CLINICAL CASE

A RARE CASE OF TROPHOBLASTIC TUMOR WITH FALLOPIAN TUBE LOCALIZATION FOLLOWING OVARIAN STIMULATION

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Abstract

The real incidence of gestational trophoblastic disease is unknown in our country and there is no reported case of tubal localization. We describe a commune case of trophoblastic tumor localization in the fallopian tube following ovarian stimulation.A 39-year-old woman was admitted in our clinic for amenorrhoea, lower abdominal pain and vaginal bleeding. She underwent ovarian stimulation with Clomiphene citrate for induction of ovulation. The clinical and ultrasound examination revealed a tumor in the right side of the uterus, a tumor of 3/4cm sensitive, belonging to the right adnexa. The human chorionic gonadotrophic hormone (-HCG) from the blood was about 19 000 IU/mL without gestational sac and embryo inside the uterus. We performed laparoscopy. The right tube was enlarged of about 6/3 cm, of purple color and adherent to the anterior wall of the urinary bladder. We performed the dissection of the adhesion and right laparoscopic salpingectomy.The postoperative outcome was favorable. The histopathological examination revealed the presence of the trophoblastic cells into the fallopian tube. The immunohistochemical examination confirmed the diagnosis. The surgical treatment was curative and the patient had no further gynecological or other related complains one year later. We presented a rare case of trophoblastic tumor localized into the fallopian tube. The particularity of this case is the clinical presentation as a persistent ectopic pregnancy and the fact that it is related to ovarian stimulation.

Keywords*: trophoblastic tumor, fallopian tube, amenorrhoea*

Introduction

The precise incidence of ectopic pregnancy was last time reported by Centers for Disease Control in the early 1990s and it seems to be about 20 per 1000 pregnancies[1]. The main cause for the increasing incidence is the inflammatory pelvic disease[2]. The prevalence of ectopic pregnancy among women who complain of abdominal pain or vaginal bleeding in the first trimester of pregnancy ranges from 6 to 16 percent[3]. It is well known that without rapid diagnosis and treatment, ectopic pregnancy represents a life-threatening condition. The human reproductive physiology explains that it is the result of a flaw in the normal physiology that allowed the zygote to implant outside the endometrial cavity[4].

Hippocrates was the first one who described the hydatidiform mole around 400 B.C. as "dropsy of the uterus." The hydatidiform mole is referred to as molar pregnancy or mole

and it represents an item of research and clinical interest among gynecologists and pathologists. The mole is part of a group of diseases classified as gestational trophoblastic diseases with origins in the placenta and the potential to invade the uterus, the surrounding tissue and the ability to metastasize. It has a unique pathogenesis because the tumor rises from gestational but not from maternal cells[5]. Trophoblastic tumor with fallopian localization is reported in less than 10 cases in the medical literature.

Case presentation

A 39-year-old nulliparous woman was admitted in our clinic for amenorrhoea, lower abdominal pain and vaginal bleeding. Her last normal menstrual period was 10 weeks ago.

The medical history revealed that she had no previous pregnancy. No other significant pathology and no prior surgical intervention in the pelvic area were recorded. In order to conceive, after the last menstrual period, the patient was given Clomiphene citrate 5 mg/daily days 3-7 of the menstrual cycle for induction of ovulation followed by Pregnyl 5000 ui on day 14.

The clinical examination at admission revealed the uterus of about 5/4 cm, on the right side of the uterus a tumor of 3/4cm sensitive, belonging to the right adnexa, left adnexa and the Douglas space were normal. She had no other associated pathology on clinical examination.

The first transvaginal ultrasound examination proved the uterus with normal volume and structure. The endometrium had a thickness of 8 mm. It was observed the existence of a 47/40 mm tumor in the right side of the uterus, with thin walls and very thin membranes inside. The ovaries and the retrouterine space were normal at the ultrasound examination.

We performed a urinary pregnancy test that was positive and we measured the values of beta fraction of human chorionic gonadotrophic hormone (-HCG) from the blood. The first particularity of this case was the high value of -HCG, of about 19 000 IU/mL without gestational sac and embryo inside the uterus. The first discussion was that the clinical and ultrasound examination were suggestive for ectopic pregnancy and the pregnancy hormone was sensitive for trophoblastic disease.

We decided to perform laparoscopy. We used the open technique known as the Hasson technique. We observed the modified aspect of the right fallopian tube that was suggestive for right ectopic pregnancy. The right tube was enlarged of about 6/3 cm, of purple color and adherent on the anterior wall of the urinary bladder. We performed the dissection of the adhesion and right laparoscopic salpingectomy (Figures 1 and 2).

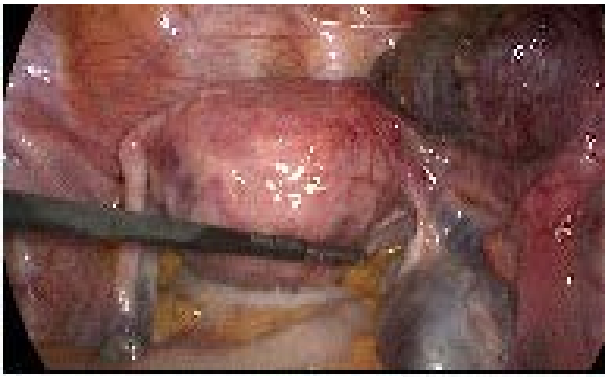

Figure 1 – Intraoperative aspect

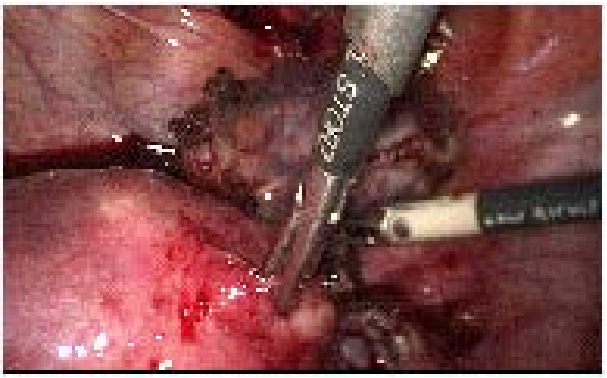

Figure 2 – Intraoperative aspect

The postoperative evolution was favorable. Postoperative follow up included clinical, laboratory and ultrasound examination. The patient presented normal biological findings. The postoperative treatment included low-molecular-weight heparin, pain killer, and antiinflammatory drugs. We monitored the HCG values until they become negative, goal which was achieved in 4 weeks after surgery.

She was discharged 3 days after the surgery and came to follow-up visit two and four weeks later. She had no symptoms and

there was no pathology according to her physical examination.

The histopathological examination revealed the presence of the trophoblastic cells with hydropic degeneration and frequent mitosis into the fallopian tube (Figures 3, 4). The immunohistochemistry examination confirmed the diagnosis. The treatment was curative and the patient had no gynecological or other related complains one year later.

Written informed consent was obtained from the patient before preparing this manuscript.

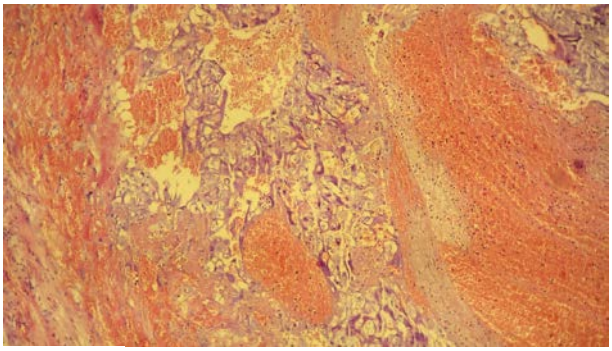

Figure 3 - Histological aspect of the fallopian tube wall with invasion of the muscular cells by trophoblastic tissue with balonised stroma showing molar degeneration of the trophoblast

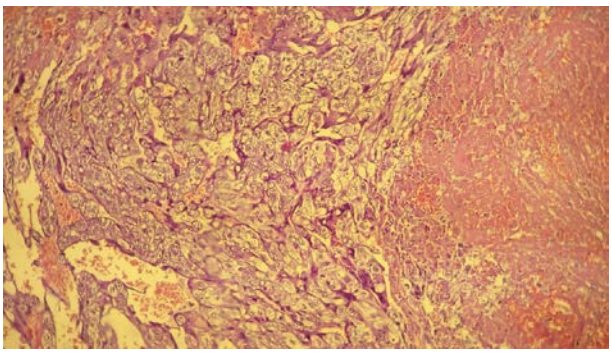

Figure 4 - Histological aspect of the fallopian tube wall with invasion of the muscular cells by trophoblastic tissue with balonised stroma showing molar degeneration of the trophoblast

Discussions

Human chorionic gonadothrophin is produced and released during pregnancy. It is supportive for pregnancy allowing the production of progesterone, which help the preparation of the uterus for implantation. It supports the formation of the cells that ultimately constitute the placental tissue, which provides nutrition to the egg after fertilization and connection to the uterine wall[6]. The human chorionic gonadotrophic hormone (-HCG) values doubles every 48-72 hours in a normal pregnancy until it reaches 10,000-20,000mIU/mL. It is known that in ectopic pregnancy mean serum β-HCG levels are lower than in healthy pregnancies.The level of β-HCG above which an imaging scan should visualize a gestational sac within the uterus in a normal intrauterine pregnancy is about 1500-1800 mIU/mL with transvaginal ultrasonography, but up to 2300 mIU/mL with multiple births[7]. The ultrasonography is the most common and important technique for diagnosing an ectopic pregnancy[8]. The ultrasound observation of an intrauterine sac, with or without fetal cardiac activity, is sufficient to exclude ectopic pregnancy. The particularity of our case was the value of β-HCG in the first evaluation (19000 IU/mL), unusual for an ectopic pregnancy, which may indicate a normal pregnancy or trophoblastic disease. The ultrasound examination excluded intrauterine localization.

Hydatidiform mole may have two distinct entities, complete hydatidiform mole and partial hydatidiform mole. These differ according to clinical presentation, gross and microscopic histopathology, basis of chromosomal pattern and outcome[9]. Molar pregnancies are considered to be premalignant because even if they are benign conditions they have the potential to develop into a malignancy. Malignant disease is characterized as gestational trophoblastic neoplasia and the histologic classes included in this category are: invasive mole, choriocarcinoma and placental site trophoblastic tumor[10]. The molecular mechanism involved in trophoblasts differentiating to an invasive phenotype is E-cadherin related. E-cadherin was evidenced in villous cytotrophoblasts, and also in non-proliferating, intermediate trophoblasts (IT) within columnal cells and islands cell into the uterine, partial molar and ectopic placentas. It is observed a temporary shift in E-cadherin expression in extravillous trophoblasts with migrating and invasive potential[11].

Choriocarcinoma represents the most severe type of trophoblastic gestation disease. The carcinomatous tissues fill out the uterine cavity, or it grows as deep nodes in the uterine

wall. It is noted that the primary ectopic localization of this tumour is extremely rare. Some authors report two cases of choriocarcinomas with ovarian or tubal localization[12]. An example is a case of a 38-year-old multiparous woman, who presented to her gynecologist for abnormal vaginal bleeding.

Clinical examinations and ultrasound showed normal findings while blood analysis demonstrated anemia and low elevated serum b-human chorionic gonadotropin. Due to hemorrhage and anemia after the curettage, the medical council decided to perform total hysterectomy. Even if the macroscopic examination of the post-operative material showed normal uterus, fallopian tubes and ovaries, a whitish brown lesion 22 mm diameter of the cervix was noted. Standard histopathology and immunohistochemical analysis diagnosed gestational choriocarcinoma[13].

Clomiphene is a nonsteroidal triphenylethylene derivative not related to diethylstilbestrol. The action mechanism is as selective estrogen receptor modulator (SERM). Clomiphene citrate is the most used treatment for fertility enhancement over the past 40 years. Clomiphene was a revolutionary advance in reproductive medicine and became common for induction of ovulation because of its easy administration and few side effects. It contains two stereoisomers: zuclomiphene (38 percent) and enclomiphene (62 percent), which were initially called the cis-isomer and trans-isomer, respectively. Enclomiphene is cleared rapidly, while zuclomiphene has a long half-life[14]. Enclomiphene is the most potent isomer with greater antiestrogenic activity and the responsible for inducing follicular development[15]. More than 50 percent of an oral dose of 14C-labeled clomiphene citrate is excreted within the first 5 days, but traces of radioactivity from the clomiphene appear in the feces up to six weeks later. Even if this observation brings concerns about fetal exposure, most studies suggest that the incidence of congenital malformations is not increased[16]. The same medical agent was administered to our patient.

A retrospective cohort study to explore factors affecting the incidence of ectopic pregnancy in assisted reproductive technology was performed. A total of 18,432 pregnancies resulting from ART treatment were retrospectively analyzed. Irrespective of the tubal infertility, for fresh in vitro fertilization cycles, the rate of EP is positively associated with ovarian stimulation; while for thawed vitro fertilization cycles, blastocyst transfer or transfer with fewer embryos reduces the ectopic pregnancy rate[17].

This clinical aspect of our case is as common ectopic pregnancy. The laboratory findings and the final pathological exam revealed tubal trophoblastic tumor. In the period 1974-1999, only 30 cases of tubal localization of hydatidiform mole were described[18]. Searching the medical database we observed less than 10 cases reported of fallopian localization of trophoblastic tumor.

Conclusion

We presented a rare case of trophoblastic tumor localized into the fallopian tube. The particularity of this case is the clinical presentation as an ectopic pregnancy and the fact that it is related to ovarian stimulation.

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