Successful Treatment of Cornual Pregnancy with 1-Day High-Dose Methotrexate Regimen and Folinic Acid Rescue

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Abstract
This report describes a woman with a cornual pregnancy, documented by laparoscopy and ultrasonography, who was successfully treated with a 1-day high-dose methotrexate regimen and folinic acid rescue. The serum β-hCG level was 2,260 and increased to 3,060 IU/l on the 5th day after treatment before it fell precipitously to below 250 IU/l 15 days after methotrexate treatment. No side effects were experienced by the patient.

Introduction
Cornual (interstitial) pregnancy accounts for about 3% of all tubal pregnancies. Rupture of cornual pregnancy occurs later, between the 8th and 16th week of pregnancy, than ampullary or isthmic tubal pregnancies due to the increased distensibility of the tube when it is surrounded by a relatively thick myometrium. Because of the rich blood supply to the site of implantation, from both the uterine and ovarian arteries, the hemorrhage that accompanies a ruptured cornual pregnancy may be rapidly fatal. Hysterectomy is commonly necessary because of the large uterine defect. Cornual resection in patients who wish to retain their reproductive function predispose the patient to uterine rupture in subsequent pregnancies.

The recent ability to make an early diagnosis of cornual pregnancy by transvaginal ultrasonography and serial assay of serum β-hCG has led to the use of methotrexate for the nonsurgical treatment of unruptured cornual pregnancy.

Treatment of cornual pregnancy with systemic administration of methotrexate was successfully accomplished using multidose regimens in 6 out of 7 cases reported over the last decade [1-4]. We report here the first case, to our knowledge, of the successful use of a 1-day high-dose methotrexate regimen with folinic acid rescue in 1 patient with a documented cornual pregnancy.

Case Report
The patient, 43 years old, gravida 7, para 4, was admitted to the hospital 5.5 weeks after her last menstrual period complaining of lower abdominal pain and vaginal bleeding. Examination revealed a slightly enlarged uterus, dilated cervix and scant bleeding. Vital signs were normal.
The serum β-hCG level was 93 IU/1 (First International Reference Standard). Transvaginal sonography revealed an amorphous material in the uterine cavity. Following the diagnosis of incomplete abortion, a dilatation and curettage was performed which yielded endometrial tissue with Arias-Stella changes and gangrenous decidua, without trophoblastic tissue or chorionic villi. The patient was readmitted to the hospital 5 days later. Pelvic examination and transvaginal sonography were normal, and the serum β-hCG level was 760 IU/1. Because of the presumed diagnosis of ectopic pregnancy, the patient underwent laparoscopy which revealed normal fallopian tubes and uterus. Bilateral salpingectomy was performed at the patient’s request. Three days later, the serum β-hCG level was 1,520 IU/1, and transvaginal sonography disclosed a right cornual pregnancy, 6 mm in diameter. An attempt to aspirate the sac under hysteroscopic guidance was unsuccessful. Two days later, the serum β-hCG level was 2,260 IU/1, and methotrexate was administered intravenously according to Goldstein’s protocol, 100 mg/m² over 30 min followed by 200 mg/m² over 12 h. Four doses of folinic acid (15 mg) were given orally at 12-hour intervals, beginning 12 h after the completion of methotrexate infusion. The serum β-hCG level increased to 3,060 IU/1 on the 5th day of treatment and then fell precipitously to below 250 IU/1 15 days after methotrexate treatment (fig. 1). Blood count and liver enzymes obtained before and 14 days after methotrexate treatment were normal. No side effects were experienced by the patient.

Discussion
Successful nonsurgical treatment of unruptured ampullar or isthmic tubal pregnancy with single [5, 6] or multi-doses of methotrexate [7] is well established. Only limited information regarding the medical treatment of cornual pregnancy with methotrexate is available. There have been only four reports involving 7 patients in whom methotrexate was administered systemically for the treatment of cornual pregnancy [1-4]. Surgical removal of the ectopic pregnancy was required in 1 of these patients because of persistently high serum β-hCG levels (5,280-5,340 IU/1) after 10 days of therapy [4]. Four of the 6 successful cases had low or declining levels of serum β-hCG (364, 436, 450 and 988 IU/1); spontaneous resolution may already have been in progress in some of these patients [2, 4]. In all 7 cases reported, one to three courses of multidose regimens of methotrexate were employed [1-4]. Using similar multi-dose regimens in patients with other forms of tubal pregnancies, an incidence of side effects related to methotrexate toxicity was in the range of 10-50% [7].
Recently, Stovall et al. [6] have demonstrated the efficacy of a single-dose methotrexate regimen (50 mg/m²), without folinic acid recovery, in the treatment of 30 cases with ampullar pregnancy. No patient required a second dose of methotrexate, and no patient experienced any side effects. Because of the more severe sequelae accompanying a ruptured cornual pregnancy we have chosen to use the higher dose 1-day course of the methotrexate regimen proposed by Goldstein [5]. To reduce the potential risk of methotrexate toxicity, folinic acid was also administered. Although our initial results have to be confirmed by a large patient sample, this report provides another alternative for the management of cornual pregnancy. Still needed are optimal dosing regimens to ensure the resolution of a cornual pregnancy with minimal side effects.

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