10

Term Extra-Uterine Pregnancy

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1. Introduction

Extrauterine pregnancies rarely reach third trimester of gestation. However, abdominal pregnancy can result in term delivery. Term cervical pregnancy has also been reported. The most unusual is term tubal ectopic pregnancy.
Our objective is to review cases of term extra-uterine pregnancy and to evaluate its consequences on the mother and the fetus. Due to its ill impact, the best management is early diagnosis and treatment. Prolongation of an ectopic pregnancy should be avoided.

2. Abdominal pregnancy (AP) reaching fetal viability or term

2.1 Introduction/definition/incidence

AP represents a variant of ectopic gestation in which the conceptus is sited in the abdominal cavity, external to the uterus, fallopian tubes and broad ligament (1, 2). Devoid of endometrial support, the placenta may attach to the peritoneum, bowel, uterine serosa and omentum. AP is the rarest form of ectopic pregnancy, with an incidence of 1% of all ectopic gestations (3).
AP is defined as advanced once fetal viability is reached. At this stage AP carries significantly high mortality rates for both mother (0-20%) and fetus/newborn (40-95%) (2, 4). The latter is partly due to a 20-40% rate of congenital fetal malformations (4).

2.2 Diagnosis

A high index of suspicion for this rare and serious condition, complemented by often nonspecific findings in the clinical history and physical examination may lead to a timely correct diagnosis. Recurrent abdominal pain and tenderness, a relatively mobile abdominal mass in an amenorrheic woman of reproductive age, painful fetal movements in the upper abdomen associated with a persistently abnormal lie, fetal heart sounds localized in the upper epigastrium, should raise the possibility of an AP and be followed by an ultrasound examination (5). In early pregnancy the diagnosis of AP might be missed by failure to obtain an image demonstrating continuity of the vagina, cervix and uterus with its pregnancy contents (1). Four ultrasound criteria have been suggested to support the diagnosis of AP: (1) absence of an intrauterine gestational sac, (2) absence of both an evident dilated tube and a complex adnexal mass, (3) a gestational sac surrounded by loops of bowel and separated

by peritoneum, (4) a wide mobility similar to fluctuation of the sac particularly evident with pressure of the transvaginal probe toward the posterior cul-de-sac (6). Characteristic sonographic features in an advanced AP are: fetal parts adjacent to the mother's abdominal content, absence of the uterine wall between the maternal urinary bladder and the fetus, a pseudo-placenta previa appearance, oligohydramnios (4). Despite the availability of prenatal ultrasound in developed countries, AP continues to be reported at a late gestation underscoring the difficulty in diagnosing this entity as well as the failure to observe basic ultrasound techniques (1). This would explain a 50-90% diagnostic failure rate and the often unexpected diagnosis of AP during elective Caesarean Sections performed for fetal malpresentation or low-lying placenta (7, 8, 9, 10). Puerperal presentations of a living heterotopic AP have been described, thus underscoring the diagnostic challenge represented by this rare entity (11, 12). In undiagnosed advanced AP cardiovascular shock due to intra-abdominal bleeding and sudden death are more ominous presentations (13). MRI offers, apart from diagnostic reassurance, no additional information to ultrasound assessment and is therefore, as an adjunct imaging modality, not central to the diagnosis of advanced AP (1, 14).

2.3 Management of AP

Management of an AP requires a careful initial evaluation of the fetus in terms of gestational age, the presence of associated fetal anomalies, the amount of amniotic fluid (as a determinant of fetal pressure deformities and pulmonary hypoplasia)(4, 15). This is best accomplished at a referral center with adequate resources: medical imaging and interventional radiology service, blood bank, intensive care unit as well as a surgical team capable of handling possible bowel, vascular, genitourinary complications that might arise. Because of the risk of sudden intra-abdominal haemorrhage due to either placental abruption or vascular invasion, most advise surgical intervention as soon as the diagnosis of AP is confirmed and regardless of the fetal condition (4). A conservative approach may be considered and delivery delayed until fetal maturity is reached, if the gestational age exceeds 20 weeks and the following prerequisites are met: absence of fetal malformations, adequate amniotic fluid volume, absence of maternal medical contraindications, placental implantation site not in the proximity of major vessels, liver or spleen, continuous maternal hospitalization in an appropriate facility, fetal surveillance with daily heartrate monitoring and serial ultrasound assessments, and informed consent from the patient (4).

In the absence of complications, delivery of an advanced AP can be planned for 34 weeks' gestation. Careful preoperative preparations should include: an adequate supply of blood and blood products, appropriate intravenous infusion access, availability of cell-saver and MAST (Military Antishock Trouser) Suit, a multidisciplinary surgical team (4, 7, 10, 15). A midline vertical skin incision should be employed for entry into the abdominal cavity as adequate exposure is paramount. Bleeding could be prevented by incising the amniotic sac in an avascular area, avoiding the proximity of the placenta, as well as by careful removal of the fetus without disturbing the placenta and surrounding membranes (4, 15). Placental management following an advanced AP has shifted towards a non-surgical approach, leaving this organ in situ (16, 17). Although this approach has decreased the high maternal morbidity and mortality associated with attempted surgical removal, leaving the placenta in situ has also potential risks for the mother: a prolonged resorption period, haemorrhage, bowel obstruction and peritonitis (18). The use of methotrexate to accelerate absorption of a retained placenta remains controversial due to the potential severe associated complications

(19). Ultrasound evaluation is of benefit in the follow-up of placental involution after delivery of an advanced AP (14).

2.4 Conclusion

Although still rare, the increasing incidence of AP in both developed and especially developing countries mandates awareness of this diagnosis, particularly in pregnant or postpartum women presenting with abdominal pain (11).

3. Term cervico-isthmic pregnancy

3.1 Introduction

Both cervical and cervico-isthmic pregnancies are rare, life-threatening forms of ectopic gestations. The former is reported to have an estimated incidence of one in 2,500 to one in 18,000 pregnancies, and represents less than 1% of all ectopic gestations (1). A cervical pregnancy (CP) results from the implantation and growth of a blastocyst within the mucosa of the endocervical canal and is located completely within the cervical canal, with no placental tissue above the internal cervical os (2, 3). Currently CP are diagnosed by transvaginal ultrasound early in the first trimester of pregnancy and terminated by conservative, fertility sparing medical and/or surgical management. Most cases are not reported and therefore the exact incidence of CP is unclear. A CP is never viable and is unlikely to progress past 20 weeks of gestation. Previous reports of CP ending in live births are now thought to have been cervico-isthmic pregnancies (CIP) (3, 4, 5). In a CIP the gestational sac implants in the uterine isthmus, between the histologic and anatomic cervical os, and subsequently extends into the lower uterine segment (3, 4). The process of incorporation of the lower uterine segment into the gestational cavity occurs from the cervix upward rather than from the uterine cavity downward, as it happens in a normally implanted pregnancy (4). CIP are even more important clinically because they can grow to advanced gestational age and have significant perinatal complications. The growing gestational sac causes premature cervical effacement and dilatation which result in preterm premature rupture of the amniotic membranes and preterm delivery (6). Trophoblastic invasion of the endocervical and isthmic mucosa and stroma result in placenta accreta, placenta increta or placenta percreta and explain the massive hemorrhage at attempted placental removal (6, 7). Since 1980, when the term CIP was coined (3), the English language literature reported thirteen CIP exceeding 24 weeks, which is considered as the gestational age of neonatal viability (3, 4, 6 – 16). Table 1 summarizes these reports.

3.2 Diagnosis

Diagnostic algorithms and clinical prediction rules for CIP are difficult to validate because of the limited number of reported cases. In five of the thirteen women (38.5%) with advanced CIPs, the correct diagnosis was made at the time of delivery, underscoring the diagnostic challenge of this entity (3, 8, 10, 13, 15).

Several associated clinical signs noted historically should be heeded for a timely diagnosis of CIP. In case of painless vaginal bleeding occurring after 20 weeks of gestation, in a nulliparous woman in the fourth or fifth decade of life, CIP should be considered in the differential diagnosis. Painless vaginal bleeding was the presenting clinical sign in six women diagnosed with CIP reaching fetal viability (46%) (6, 7, 9, 11, 14, 16). Maternal age

was 35 years or above in seven of the thirteen CIP (54%) and 54% of women had no prior deliveries.

After an ultrasound examination confirmed normal placental localization in a woman with painless vaginal bleeding, speculum examination could reveal premature cervical

Author, Year Reference	Maternal age Parity	Gestational age at diagnosis	Gestat age at delivery/Outcome	Treatment Blood transfusion in Units
David 1980 (3)	28 years; P0	At delivery	40 weeks/alive	CS + TAH No transfusions
Kalakoutis 1985 (8)	43 years; P1	At delivery	28 weeks/alive	VD + TAH 18 Units
Cohen 1985 (9)	36 years; P0	At 25 weeks	27 weeks/alive	CS + TAH 5 Units
Hoffman 1987 (10)	42 years; P2	At delivery	32 weeks/alive	CS + TAH Not stated
Weyerman 1989 (11)	38 years; P0	16 weeks	26 weeks/ Neonatal death	CS + TAH 4 Units
Jelsema 1992 (12)	30 years; P1	5.5 weeks	38 weeks/ alive	CS + TAH 8 Units
Iloabachie 1993 (13)	26 years; P0	At delivery	37 weeks/twins alive	CS 16 Units
Souter 1995 (14)	27 years; P0	21 weeks	28 weeks/ Alive	CS + TAH 52 Units
Strobelt 2001 (4)	41 years; P2	7 weeks	30 weeks /Alive	CS + TAH 7 Units
Mesogitis 2001 (15)	26 years; P0	At delivery	37 weeks /Alive	VD + TAH 4 Units
Honda 2005 (6)	39 years; P0	6 weeks	32 weeks /Alive	CS + TAH 5 Units
Kayem 2008 (16)	32 years; P2	25 weeks	34 weeks/ Alive	CS + Segmental resection of the uterine wall and placenta; No Transfusions
Avery 2009 (7)	35 years; P2	5 weeks 6 days	38 weeks /Alive	CS + TAH 20 Units

Table 1. Summary of CIP reaching neonatal viability (1980-2009)

effacement and dilatation and a bulging lower uterine segment. These findings are indicative of two impending perinatal complications of CIP: preterm premature rupture of amniotic membranes and preterm birth. Eight of thirteen CIP (61.5%) delivered prematurely. The gestational age range at delivery was 26 to 34 weeks (4, 6, 8-11, 15, 16). Seven out of eight prematurely born babies survived (87.5%). One neonatal death occurred following delivery at 26 weeks of gestation (11).

The diagnosis of CIP is confirmed by medical imaging and intraoperative findings.

Sonography has made early diagnosis of CP and CIP possible and has replaced histologic diagnosis (7). Transvaginal ultrasound has been able to identify CIP at 6 and 7 weeks of gestation in four patients with CIP which reached neonatal viability (4, 6, 7, 12), whereas abdominal ultrasound diagnosed three CIP in mid-trimester (9, 11, 16). Two ultrasound criteria have been proposed to support a diagnosis of CIP and differentiate it from CP: a well-preserved and closed cervical canal, thus ruling out CP and more than half of the uterine cavity above the gestational sac uninvolved by gestational sac implantation (4, 6) Image 3.1. Magnetic Resonance Imaging was useful in distinguishing between CP and CIP (17, 18) Image 3.2.

Intra-operatively the diagnosis of CIP is confirmed by the following findings: a small sized, empty uterine corpus and fundus, an abnormally distended and thin walled lower uterine segment, a placenta implanted below the peritoneal reflection of the anterior and posterior surfaces of the uterus, a densely adherent placenta, placental penetration and neovascularization visible under the serosal surface (6, 7, 12).

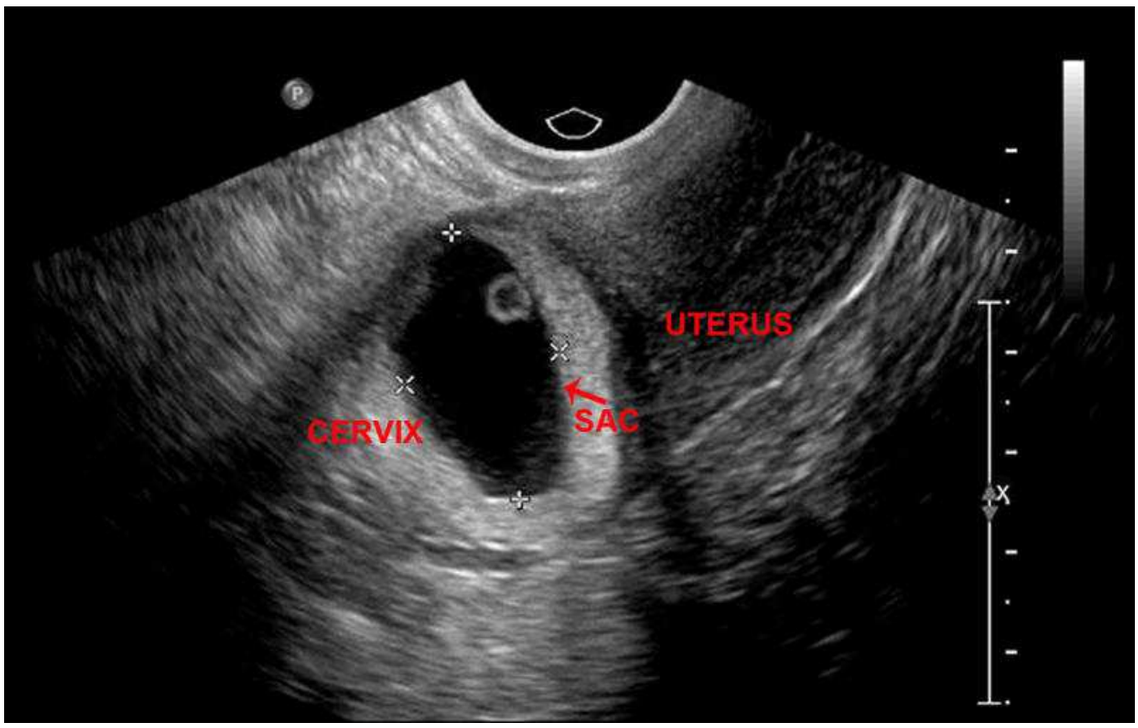

Image 3.1. Ultrasound of Cervical pregnancy

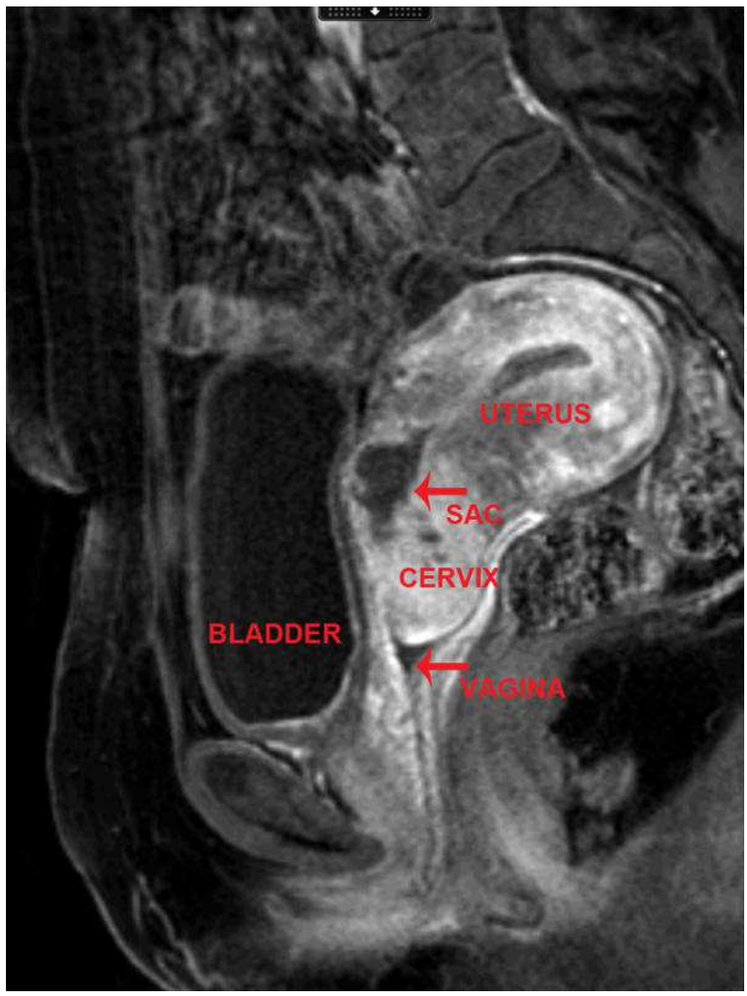

Image 3.2. MRI of Cervical pregnancy

3.3 Treatment

There are no clinical guidelines for the management of CIP as no center has accumulated enough data and experience with the treatment of this rare entity. Individual case reports, despite their inherent shortcomings, serve as reference in formulating management strategies for CIP which attained neonatal viability.

The management of CIP is dictated by the timing of the diagnosis.

If the diagnosis of CIP is made un-expectantly at the time of delivery, as it occurred in 38.5% of the reported advanced CIP, the therapeutic priority is to minimize the risks of catastrophic postpartum hemorrhage. This can be achieved by controlling the bleeding and replacement of the blood loss. Surgical occlusion of the internal iliac and uterine arteries or segmental resection of the uterine wall and attached placenta (16) could be initially employed if continuing fertility is desired and surgical expertise is available. Of the five women diagnosed at the time of delivery four required a total abdominal hysterectomy (3, 8, 10, 15) for control of postpartum hemorrhage, including the two women who were delivered vaginally (8, 15). This underscores the difficulty in controlling massive postpartum hemorrhage in previously unsuspected advanced CIP.

Once a CIP is diagnosed in the first trimester or early mid-trimester, termination of pregnancy should be offered after patient counseling. The latter should emphasize the possibility of severe life-threatening maternal and neonatal morbidity associated with continuation of the pregnancy (preterm delivery, postpartum hemorrhage, and hysterectomy) as opposed to the high success rate of early pregnancy termination by conservative, fertility sparing management (1, 6, 7, 17). If continuing the CIP is the patient's request after informed consent, then careful antenatal and perinatal management planning is imperative. Consideration should be given to timely transfer to a referral center with adequate resources: medical imaging and interventional radiology, extensive blood bank capabilities, adult and neonatal intensive care unit and surgical expertise to control massive postpartum hemorrhage. Continuous maternal hospitalization is advised in women with repeated antepartum bleeding or reduced cervical length (6). Transvaginal cervical length assessments should complement serial fetal ultrasound surveillance and alert the clinician about the possibility of preterm delivery (4, 6, 12). Delivery planning should ensure the availability of a large supply of blood and blood products. Eleven of thirteen women (84.6%) with advanced CIP received intra and/or postpartum blood transfusions (4, 6 - 15). Ten women were transfused 139 units of packed red blood cells, an average of 14 units per patient (4, 6 – 9, 11-15). These figures underscore the life-threatening nature of postpartum bleeding and the need of adequate blood bank services. Cesarean section is considered the safest route of delivery (6). Vaginal delivery remains an option and was accomplished in two women (8, 15). In the absence of a hemorrhagic emergency, placement of hypogastric artery catheters prior to delivery enables immediate internal iliac and uterine artery occlusion by embolization in the event of massive postpartum bleeding. (4).Eleven out of thirteen women with advanced CIP (84.6%) had a total abdominal hysterectomy after delivery of a viable newborn. The high postpartum hysterectomy rate has several reasons: the diagnosis is un-expectantly entertained at the time of delivery, the life-threatening nature of the postpartum hemorrhage and the lack of expertise in conservative operative techniques employed to control postpartum hemorrhage. Despite these challenges, the overall neonatal survival rate was 93%. Thirteen out of fourteen babies survived and one CIP was a twin gestation delivered at term (13).

The subsequent reproductive performance after CP was reassuring in 37 reported gestations: 54% of women had a term delivery, 14% had a premature delivery and 8% experienced a first trimester spontaneous abortion (19). Notwithstanding this argument, recurrent, consecutive CP were reported after use of assisted reproductive technology (20, 21). The subsequent successful obstetric experience after CP, reaffirms the enthusiasm for conservative, fertility sparing treatment enabled by early diagnosis. The reproductive performance after CIP remains elusive as the obstetric experience is limited to a single gestation that occurred in one of the two women whose uterus was preserved after term delivery of a CIP (16).

4. Term tubal pregnancy

4.1 Introduction

Term tubal pregnancy, however is extremely rare. Review of the literature revealed that at least over 13 cases of term tubal pregnancy have been reported. Most of them were published in the nineteen fifties. The most recent article on this subject was published in 2010. So, despite being a rather rare event, it can still be encountered especially in places with limited medical facilities.

4.2 Diagnosis

McElin and Randal (2) established 4 criteria of tubal pregnancy near or at term without rupture of the tube: 1) that comp lete extirpation of the fetal sac and products of conception be achieved by salpingectomy 2) that there be no gross or microscopic evidence of tubal rupture, 3) that ciliated columner epithelium be demonstrated at a few points in the inner lining of the sac and 4) that smooth muscle be found in the sac wall at multiple sites and at considerable distances from normal, undilated tube.

4.3 Conclusion and management

Tubal ectopic pregnancy accounts for approximately 1% of all pregnancies. Term tubal pregnancy, however is extremely rare. Review of the literature revealed that at least over 12 cases of term tubal pregnancy have been reported. Most of them were published in the 1950s [1–11]. The most recent article on this subject was published by us in 2010 [12]. With the recent advances in ultrasound and diagnostic imaging, it would be quite rare for ectopic pregnancy to reach up to term. In the event this would happen, an urgent laparotomy and salpingectomy with the removal of the affected fallopian tube would be the recommended option. Figure 1 and 2 demonstrate term tubal ectopic pregnancy with normal uterus and dilated fallopian tube after surgically opening it (figure 4.1). Then the term macerated fetus inside the tube (figure 4.2).

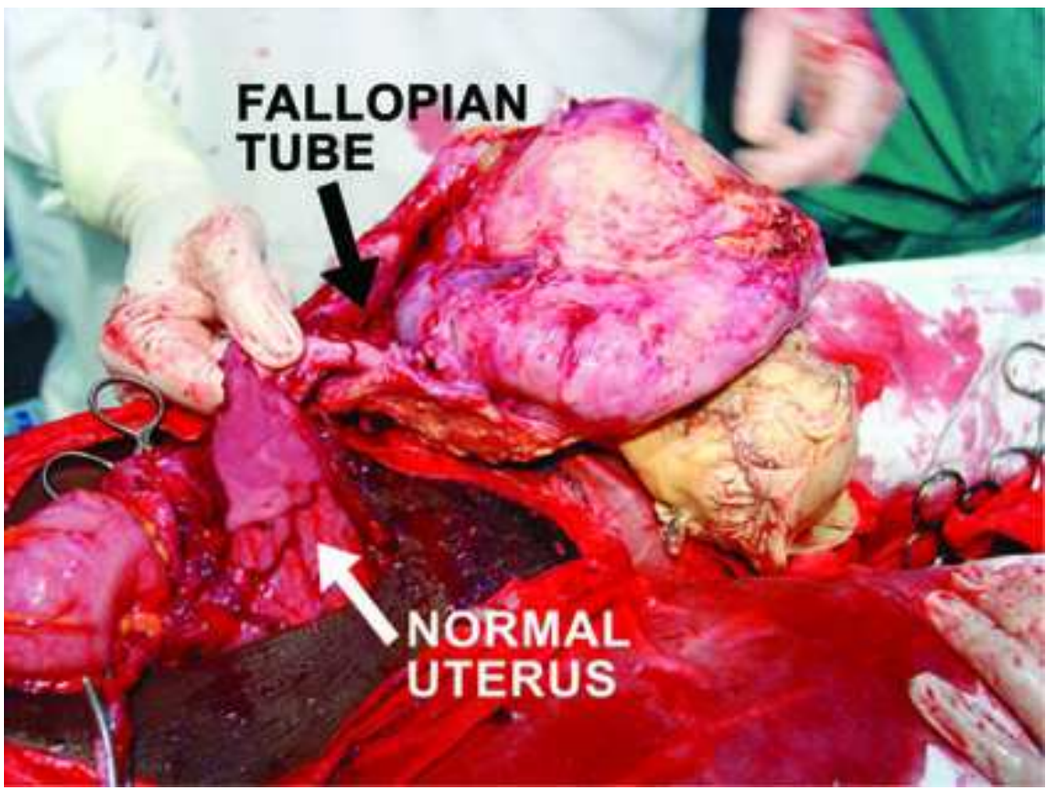

Fig. 4.1. Reatained term tubal pregnancy

Fig. 4.2. Reatained term tubal pregnancy

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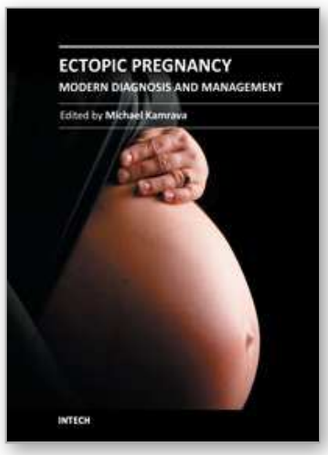

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Ectopic pregnancy is the second major cause of maternal mortality in the United States and a leading cause of maternal morbidity and mortality in the world. This book contains the practical methods to early diagnosis of various forms of ectopic pregnancies and their modern management. Ectopic Pregnancy - Modern Diagnosis and Management is a comprehensive book which guides the reader through all features of ectopic pregnancy, both practical and academic, covering all aspects of diagnosis and management of ectopic pregnancy in a clear, concise, and practical fashion. The book is organized so that it can either be read cover to cover for a comprehensive tutorial or be kept desk side as a reference to the ectopic pregnancies. Each chapter introduces a number of related ectopic pregnancy and its diagnosis, treatment and co-morbidities supported by examples. Included chapters bring together valuable materials in the form of extended clinical knowledge from practice to clinic features.

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