Bleeding Warrants US For Ectopic Pregnancy

BY MICHELE G. SULLIVAN

KISSIMMEE, FLA. — Women who present with vaginal bleeding—with or without abdominal pain—in the first trimester of pregnancy should undergo an ultrasound scan to rule out an ectopic pregnancy in the cervix, according to Dr. Valerie Shavell.

Because cervical pregnancy is so rare—about 1 in 9,000 pregnancies—it may not be on the diagnostic radar when a woman arrives in the emergency department with such common symptoms. Thus, a cervical pregnancy can easily be misdiagnosed as a threatened spontaneous abortion, she said at the annual meeting of the AAGL.

If the patient is then discharged under watchful waiting, rupture may occur with a potentially fatal bleed. Hemorrhage is also possible if she undergoes a dilation and curettage for a suspected threatened abortion. Either way, the outcome may be a hysterectomy, said Dr. Shavell of Wayne State University, Detroit.

Ultrasound can identify more than 80% of cervical pregnancies in time for medical or minimally invasive therapy, which can prevent hysterectomy and preserve fertility, said Dr. Shavell and her colleague, Dr. Mark Zakaria.

Dr. Shavell discussed symptoms and ultrasound findings in a case series of 14 women (mean age 32 years) who were treated for cervical pregnancy at the Detroit Medical Center over a 10-year period. Most of the patients (eight) presented directly to the hospital's emergency department. Four were transferred from other hospitals, and two were admitted from the resident clinic. Their mean gravidity was 5, and their mean parity was 2.

Consistent with the area's demographics, 71% were black. Eleven of the women had a risk factor for cervical pregnancy: prior termination of pregnancy (9), cesarean section (4), or cervical cone biopsy (2). The gestational age at presentation ranged from 5 to 11 weeks.

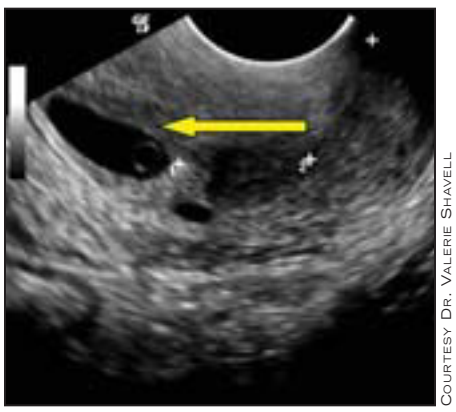
All patients presented with vaginal bleeding, which was mild in seven, moderate in four, and heavy with clots in three. Six patients also reported some abdominal pain or cramping.

"In all cases, ultrasound identified a gestational sac and yolk sac consistent with the gestational age as measured by the last menstrual period," Dr. Shavell said. "We also saw prominent vascularity surrounding the gestational sac in every case."

Fetal heart activity was present in 64%. The distance between the external cervical os and the leading edge of the gestational sac ranged from 7 to 25 mm.

Dr. Zakaria reported treatment outcomes for all 14 of the patients, plus 1 additional patient. All received the first-line therapy of methotrexate and leucovorin (used to protect healthy cells from methotrexate); this was sufficient to terminate the pregnancy in five. Six women received additional therapy and also underwent a uterine artery embolization. In four patients, the methotrexate combination was delivered in conjunction with a fetal intraembryonic potassium chloride injection, followed by uterine artery embolization.

It's important to carefully assess both the patient and the services available to her while making treatment decisions, Dr. Zakaria said. "Methotrexate is a reasonable first-line therapy. It's easy to administer and can be given in any hospital. The other treatments require an interventional radiologist, who might not always be available at a community hospital. If the patient comes to the emergency department and the physician suspects a cervical pregnancy, that physician should consider whether the hospital is equipped to do these interventions, or whether a transfer might be necessary."



COURTESY DR. VALERIE SHAVELL

Ultrasound can identify more than 80% of cases in time for therapy.

"Generally, those who had lower human chorionic gonadotropin levels required less intervention, although it's hard to say what that means," he said in an interview. "It could have been that these women were in an earlier stage of pregnancy, or we could have also caught them at a later stage, when the pregnancy was already failing and the hormones were already on the way down." ■

DRUGS, PREGNANCY, AND LACTATION

Anticonvulsant Use in Pregnancy

It is estimated that approximately 500,000 women in the United States who have a diagnosed seizure disorder are of reproductive age. Anticonvulsant medications used to prevent seizures, such as phenytoin, were among the first medications identified as human teratogens more than 30 years ago. Since that time, it has been generally accepted that women with a seizure disorder have an increased risk of having a child with developmental disabilities, and that this risk is higher among women who are treated with polytherapy as opposed to monotherapy. It is also generally accepted that this risk is not due entirely to the mother's underlying seizure disorder, but rather is associated with the medication exposure itself.

BY CHRISTINA CHAMBERS, PH.D., M.P.H.

However, there are several important questions that have not yet been definitively answered: What are the comparative risks of specific anticonvulsants, does lowering the dose decrease the risk, does periconceptional folic acid supplementation modify anticonvulsant-attributable risk, does the same risk apply to anticonvulsant medications when used to treat psychiatric disorders, and what are the long-term consequences such as cognitive deficits in children with prenatal exposure?

In recent years, some of these questions have been addressed by several ongoing population-based or registry-type studies being conducted in multiple countries throughout the world. Although sample sizes for specific medications tend to remain relatively small, and careful long-term follow-up for neurodevelopmental deficits is rare, new information is emerging. Most studies have confirmed a relative excess of congenital malformations with first-trimester exposure to valproate mono- or polytherapy, compared with other anticonvulsants or no anticonvulsant exposure. As expected with human teratogens, the malformations associated with valproate exposure represent a specific pattern including neural tube defects, facial clefts, and hypospadias. Similarly, as expected for human teratogens, in many studies the risk appears to be dose related, and not all exposed fetuses are affected.

Most recently, investigators from a multicenter study based at Emory University, Atlanta, and the United Kingdom have completed 3-year follow-up on the neurodevelopmental effects of anticonvulsant drugs, and report a significant dose-related effect of valproate across several domains of cognitive development. Other commonly used drugs, such as carbamazepine, phenobarbital, lamotrigine, and phenytoin are currently being evaluated in the same study.

Recently, an expert panel assembled by the American Academy of Neurology conducted an evidence-based review of the safety of anticonvulsant medications in pregnant women with epilepsy. The panel's summary, published last May (Epilepsia 2009;50:1237-46), concluded that there is a high probability of comparative teratogenicity of first-trimester valproate exposure relative to carbamazepine, and possibly compared with phenytoin or lamotrigine.

The panel also concluded that intrauterine exposure to anticonvulsant polytherapy or to valproate monotherapy probably results in poor cognitive outcomes, but panel members were less confident regarding the current weight of evidence for phenytoin or phenobarbital. The risk for impaired cognitive development may be related to the use of anticonvulsants throughout pregnancy or at least into the third trimester.

As ongoing anticonvulsant studies continue to accrue sample size, the panel's recommendations at present are as follows:

► Clinicians should consider avoiding first-trimester treatment of patients with valproate and/or with polytherapy in order to decrease the risk for major congenital anomalies.

► Clinicians should avoid if possible valproate and/or polytherapy treatment throughout pregnancy in order to reduce the risk for cognitive deficits. Avoidance of phenytoin and phenobarbital throughout pregnancy might also be considered.

The panel concluded that periconceptional folic acid supplementation (at a range of doses) was possibly effective in reducing the risk of major congenital malformations in women with epilepsy, but recommended that clinicians consider supplementation at or above the 0.4 mg/day currently recommended for all women of reproductive age (Epilepsia 2009;50:1247-55).

As with many other chronic maternal conditions, these recommendations must be evaluated in the context of appropriate treatment for the mother with a seizure disorder, in consideration of any treatment changes before pregnancy occurs, and in consideration of the safety of alternative medications.

To date, there are insufficient data on the absolute risks for most specific anticonvulsants in pregnancy, and especially for the newest medications. Well-conducted long-term neurodevelopmental studies with sufficient sample size are also lacking for most anticonvulsants. While specific mechanisms of teratogenesis have been suggested, susceptibility factors that might help identify individual pregnancies at higher or lower risk have not been clarified. International efforts to address many of these questions are underway.

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