILICAL CORD

Central nervous system anomalies are the most common malformations associated with triploidy (Fig. 4), with a frequency of approximately 50%. Cardiac anomalies have been detected in 31.4% of triploid fetuses; ventriculoseptal and atrioseptal defects (Fig. 5) are the most common[2]. Truncus anteriosis, Ebstein's anomaly and aortic stenosis have also been described[12]. Omphalocele and gastroschisis are present in 10-18% of triploid fetuses. 86% of 2nd trimester triploid fetuses will have more than one major structural malformation (Figs. 6-9)[6].

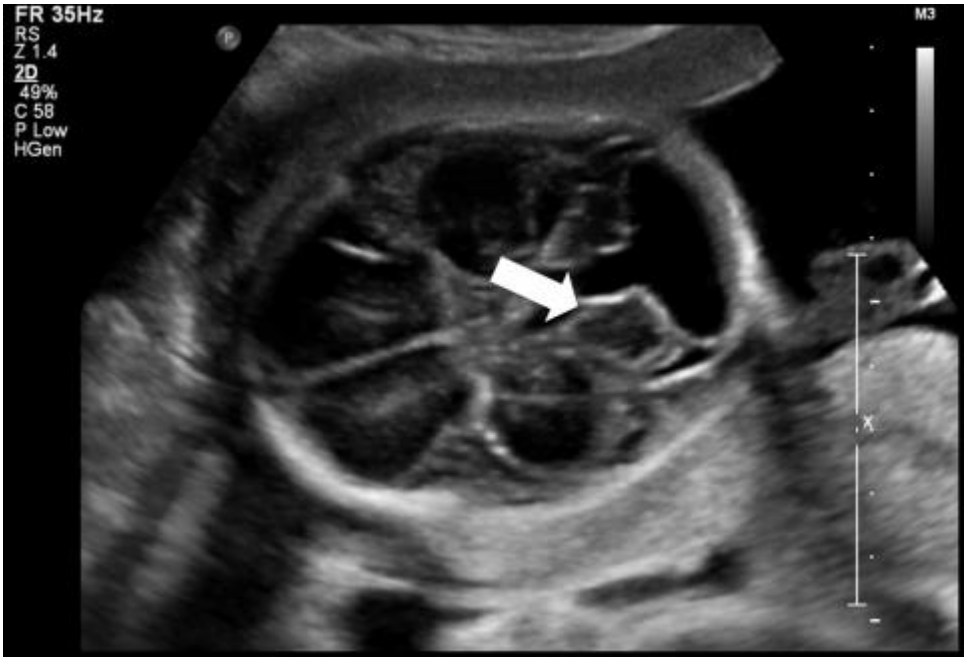

Figure 4. Dandy-Walker malformation; absence of the vermis (arrow). Click for bigger image.

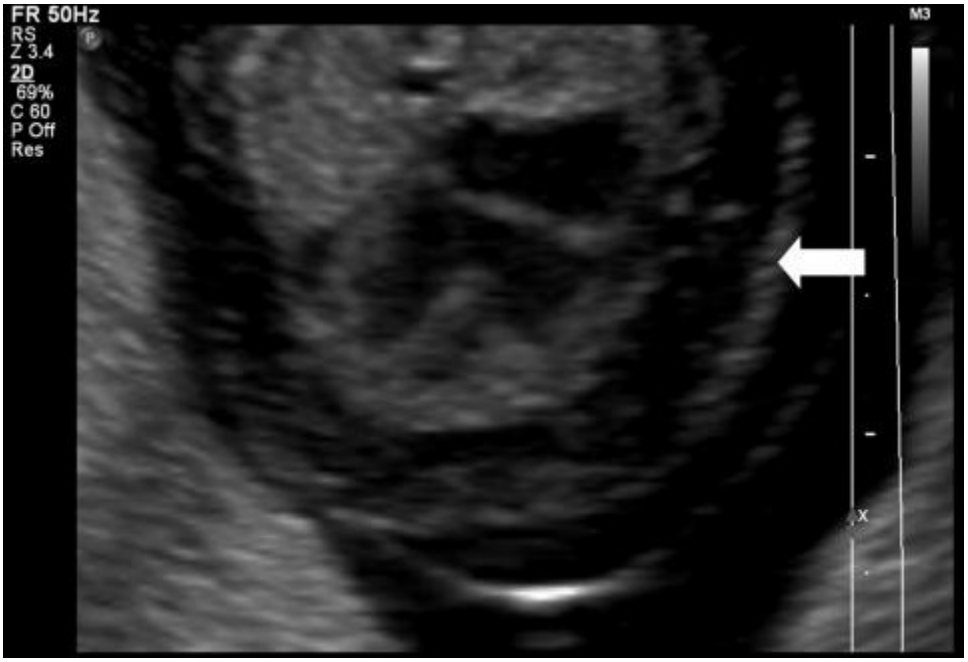

Figure 5. Triploidy with anasarca (arrow) and an atrio-ventricular septal defect. Click for bigger image.

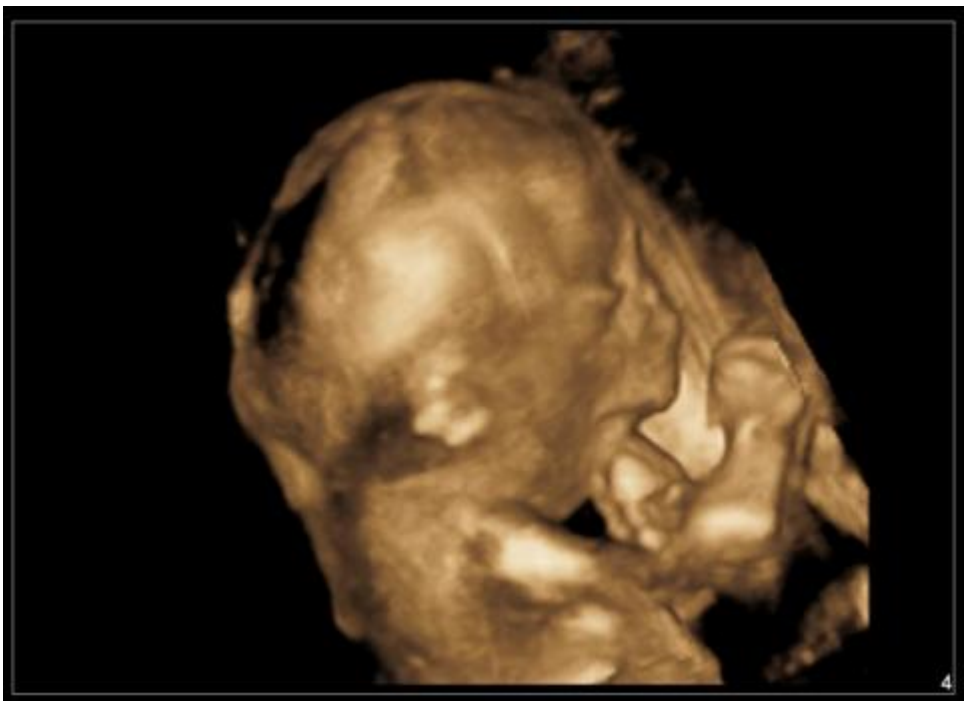

Figure 6. 2nd trimester triploidy fetus with micrognathia and low set ears. Click for bigger image.

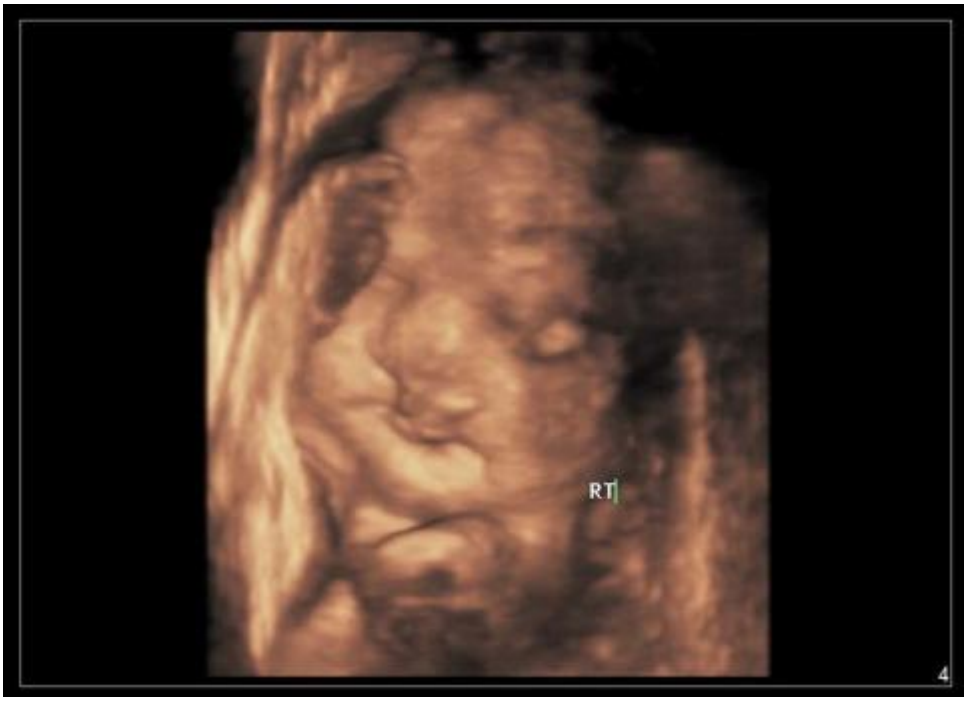

Figure 7. 2nd trimester triploidy fetus with a bilateral cleft lip. Click for bigger image.

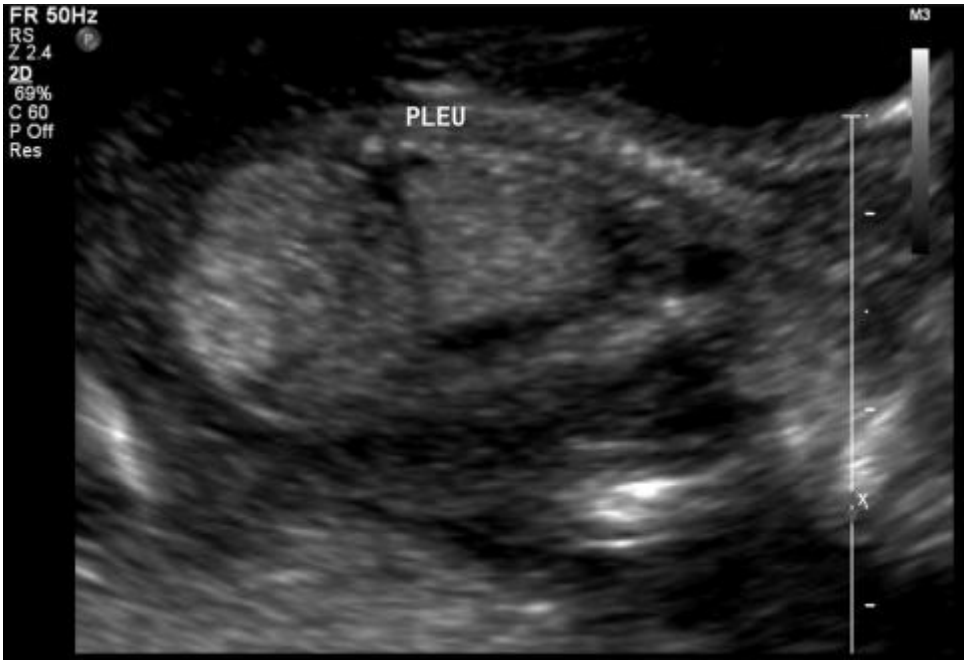

Figure 8. 2nd trimester triploidy fetus with a pleural (pleu) effusion. Click for bigger image.

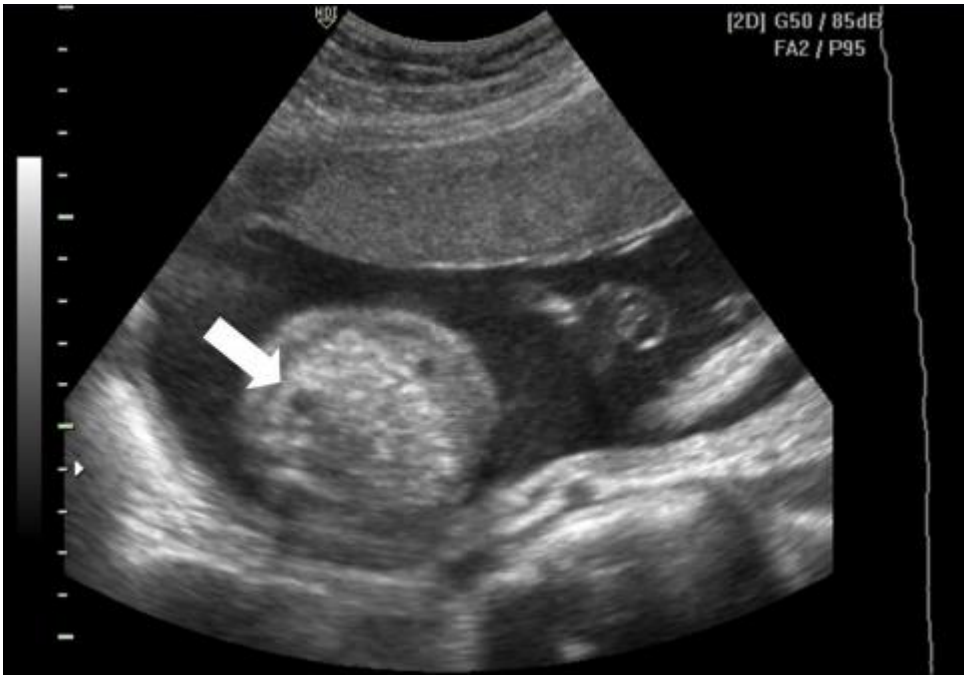

Figure 9. 2nd trimester triploidy fetus with echogenic bowel (arrow). Click for bigger image.

Approximately 40-60% of triploid fetuses have oligohydramnios and an additional 5% have polyhydramnios[13]. Due to the frequent presence of oligohydramnios, the sonographic detection rate of congenital anomalies is less than would be expected with a normal amniotic fluid volume.
In 7%[14] to 15%[6] of 2nd trimester triploidy cases, there are not any major congenital anomalies detected on an extended fetal anatomic survey[15]. Interval 2nd trimester growth of the biparietal diameter has been described as normal in some cases[15].
As previously stated, placental abnormalities are associated with triploidy[10,15,16,17]. The finding of triploidy in a molar pregnancy is associated with a small risk for persistent trophoblastic disease. Complete moles contain only paternal chromosomes and have a 15-25% risk for persistent trophoblastic disease[18].
Early onset (16-24 weeks) preeclampsia is an acknowledged complication of triploidy with a partial mole[16].
The differential diagnosis for the sonographic findings associated with triploidy include: 1) a normal fetus with growth restriction and a small placenta; 2) a complete mole with a co-existent fetus; 3) trisomy 13; 4) trisomy 18; and 5) a normal fetus with placental mesenchymal dysplasia (PMD).
Placental mesenchymal dysplasia is characterized by an enlarged hydropic placenta with multiple cysts. Sonographically this is indistinguishable from a mole or partial mole. Unlike a molar placenta, trophoblastic proliferation is absent. PMD is associated with a predominance of female fetuses. Other fetal complications associated with PMD include polyhydramnios, intrauterine growth restriction, intrauterine fetal demise and prematurity[19].

SUMMARY

Second trimester intrauterine growth restriction, marked asymmetry between the head and abdomen with relative macrocephaly and a cystic appearing placenta are the triad of sonographic findings that are highly suggestive of triploidy. Since several diseases overlap phenotypically with triploidy, early detection and karyotypic confirmation are essential.

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