Case Report

Cervico-Isthmic Pregnancy: Early Diagnostic Imaging and Successful Dual Therapy for Uterine-Sparing Treatment

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ABSTRACT

Cervico-isthmic pregnancy is a rare and potentially life-threatening form of ectopic gestation in which the blastocyst implants in the uterine cervico-isthmus between the histological and anatomical internal os, followed by subsequent extension to the lower uterine segment. Early diagnosis may allow a conservative therapeutic approach that avoids catastrophic hemorrhage requiring hysterectomy. Here we report the case of a 43-year-old primigravida woman whose cervico-isthmic pregnancy complicated by massive hematometra was diagnosed at 6 weeks gestation by multimodal imaging and successfully treated by hysteroscopic resection, securing adequate hemostasis, after transcatheter arterial chemoembolization. Journal of Minimally Invasive Gynecology (2015) 22, 678–683 © 2015 AAGL. All rights reserved.

Keywords: Cervico-isthmic pregnancy; Diagnostic imaging; First trimester; Hysteroscopy; Transcatheter arterial chemoembolization

DISCUSS

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On the surface of the nongravid uterus, approximately midway between the apex and base, is a slight constriction known as the isthmus. Corresponding to this in the interior is a narrowing of the uterine cavity. The portion above the isthmus is termed the body, and that below, the cervix (Fig. 1A). The isthmus of the uterus is therefore the constricted part of the uterus between the body and the cervix. The isthmus is approximately 0.5 to 1 cm long, and its cavity enters the internal os. During pregnancy, the isthmus expands from a length of 0.5 cm to 2.5 cm at term to become the lower part of the uterine cavity, called the lower uterine segment [1].

The uterine cervix is limited cranially by the internal os, which can be defined histologically or anatomically. Histologically, the internal os is the transition point from the endocervical mucosa to the isthmic mucosa that resembles the corporal mucosa, although thinner and richer of supporting tissue. The anatomical internal os, the zone of transition between the isthmus and uterine corpus, is located 0.5 to 1.6 cm cranially to the histological os [2]. The term “obstetrical internal os” describes the junction of the ovum chamber and cervical canal. In the nonpregnant uterus, it coincides in position with the anatomical os, but this relationship is lost in pregnancy as described in Danforth’s concept of “unfolding” of the isthmus [1].

Both cervical (Fig. 1B) and cervico-isthmic (Fig. 1C) pregnancies are rare and potentially life-threatening forms of ectopic gestation developing in the lower uterine segment (Fig. 1A) [2,3]. A cervical pregnancy results from the implantation and growth of a blastocyst (Fig. 1B, arrowhead) within the mucosa of the endocervical canal and is located completely in the cervical canal, with no placental tissue above the internal cervical os (Fig. 1B, arrow) [4]. In contrast, in a cervico-isthmic pregnancy, the gestational products (Fig. 1C, arrowhead) implant in the uterine cervico-isthmus between the histological (Fig. 1C, long arrow) and anatomic...
Clinically, these 2 pathological conditions should be carefully differentiated [4,5], because cervical pregnancies are unlikely to progress past 20 weeks of gestation, whereas some cervico-isthmic pregnancies are known to grow to an advanced gestational age [2,4–9] and can cause significant perinatal complications, including massive hemorrhage from the placental bed [2,5,6,8]. Therefore, early detection and appropriate management of cervico-isthmic pregnancy are important to avoid the potential morbidity necessitating life-saving hysterectomy with loss of fertility [3,10].

Furthermore, owing to certain similarities, cervico-isthmic pregnancy with cervical placenta can be mistaken for major placenta previa. However, there are important differences between these 2 morbid conditions; in major placenta previa, the placental implantation site is within the uterine cavity, whereas cervico-isthmic pregnancy with cervical placenta remains in the lower uterine segment and the cervical region [5].

Here we report a rare case of early cervico-isthmic pregnancy complicated with massive hematometra, which was diagnosed by multimodal imaging and managed by hysteroscopic resection after transcatheter arterial chemoembolization (TACE) [11]. The Gifu Prefectural Tajimi Hospital’s Institutional Review Board approved this report.

**Case Report**

A 43-year-old married primigravida woman without previous disease history was referred for suspected cervical ectopic pregnancy after presenting with a 6-week, 5-day history of amenorrhea, positive urinary pregnancy test, and increased vaginal bleeding. At the initial examination, her hemoglobin value was 8.3 g/dL. Coagulation disorder was not identified, with a prothrombin time–international normalized ratio of 1.05 and an activated partial thromboplastin time of 27.0 seconds. Her serum β-human chorionic gonadotropin (β-hCG) value elevated at 66 459 mIU/mL (normal value, <6 mIU/mL) (Fig. 2).

Ultrasonographic examination demonstrated the presence of a gestational sac with a diameter of 17.3 mm in the lower uterine segment (Fig. 3A). Prominent peritrophoblastic blood flow was identified by color-Doppler flow analysis (Fig. 3A, inset, arrow). A viable fetus was not observed.

Precise localization of the gestational sac could not be determined solely by ultrasonography because of an enlarged uterine corpus due to massive hematometra. On the same day, sagittal T1-weighted dynamic magnetic resonance imaging MRI with enhancement by gadopentetate dimeglumine (Magnevist; Japan Schering, Osaka, Japan) clearly located a mass with heterogeneous signal intensities (Fig. 3B, arrowhead) in the uterine cervico-isthmus between the anatomical (Fig. 3B, short arrow) and presumably histological (Fig. 3B, long arrow) internal os. A closed cervical canal was evident, along with a markedly dilated uterine cavity with pooled blood.

On the arterial phase of sagittal 3-dimensional computed tomography (CT) angiography [11] performed for further assessment of the uteroplacental neovascularization around the gestational products, a prominent vascular lesion (Fig. 3C, arrow) with feeding branches from bilateral uterine arteries was identified in the lower uterine segment.

On the basis of these findings, which fulfill the diagnostic criteria of cervico-isthmic pregnancy, including a well-preserved and closed cervical canal and more than one-half of the uterine cavity above the gestational sac uninvolved by gestational sac implantation [2], a cervico-isthmic pregnancy with prominent neovascularization was diagnosed. After receiving counseling on the potential risk of hemorrhage during conservative management, the patient strongly wished to preserve her uterus and opted to undergo TACE [11] as an initial conservative measure to devascularize the ectopic gestational products.

On the next day, a vascular mass (Fig. 3D, arrow) was reconfirmed in the lower uterine segment on digital subtraction
therapy in this case, hysteroscopic resection of the gestational mass was performed as well [12]. The uterine cavity was inspected using a continuous-flow resectoscope with an outer diameter of 8 mm (Karl Storz Endoscopy Japan, Tokyo, Japan) with distension by sorbitol medium (Uromatic S; Baxter Ltd., Tokyo, Japan) by gravity flow.

After 210 mL of pooled blood was drained from the uterine cavity, a necrotized gestational mass firmly attached to the left posterior portion of the cervico-isthmic uterine wall was identified (Fig. 3E, arrow). Then gestational products were selectively removed using the cutting loop of a resectoscope. When retained gestational products were shaved, electrodisssection was minimized by using the cutting loop as a curette with gentle repetitive motions, to avoid potential thermal damage to the cervico-isthmic uterine wall. Placenta forceps was also used to retrieve the partially detached gestational tissue. Hysteroscopic resection of the gestational products was completed with minimal blood loss. The duration of surgery was 29 minutes.

Histopathological examination confirmed the diagnosis of cervico-isthmic pregnancy by the presence of partially viable ectopic villous tissue, but no cervical tissue was resected with the gestational mass specimen to demarcate the cervical mucosa and margins of the tissue in relation to the histological or anatomical os. The postinterventional course was uneventful. Serum \( \beta \)-hCG returned to a normal level by 49 days after the initial TACE (Fig. 2), and the gestational products (Fig. 3F, arrow) resolved without any additional treatment.

**Discussion**

Aberrant implantation in the lower uterine segment can occur in the cervical canal, cervico-isthmus, and a previous cesarean scar [13]. Cervico-isthmic pregnancy, which implants in the uterine cervico-isthmus between the histological and anatomical internal os (Fig. 1C), is the least frequent among low-lying implantation ectopic pregnancies [13], with an estimated incidence of approximately 1 in 10 000 gestations [3]. Because of its rarity, cervico-isthmic pregnancy is often confused with cervical pregnancy and has been poorly characterized diagnostically as well as therapeutically [2]. As a result, in the past the final diagnosis of cervico-isthmic pregnancy was made by postsurgical examination after an initially incorrect or late diagnosis, with most cases resulting in salvage hysterectomy owing to catastrophic hemorrhage from the placental bed [3].

With the advent of diagnostic procedures, ultrasonographic scan with color-flow mapping became an initial modality of choice by allowing the suspicion for a cervico-isthmic pregnancy to be raised [9] when implantation of the gestational sac is identified in the lower uterine segment. Furthermore, it has been suggested that in patients with cervico-isthmic pregnancy, the cervical canal should be preserved and closed, and more than one-half of the uterine...
cavity above the gestational sac should be uninvolved by gestational sac implantation [2,14].

But because ultrasonography does not always accurately distinguish the transition between isthmus and cervical canal [2,5] owing to its inherent limitation of space-resolving power, differentiation of cervico-isthmic pregnancy from cervical pregnancy could still be a diagnostic challenge, especially in the early gestational period.

Because the stationary view obtained by MRI can detect the specific characteristics of tissues and fluids in the pelvic...
organs, it may be more informative than ultrasonography when the relationship between low-lying implantation gestational products and surrounding tissues must be determined [15]. Although MRI reportedly allows the correct diagnosis of cervico-isthmic pregnancy in the late first trimester [14] and in the second trimester [7], the value of MRI in diagnosing cervico-isthmic pregnancy in the early gestational period has not been described previously.

In the present cervico-isthmic pregnancy, dynamic MRI with contrast enhancement clearly showed that the gestational mass situated in the cervico-isthmic region with a well-preserved and closed cervical canal at 6 weeks gestation after equivocal localization of the gestational sac by ultrasonography. Therefore, contrast-enhanced MRI could be potentially useful when cervico-isthmic pregnancy needs to be differentiated from cervical pregnancy in the early gestational period. Its feasibility for diagnosing cervico-isthmic pregnancy even in the first trimester should be validated with further accumulation of cases, and, with increased vigilance of this diagnosis, case reports, and use of dynamic MRI, further investigation of the preferred imaging modality for cervico-isthmic pregnancy should be analyzed.

Even after correct diagnosis of a cervico-isthmic pregnancy in the early gestational period became possible, its management remains difficult for treating physicians [2,5,6,8,9,14]. Previous clinical experience has shown that a limited number of cervico-isthmic pregnancies diagnosed in the first trimester can result in successful live birth at an advanced gestational age after conservative management [2,5,6,8,9]. However, on the other hand, carrying the conceptus later than the second trimester can pose a serious threat to the maternal health, because these pregnancies also may be exposed to potential risks, such as spontaneous abortion, premature delivery, premature rupture of the membranes, placenta accreta, postpartum hemorrhage, and uterine rupture, which may necessitate salvage hysterectomy as a life-saving measure [2,5,9-14].

Therefore, earlier termination could be a feasible therapeutic option for women desiring uterine preservation to avoid the potential complications associated with life-threatening hemorrhage [3,10,16-18]. In the present case, early termination was chosen because continuation of pregnancy was deemed difficult owing to persistent bleeding with massive hematomata. Despite the advent of conservative strategies enabling uterine preservation, the most appropriate technique to terminate early cervico-isthmic pregnancies remains undetermined. As a result, a variety of therapeutic procedures, including hysteroscopic resection after 1 systemic dose of methotrexate and 1 intra-sac injection of methotrexate [10], laparoscopic surgery after methotrexate therapy [16], multiple doses of methotrexate therapy alone [17], or laparotomic removal of gestational products after potassium chloride injection into the fetal heart and methotrexate infusion into the amniotic sac [18], have been individually implemented without a clear management consensus.

The lower uterine segment is an area that receives an abundant blood supply from the complex vascular network from the anastomosing uterine and vaginal arteries [11]. Therefore, assessment of uteroplacental neovascularization around the cervico-isthmic portion of the uterus at an initial stage of diagnosis could play a significant role in avoiding the potential risk of catastrophic hemorrhage leading to hysterectomy when conservative management must be considered for early cervico-isthmic pregnancy [3].

Along with improved scanner speed after the introduction of multirow detector CT scanners and the ability to create thin-section images, recently evolving 3-dimensional CT angiography could be a useful modality for diagnosing abnormal placentation associated with vascular disorders and is replacing more invasive diagnostic pelvic angiography as an initial diagnostic measure [11,12]. In the present cervico-isthmic pregnancy with massive hematomata, uteroplacental neovascularization could be precisely evaluated by 3-dimensional CT angiography, when the potential risk of hemorrhage during conservative management was assumed to be high owing to increased blood flow around the gestational products by color Doppler ultrasonography.

TACE was chosen for immediate devascularization of the prominently neovascularized cervico-isthmic gestational mass identified by 3-dimensional CT angiography. Although the value of TACE for the management of cervico-isthmic pregnancy has not yet been established, it could be a feasible option as an adjunctive preoperative measure instead of methotrexate therapy before surgical resection of low-lying implantation, because immediate and efficient devascularization has already been demonstrated for the management of cesarean scar pregnancy [11], retained gestational products forming a placental polyp [12], and proximal interstitial pregnancy [19]. Although recanalization of the embolized arteries and the development of an aberrant blood supply should be carefully monitored even after successful devascularization, as in the present case, TACE could be a feasible interventional option when hysteroscopic resection of an early cervico-isthmic gestational mass with prominent neovascularization is attempted.

In conclusion, precise evaluation by diagnostic imaging could accelerate the uterus-conserving management for early cervico-isthmic pregnancy with massive hematomata by hysteroscopic resection after transcatheter arterial chemoeMBOLIZATION.

References