ECTOPIC PREGNANCY - DIAGNOSIS AND MANAGEMENT - A BRIEF REVIEW

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REVIEW

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Abstract

Any pregnancy implanted outside the endometrial cavity is defined as an extrauterine pregnancy (EUP) or ectopic pregnancy (EP). It is a acute and serious complication of frist trimestre of pregnancy that can be associated with high risk of morbidity and mortality for the patient. Most extra uterine pregnancy (EUP) (more than 95%) are usually found in the salpinx. In the fallopian tube, locations are found to be 13% isthmic, 75% ampullary and 12% fimbrial. The prevalence of ectopic pregnancy ranges from 6-16% of all pregnancies, with an increasing incidence in recent years due to assisted reproductive technologies. Half of women of reproductive age who are diagnosed with ectopic pregnancy have no known risk factors.

Keywords: extrauterine pregnancy, ectopic pregnancy, cervical ectopic pregnancy, post-caesarean scar ectopic pregnancy

Introduction

Extra-uterine or ectopic pregnancy is a gestation located externally from the uterine cavity. It's a medical condition that commonly complicates the first trimester of pregnancy. The medical suspicion of an ectopic pregnancy is raised by pelvic pain and abnormal vaginal bleeding associated with an elevated serum ßHCG or urine positive pregnancy test [1]. The fallopian tube is responsible for more than 90% of the ectopic pregnancy's locations [2]. The abnormal gestation can also be found in other locations, such as the abdomen (1%), the ovary (1-3%), uterine cervix (1%), as well as post-cesarean section scar (1-3%). Those are usually associated with high mortality and morbidity due to tardive diagnosis and options of treatment. Previous ectopic gestation increases the risk of developing another EUP. While one extra-uterine pregnancy rises the recurrence risk by 10%, two or more could increase it to 25%. Abnormalities or previous surgery of the salpinx, pelvic infections, and reproductive techniques are among the risk factors of developing an ectopic gestation [3], [4]. Symptoms of ectopic pregnancy include pelvic pain, which may be bilateral or localized to the right or left iliac fossa, pain at the top of the shoulder, vaginal bleeding, nausea, vomiting, diarrhea, dizziness, or collapse. Some women with EUP may be asymptomatic [5].

An unusual medical condition is a heterotopic pregnancy, when both the intrauterine and extra-uterine pregnancy occur simultaneously, commonly following multiple ovulation. In those cases, ectopic pregnancy

diagnosis delays due to ultrasound confirmation of the intrauterine gestational sac and the rareness of the condition. When diagnosed early, the EUP can be easily treated either by minimally invasive surgical treatment or non-invasive medical medication, such as methotrexate. [2], [6] Both maternal mortality and morbidity decreased following improved methods of diagnosis and therapeutic management protocols [7].

The pathophysiology of EUP includes tubal anatomy and functionality. Congenital or acquired tubal obstruction, altered tubal motility, and ciliary dysfunction, as well as molecular chemotactic factors, are among the factors that impair the physiological progression through the salpinx to the uterine cavity and promote abnormal tubal implantation [4], [7].

Any pregnancy outside the endometrial cavity is defined as extra-uterine pregnancy (EUP) or ectopic pregnancy (EP). It is a critical complication of the first trimester of pregnancy that can be associated with a high risk of morbidity and mortality for the patient. Most extra-uterine pregnancies (EUP) (more than 95%) are in the salpinx. In the fallopian tube, the locations are 13% isthmic, 75% ampullary, and 12% fimbrial. The prevalence of ectopic pregnancy ranges from 6-16% of all pregnancies, with an increasing incidence in recent years due to assisted reproductive technologies. Half of the women of reproductive age diagnosed with ectopic pregnancy have no known risk factors.

Material and methods

The PubMed database was used for this descriptive review, obtained from peer-reviewed studies published between 2012-2021, studies searched using keywords such as extrauterine pregnancy, ectopic pregnancy, pregnancy with unspecified location, cervical ectopic pregnancy, post-cesarean scar ectopic pregnancy, abdominal ectopic pregnancy, methotrexate, laparoscopy that analyzed the most common causes as well as evaluation and management of this condition. This review aims to highlight the involvement and impact of ultrasound in the immediate diagnosis, management (risk assessment), and therapeutic measures (prevention and treatment) of extrauterine pregnancy. Indications, contraindications of methotrexate treatment protocol of the condition, along with the follow-up and monitoring criteria for this abnormal pregnancy have been reviewed.

Results and Disscussions

Etiology

The etiology is difficult to define the mechanism of action is a combination of defective embryo-tubal transport and altered tubal environment allowing early implantation. Any mechanism that disrupts tubal functionality increases the risk of ectopic pregnancy [8].

Recent studies have shown that history of pelvic inflammatory disease, often caused by Chlamydia infection, endometriosis, injury or surgery to the fallopian tubes, use of assisted reproductive technology due to the infertility factor, smoking, use of intrauterine devices (induced inflammation), and age over 35 years correlate with a higher risk of EUP [6], [9], [10]. They may be major risk factors for recurrent ectopic pregnancy [4] (Table 1).

Previous extrauterine pregnancy increases the risk of future ectopic gestation. Little information was retrieved regarding the outcome of intrauterine pregnancy following an ectopic one [11].

Melanie Chouinard et al. demonstrated in a retrospective study that a large percentage of women diagnosed for the first time with ectopic pregnancy (subsequently treated surgically), the risk of a second ectopic pregnancy increases with age, while the chance of a future intrauterine pregnancy decreases. Women with a previous ectopic pregnancy who subsequently achieved an intrauterine pregnancy had higher risks of

complications such as preterm birth, low birth weight, placental disorders, and delivery by cesarean section. Complications of intrauterine pregnancy were present regardless of age, although older women were at higher risk of abruptio placentae and placenta previa [11].

History of previous EUP
Tubal surgery
Previous PID or STD
Age > 35 years
> 20 cigarettes/day
IUD use
Infertility > 1 year
Previous abortion (medical or surgical)

Table 1 - Risk factors for EUP [3,6,9]

Assessment and diagnosis

Obtaining a pregnancy test should be one of the first diagnostic tests to be performed. A negative pregnancy test virtually rules out a live ectopic pregnancy, assuming that the available pregnancy test has sufficient sensitivity to detect human chorionic gonadotropin levels commensurate with early pregnancy. A positive pregnancy test establishes the presumptive diagnosis of pregnancy but cannot assess the location or the viability. The most widely available and used biomarker to manage women with a pregnancy with unspecified location is serum human chorionic gonadotropin (hCG) [12]. A single measurement of hCG concentration can offer information regarding the presence of pregnancy, offering little information, especially when the result is with normal limits. Dynamically measured serum hCG concentrations are commonly used to establish whether a pregnancy is normally developing, or it rises the suspicion of pathological gestation [2].

It should be noted that chronic ectopic pregnancies can coexist with low hCG levels and are usually associated with chronic pelvic pain [10].

Suspected abnormal pregnancy should be confirmed and properly evaluated. Both measurements of urinary or serum ß-hCG levels and by transvaginal ultrasound (TVUS) are often necessary to confirm or infirm the diagnosis. A pregnancy test should be performed for every reproductive age, a sexual-active woman that is accusing pelvic pain and/or abnormal vaginal bleeding, regardless of the contraceptive method that she is using or in the presence of tubal sterilization. The suspicion of ruptured EUP is increased when the patient presents specific clinical signs and symptoms, such as the acute abdomen and hemodynamic instability. The evaluation and immediate surgical treatment are crucial when the diagnosis is confirmed [12]. For patients at risk, the evaluation of a possible ectopic gestation should be performed regardless of the clinical signs or symptoms.

When ultrasound examination is inconclusive for the location of the pregnancy, the pregnancy will be classified as pregnancy with an unspecified location. Repeat TVUS and dynamic determination of ß-hCG will allow a definitive diagnosis in most cases. Intensive follow-up is usually required for women with an outcome of ectopic pregnancy [12] (Table 2).

Ultrasound criteria	Gestational age (weeks)
Gestational sac	5
Yolk sac	5–6
Fetal pole	6
Cardiac activity	6–7

Table 2 - Ultrasound findings in normal pregnancy [13]

Serum progesterone

A meta-analysis of the accuracy of using serum progesterone levels to predict pregnancy outcome showed that it is a good indicator of pregnancy viability but not of location. Serum progesterone level below

10nmol/L was not proven to be associated with EUP, and it can be utilized as a selection criterion together with dynamic serum ß-hCG levels [1]. Levels of <20 nmol/L have a positive predictive value for failed pregnancies, while levels of >25 nmol/L predict future pregnancy, and levels of >60 nmol/L are strongly associated with evolving pregnancy [8].

Ectopic pregnancy may be completely asymptomatic (in case of intact tubal pregnancy or intact fallopian tube with the presence of the embryo with discernible cardiac function) or present with intensifying pelvic pain (tubal abortion) or severe hemorrhagic shock (ruptured tubal pregnancy) leading to hemodynamic instability, even death [7].

Ultrasound criteria in the diagnosis of ectopic pregnancy

A diagnosis of ectopic pregnancy cannot be A diagnosis of ectopic pregnancy cannot be confirmed by a peculiar characteristic of the ultrasound appearance of the endometrium. In the uterine cavity, in 20% of the cases, a collection of fluid can appear as an abnormal "pseudo sac". The ultrasound characteristics of the uterine hypoechoic area are often suggestive for early pregnancy and, therefore, the diagnosis of either intrauterine or extrauterine pregnancy should not be made on an ultrasound finding alone [8]. Intrauterine pregnancy can be confirmed by ultrasound from 5 weeks of gestation and includes visualization of the yolk sac or embryo within the pregnancy sac [2]. For the diagnosis of EUP, TVUS has a sensitivity of 87.0 - 99.0% and a specificity of 94.0 - 99.9%. The technique can confirm the presence of a gestational sac with or without an embryo inside both inside and outside of the uterine cavity [13], [14]. Most EUP do not reach the stage when an embryo can be visualized within the gestational sac. When an ectopic pregnancy is suspected, an adnexal mass with a hypoechoic area is found to be both outsides of the uterine cavity and ovarian tissue. Though ultrasound finding has an 80% predictive value, the differential diagnosis should be performed with corpus luteum, para tubal cyst, hydrosalpinx/ sactosalpinx, endometrioma, and bowel [14] (Table 3).

Normal pregnancy
Miscarriage (threatened or imminent)
Extrauterine pregnancy
Symptomatic ovarian mass (yellow body/hemorrhagic/dermoid cyst, adnexal torsion)
Dysfunctional metrorrhagia
Pelvic inflammatory disease
Gastrointestinal origin
Urinary origin

Table no. 3 - Differential diagnosis in a woman of reproductive age presenting with pelvic-abdominal pain and vaginal bleeding [10]

Ultrasound findings suggestive of a EUP include an empty uterus, free fluid (especially if hyperechogenic), an adnexal mass or ring separated from the ovary, ring of fire sign (although commonly seen around a yellow corpus cyst), and most specifically, the finding of extrauterine embryonic heart activity [1] (Table4).

Pregnancy with unspecified location (PUL) is not a diagnosis. It is a term used to classify a pregnancy until the final clinical outcome is known.

Women often present at an early stage of pregnancy making identification of implantation site, difficult. This is why the general term PUL was introduced. It can be used until the implantation site of the pregnancy is determined [15], [16].

Any woman classified as having a pregnancy with an unspecified location requires careful follow-up to determine the outcome, which may be an early intrauterine pregnancy, a failed pregnancy, a EUP, or rarely a persistence of a pregnancy with an unspecified location [8].

TYPES OF EUP		SONOGRAPHIC CRITERIA
Tubal pregnancy (isthmic, ampullary, infundibular, fimbrial)	fallopian tube pregnancy, different portions	• clear uterine cavity • inhomogeneous adnexal mass or clear extrauterine pregnancy sac or yolk sac or fetal pole in an extrauterine sac with present cardiac activity
Interstitial pregnancy	interstitial salpinx pregnancy	• empty uterine cavity • gestational sac/conception product located in the interstitial (intramyometrial) portion of the fallopian tube surrounded by a continuous edge of myometrium • interstitial line mark (thin hyperechogenic line extending from a central echo of the uterine cavity to the periphery of the interstitial sac)
Cornual pregnancy	pregnancy located in the uterine horn, near the tubal interstitial portion near the internal ostium of the fallopian tube	• a single interstitial portion of the fallopian tube in the main uterine body • mobile gestational sac/conception product separate from the uterus surrounded by myometrium • the vascular pedicle connecting the gestational sac to the unicornuate uterus
Caesarean scar pregnancy	implantation is at the level of the old post-caesarean scar	• empty uterine cavity • conception product/gestational sac anteriorly located at the level of the internal os covering the post-caesarean lower segment site • negative sign of the sliding organ • evidence of peritrofoblastic flow on colour Doppler examination
Abdominal pregnancy	***Primary*** - implantation is performed from the beginning on the peritoneal surface ***Secondary*** - initial implantation at the tubal ostium, followed by tubal abortion and re-implantation on the peritoneal surface	• empty uterine cavity • no evidence of a dilated fallopian tube or complex adnexal mass • gestational sac surrounded by intestinal loops and separated from the peritoneum • wide mobility similar to fluctuation of the sac
Cervical pregnancy	implantation in the cervical canal	• empty uterine cavity • barrel-shaped cervix • product of conception/gestational sac below the internal cervical os • negative sign of the sliding organ
Intramural pregnancy	grafting and development of pregnancy in the uterine wall thickness	• empty uterine cavity • conception product/gestational sac completely surrounded by myometrium and separated from endometrial cavity
Ligamentous pregnancy	secondary form of ectopic pregnancy, in which the primary tubal	• empty uterine cavity • conception product/gestational sac near the lower part of the uterus

	pregnancy erodes the mesosalpinge and is located between the broad ligament sheets	• free fluid in the Douglas space
Ovarian pregnancy	pregnancy implants in the ovarian cortex	• empty uterine cavity • cystic structure with large hyperechogenic ring, inside the ovary or surrounded by the ovarian cortex and separated from the corpus luteum
Heterotopic pregnancy	condition in which an ectopic pregnancy and an intrauterine pregnancy coexist	• the sonographic appearance is that of an intrauterine pregnancy plus an abnormally implanted pregnancy, most often tubal

Table 4 - Sonographic characteristics in types of extrauterine pregnancy [8,17]

Cervical ectopic pregnancy

Approximately less than 1% of ectopic pregnancy is found to be located in the cervix (Figure 1). The blastocyst progresses through the uterine cavity towards the cervical area and implants in the endocervical canal below the internal ostium. The exact mechanism of cervical ectopic pregnancies is unknown, however, a risk factor for this type of EUP is a history of uterine dilatation and curettage in a previous pregnancy [5], [6], [18].

For a cervical ectopic pregnancy to be diagnosed, two criteria must be met: 1) the cervical glands must be opposite to the placental attachment site and 2) a portion or even the entire placenta must lie beneath the uterine vessels or peritoneal reflection on the uterine surfaces.

Painless vaginal bleeding is a common symptom for which women present to hospital, while one-third of the patients seek medical care due to massive bleeding [5], [18].

It is recommended to avoid digital exploration of the cervical canal, as this may result in the development of a major hemorrhage. This condition can be associated with increased morbidity and mortality if the diagnosis is omitted or if the treatment is delayed, as they have a potential for massive hemorrhage, which could lead to hysterectomy and even death [6], [19].

They represent a real challenge because they are often diagnosed as miscarriage or an intrauterine pregnancy with a low implantation base and are managed differently than a cervical ectopic pregnancy (expectant, misoprostol drug management or surgical management by dilation and curettage VS methotrexate drug management or surgical management by resection or hysterectomy) [5], [19].

For hemodynamically stable women and pregnancies with gestational age < 12 weeks, uterine preservation and pregnancy termination can be achieved by systemic methotrexate treatment. A single systemic dose of MTX 50 mg/m² is widely accepted as the first-line therapy regardless of fetal cardiac activity.

Some studies have pointed to higher risks of systemic methotrexate treatment failure in women with pregnancies with GA > 9 weeks, fetal CRL of 10 mm, cardiac activity present, and ß-hCG levels > 10,000 IU/L. Some clinicians choose to induce fetal death by intrathoracic or intracardiac injection of potassium chloride [5], [6], [19].

To limit complications due to bleeding, uterine artery embolization can be used as a conservative and minimally invasive treatment alternative, characterized by the injection of embolic material which obstructs the uterine arteries with the cervical branches, thus devascularizing the embryo sac, stopping the pregnancy, and resorbing it (Figure 2), (Figure 3) [6].

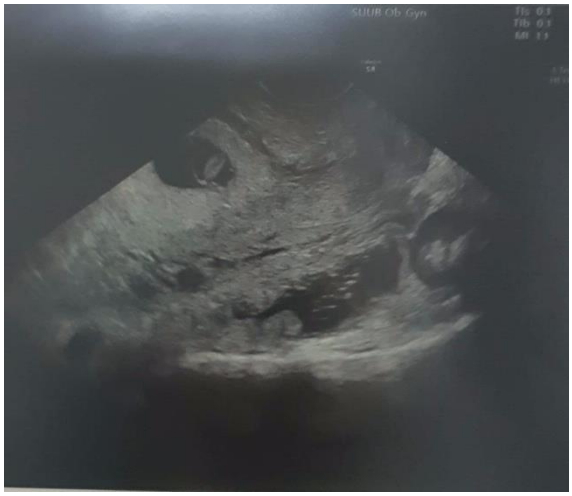

Figure 1 - 2D TVUS: cervical ectopic pregnancy

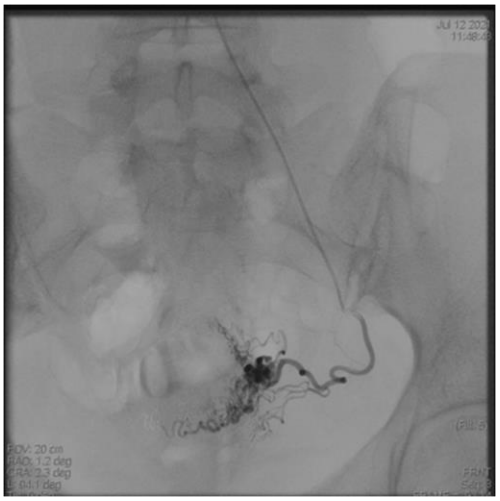

Figure 2 - Pre-embolization aspect of the cervical pregnancy

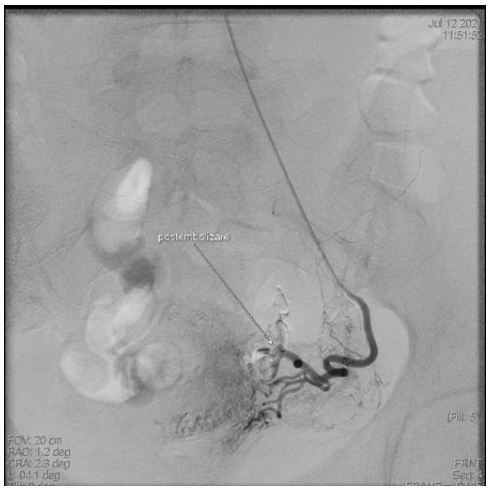

Figure 3 - Post-embolization aspect of the cervical pregnancy

Note that dilation and curettage carry a 40% risk for hysterectomy. Attempts to evacuate the uterus, digitally or instrumentally will produce violent hemorrhage, necessitating hysterectomy in most cases [18].

Early ultrasound diagnosis of cervical ectopic pregnancy allows procedures to be performed with preservation of the uterus and the patient's fertility [20].

Post-caesarean scar ectopic pregnancy

Different terms have been and still are used, such as ectopic cesarean pregnancy, ectopic cesarean scar, isthmic, or post-cesarean pregnancy.

Post-cesarean scar pregnancy is a medically induced, potentially dangerous consequence of a previous pregnancy completed by cesarean section. It occurs when the blastocyst implants (microscopically or macroscopically) on the uterine scar or in the 'niche' (or dehiscence) left behind by the incision site of the previous operation. The only risk factor for PCSEP is one or more previous cesarean deliveries [21].

Pregnancy located in the old cesarean scar is the precursor of placenta accreta, having the same histological picture.

Sonographic criteria of pregnancy with localization at the level of the old cesarean scar:

- myometrium is extremely thin under the bladder
- bladder distortion by deformation or disruption of the bladder line
- increased vascularity at the implantation site (color Doppler) [21].

As in every intrauterine pregnancy, vaginal bleeding of varying degrees may be the first sign [22].

Patients may be asymptomatic and only become aware of a PCSEP when detected by TVUS (Figure 4). Every patient with previous cesarean deliveries should be screened for cesarean scar pregnancy [21].

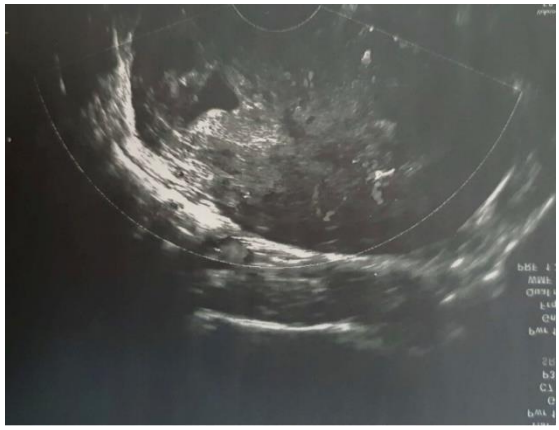

Figure 4 - 2D TVUS: post-cesarean scar ectopic pregnancy

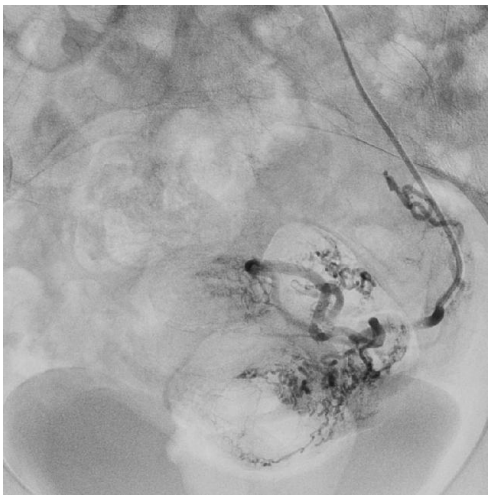

Figure 5 - Pre-embolization aspect of the post-cesarean scar ectopic pregnancy

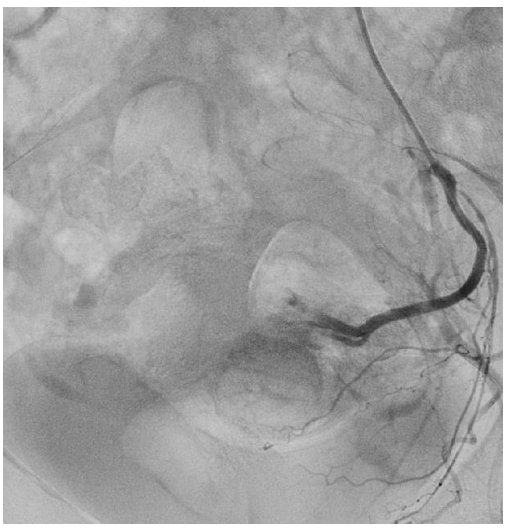

Figure 6 - Post-embolization aspect of the post-cesarean scar ectopic pregnancy

The first-line method in the treatment of post-cesarean scar pregnancy is methotrexate. Uterine artery embolization is another conservative treatment option (Figure 5), (Figure 6). For the removal of the ectopic pregnancy, laparoscopic or hysteroscopic procedures are the most preffered. Laparotomy should be performed in cases of rupture or unavailability of the other treatment options [9], [21].

Abdominal ectopic pregnancy

Abdominal ectopic pregnancies are intraperitoneal pregnancies, which exclude tubal and ovarian locations. Intraligamentous pregnancy could be considered a form of extraperitoneal abdominal ectopic pregnancy. Abdominal ectopic pregnancies are intraperitoneal pregnancies, which exclude tubal and ovarian locations. Intraligamentous pregnancy could be considered a form of extraperitoneal abdominal ectopic pregnancy. Abdominal ectopic pregnancy accounts for about 1% of all extrauterine pregnancies and has a mortality rate of 5% [5].

The location is secondary to either expulsion of the blastocyst from the fimbrial end of the salpinx or following the rupture of tubal pregnancy. Risk factors are general in EUP and include tubal injury, pelvic inflammatory disease, endometriosis, and assisted reproductive techniques [3].

A specific feature of abdominal ectopic pregnancies is that they can present at a very advanced, viable gestational age, even at term. Sonographic characteristics of an abdominal pregnancies include the absence of myometrial tissue framing the ectopic gestational sac, a mobile gestational sac closely limited by the intestine loops and separated from them by a layer of peritoneum, associated abnormal placentation, amniotic liquid abnormalities (often oligohydramnios), and unusual fetal position [1], [5].

Ideally, the ectopic pregnancy should be removed laparoscopically. In advanced abdominal pregnancy (when the placenta is

attached to major vessels or vital organs), optimal treatment consists of removal of the gestational sac via an open surgical approach, avoiding the excision of the placenta, which is left in situ, in order to minimize the possibility of excessive bleeding. Postoperatively, methotrexate or arterial embolization may be used to accelerate the involution of the remaining tissue [9].

Treatment with methotrexate

For most women presenting to the hospital with first-trimester vaginal bleeding or pelvic-abdominal pain, 6%-16% will have an ectopic pregnancy [1].

Women diagnosed with ectopic pregnancy are usually treated either medically with methotrexate or surgically. Clinical criteria are used to determine treatment (medical versus surgical treatment). There are recent data promoting the benefits of tubal preservation, optimizing fertility without excessive risks of recurrent ectopic pregnancy. Expectant management is an alternative when the extrauterine pregnancy is nonviable [23].

Methotrexate is widely accepted as a first-line in the treatment of EUP. It may be suitable in the case of a confirmed, unruptured, hemodynamically stable ectopic pregnancy [7]. Methotrexate is a chemotherapeutic agent that prevents trophoblast growth by inhibiting DNA synthesis and cell division. However, it is contraindicated in renal or hepatic disease or in the presence of leukopenia or thrombocytopenia [2], [9], [18]. The success rate of the non-invasive medical treatment with methotrexate for ectopic pregnancy is considered to be as high as 90%. Contraindications for methotrexate protocol include pre-treatment ß-hCG levels greater than 5,000 mIU/mL, fetal cardiac activity (FCA) of the embryo, and ectopic pregnancy sac greater than 4 cm in size [24]. Failure of methotrexate therapy can lead to tubal rupture and physicians should be aware of the risk of methotrexate failure and be suspicious that patients may return with ruptured EP unless a proper follow-up is performed [7].

There are data indicating severe toxicity and mortality risk following MTX administration in ectopic pregnancy, adverse effects occurring after administration either after single, double, or multi-dose regimen in women without comorbidities [25] (Table 5), (Table 6).

ABSOLUTE
intrauterine pregnancy
immunosuppression
hypersensitivity to methotrexate
active peptic ulcer
active lung disease
significant renal or hepatic dysfunction
breast-feeding
ruptured ectopic pregnancy
RELATIVE
embryonic heart activity detected by transvaginal ultrasonography
high initial hCG concentration
ectopic pregnancy > 4 cm
refusal of blood transfusion

Table 5 - Contraindications to methotrexate use [2, 7]

Monitoring consists of clinical, biological and imaging follow-up of patients treated expectantly or medically.

Follow-up after methotrexate protocol includes weekly ßhCG measurement until normalization. A repeated methotrexate therapy or minimal invasive surgery are suitable options for an ongoing extrauterine pregnancy or trophoblastic tissue [7]. Also, it is recommended that women should postpone the following pregnancy for at least 3 months after medical methotrexate protocol [9].

	DOSE, MODE OF ADMINISTRATION	TIME OF ADMINISTRATION	HCG MEASUREMENT	ADDITIONAL ADMINISTRATION
SINGLE DOSE	MTX 50 mg/m² body surface area IM	• day 1	before treatment • day 1 • day 4 • day 7	• MTX 50 mg/m² body surface area, IM activated • day 7: if hCG decreases < 15% from day 4 to day 7
MULTI DOSE	MTX 1 mg/kg IM LEU 0,1 mg/kg IM	• day 2 LEU possibly • day 3 MTX • day 4 LEU possibly • day 5 MTX • day 6 LEU possibly • day 7 MTX • day 8 LEU	before treatment • day 1 • day 3 • day 5 • day 7	• 2nd, 3rd, or 4th dose of MTX 1 mg/kg IM followed by LEU 0.1 mg/kg IM: if hCG decreases < 15% from previous hCG value

LEU = leucovorin, MTX = methotrexate

Table 6 - Methotrexate treatment protocols for ectopic pregnancy [7]

Surgical treatments in ectopic pregnancy

Laparoscopy, a minimally invasive surgery, is the gold standard of surgical treatment for extrauterine pregnancy. When the procedure cannot be performed due to medical, logistical, or technical reasons, laparotomy is a viable option. Fast access within the abdominal cavity, minimal operating time, decreased blood loss and postoperative adhesions, as well as faster recovery, are among the advantages of laparoscopy compared to laparotomy [7].

Indications for surgery are the presence of a EUP with cardiac activity on ultrasound or an adnexal mass >35 mm and a β-hCG level >1500, respectively 5000 IU/L. Significant abdominal pain is an imminent sign of ruptured ectopic mass, which should, prompt clinicians to decide in favor of surgery [9].

Immediate indications for surgical treatment include tubal rupture, hemodynamic instability, acute abdomen (symptoms such as acute pain), diagnostic laparoscopy, and suspicion of heterotopic pregnancy [7].

Surgical organ-preserving procedures include salpingotomy, partial salpingectomy (segmental resection), and transampullary expression ("milk-out method"). Salpingectomy, an ablative surgical procedure, is indicated in case of uncontrollable bleeding or the presence of tubal destruction. Also, ablation is to be considered in ipsilateral prior sterilization or recurrence [7].

Surgical tubal trauma should be minimal if the procedure performed is salpingotomy. Patients will be properly informed and close monitoring should be performed using weekly serum b-hCG levels, due to the increased risk of trophoblast persistence. In case of a negative outcome, the procedure can require additional treatment such as systemic methotrexate or salpingectomy [14].

Heterotopic pregnancy and hemodynamically stable patients with ectopic pregnancy can also benefit from intragestation administration of potassium chloride or hyperosmolar glucose injection, followed by the aspiration of the gestation sac contents.

This simple and efficacious method can be performed without compromising a coexisting intrauterine pregnancy [14].

Cornual pregnancy, a rare form of ectopic gestation that represents approximately 2% of all EUP, treatment involves surgical resection of the pregnancy and hemostasis of the corneal portion in case of hemorrhagic rupture. Hemostasis of the uterine horn can be performed laparoscopically, by resecting both the horn and the fallopian tube. However, for subsequent pregnancies, there remains a risk of interstitial pregnancy and uterine rupture [26].

Ectopic pregnancy after an interanexial hysterectomy is an uncommon event that is often overlooked. Some studies have shown the importance of a pregnancy test being recommended to all young or reproductive age, sexually active women addressing medical assistance with clinical signs and symptoms of ectopic pregnancy, regardless of the type of hysterectomy in the past. The most commonly reported type of hysterectomy preceding ectopic pregnancy was a vaginal hysterectomy, followed by abdominal and laparoscopic hysterectomy. Ectopic pregnancies have also been reported after subtotal hysterectomies [27].

After surgical treatment, follow-up includes weekly hCG measurement until normalization. For persistent extrauterine pregnancy or trophoblastic tissue, re-laparoscopy, as well as drug therapy (methotrexate), can be indicated [7].

Conclusions

The EUP rate is about 1-2% of all births in developed countries. It is the most frequent cause of death in the first trimester of gestation, about 10% of all pregnancies. Although the etiology of EUP is multifactorial, 50% of women have no identifiable risk. Any EUP should be suspected in any woman of reproductive age, with amenorrhoea, positive pregnancy test (serum or urine), pelvic abdominal pain, with or without vaginal bleeding, and pregnancy not sonographically located in the uterine cavity associated with risk factors. Risk factors such as Chlamydia trachomatis can damage tubal anatomy, disrupting ciliary action, tubal obstruction, and pelvic adhesions.

Most women with EUP have minimal or absent symptoms and are hemodynamically stable. Using TVUS as the primary tool to diagnose EUP is highly sensitive and specific, with women being diagnosed rapidly and accurately. Tubal ectopic pregnancies are positively identified by ultrasonographic visualization of an adnexal mass moving separately from the ovary.

Ectopic implantations pose a risk of organ rupture and massive bleeding, and immediate diagnosis of a suspected ectopic pregnancy is essential for case management. The use of methotrexate for the treatment of early unruptured EUP is reported to be effective and safe. Surgical removal of ectopic pregnancy performed by laparoscopy is the method of choice for hemodynamically unstable women but may also be an option in the case of hemodynamically stable women. The treatment choice after assessment should be guided by the outcome, risks, and benefits of the approach. Prevention is the reduction of risk factors through screening and treatment.

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