New anomalies due to methotrexate and misoprostol exposure in early pregnancy

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ARTICLE INFO

Article history:
Received 21 December 2012
Received in revised form 25 March 2013
Accepted 17 May 2013

Keywords:
Canada
Case report
Medical abortion
Methotrexate
Misoprostol
Teratogen

Induced abortion is common worldwide, with an estimated 1 in 5 pregnancies ending in abortion in 2008 [1]. Abortion may be performed surgically or with medication. In Canada, medically induced abortion requires methotrexate followed by misoprostol.

The present paper describes a case illustrating previously unreported teratogenic effects of methotrexate and misoprostol when administered unsuccessfully to induce an early medical abortion. It is important for physicians and women considering methotrexate and misoprostol for medical abortion to understand these findings and the implications for ongoing pregnancy.

An 18-year-old woman presented to her physician requesting a medical abortion. Ultrasound at an accredited facility documented an intrauterine pregnancy at 6 weeks of gestation. The woman received 50 mg/m² of intramuscular methotrexate 4 days after the ultrasound, followed by 800 μg of misoprostol 7 days later. She experienced vaginal bleeding and noted the passage of solid material she thought to be the placenta and fetus. She did not attend either the scheduled follow-up visit with her physician or the requested serum quantitative β-human chorionic gonadotropin testing.

The woman reported having 1 alcoholic drink every 2 or 3 weeks in the subsequent 3 months, except when she had 6 drinks in 1 evening at 16 weeks of gestation; she smoked half a packet of cigarettes daily and occasionally used marijuana. The woman had no occupational or other exposure to toxins. She was unaware of an ongoing pregnancy until 19 + 3 weeks (based on her original ultrasound), at which time she presented again to her physician. An ultrasound performed that day showed significant fetal anomalies and she was referred to a tertiary care hospital. A second-trimester abortion was induced at 22 weeks and an autopsy was performed.

The fetus displayed features of methotrexate teratogenesis consistent with those previously described in the literature [2], including intrauterine growth restriction, microcephaly, hypertelorism, low-set ears, micrognathia, broad clenched hands, fifth-finger clinodactyly, and placental 2-vessel umbilical cord (Supplementary Material S1). Methotrexate exposure is characterized by growth retardation; limb defects; craniofacial anomalies; and digit, vertebral, genital, and cardiac abnormalities. The present case involved abnormalities not previously described: small nose; absent uvula; prominent heels; 11 pairs of ribs; and 6 lumbar vertebrae. Internal-organ examination showed bilobed right lung, unilobed left lung (Fig. 1), and subhepatic cecum. These abnormalities are consistent with a recent theory that exposure to methotrexate very early in pregnancy may trigger a range of possible neural crest cell-related anomalies [3]. Features of fetal alcohol syndrome were not identified.

Teratogenicity resulting from low-dose methotrexate exposure in the first trimester—such as doses used to treat rheumatoid conditions—has been well documented, with a specific pattern termed aminopterin/methotrexate syndrome [2]. There have been few reports on the patterns of malformations seen with higher doses used for termination of pregnancy. The possible teratogenic effects of misoprostol are less clear, with evidence indicating that defects are related to vascular disruption with short limbs, orofacial abnormalities, and defects of the brain and skull [4].

Characteristics of methotrexate teratogenicity are dependent on dose and timing. In Canada, most medical abortions are performed between 4 and 7 weeks of gestation. The suggested critical teratogenicity period is 8–10 weeks of gestation; however, these assumptions remain speculative and there are reports of abnormalities after exposure at 4–12 weeks of gestation (Supplementary Material S1). The limb bud, lung, and facial anomalies in the present case support teratogen exposure at 6 weeks of development and illustrate that exposure at 6.5 weeks can be highly teratogenic.

The present case illustrates a typical presentation and initial management protocol for a medication-induced abortion using methotrexate and misoprostol. The patient was aware of clear instructions to ensure completion of the abortion but she did not believe they were necessary and was lost to follow-up. Before receiving methotrexate and misoprostol, all pregnant women—and all physicians managing their care—should be aware of the potential consequences of ongoing pregnancy. Appropriate measures to prevent this possibility, and a plan for ensuring follow-up, should be agreed in advance.

Physicians offering methotrexate and misoprostol to induce abortion medically should consider screening to select patients appropriate for both this treatment and the follow-up required. A wide range of teratogenic consequences in an ongoing pregnancy is likely, including the new anomalies described in the present paper. The possibility of significant teratogenesis should be included in the counseling session prior to initiating these medications. Vigilance to complete timely follow-up after methotrexate and misoprostol administration in early pregnancy is critical.

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Reproductive health concerns of women contending with spousal violence and husband’s alcohol use in a Mumbai slum community

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Mumbai, India, has diverse slum communities consisting primarily of migrants struggling to survive in a high-cost living environment [1]. Financial and survival stressors and increased access to low-cost alcohol have been cited as reasons for increased alcohol problems and spousal violence in these slums [2]. Studies from India indicate heightened risk for spousal violence among men reporting alcohol use, and poorer reproductive health outcomes among women contending with such violence [3]. Less is known about reproductive health risks among women who report risky alcohol use by their husband. The present study examined the effects of recent spousal violence and husband’s frequent drinking on poor reproductive health among women with these issues in Mumbai slums.

The study group was a household-recruited sample of married women aged 18–40 years who reported spousal violence ever and/or husband’s risky alcohol use in the past 30 days (heavy alcohol use ["drunken" behavior as perceived by the wife] or frequent alcohol use [≥ 3 days of use in a typical week]). These women were recruited as part...