Polyhydramnios: An Update

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Abstract: Maternal, fetal or placental pathologies may result in an excessive amount of amniotic fluid (AF) volume. Therefore, the surveillance of the AF volume, predominantly by ultrasound, has become an important instrument for the assessment of fetal well-being. An excessive accumulation of amniotic fluid, as a consequence of a disturbed balance between production, fetal resorption and secretion, is defined as polyhydramnios. Its degree correlates significantly with fetal morbidity and mortality. Therefore, polyhydramnios is an important clinical pattern in perinatal medicine. Approximately 20 percent of the fetuses with severe polyhydramnios show a congenital anomaly, whereas 50 percent of all cases are considered to be idiopathic, mostly with mild patterns. Furthermore, the likelihood of aneuploidy varies from 0.4 to 10 percent. Early detection, provides a correct diagnosis and allows a individual therapy. A referral to a tertiary center is advised in case of severe polyhydramnios and unknown etiology.

In this review, current diagnostic as well as therapeutical aspects are discussed.

Key words: amniotic fluid, prenatal diagnosis, pregnancy, therapy

BACKGROUND

The amniotic fluid (AF) that surrounds the fetus is essential for its continuous development, as well as for its protection. It prevents the growing fetus from physical trauma, permits fetal lung growth, and provides together with the amnion membrane an efficient barrier against ascending infection. Normal amniotic fluid values may vary; however, the average volume steadily increases with gestational age, peaking at 800 to 1000 ml at 36 to 37 weeks of gestation. An excessive amount of amniotic fluid may give a hint to possible fetal malformations or maternal diabetes and should lead to a profound examination.

The surveillance of the amniotic fluid volume, predominantly by ultrasound, has become an important instrument in the assessment of fetal wellbeing. An excessive accumulation of amniotic fluid, somewhat arbitrary, more than 2 liters at term, is defined as polyhydramnios. Its degree correlates with fetal morbidity and mortality.[1] Severe polyhydramnios is associated with poor fetal and neonatal outcome, even with a death rate up to 30 percent. Approximately 25 percent of it is the consequence of prematurity.

An excessive amount of amniotic fluid volume is often diagnosed clinically. A clinical examination may reveal a rapidly enlarging uterus of the pregnant women. The diagnosis is usually confirmed by a subsequently performed ultrasound examination and can be described with various methods (qualitatively or quantitatively).

Excessive amniotic fluid volume is observed in about 1 percent of all pregnancies, with a similar prevalence among different populations (Range: 0.4 to 3.3%). The diagnosis depends on the population and gestational age at diagnosis as well as on the sonographer's experience and methods of ascertainment.

DIAGNOSIS

The diagnosis is based upon sonographic visualization of the increased amniotic fluid volume. This may be qualitative or quantitative, but has always a more or less subjective component of the examinator.

Polyhydramnios is defined as an excessive volume of AF (> 2000 ml). With the appearance of routinely performed ultrasound during pregnancy, several methods have been used to describe the amount of AF. The monitoring can be performed by measuring the biggest depot, although this method has its limitation. The assessment of AF volume is the value of the arithmetic median of two measured section standing vertical to each other. A value > than 80 mm is defined as polyhydramnios. Three different severity codes are differentiated:

- Mild (80 to 99 mm)
- Medium (100 to 120 mm) and
- Severe (> 120 mm).

Phelan[2] quantified the volume by introducing the amniotic fluid index (AFI). The AFI measurement is calculated by adding the vertical depths of the largest pocket in each of the four equal uterine quadrants, not containing umbilical cord or fetal extremities.

The sum is the AFI.

It is interpreted according to the following thresholds:

- Low volume (Ahydramnios-oligohydramnios) : 0 to 5 cm
- Normal volume : 5.1 to 24 cm
- Polyhydramnios : greater than 24 cm

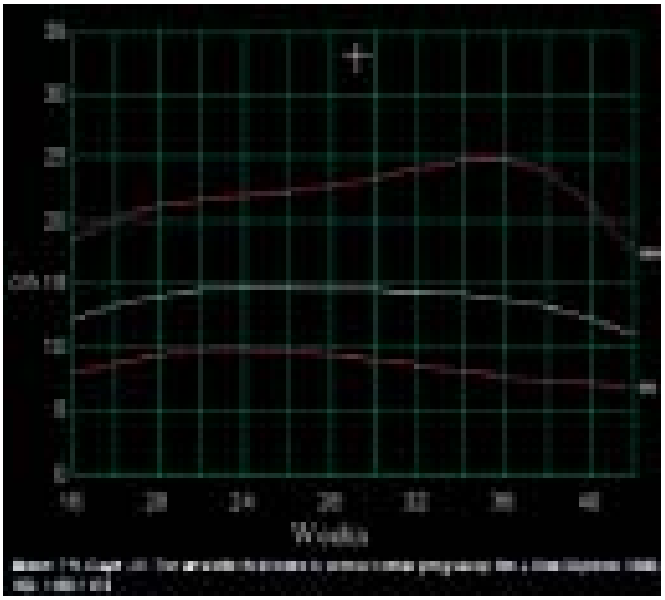

Fig. 1: Amniotic fluid index: Polyhydramnios (AFI > 30 cm) at the 29th week of gestation

It has been shown that the AFI is quite reliable in determining normal or elevated AF volumes.

Recent data have shown that age-specific percentiles are not more helpful than constant cut-off values used either with the single pocket or AFI method.[3]

Nevertheless, standardized objective indices provide accurate reproducibility and are indispensable for the monitoring of the ongoing pregnancy at risk (Fig. 1).

PATHOPHYSIOLOGY

The balance between production, fetal resorption and secretion are crucial for a normal amniotic fluid volume. In the first trimester, the AF is mainly produced by the placenta and the amnion membrane. In the second trimester fetal kidneys are increasingly responsible for its production. Later in the ongoing pregnancy, the urogenital and pulmonary tract of the fetus are participating in the maintenance.

Excessive accumulation of amniotic fluid is normally related to either decreased fetal swallowing/diminished absorption or increased fetal excretion. Therefore, minor changes in fetal urine production or absorption may result in significant changes in AF fluid volume.

ETIOLOGY OF POLYHYDRAMNIOS

In pregnancies affected by polyhydramnios, approximately 20 percent (Range 8 to 45%) of the neonates are born with a congenital anomaly. Similar, the likelihood of aneuploidy varies from 0.4 to 10 percent.

Therefore, the delivery of these affected fetuses in a tertiary care setting is recommended. Today about 50 percent of all polyhydramnios case are considered idiopathic, mostly with mild patterns.

In case of diagnosed polyhydramnios, the following etiologies should be included in the differential diagnosis:

A. **Maternal**
   a. Diabetes mellitus
   b. Infections (TORCH)

B. **Fetal**
   a. Malformations
      - Cerebral (intracerebral pathology, anencephaly, spina bifida)
      - Pulmonal malformation (CCAM, neuromuscular)
      - Gastrointestinal (anatomic/neuromuscular) disorders, e.g. esophageal atresia
      - Urogenital (Elevated urine production, reduced concentration, tumors)
   b. Cardial
      - Congenital cardiac-rhythm anomalies (associated with hydrops), cardiopathy
   c. Fetal tumors
      - e.g. sacrococcygeal teratoma
   d. Musculoskeletal disorders/fetal akinesia
      - e.g. arthrogryposis
   e. Chromosomal disorders
      - Trisomies 13, 18, 21, triploidy
   f. Immunologic hydrops
      - Anti-D, anti-C, anti-kell antibodies
   g. Non-immunological hydrops
      - Structural abnormality
      - Anemia (e.g. parvovirus infection)
      - Metabolic disorders (e.g. Glucose-6-phosphatase deficiency)
   h. Multiple gestations
      - Twin-twin transfusion syndrome
      - Acardiac twin/TRAP

C. **Placental anomalies**
   - Chorioangioma

Bacterial or viral infections transmitted *in utero* to the fetus are significant causes of fetal mortality and morbidity. The TORCH Group (Toxoplasmosis, other (e.g. syphilis), rubella, cytomegalovirus (CMV) and herpes simplex virus (HSV)) can be responsible for the development polyhydramnios. Polyhydramnios that develops with maternal diabetes is thought to be due to osmotic diuresis as a result of fetal hyperglycemia.

The increasing percentage of fetal pathologies diagnosed *in utero* during the first and second trimester as well as the nowadays effective prevention of isoimmunization against Rh(D) have changed the relative frequencies of all of these etiologies over the past few decades and reduced the number of idiopathic cases (Table 1).

Table 1: Distribution of the etiology of polyhydramnios in accordance to the years of assessment

Cause	*1970 (%)*	*1987 (%)*	*2004* (%)*
Idiopathic	35	66	60
Diabetes mellitus	25	15	7.5
Malformations	21	13	24.1
Rh incompatibility (and non-immun hydrops*)	11	1	3.5*
Multiple gestation	8	5	4.5

(John T. Queenan. High-risk Pregnancy (3rd edition).
*data from the University Women's Hospital Basel, Switzerland)

In 2004 we reviewed the computerized records of 174 cases with polyhydramnios, which have been examined in our ultrasound unit at Women's University Hospital Basel, Switzerland, between 1998 and 2004. 104/174 fetuses (60%) had no associated pathology, whereas 42 (24.1%) had a prenatally diagnosed malformation, with or without aneuploidy (Table 1).

Many fetal anomalies have been linked with an excessive amniotic fluid volume. The most important anomalies causing polyhydramnios are those that interfere with fetal swallowing, such as absence or disability of swallowing (anatomic malformations such as cleft lip, cleft palate, or cerebral and neuromuscular deficiencies), or a blockage of the fetus' gastrointestinal tract (esophageal, duodenal, or intestinal stenosis, atresia or intestinal shift due to hernias (Figs 2 and 3).[4] Decreased swallowing may also be the consequence of cerebral and neuromuscular disorders, such as anencephaly, myotonic dystrophy, arthrogryposis or as a complication due to a secondary obstruction of the intestinal tract from pulmonary (Fig. 4) or intra-abdominal pathologies.[5]

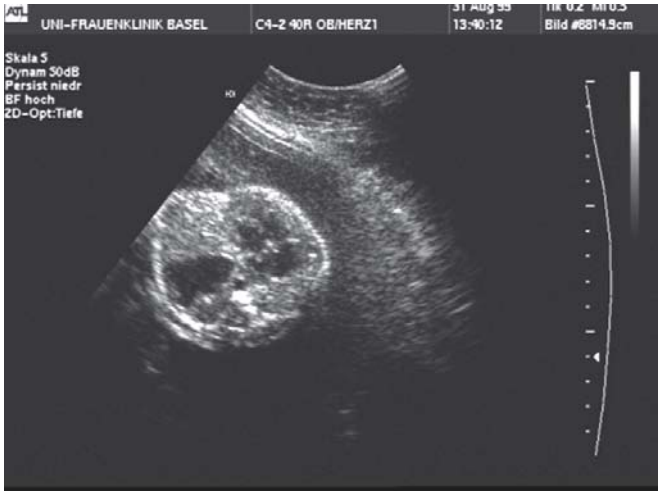

Fig. 2: Fetus with trisomy 18 and left sided diaphragm hernia with dislocation of the fetal heart

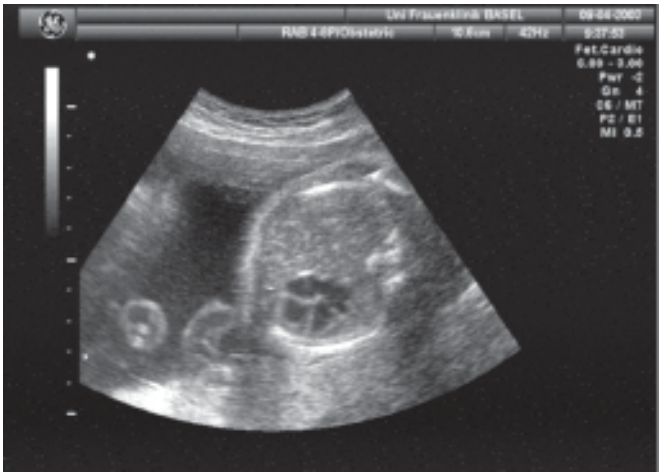

Fig. 3: Right fetal diaphragm hernia with dislocation of the intestine. Normal karyotype (in contrast to Figure 2)

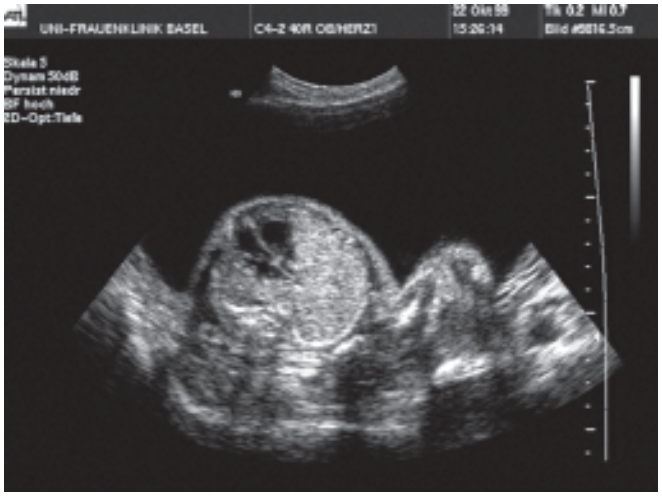

Fig. 4: Polyhydramnios associated with lung malformation (CCAM, type III)

In case of primary or secondary intrauterine heart failure (Fig. 5) (e.g. AV-shunting, cardiac rhythm anomalies), sacrococcygeal teratoma (Fig. 6),[6] immunologic hydrops, non-immunological hydrops), a polyhydramnios may develop. Other rare etiologies of polyhydramnios include VACTERL syndrome (Fig. 7), neonatal Bartter's syndrome, an inherited hypokalemic salt-losing nephropathy or a severe fetal anemia, due to infection (e.g. parvovirus), isoimmunization and inherited disorders like α-thalassemia and glucose-6-phosphatase deficiency.

Besides organ specific pathologies like osteogenesis imperfecta (Fig. 8), chromosomal disorders may be also associated with excessive fluid volume. The incidence of chromosomal anomalies is about 1:200 live births. Many of the

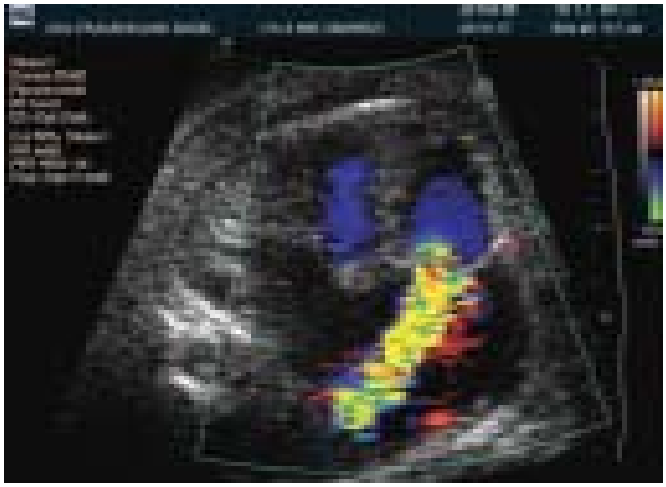

Fig. 5: Tricuspid insufficiency, associated with polyhydramnios, with retrograde flow and turbulences

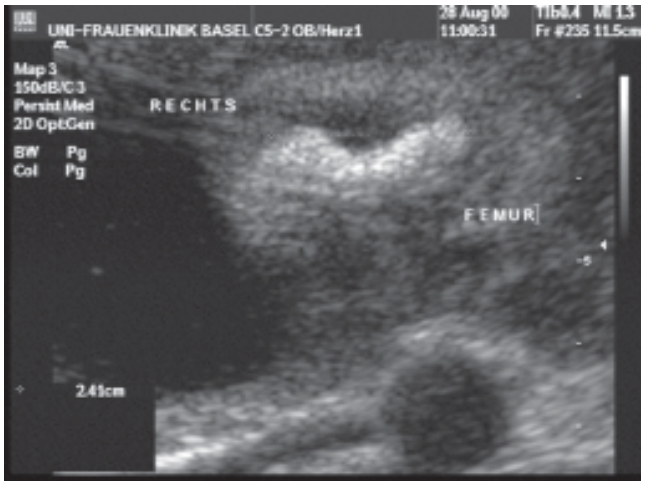

Fig. 8. Short femur at the 24th week of gestation in a case of osteogenesis imperfecta and associated polyhydramnios

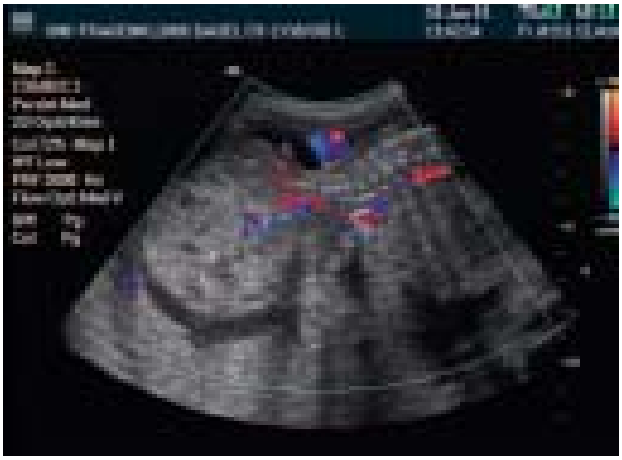

Fig. 6: Sacral teratoma in the 25th week of gestation. Two weeks later a polyhydramnios developed due to heart failure

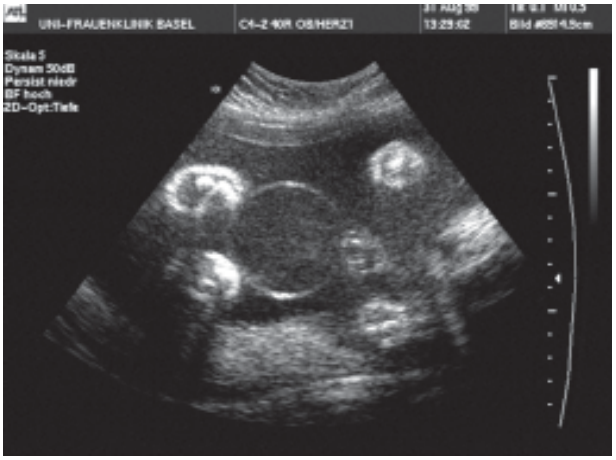

Fig. 9: Fetal trisomy 18 with associated polyhydramnios. In the center a large umbilical cyst is visible

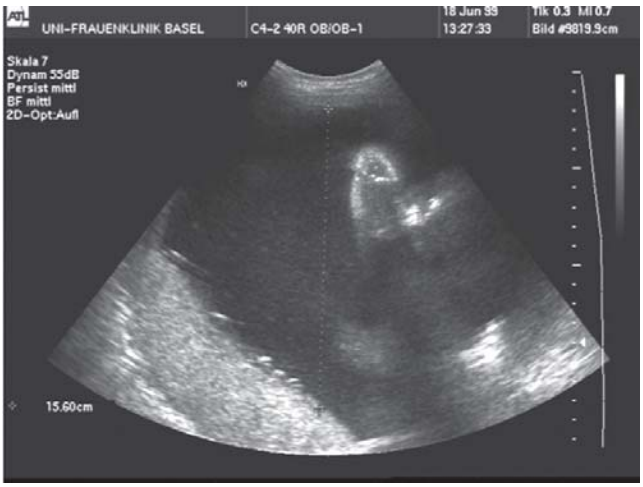

Fig. 7: Polyhydramnios, associated with VACTERL syndrome (measurement of one pocket: 15.60 cm)

disorders are associated with malformations, which may result in polyhydramnios. Even when there are more common distinctive features in each disease pattern, the possibility of an aneuploidy should always be a differential diagnosis in the clarification of an excessive amniotic fluid volume. Most commonly fetuses with trisomy 18 (Edward's syndrome) (Figs 2 and 9 to 11), trisomy 21 (Fig. 12) and trisomy 13, are affected.

In twin pregnancies, twin to twin transfusion syndrome (TTS) is an important differential diagnosis of excessive amniotic fluid volume, especially when fetal malformations are not present. The TTS complicates about 15 percent of monochorial twin gestations. Pathological shunting of blood leads to a increasing volume imbalance between both fetuses. The hypervolemia of the so called recipient with increased renal perfusion leads to consecutive polyhydramnios. The end-stage of this disease pattern is formed by high output cardiac failure, hydrops and polyhydramnios of the recipient twin.

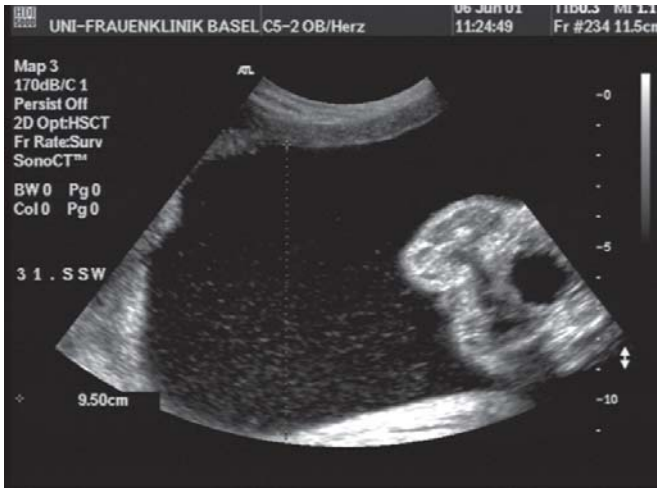

Fig. 10: Fetal trisomy 18 at the 31st week with a polyhydramnios. Transabdominal sonographic measurement of one pocket (9.50 cm)

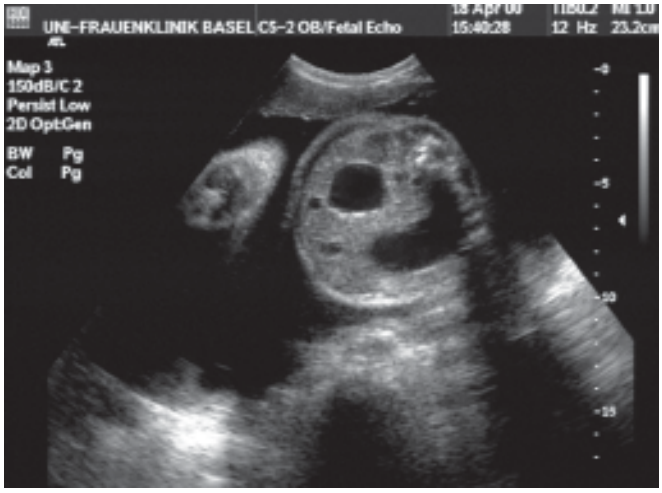

Fig. 12: Duodenal stenosis in a case of trisomy 21 with the sonographic double-bubble sign and associated polyhydramnios

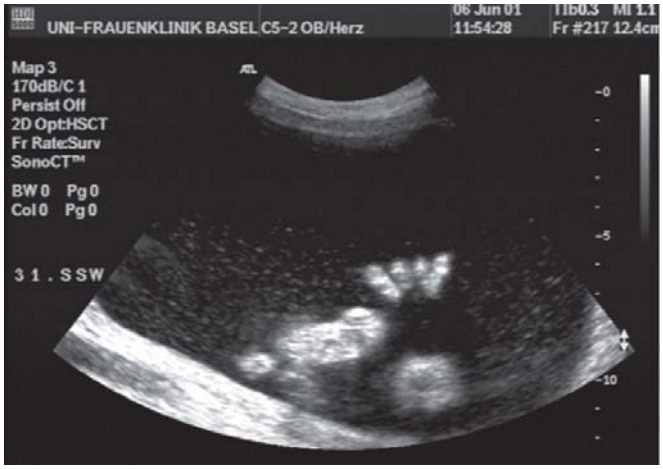

Fig. 11: The same case (trisomy 18) as in Figure 10. Typical intersected position of the fingers (polyhydramnios at 31st week)

A rarer conditions represents the "Twin-reversed arterial perfusion" (TRAP) sequence, with an estimated incidence of 0.3:10,000 births. It occurs also in monochorionic twin pregnancies. In coexistence with a normal twin, an acardiac fetus is connected with artery-to-artery and vein-to-vein anastomoses, combined with a delayed cardiac function of one of the twins during the evolution. It usually results in heart failure with secondary polyhydramnios of the healthy twin.

ASSESSMENT

In case of polyhydramnios, a targeted ultrasound examination should be performed. We recommend a referral of each patient with an excessive amniotic fluid volume to a perinatal center. A profound ultrasound examination should be performed to exclude malformations, and possible evidences of aneuploidy. Further testing (e.g. laboratory evaluation, karyotyping, glucose tolerance test) may help elucidate the final diagnosis.

Karyotyping (amniocentesis, or more infrequent due to the gestational age at diagnosis, chorionic villi sampling), is recommended in case of fetal anomalies. The risk of aneuploidy in case of associated malformation is up to 10 percent. If a congenital infection is suspected, additional polymerase chain reactions (PCR) may be performed to search for viruses.

Steps of Clarification in Case of Polyhydramnios

- Accurate ultrasound examination to exclude fetal malformations
- Fetal karyotyping for aneuploidy in case of malformation
- Oral maternal glucose tolerance test
- Screening for maternal antibodies to D, C, Kell, Duffy (FY), and Kidd (JK) antigens to determine mother's immunity
- Kleinhauer-Betke test (analysis for the presence of fetal cells in maternal blood) to evaluate a possible fetal-maternal hemorrhage
- Screening for TORCH
- Hemoglobin Bart in Asian patients (who may be at risk for heterozygous alpha-thalassemia)
- Test for congenital virus infection in the amniotic fluid by using PCR
- After excluding frequent causes, a distinctive search for fetal hypokalemic salt-losing nephropathies (assessment of chloride and prostaglandin E2 in the amniotic fluid) may be appropriate.

Symptoms of Polyhydramnios

Maternal symptoms of severe polyhydramnios are primarily the result of the weight gain and the pressure of the distended

uterus and abdominal wall. A compression of the vena cava during bed rest, dyspnea or orthopnea, as well as compression symptoms like congestion of the kidneys and edema of the lower extremities, are common features.

An excessive amniotic fluid volume may be also associated with an increased risk of obstetrical complications such as preterm labor, fetal malposition as well as umbilical cord prolapse after rupture of membranes and postpartum hemorrhage due to postpartum uterine atony. Furthermore, a significant water retention in a pregnant woman may mirror fetal hydropic changes, including hydramnios and fetal ascites. This clinical entity is called the "mirror syndrome."

TREATMENT

In most cases an expectant management after exclusion of the above mentioned associations is the best way of proceeding. Controls should be performed with regular, weekly sonographic measurements of the AFI, besides close surveillances of the fetus, including biometry and in certain indications Doppler measurements of fetal perfusion, as well as cervical length measurement. Many, especially idiopathic cases remain stable or ease during the ongoing pregnancy. A therapeutical approach should be discussed in case of severe maternal discomfort, additional complications, or impending preterm delivery. A reduction of the AF volume relieves maternal discomfort and may be helpful in prolonging the pregnancy, but usually the refilling is rapid. The following options are adequate in the treatment of a polyhydramnios.

Amnion Drainage for Reduction of the AF Volume

Drainage of the amniotic volume has been used for decades in the treatment of severe polyhydramnios, either to relieve maternal discomfort or to prevent complications, such as outflow obstruction of maternal kidneys, preterm labor, premature rupture of membranes (PROM), and fetal hypoxemia. Several clinical methods are used, allowing a drainage of up to 3.5 L of fluid in < 30 minutes.[7,8] Traditionally, amniondrainage has been performed using an 18- or 20-gauge spinal needle, the amniotic fluid being resolved with a three-way stopcock and a syringe. As an alternative, a vacuum bottle aspiration system can be used.

No more than 5 liters should be removed at one time. Normally the procedure is discontinued when the AFI is normal (< 25 cm). Antibiotics or tocolysis are recommended in indicated situations. Sometimes it is necessary to repeat the procedure. Serial amniondrainage has been introduced in the treatment of severe twin-twin transfusion syndrome. The procedure itself can be complicated by PROM, uterine contractions, placental abruption and in twin pregnancies, inadvertent septostomy, resulting in a iatrogenic monoamniotic twin pregnancy with the risk of cord entanglement. Further complication of any procedure *in utero* may be a chorioamnionitis. Yet the risk seems to be quite small, comparable to that of amniocentesis, if the procedure takes 20 to 30 minutes.

Prostaglandin Synthetase Inhibitors

Beside invasive punctures, the administration of prostaglandin synthetase inhibitors is an alternative treatment option.[9] The therapeutic use of these agents (predominantly indometacine, in a daily dose of 3 × 25 mg before 32 weeks of gestation [max. 5 × 25 mg]) lead to a decreased amniotic fluid volume beside prevention of premature labor, a common side effect of polyhydramnios, in influencing the prostaglandin synthesis in myometrium, amnion, chorion and decidua. Because of the high risk of severe maternal and fetal adverse effects, however, the drug administration must be performed with great caution. We should also be aware of fetal risks such as premature closure of the ductus arteriosus with fetal pulmonal hypertension, leading to tricuspid insufficiency, and impaired fetal renal function. Weekly sonographic monitoring, including the visualization of narrowing of the ductus arteriosus by Doppler ultrasound and the quantification of amniotic fluid volume should be performed, if duration of therapy exceeds several days. Maternal side effect of the orally administered therapy include gastrointestinal symptoms (nausea, vomiting, esophageal reflux, gastritis, and diarrhea).

Polyhydramnios and Elevated Cell-free Fetal DNA in Maternal Plasma

Abnormal amniotic fluid volume may indicate fetal, placental or maternal pathologies. In case of polyhydramnios, elevated levels of cell-free fetal DNA in maternal plasma were detected by real-time polymerase chain reaction (PCR).[10] The concentration of extracellular fetal circulatory DNA in maternal plasma is up to two-fold elevated, compared to controls. It can be speculated that the increased intrauterine pressure in polyhydramnios leads to an enhanced influx of cell-free fetal DNA into the maternal circulation and cell-free fetal DNA may be a valuable marker of the severity of this disease.

CONCLUSION

Polyhydramnios is an important clinical pattern in perinatal medicine. Early diagnosis, mostly with ultrasound, provides a correct diagnosis and allows a specific therapy. A referral to a tertiary center is advised in case of severe polyhydramnios and unknown etiology.

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