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## Case Report / Приказ случаја

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### Unruptured tubal pregnancy in early second trimester

Неруптурирана тубарна трудноћа у раном другом триместру

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### Неруптурирана тубарна трудноћа у раном другом триместру

#### SUMMARY

**Introduction** Most ectopic pregnancies are tubal pregnancies. They are potentially life-threatening conditions with a high mortality rate if unrecognized. The diagnosis is established when the first warning symptoms occur, or during the first prenatal visits to a gynecologist. The diagnosis in the second trimester is extremely rare, since clinical presentation resulting either from the expulsion of a fetus into the peritoneal cavity or the tubal rupture is manifested by that time. If there is no rupture or the expulsion of a fetus, the pregnancy is allowed to continue and an ectopic pregnancy diagnosis may be established in the second trimester

**Case study:** We present a case of a 31-year-old second gravida with a confirmed vital intrauterine pregnancy at the first examination. In the early second trimester the patient visited her doctor due to vaginal bleeding. After a gynecological examination and ultrasonography an ectopic pregnancy was suspected, so the patient underwent laparotomy. An ectopic pregnancy was confirmed and the adnexectomy was performed.

**Conclusion:** Early ultrasound examinations have to confirm whether a eutopic pregnancy is present. A misdiagnosis and monitoring an ectopic pregnancy as a eutopic one are potentially life-threatening for a pregnant woman.

**Keywords:** unruptured; tubal pregnancy; early second trimester

#### САЖЕТАК

**Увод** Најчешћа ектопична трудноћа је јајоводна. Ради се о потенцијално животно угрожавајућем стању са високом смртношћу код непрепознатих случајева. Дијагноза се поставља при појави првих симптома или приликом првих посета гинекологу. Дијагноза у другом триместру је значајно ређа јер до тада обично долази до манифестовања потпуне клиничке слике која је последица или експулзије заетка у перитонеалну шупљину или руптуре јајовода. Уколико до руптуре јајовода или експулзије заетка не дође, могућ је наставак трудноће и дијагноза ектопичног гравидитета у другом триместру.

**Приказ болесника** Тридесетједногодишња секунди-гравиди, са првом виталном интраутерином трудноћом, у раном другом триместру јавила се лекару због појаве вагиналног крварења. После гинеколошког и ултрасонографског прегледа постављена је дијагноза ектопичне трудноће и урађена лапаратомија. Потврђена је тубарна трудноћа и урађена аднексектомија.

**Закључак** Прве ултразвучне контроле морају да потврде еутопичност трудноће. Погрешна дијагноза и праћење ектопичне као еутопичне трудноће је потенцијално угрожавајуће за трудницу.

**Кључне речи:** неруптурирана, тубарна трудноћа, рани други триместер

#### INTRODUCTION

An ectopic pregnancy is a condition where an embryo implants in a location other than the uterus. The most common site for an ectopic implantation is the Fallopian tube, but it can occur at other locations as well. Potential locations of ectopic gravidities include the ovary, the abdomen, the cervix, intraligamentous locations, and the intramyometrial segment [1-3].

The incidence of ectopic pregnancies is about 1.3–2.4 % in relation to the total number of registered pregnancies [4]. The incidence of ectopic pregnancies has been increasing since the 1970s (0.5%) till nowadays (2%) [5]. In the USA the incidence of ectopic pregnancy is about 2.3 %. The rate among the African-American women is almost double and mortality risk is a 5 fold higher than in white women in all the states in the USA [6, 7].

Risk factors responsible for the development of ectopic pregnancy include previous pelvic inflammatory diseases, abdominal surgeries, previous ectopic pregnancy, hemoperitoneum of any etiology, the use of intrauterine devices, and previous Cesarean section [8, 9]. The probability of ectopic pregnancy is 2.5-5 fold higher following assisted reproduction methods. The incidence of ectopic pregnancy after in-vitro fertilization is between 1.4% and 5.4%. The patients with reduced ovarian reserve and confirmed tubal pathology are also at high risk [10, 11]. Previous pelvic surgery,

manipulation and surgical procedures including the Fallopian tubes, increase the probability of ectopic pregnancy development [3, 12].

Failure in diagnosing ectopic pregnancy, especially at uncommon sites of an embryo implantation, is one of the leading causes of maternal deaths in early pregnancy [6, 7, 13, 14]. Careful clinical monitoring and timely diagnosis reduce the probability of potentially fatal maternal risks [15]. Ectopic pregnancy is usually diagnosed in the first trimester of pregnancy and it is the most common life-threatening condition in an early pregnancy [3, 6, 7, 12, 13]. However, the diagnosis can be established in the second or third trimester in patients without tubal rupture. Late diagnosis is rare, since the ultrasound examination in the first trimester confirms the diagnosis of ectopic-ectopic pregnancy during the first examination [14].

### CASE REPORT

Our patient is a 31-year-old primipara, second gravida. She was referred to our Institution by a doctor from the local health center at 17<sup>th</sup> week of amenorrhea, with fetal death and suspected abdominal pregnancy.

The patient had no pain and visited her gynecologist due to vaginal bleeding. It was her second examination regarding the pregnancy. After clinical and ultrasound examinations, a practicing gynecologist suspected ectopic pregnancy and referred the patient to the regional health center. Due to suspicion of abdominal pregnancy, the patient was transported to the tertiary health care center.

She has been a healthy person, non-smoker, without significant diseases, allergies or surgeries. Menarche occurred at the age of 16. Menstrual cycle was with bleeding at 35-38 days. The bleeding lasted 7-10 days. The patient had one pregnancy with vaginal delivery on due date, without obstetric surgery or postpartum complications. The delivery had been two years before she presented to our Clinic. She reported no usage of intrauterine contraception, but used a condom as a physical barrier contraception.

The patient contacted a gynecologist for pregnancy confirmation and underwent clinical and ultrasound examinations. During that first examination, she reported that amenorrhea lasted 9 weeks. On that occasion, the presence of a gestational sac and a vital embryo with a biometry consistent with about eight weeks were confirmed. Extrauterine pregnancy was not suspected and it was monitored as intrauterine pregnancy.

Then, fetal biometry was performed (crown-lump length CRL was 16 mm - corresponding to a gestational age of 8 weeks and 2 days, gestational sac diameter of 40.1 mm corresponded to a gestational age of 9 weeks), and fetal viability was confirmed by fetal cardiac activity. Such an examination should have detected the position and shape of the gestational sac, as well as a double decidua sac halo. The position of the sac and the absence of this sign on initial ultrasound examination could have raised doubts about an ectopic pregnancy. Chorionic gonadotropin values were not determined in the pregnant woman's blood. The patient has had no health problems until scarce

vaginal bleeding occurred with amenorrhea lasting 16 weeks and 5 days. The patient visited the same gynecologist who performed the first examination. On that occasion fetal death and ectopic pregnancy were confirmed and the patient was referred to the General Hospital. After an ultrasound examination there, an ectopic pregnancy was confirmed, as well as fetal death. Due to suspected ectopic, probably abdominal pregnancy, the patient was referred to the specialized clinic.

On admission to our Clinic the patient was conscious, afebrile, normotensive, and painless, with scarce vaginal bleeding and she was cardiocirculatory stable. The abdomen was insensitive to superficial and deep palpation. Speculum examination revealed cylindrical cervix, transversal orifice, moderate bleeding from external orifice, and dark blood. Proust pain sign was negative. On bimanual examination the uterus was enlarged and softened, slightly shifted to the left in retroversioflexion (RVF). The left adnexal region was palpable without tumefactions. In the right adnexal region and below the uterus, a soft, tense and insensitive formation about 10 cm in diameter was palpated. Transabdominal ultrasonography examination (Toshiba Nemio, XG, 6 MHz ) with the bladder not full enough revealed the presence of the gestational sac with developing anterior wall placenta and the fetus without heart action and with positive Spalding's sign (overlapping of skull bones) (Figure 1).



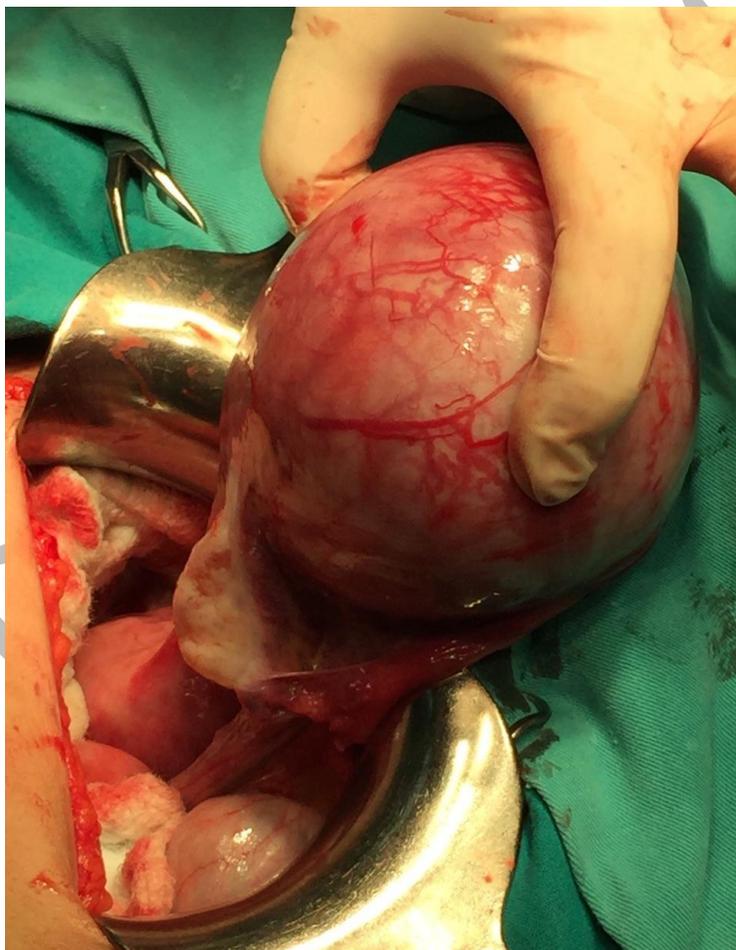
**Figure 1. An embryo, a dilated tube, the uterus – transverse imaging.**

Transvaginal ultrasonography revealed the uterus shifted to the left in RVF (dimensions: 80mm x 54mm x 56 mm, endometrium 14 mm). In the right adnexal region a cystic formation was observed and suspected to be a dilated right fallopian tube. The borders and the walls of the cystic formation were clear, with the dimensions 92mm x 84mm x 65mm). No fluid was collected around the tumefact in the Pouch of Douglas. On the upper pole of the formation a hyperechogenic formation was observed and considered to be the placenta. Fetal biometry was as follows: biparietal diameter (BPD) 28.5, head circumference (HC) 101.8mm, abdominal circumference (AC) 85.9 mm, femur length (FL) 14.5 mm. Fetal biometry was consistent with fetal gestational age of 14 weeks and 5 days. Below the cystic formation (gestational sac and the embryo) the right ovary was registered, 44 mm x 38mm x 28mm in size. The left ovary was normal, 28 mm x 22mm x 17mm in size. Both ovaries had normal sonographic features. Upon the completion of the ultrasound examination, an intact right tubal pregnancy was suspected.

The patient was admitted to hospital and upon anamnestic, clinical and ultrasound procedures, laboratory investigations were performed. Laboratory analyses on admission were as follows: blood group A Rh (D) negative; biochemical analyses and coagulation factors within referential values. Coagulation status: the prothrombin time: 93%; activated partial thromboplastin time – a PTT- 25 seconds; factor I 2.3g/l; the prothrombin time- INR: 1.0. After anamnestic, clinical and ultrasound procedures and after obtaining laboratory results, we decided to perform a laparotomy. The patient was prepared for surgery that was performed under general endotracheal anesthesia.

### **Surgical procedure and findings**

Lower transversal laparotomy was performed, as well as the tamponade of the bowels; there was no free fluid in the abdominal cavity. A cystic, tense tumefact, with leaden-coloured walls and about 10 cm in diameter dominated in the pelvis minor . The uterus was enlarged and shifted to the left. There were no morphological changes in the left adnexal region. The tumefact was shifted from the pelvis and after the positions of the right ovary, ligament of the uterus and tumefact were defined, it was confirmed that the ampullary portion of the tube was highly distended. The wall of the tube was very tense, with stretched and highly dilated infundibulopelvic ligament (Figure 2). The tumefact was semi-torquated around the isthmic portion of the tube. The ovary was in close contact with ampullary and isthmic sections of the tube.



**Figure 2. The uterus, a dilated tube with a product of conception, an ovary.**

There was no bleeding on the fimbria of the affected tube. Due to heavily distended and stretched ligaments and the vicinity of the ovary it was almost impossible to preserve the ovary with an adequate hemeostasis, so it was decided to perform adnexectomy. A straight clamp was applied next to the uterus and the tube next to the uterus was fastened, as well as a dilated and stretched ovary clamp with the uterus. Curved peans were used to fasten distended infundibulopelvic ligament to the right. Sample: entire adnexa was removed without serious bleeding. Cut sections were sutured. Hemeostasis was checked and after peritonization and rinsing a control

drain was placed in the pouch of Douglas pararectally. The abdomen was then closed in layers. The sample was carefully cut, so all the structures and the embryo described by the ultrasound were observed (Figures 3, 4). After closing the abdomen, the patient was placed in lithotomic position and instrumental revision of the uterine cavity was performed because of heavy vaginal bleeding during the surgical procedure. An abundant specimen was obtained. Both the removed adnexa and the specimen were subjected to a histopathological examination. The surgical procedure lasted 50 min. The postoperative course was normal. The control drain in the pouch of Douglas was removed on the third postoperative day. The patient was discharged on the fifth postoperative day with fully restored passage and normally healing wound. Postoperative ultrasound finding was normal. On the second postoperative day the patient was given Immunorh. No I immunoprophylaxis.



**Figure 3. Cut tubal wall and peeled gestational sac. Figure 4. An embryo, placenta, cut tubal wall.**

Histopathological examination confirmed the embryo age of 15 gestational weeks. No fetal anomalies were detected. In the samples obtained by the check-up curettage, decidual endometrial alterations without the presence of fetal elements were confirmed. The presence of the yellow body was detected in the removed ovary.

## **DISCUSSION**

It is necessary to determine whether a eutopic pregnancy is present on receiving the first ultrasound examination. If the pregnancy in the uterine cavity is not confirmed in the presence of amenorrhea, pregnancy signs and positive pregnancy tests, a pregnant women requires careful monitoring until ectopic/eutopic pregnancy is diagnosed. The diagnosis is established by repeated application of transvaginal ultrasound and adnexal mass identification, or by the diagnosis of

intrauterine pregnancy. The use of maternal serum serial chorionic gonadotropin levels is also significant [15]. The possibility of heterotopic pregnancy, especially in patients after *in vitro* fertilization, should not be ignored.

Errors are possible due to poorly trained staff, uncooperative patients, atypical symptoms, and unusual localizations [16]. A complete clinical manifestation of an ectopic pregnancy is most commonly symptomatic in the period of 6-8 gestational weeks, unless diagnosed earlier. The tube is not a well-suited site of embryonic implantation and the decidual reaction is minimal. The trophoblasts spread and erode maternal blood vessels. The tube is thinned and muscle fibers undergo hypertrophy, but limited hyperplasia. Timing of the tubal rupture depends on the nidation site and the degree of the tubal wall invasion and the level of hemorrhage in the tubal wall as well [17]. Unrecognized ectopic pregnancy develops in the ampullary region and its progression depends on the degree of tubal invasion and the way of trophoblastic growth. The trophoblast growth can be intraluminal, extraluminal and combined. In predominately intraluminal trophoblastic invasion, the degree and velocity of hemorrhage development depend on the degree of maternal blood vessels involvement. The tubal rupture does not necessarily occur immediately after a bleeding attack. Tubal distension occurs as a consequence of conceptual mass growth and bleeding. The possibility of intact endosalpinx epithelium and the absence or minimal hemorrhagia can be seen in intraluminal trophoblastic spread, but trophoblastic invasion of the maternal blood vessels is more intensive and tubal rupture occurs earlier in extraluminal extension [18]. The appearance and regularity of the gestational sac and the presence of crescent-shaped visible placental tissue (other authors also used similar diagnostics criteria before surgery) were the guidelines in making differential diagnosis between abdominal and tubal pregnancy [19]. We decided to perform lower transverse laparotomy due to low probability of abdominal pregnancy. In the case of our patient fetal death occurred. There was no blood in the abdomen, nor tubal rupture. Other authors also reported their experience in patients with unruptured tubal pregnancy. There are no literature data on preserving the affected tube following an ectopic pregnancy in the second trimester. After abdominal opening and confirmation of the right tubal ectopic pregnancy diagnosis, we made an assessment and decided to perform adnexectomy as a safe alternative in our patient to maintain more effective hemeostasis. The vicinity of the right ovary and the tube with the conceptus, as well as heavily distended thinned ligaments made us doubt on performing salpingectomy as the most sparing surgery, so we performed adnexectomy. Clinical manifestation of ectopic pregnancy in the second trimester may be severe, with prominent hemorrhage and life-threatening to the mother [20, 21]. Surgical treatment of the second trimester ectopic pregnancies is an inevitable procedure, most commonly including salpingectomy, but adnexectomy may be performed as well, depending on the findings obtained [22] Hysterectomies in patients with advanced tubal pregnancies have also been described [23]. Timely diagnosis (38-68 gestational day) provides successful surgical treatment by using minimally invasive procedures, while preserving the affected tube [24]. Embryo implantation outside the uterus is always associated with

endometrial changes. Proliferation, cystic hyperplasia, secretory transformation, hyper-secretory changes, asynchronous secretory changes between the glands and the stroma, and decidua reaction were histopathologically verified [25,26]. Instrumental curettage of the uterine cavity is not a standard post-surgical line of therapy in ectopic pregnancy management, except in heavy or prolonged uterine bleeding, or in cases of suspected heterotopic pregnancy.

Early ultrasound examination is performed to confirm whether the pregnancy is eutopic. A misdiagnosis and monitoring ectopic pregnancy as an eutopic one are potentially life-threatening for a pregnant woman. Surgical treatment should be as sparing as possible, regarding preservation of reproductive organs, especially in patients wishing to have more children. Early diagnosis of tubal ectopic pregnancy may also enable the preservation of the tubes. The advancement of an ectopic pregnancy towards the second trimester decreases the likelihood that the patient will have a sparing surgery.

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