ORIGINAL ARTICLES

Medicolegal Review of Methotrexate Administration to Viable Intrauterine Pregnancies

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OBJECTIVE: To examine 3 legal cases in which physicians prescribed methotrexate to women with a viable intrauterine pregnancy, presumed to be ectopic, resulting in adverse fetal outcomes.

STUDY DESIGN: We conducted an electronic literature search for legal cases using the keywords "methotrexate" and "pregnancy" in the LexisNexis legal research engine as well as an Internet-wide search using the additional keyword "verdict." We manually searched the resultant list of identified cases and categorized the studies identified in the search by verdict, award amount, and outcome of the embryo exposed to methotrexate.

RESULTS: The monetary awards are typically greater when the embryo exposed to methotrexate lives and requires continuous medical and custodial care as compared to when the fetus dies in utero or shortly after birth.

CONCLUSION: Physicians who, with all good intentions, prescribe methotrexate to women with a viable pregnancy, presumed to be ectopic, could find themselves liable for an adverse fetal outcome. For the benefit of patients, their unborn offspring, and the liability exposure of the physician, it is important to be very cautious when prescribing methotrexate. (J Reprod Med 2017;62:97–101)

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Keywords: ectopic pregnancy; lawsuits; legal outcomes; litigation; medicolegal aspects; methotrexate; pregnancy; pregnancy, extrauterine.

Administration of methotrexate to a patient with a viable intrauterine pregnancy mistakenly presumed to be an ectopic pregnancy carries devastating consequences to the unborn embryo. This mistake can tarnish the reputation of even the best physicians and lead to legal ramifications. Despite good intentions and efforts to ensure proper treatment, misdiagnosis of ectopic pregnancy can still occur. Preliminary or erroneous ultrasound readings, sole dependence on ultrasound without serum human chorionic gonadotropin (hCG) levels, and anchoring on a diagnosis in the setting of equivocal test results may contribute to a misdiagnosis of ectopic pregnancy. Methotrexate is a category X drug approved by the FDA for neoplas-

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tic diseases, psoriasis, and rheumatoid arthritis. Its off-label use to treat ectopic pregnancy may result in congenital malformations when administered in a viable intrauterine pregnancy. The existence of an ectopic pregnancy must be established with a high degree of certainty before treating a patient with methotrexate. By examining several legal cases, this medicolegal review seeks to bring awareness to the medical and legal ramifications of administering methotrexate to patients with misdiagnosed ectopic pregnancy.

The number of viable intrauterine pregnancies to which methotrexate is administered is unknown and probably underreported. Although there are no exact data on the subject, studies suggest that there are a number of increasing legal actions related to this issue.[1,2] In addition, national news sources have reported cases of pregnant women receiving methotrexate following misdiagnosed ectopic pregnancies.[3,4] Online support groups for individuals who were administered methotrexate and were later confirmed to have intrauterine pregnancies on subsequent ultrasound can be found across the Internet on various websites, including babycenter.com and supportgroups.com.[5,6] One Facebook support group founded by an affected individual currently has 327 members as of March 2017.[7] These groups capture only the women who seek online support.

For a medical malpractice claim to succeed, a plaintiff attorney must demonstrate several components. It must be established that the physician had a duty of care for the patient and that this duty was breached. In addition, an injury must be present and a causal connection must be demonstrated that this breach in duty led to the proximate alleged injury. If the suit is in favor of the plaintiff, the resultant damages recovered are typically economic and noneconomic. Economic damages are objectively verifiable monetary losses. In the case of methotrexate administration to a viable pregnancy resulting in physical deformities, economic damages may include hospital bills, custodial care for the child, lost wages of both parents, and future lost wages of the child. Noneconomic damages refer to compensation for subjective, nonmonetary losses and can take the form of pain and suffering along with emotional distress. Damage awards can accumulate to an astronomical amount and easily surpass a physician's medical malpractice policy limits.

A separate but intertwined potential cause of action against physicians may be failure to obtain informed consent. There are 2 standards for informed consent against which a physician's actions can be judged when examining how the physician presented information to a patient: the prudent physician standard and the reasonable patient standard. The prudent physician standard is what a prudent physician would have disclosed to a patient under similar circumstances and is the majority standard applicable in most states.[8] This standard typically requires expert testimony by a physician as to what a prudent physician should disclose to a patient. The other standard is the reasonable patient standard and requires the physician to disclose the risks a reasonable patient would want to know. Both standards involve informing the patient of the risks of the proposed therapy and the alternatives to the treatment. Depending on the patient's clinical presentation, ultrasound findings, and quantitative hCG values, providing informed consent to a patient with a suspected ectopic pregnancy may include a discussion about the risks and benefits of expectant management, surgical management, and methotrexate therapy.

Materials and Methods

We searched for legal cases pertaining to methotrexate administration to viable intrauterine pregnancies and their verdicts by using the LexisNexis legal research engine. LexisNexis and VerdictSearch are commercial online legal research engines for legal-related materials commonly used by attorneys, law students, judges, and paralegals. We used the keywords "methotrexate" and "pregnancy." Case verdicts and monetary awards were also found using VerdictSearch and by contacting courthouses. Medical record information pertaining to each patient's care was limited to public court documents. We present 3 cases that differ in medical outcomes and discuss the legal results of each one.

Results

Case 1

In the case *Newmark-Shortino v Buna,* the patient filed a lack-of-informed-consent claim against the obstetrician for failing to present her with alternative treatment options.[9] According to the lawsuit, a woman presented to her obstetrician with a presumed gestational age of 7 weeks. Legal records indicate that a transvaginal ultrasound showed a

right adnexal complex mass and fluid in the uterus without evidence of an intrauterine gestation. The records state a second ultrasound the following day again did not show an intrauterine pregnancy, and bloodwork revealed an hCG level of 917 mIU/mL. The lawsuit alleges she received a dose of methotrexate and was instructed to return for a follow-up appointment 6 days later. The patient claims she was neither informed nor advised of any option other than methotrexate therapy.

Legal records state that a repeat bloodwork at her follow-up appointment showed her serum hCG level had risen to 4,757 mIU/mL. According to the lawsuit, the patient claims the obstetrician told her that the bloodwork must have been an error, but the rising number could be an indication of a normal pregnancy. Legal documents show that a second dose of methotrexate was administered to the patient. According to the lawsuit, additional bloodwork was ordered which showed the hCG levels continuing to rise. A repeat ultrasound confirmed a 5-week embryo with cardiac activity within the uterus. The patient underwent a dilation and curettage (D&C) and filed a lawsuit against the physician for medical negligence, lack of informed consent, and emotional distress.

An obstetrician retained by the plaintiff testified that "if [the obstetrician] did not tell [the patient] the pregnancy could potentially be a normal intrauterine pregnancy, that would be a deviation from the accepted standard of care because he would not have given her information to which she was entitled about her pregnancy." The trial judge initially did not allow the lack of the informed consent claim to be presented to the jury, and the jury ruled in favor of the obstetrician. The patient appealed the case on the grounds that the lack of informed consent claim should have been allowed to go before the jury, and the appellate court agreed. The case was sent back to the lower court so that the claim of lack of informed consent could be presented before the jury. The case was tried and the jury awarded the patient $300,000 plus interest for lack of informed consent.

Case 2

In the case *Tindall v Stewart*, a woman who received methotrexate for a presumed ectopic pregnancy filed a lawsuit after giving birth to an infant with congenital malformations.[10,11] The 27-year-old woman, believed to be at 6 weeks' gestation, had an ultrasound performed by a radiologist to confirm her pregnancy. According to the lawsuit, the radiologist contacted her obstetrician informing her of the strong possibility of an ectopic pregnancy. The obstetrician administered methotrexate to the patient to treat the ectopic pregnancy. Legal records show it was later discovered that the patient had an intrauterine pregnancy rather than an ectopic pregnancy. According to the suit, the patient claims she was told that the risk of congenital malformations from the methotrexate injection was low and therefore decided to continue her pregnancy. The lawsuit states the infant was born with multiple malformations and died 3 months later as a result of complications caused by cardiac problems.

The patient later filed a lawsuit against both the obstetrician and the radiologist. The patient alleges that the obstetrician relied solely on the ultrasound report without ordering additional tests. The lawsuit reports that the obstetrician stated that the hCG level drawn before administering methotrexate was consistent with the existence of an ectopic pregnancy. According to legal documents, the attorney representing the patient argued that the obstetrician should have ordered at least 2 hCG levels prior to administering methotrexate. The radiologist and his group settled the suit prior to trial for $950,000. The claim against the obstetrician went to trial and the jury rendered an award against the obstetrician for $615,000. The obstetrician was given a set-off of $380,010 as a result of the radiology group's settlement, and the total award to the patient was approximately $1.2 million.

Case 3

In the following case of *Sheppard-Mobley v King*, a woman filed a lawsuit after giving birth to a child with multiple congenital malformations from methotrexate administration.[12] According to legal records, the patient was 5–6 weeks pregnant when she presented to her obstetrician. An ultrasound performed by a radiologist did not show an intrauterine pregnancy. Relying on the radiologist's ultrasound findings, the obstetrician prescribed methotrexate. According to the lawsuit, the patient presented several times to the obstetrician following methotrexate treatment with complaints of not having a menses. An ultrasound was performed 5 months later by a different radiologist that showed an intrauterine pregnancy at 28 weeks' gestation.

The legal documents state that the child was

born with 4 toes on each foot, wide set eyes, a cleft palate, a heart defect, cognitive difficulties, and 85% hearing loss. According to legal records, the child underwent surgery for his cleft palate, and by the third year of life had received 2 cranial reconstructive surgeries and one surgery for his hearing difficulties.

The lawsuit states that the child required a full-time "pusher" to care for him during his classes and that he will never be able to live independently or without lifelong medical monitoring as a result of his medical conditions. The patient's claim sought damages from pain and suffering, monetary compensation for past and future medical expenses, and recompense for a projected loss of $20 million in future earnings of the child. Before the case was brought to trial, a settlement of $4.15 million was reached, in which the obstetrician paid $3.3 million and the radiologist paid $850,000.

Review of Diagnostic Criteria for Nonviable Pregnancy

Proper transvaginal ultrasound examinations are invaluable in determining intrauterine versus ectopic pregnancies. Doubilet et al provide the following criteria for diagnosing pregnancy failure, with the first 2 points "yield[ing] a specificity and positive predictive value of 100% (or as close to 100% as can be determined)"[13]:

- Crown-rump length of ≥7 mm and no heartbeat
- Mean sac diameter of ≥25 mm and no embryo
- Absence of embryo with heartbeat ≥2 weeks after a scan that shows a gestational sac without a yolk sac
- Absence of embryo with heartbeat ≥11 days after a scan that shows a gestational sac with a yolk sac

In cases of equivocal ultrasound readings, especially early in pregnancy, serum hCG measurements are essential. A single hCG level above the discriminatory zone of approximately 3,500 mIU/mL is associated with a visible singleton intrauterine pregnancy on ultrasound.[14] However, experts disagree on the effectiveness of the discriminatory zone to rule out intrauterine pregnancies.[13,15-17] Furthermore, a single hCG level above the discriminatory zone without a finding on ultrasound may be confounded by twin gestations or heterotopic pregnancies.[18] Therefore, a single hCG level in a clinically stable patient may not be as valuable as 2 hCG levels taken 48 hours apart. An increase in serum hCG of <53% in 48 hours confirms with 99% sensitivity an abnormal pregnancy.[18]

Discussion

Despite using ultrasound and hCG levels, misdiagnosis remains a distinct possibility. In cases of clinically stable patients, erroneously diagnosing a pregnancy as a nonviable pregnancy can carry devastating consequences. The risk of treating a perceived ectopic pregnancy with methotrexate will likely induce congenital abnormalities or cause fetal death to an otherwise viable fetus.[19] There are reports of physicians having recommended surgical abortion to patients with intrauterine pregnancies that had received methotrexate based on fear of medicolegal repercussions ensuing from adverse fetal outcome.[19]

In Case 1, where the award amount was the least amongst the 3 cases, the patient elected to undergo a D&C. The child in Case 2, however, did not survive beyond 3 months and required a shorter and presumably less costly length of care. In Case 3, the economic damages included compensation for the child's caretaker and past and future medical expenses. Additionally, the lawsuit accounted for the loss of the child's future wages as an adult. Of the $4.15 million paid by the obstetrician and the radiologist, $300,000 was allocated to the mother for emotional distress, while the remainder was assigned to her child. The monetary awards are typically greater when the infant exposed to methotrexate lives and requires continuous medical and custodial care as compared to when the fetus dies in utero or shortly after birth.

Many states have passed laws limiting the amount of compensation a plaintiff can receive as a result of a medical malpractice suit. Even with tort reform, most states still do not have limits on economic damages. These limits, or "caps," typically apply to noneconomic damages only and do not apply to economic damages, which include hospital care, long-term custodial care, lost wages of the parents, and projected future lost wages of the child.[20] In cases of children born with deformities caused by methotrexate, these damage awards can easily exceed the policy limits of the physician's malpractice insurance.

Prior to giving methotrexate, it is important to properly inform patients of the risks and benefits of the proposed therapy and alternatives to treatment as well as to document the informed consent.

Not only will this improve patient care but will also likely deter future claims of lack of informed consent. In a clinically stable patient, it is essential to obtain quantitative hCG trends as an adjunct to ultrasound findings, especially if the ultrasound result is nondiagnostic or indicative of a possible early intrauterine pregnancy. It is also prudent to have a proper understanding of the usefulness and limitations of the discriminatory zone.

For the benefit of patients and their unborn offspring and the liability exposure of the physician, it is important to be very cautious when prescribing methotrexate. When there is any doubt, it is better to err on the side of expectant or surgical management as compared to giving methotrexate.

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