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The Medical Evaluation in Cases of Fetal Demise

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One of the most emotionally trying events surrounding pregnancy is the delivery of a stillborn infant. A fetal death may occur at any point in time during a pregnancy. If fetal death occurs prior to 20 completed weeks of gestation, it is considered a spontaneous abortion; a fetal demise occurring after 20 completed weeks of gestation is considered an intrauterine fetal death (IUFD, also commonly known as a "stillbirth").[1] Another common, and perhaps more accurate, definition of IUFD is the delivery of a fetus weighing 500 grams or more. Twenty-seven states, however, require the reporting of a fetal death based upon gestational age, not weight.[2] Each practitioner should become familiar with their individual state requirements regarding the reporting of fetal deaths.

Although 15% of recognized pregnancies lead to spontaneous abortion, many studies indicate that the actual prenatal spontaneous death rate in human gestation may be as high as 50%.[3] The vast majority of these losses occur in early embryos, prior to recognition of pregnancy; most of these embryos are malformed, the majority having chromosomal anomalies.[4]

The occurrence of multiple (more than three) spontaneous abortions should prompt the clinician to refer the couple for genetic evaluation, since 1-2% of such individuals have been found to have otherwise asymptomatic chromosomal rearrangements predisposing to recurrent pregnancy losses. The magnitude of the role of fetal anomalies in the causation of pregnancy loss decreases as gestation progresses.

In the United States, approximately nine intrauterine fetal deaths occur per every 1000 live births, accounting for almost one-half of total perinatal mortality. This paper will focus on intrauterine fetal death (IUFD) as defined above.

The etiology of IUFD can be identified in approximately half the cases, with the following conditions most commonly associated with IUFD[1]:

- hypertensive diseases of pregnancy
- diabetes mellitus
- erythroblastosis fetalis
- fetal congenital anomalies
- chromosomal abnormalities
- umbilical cord accidents
- placental insufficiency or abnormalities
- fetal or maternal infection.

Identification of the cause of spontaneous abortion or IUFD allows for accurate counseling regarding the risks for recurrence of spontaneous pregnancy loss and/or the risks for having a malformed liveborn infant. Due to the emotional duress for everyone involved during the delivery of a stillborn infant, it is not uncommon for the clinician to later realize that an incomplete evaluation to identify possible causes of the IUFD was done.

The following components are suggested to be included in a protocol developed by each IHS Service Unit to appropriately evaluate a stillborn infant:

Review of family and obstetric history. The mother's medical, family, and obstetric history, as well as the father's medical and family history, should be reviewed for possible conditions that may have contributed to the fetal demise. Any family history of recurrent pregnancy loss, mental retardation, malformed children, or genetic disorders should be sought. Rh isoimmunization, diabetes, preeclampsia, and pregnancy-induced hypertension (PIH) are medical complications commonly associated with IUFD.

Acute and chronic maternal infections can also be associated with IUFD. Such maternal infections as chicken pox, mumps, syphilis, and the TORCH complex (toxoplasmosis, other, rubella, cytomegalovirus, herpes simplex virus) have been associated with congenital infection and IUFD.

Recent maternal trauma has been associated with fetal compromise and demise, especially blunt abdominal trauma, falls, motor vehicle crashes, and battery. Though rare, IUFD has occurred following obstetrical procedures, such as external version and amniocentesis. The use of street drugs has been associated with an increased incidence of preterm birth, congenital abnormalities, and fetal demise. Exposure to alcohol, cocaine, and toluene has been associated with increased stillbirth and sudden infant death syndrome (SIDS). For medicolegal reasons, use of street drugs should be documented prenatally, and a maternal drug screen should be considered in the event of an IUFD. Additionally, it may be helpful to document when the patient last noted active fetal movement. as well as the last time fetal heart tones were noted.

Physical examination of the fetus. A complete physical examination of the fetus should be performed and recorded, including documentation of the fetal weight, length, and (if possible) head circumference. It should be recorded if the fetus appears morphologically normal. *All observed abnormalities should be compulsively documented*. Total-body photographs should be obtained to aid in future dysmorphology evaluation and genetic counseling.

Autopsy. An autopsy should be sought to evaluate the fetus for possible abnormalities or other causes that may have contributed to the demise. Even if an obvious diagnosis, such as anencephaly, can be made by the physical examination, an autopsy should be sought, since the presence of occult internal anomalies may alter the overall diagnosis assigned and subsequent risk counseling. If the family is unwilling to have an autopsy done, it is advisable to record this in the medical record.

Radiographic examination. A fetogram (total-body fetal roentgenogram) should *always* be obtained. A fetogram can differentiate among the various forms of lethal dwarfing conditions. It can also identify bony abnormalities that could be associated with a possible cause of the IUFD. In general, permits are not usually needed for noninvasive procedures such as this. It is important to note that in a stillbirth the parietal sutures will naturally overlap.

Placenta. Careful examination of the placenta, cord, and membranes is desirable in every delivery. Especially in the case of an adverse outcome, a complete inspection of the placental condition (abnormalities or absence thereof) should be documented within the medical record. The placenta should also be sent for pathological evaluation. Placental tissue is best stored in a labeled, plastic, or styrofoam container and placed in refrigeration at 1-6 degrees Centigrade. This will prevent tissue dehydration and color change. Freezing of the entire placenta should be avoided, because it causes irreparable tissue damage, making histological studies difficult. Samples of placental tissue and membranes can be frozen or placed in formalin for preservation and/or later examination if necessary.

Knots in the umbilical cord and other placental deviations should be sent for pathological examination as they are found. False knots (kinking of the cord) should be distinguished from true knots in the umbilical cord. Pathological examination can identify meconium, chorioamnionitis, and occult placental abruption in the absence of overt clinical manifestations. Placental chorioangiomas, choriocarcinoma, and umbilical vein thrombosis can also be identified. These conditions have been associated with fetal-maternal hemorrhage resulting in fetal demise.

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Cytogenetic studies may also be obtained using amniotic and placental tissues. Tissue should be obtained using sterile instruments and placed into a sterile container of tissue transport medium or sterile saline. Tissue for karyotyping *must not* be placed in formalin.

Bacterial cultures. A number of maternal or fetal infections have been associated with adverse fetal consequences including congenital anomalies and IUFD. If possible, both aerobic and anaerobic endocervical and placental (maternal and fetal sides) bacterial cultures should be obtained to evaluate the possibility of infection. Consideration may also be given to obtaining viral, chlamydial, fungal, and acid fast bacterial cultures.

Chromosomal studies. Consideration may be given to obtaining chromosomal studies, if the physical examination or autopsy reveal multiple major and/or minor anomalies. Chromosomal studies may be done to confirm recognizable chromosomal anomalies and to identify chromosomal abnormalities which do not present with identifiable features. If the death is recent (within 12 hours), karyotyping can be attempted from fetal blood and/or skin. Tissue can be collected from the fascia lata of the thigh or deep

tendon of the knee if the fetus has been dead for some time. Tissue specimens should be obtained using a sterile scalpel, forceps, and scissors and placed into a sterile container of tissue transport medium or sterile saline. Sending several tissue samples will increase the chance of obtaining useable results. Tissue may be placed in a sterile container with tissue transport medium or sterile saline. It may be of benefit to consult the receiving laboratory as to what tissue samples should be obtained and how to properly store and transport the samples prior to obtaining the tissue specimen.

Blood should also be obtained using sterile technique, and placed in a sodium heparinized tube. Chromosomal studies are generally recommended in the evaluation of all cases of IUFD. The exception is the full term (by weight) infant which is morphologically normal.

Kleihauer-Betke and Lupus anticoagulant exams. Maternal serum for detection of fetal to maternal bleeding (Kleihauer-Betke examination) should be drawn. Transplacental hemorrhage has been identified to be the cause of death in a small percentage of unexplained IUFD without a positive maternal history for some type of trauma.

The presence of lupus anticoagulant (LAC) antibody is associated with increased fetal loss. Stillbirths, as well as prematurity and fetal growth retardation, are more common in patients with systemic lupus erythematosis (SLE). Yet, only 5 to 10% of patients with SLE have the LAC antibody.[1] LAC functions as an anticardiolipin antibody detectable with an ELISA technique. It is therefore suggested that both the lupus anticoagulant and anticardiolipin antibody be obtained.

Other laboratory tests. Consideration should be given to obtaining TORCH (toxoplasmosis, other, rubella, cytomegalovirus, and herpes simplex virus) IgM titers. Use of the acronym TORCH is becoming outdated because the "other" category has markedly expanded. "Other" organisms that are associated with IUFD include coxsackievirus, enterovirus, hepatitis, human immunodeficiency virus, listeria, parvovirus, syphilis, varicella, and echovirus. As part of a general maternal evaluation, basic laboratory testing, such as a CBC with differential, a Chemistry 7 Panel (including glucose), and a fibrinogen level may be considered.

Identifying the Patient at Risk for IUFD

Although imprecise, one of the earliest signs that may alert the mother and clinician to the possibility of fetal demise is the loss of fetal movement. Especially at term, a mother's perception of decreased fetal movement is an indication of a need for prompt further fetal evaluation. Studies have found that a significant increase in perinatal mortality and fetal compromise is associated with pregnancies in which fewer than 10 fetal movements are perceived within 12 hours. It is important to educate prenatal patients to be aware of fetal movement and to report any marked decrease. *Additionally, it is prudent to formally document the mother's perception of fetal movement at each pregnancy-related visit.*

A patient presenting at term with complaints of decreased fetal movement should receive immediate evaluation by electronic fetal heart rate (FHR) monitoring, including a nonstress test (NST). As identified in the ACOG/IHS reference text "Obstetric, Neonatal, and Gynecologic Care,"[5] other indications for electronic FHR surveillance testing are:

- women with diabetes, hypertensive disorders, or a history of previous wastage
- suspected intrauterine growth retardation (IUGR)
- postdatism
- multiple pregnancy
- patients with abnormal results from other means of antenatal fetal surveillance (e.g., an abnormal modified biophysical profile or an ultrasound indicating oligohydramnios).

According to the ACOG/IHS reference text, a reactive FHR pattern is defined as two accelerations occurring within a 20 minute period; an acceleration is defined as an increase of 15 beats per minute (bpm) over the baseline and lasting 15 or more seconds.[5] Following a reassuring (reactive) NST, it recommended that the patient be reevaluated within 3 to 7 days.

In the event of a non-reactive (non-reassuring) NST, it is generally recommended that a contraction stress test (CST) be performed in less than 24 hours. By IHS guidelines, "special personnel and facility requirements exist for contraction stress testing other than that which occur when monitoring spontaneous contractions. Therefore, contraction stress tests are generally best performed and interpreted in a service supervised by an obstetrician."[5] A consultation should be sought on any patient not exhibiting reassuring electronic fetal monitoring patterns.

The NST is not a "stand-alone" evaluation and has definite limitations. Studies have indicated the false positive rate to be from 7-99% (therefore a nonreactive NST indicates more definitive testing is required) and the false negative rate to be 1-28% (therefore a reactive NST is reassuring) depending on specific criteria used for the test.[3(p365-368)] The advantage of the NST is that it is noninvasive with no clear contraindication. In addition to obtaining false positive or false negative results, the main

risks seem to be inaccurate test interpretation, and errors in how the NST information is used in patient management.

Emotional Support of the Patient

Studies have shown that a spontaneous pregnancy loss initiates a normal grieving process in the family, similar to that following the death of an older child. All involved health care providers should understand this process and support the parents though the stages of grief. This support may include frequent followup visits, counseling regarding the cause(s) of the loss and risk for recurrence, and discussion of and counseling about appropriate contraceptive measures until the parents have dealt with their grief in a healthy manner. The clinician should understand that the IUFD represents the loss of a real individual to the family and that a future child cannot "take the place of" the potential child who was lost.

Summary

Even with present technologic advancements, the cause of spontaneous abortion or IUFD can only be identified in 50% of cases. Investigation of the cause of every loss of pregnancy is important for reasons of ongoing health supervision, counseling regarding potential recurrence, genetic counseling, and ongoing emotional support of the family. Finally, identifying the cause of a IUFD can be helpful in avoiding medicolegal entanglements. It is suggested that all IHS and tribal health facilities review their protocols related to IUFD to ensure that the above criteria are addressed in each case.

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