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□ 증례 □

Delayed Resolution of Cervical Lesion of Ectopic Pregnancy Treated by Intra-amnionic Methotrexate (MTX) Instillation : A Case Report

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양막강내 Methotrexate (MTX) 투여로 치유된 자궁경관 임신에서 자궁경부 병변의 지연 관해 : 증례 보고

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- 초 록 -

자궁경관 임신은 최근에 인공유산의 증가와 인공 보조 생식술(assisted reproductive technology) 등에 의하여 증가되는 양상을 보인다. 과거에는 자궁경관 임신은 대량의 무통성 질출혈로 진단을 내리고 치료 방법은 전자궁적출술이 유일한 수단이었으나, 지금은 질식 초음파의 개발로 자궁경관 임신을 조기에 진단하고 자궁 보존적 방법으로 치료하여 차후 임신을 기대할 수 있게 되었다. 그 치료 방법 중 하나로 Methotrexate (MTX)를 주사하여 성공적으로 치유된 많은 보고들이 있었다.

본 저자들은 임신 8주에 자궁경관 임신으로 진단된 환자에서 전신적 MTX 투여와 복식 초음파 관찰 하에 양막강내 MTX 투여 병합 요법으로 치료한 1 례를 보고하고 치료과정에서 자궁경부 병변의 지연 관해에 대해서 문헌 고찰과 함께 보고하는 바이다.

핵심용어: 자궁경관 임신, Methotrexate (MTX)

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Introduction

Cervical pregnancy is a rare form of ectopic pregnancy but causes serious complications of gestation. The incidence varies from 1 : 2,500 to 1 : 12,422 during 1978 to 1994(Parete et al., 1983; Dicker et al., 1985). The traditional method of management of cervical pregnancy has been hystrectomy because life threatening hemorrhage is main side effect. Aggressive surgical management has successfully decreased mortality from 40% to near 0%. Unfortunately, complete compromise of fertility has resulted.

Conservative therapy in the management of an ectopic gestation, for preservation of fertility, is increasing. MTX has been utilized recently in the management of tubal (Stovall et al., 1991), interstitial (Tanaka et al., 1982), and cervical pregnancies (Oyer et al., 1988).

Recently, reports of successful management of cervical pregnancy by systemic and local injection of MTX was presented (Hsu et al., 1995; Marston et al., 1996). But, the potential disadvantages of this procedure include prolonged follow-up of slowly resolving β -hCG levels, MTX-related side effects, and treatment failure resulting in complication and necessitating alternate methods of management (Ash et al., 1996).

In this report, we present a case of delayed resolution of cervical ectopic lesion with systemic MTX and intra-amnionic injection of MTX guided by transabdominal ultrasonograpy.

Case History

A 27-year-old woman, gravida 2, para 1, abort 0, presented at 8 weeks of gestation, with the complaint of vaginal spotting for several days. Her history was significant for an uncomplicated preterm vaginal delivery seven years before admission. Her past medical history and gynecological

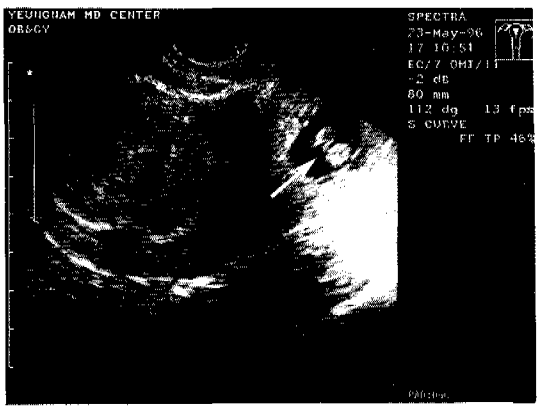

Fig. 1a

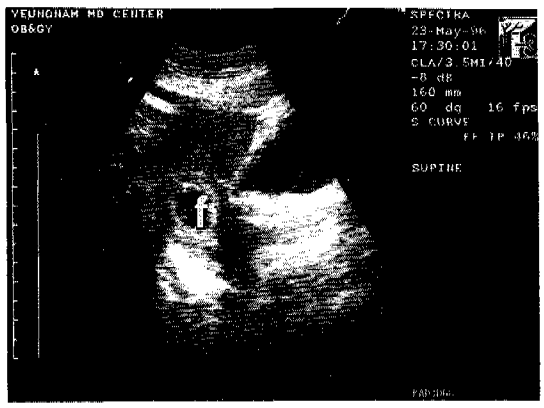

Fig. 1b

Fig. 1. Ultrasonographic study of Pelvis.
a. Transabdominal longitudinal ultrasound scan showing expansion of the lower uterine segment, with gestational sac (arrows) containing viable fetus.
b. Transverse image of the cervix. fluid (f) is also noted within the endocervical canal.

history were unremarkable.

On evaluation the patient's vital signs were stable, and her abdomen was soft and nontender. Pelvic examination revealed a bulky, purple cervix and mild bleeding from the slightly dilated external os. The uterus was nontender and was enlarged to the size of a 7- to 8- week gestation. The adnexa were normal.

Transabdominal sonogram of the pelvis demonstrated the typical hourglass appearance of the uterus and an empty uterine cavity. A gestational sac containing fetal echoes was located within cervix(Fig. 1). Cardiac activity was identified and a viable cervical pregnancy was diagnosed at this time. The initial quantative β-hCG level was 93,523 mIU/mL. The hemoglobin and hematocrit were 12.1 g/dL and 36%, respectively. Pretreatment blood counts, liver function tests, blood urea nitrogen, and creatinine levels were normal.

The patient, with a strong desire to retain her fertility potential, agreed to treatment with MTX after the potential risks and alternative methods of treatment were discussed and informed written consent was obtained.

The management protocol was 1mg/kg MTX intramuscular (IM) on days 1, and 0.1 mg/kg folinic acid on treatment days 2. Both serial pelvic sonograms and β-hCG levels were obtained to assess the response to therapy. Treatment consisted of one course of MTX. The patient showed a plateauing of her β-hCG levels at 92,026 mIU/mL. and serial sonograms demonstrated continuing cardiac activity.

On day 3, MTX was injected into gestational sac after amnionic fluid aspiration. In the operating room, preparations were made to do a hysterectomy if this became necessary. After preparation of vagina with betadine solution, the gestational sac was punctured and approximately 3ml of hemorragic amniotic fluid was aspirated with transabdominal ultrasound guidance. And then, 50mg of MTX was instilled into the amnionic sac. The patient tolerated the procedure without difficulty. The serum β-hCG titer at this time was 104,975mIU/mL.

On the fourth postoperative day, patient complained pustule on the face and anterior chest. Otherwise, the patient's postoperative course was unevenful and her liver function test and complete blood count remained within normal limits. The patient was then monitored with serial quantitative serum β-hCG levels (Fig. 2).

The patient was discharged on the sixth postoperative day. Serial β-hCG titers showed rapid resolution. But subsequent serial sonography of cervical lesion,

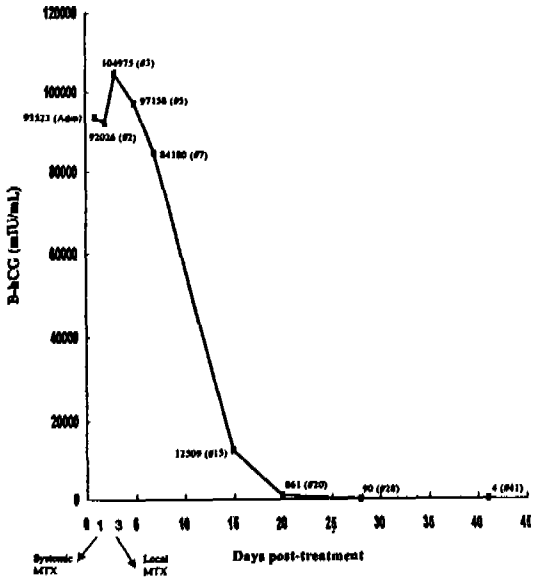

Fig. 2. Plot of β-hCG titres versus days since initiation of chemotherapy in the patient.

possible representing a focus of residual trophoblastic tissue, did not reveal a significant decrease in size and the density of the shadow. The resolution of cervical lesion was not satisfied in spite of decreasing titer of serum β-hCG. By day 41, the quantitative β-hCG was undetectable. Three months after discharge, she had experienced massive vaginal bleeding of three days duration. On examination, her vital sign were stable. Pelvic ultrasound showed unremarkable. A quantative β-hCG level was normal (< 2 mIU/ml). The bleeding at its heaviest was suspected equivalent menstural flow or bleeding from the cervical residual lesion. After then, she had not been pregnant, even though she has being try to be pregnant.

Discussion

In the past, the diagnosis of cervical pregnancy was rarely made before curettage following heavy vaginal bleeding. Currently, higher resolution transvaginal ultrasonography and sensitive β-hCG tests have permitted early diagnosis. Early detection was permitting efforts at conservative management when future fertility is desirable.

Conservative managements for cervical pregnancy include: placenta left in situ (Morton, 1949), curettage and tamponade (Sheldon et al., 1963), amputation of cervix (Rabbon et al., 1962), cervical cerclage (Bernstein et al., 1981), Foley catheter placement into the cervical canal (Reginald et al., 1985), ligation of the descending branches of the uterine artery (Kuppuswarmi et al., 1983), bilateral ligation of the internal iliac artery (Nelson et al., 1979), preoperative angiographic uterine artery embolization (Pilskow et al., 1991), systemic administration of MTX (Kaplan et al., 1989; Stovall et al., 1991), or intra-amniotic instillation of MTX (Kaplan et al., 1990).

Palti et al. (1989) described the first success of multi-dose intramuscular and intracervical MTX in treating viable cervical pregnancy. Yankowitz et al. (1990) reported the success of single high dose intravenous MTX. Timer-Tritsch et al. (1994) reported on a series of five cases using intra-amniotic injection of MTX. But, MTX treatment for cervical pregnancy must be individualized and based on the clinical parameters.

The clinical outcome of the cervical pregnancy is dependent on clinical parameters, including gestational age, initial size of the mass, fetal cardiac activity, and initial and/or maximum β-hCG level (Hsu et al., 1995). A number of failures have been reported when this treatment has been used to manage a viable cervical pregnancy (Yankowitz et al., 1990; Marcovici et al., 1994). Failures have been noted with advanced gestation (fetal heart motion documented) or with technical problems, particularly with intra-amniotic instillation of drug (Marcovici et al., 1994). It was suggested that local administration may be complicated with gestational sac collapse during aspiration and profuse bleeding, which may require surgical hemostasis (Marcovici et al., 1994). For the successful local administration, the amnionic sac must be kept intact. In our case, we treated successfully with local administration of MTX with keeping intact gestational sac.

In other reports, side effects and toxicities from MTX, which is dose related, includes gastrointestinal irritation, myelosuppression, and occasionally hepatic irritation (Stovall et al., 1991). Side effects of MTX reportedly occur in approximately 20% of patients. In our case, the patient experienced no side effects and except mild pustule on the face and anterior chest. The advantages of administration of MTX directly into amnionic sac are greater effectiveness, shorter treatment time, and absence of side effect (Leeton and Davision, 1988).

General contraindications to the treatment with MTX include renal or hepatic disease and immunocompromised state. Specific contraindications include a far advanced cervical pregnancy in which case it would be dangerous to postpone surgical treatment. The resolution time after chemotherapy, which could be determined by β -hCG levels, and sonographic appearance of the cervix, has been reported to be variable from 11 days to 5.5 months (Stovall et al., 1988; Chao et al., 1993).

Our present case is another example of a successful treatment cervical pregnancy by transabdominal ultrasound guided intra-amniotic administration of MTX and combined with systemic injection of MTX. The regression of cervical size and resolution of cervical lesion did not show correlation with changes of serum β -hCG level and these fingings were inconsistent with Hsu et al. (1995).

Recently, diagnostic hysteroscopy has been used in the management of cervical pregnancy. Roussis et al. (1992) used the hysteroscope to visualize a cervical pregnancy 40 days after systemic MTX treatment. Hysteroscopy enabled the clinician to confirm that the ectopic gestational sac was in the cervix. Since the implantation site would be visualized directly, it would have been possible to use laser coagulation through the hysteroscope directed at specific bleeding points, had it been needed. Ash et al. (1996) reported hysteroscopic resection of a cervical pregnancy and complete resolution of the ectopic pregnancy with rapid normalization of β -hCG level. In his case, uncertain and prolonged follow-up associated with intra-amniotic instillation of MTX could be avoided.

We have two successful experiences to remove of cervical pregnancy using hysteroscope (unpublised, Koh, 1997). If it may be the appropriate treatment of choice, attempting hysteroscopic resection may be more efficacious than MTX treatment. In this report we present that MTX treatment of cervical pregnancy may not always be most likely to method and result in subsequent fertility.

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