J Gynecol Obstet Hum Reprod 48 (2019) 213–216

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Review

Peritoneal reimplantation of trophoblastic tissue following laparoscopic treatment of ectopic pregnancy: A case report and review of literature

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ARTICLE INFO

Article history:
Received 22 June 2018
Received in revised form 29 August 2018
Accepted 31 August 2018
Available online 3 September 2018

Keywords:
Ectopic pregnancy
Laparoscopy
Methotrexate
Reimplantation
Salpingectomy

ABSTRACT

Reimplantation of trophoblastic tissue in the abdomen after treatment of an ectopic pregnancy is rarely reported but is very likely an underestimated complication to laparoscopy. We present a case report and review of the literature. A total of 25 cases of reimplantation of trophoblastic tissue following laparoscopic removal of ectopic pregnancy (EP) have been reported in the period January 1989 to January 2018 including our case. No cases have been reported before 1989. The use of salpingostomy vs. salpingectomy as the primary treatment of EP prior to the complication is comparable. In approximately half of the cases the reimplanted trophoblastic tissue was placed in the peritoneum and the rest in the omentum, on the bowel, in the uterosacral ligament and on the uterine body. During surgery it is important to remove all pathologic tissue and the Trendelenburg position should be considered avoided. Treatment using a single-dose Methotrexate should be performed when there is a potential risk of retaining tissue or if the serum human chorionic gonadotropin (S-hCG) is insufficiently decreasing after surgery. All patients treated for an ectopic pregnancy should be considered monitored until S-hCG is undetectable.

1. Introduction

The incidence of ectopic pregnancy (EP) is approximately 1–2% of all pregnancies. The condition is defined by the implantation of a fertilized egg outside the uterine cavity and is the most common cause of death in pregnant women in the first trimester. In fact, EP is the cause of 4–6% of all pregnancy related deaths. More than 95% of ectopic pregnancies are localized in the fallopian tube (tubal pregnancy). The remaining 5% are located in the ovary, the abdomen, the cervix or in a cesarean scar [1,2]. There is an increased risk of developing an ectopic pregnancy in case of a previous EP, tubal sterilization, tubal pathology (e.g. chlamydia or other causes of infection/inflammation) and during current use of an intrauterine contraceptive device (IUD), though the risk of pregnancy in this case is low. In addition to the regular symptoms of pregnancy, an EP often presents with abdominal pain, vaginal bleeding and amenorrhea for 6–8 weeks. Rupture and hemoperitoneum must be considered in case of hypotension, tachycardia, abdominal tenderness with abdominal guarding, and low grade fever [1].

Persisting trophoblastic tissue after surgical removal of EP is defined by a post-surgical rise or an insufficient fall in serum human chorionic gonadotropin (S-hCG). This complication occurs in 4–15% of all cases where linear salpingostomy is performed (comparable data in case of salpingectomy has not been found). Most often, the persisting tissue is retained in the tube and in more rare cases the tissue is reimplanted outside the tube e.g. in the peritoneum [1,3]. In this work we would like to highlight this rarely reported, but possibly underestimated condition, based on a case report and an updated review of the literature.

2. Case

A 16-year-old previously healthy young woman, first time pregnant, was seen at the hospital due to an unwanted pregnancy in order to have an elective abortion. The gestational age was

Abbreviations: EP, ectopic pregnancy; S-hCG, serum human chorionic gonadotropin; TVUS, transvaginal ultrasound; MTX, Methotrexate; LS, laparoscopy; LT, laparotomy.

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https://doi.org/10.1016/j.jogoh.2018.08.019
2468-7847/

unknown. No pathology was detected during the initial transvaginal ultrasound (TVUS) and S-hCG was measured and checked again after 2 days. The values were 8900 IU/L and 13,600 IU/L respectively which raised the suspicion of an ectopic pregnancy and the diagnosis was subsequently confirmed with TVUS – a small fetus with crown rump length of 5 mm and a yolk sack. There was not detected any free fluid in the abdomen.

Laparoscopically the EP was found on the right fallopian tube. The attempt to remove the pregnancy product through linear salpingostomy failed due to strongly adhesive pregnancy tissue in the tube, and the whole tube had to be removed. Hemostasis was achieved and flush and suction used. The total bleeding was less than 100 mL.

The patient was discharged from the hospital later on the same day in a state of well-being.

Histology confirmed gestational tissue including chorionic villi in the fallopian tube.

Fourteen days after surgery the patient was admitted to the hospital due to acute onset severe pain in the right side of her abdomen. For the past 10 days the patient had experienced vaginal bleeding which had decreased at the time of presentation, though. The patient was in pain but with stable vital signs. Clinically the abdomen was soft but with localized pain in the right lower quadrant. TVUS showed free fluid (the amount was not further described) and several clots in the pouch of Douglas. The blood samples showed a high S-hCG level (944), and hemoglobin of 7.1. After some hours the hemoglobin fell to 6.0. A diagnostic laparoscopy confirmed 300 mL of blood in the pouch of Douglas. On the pelvic wall, under the right ovary, an organized blood clot was placed and found to be adherent to the peritoneum and light, active bleeding was detected in the area. Further bleeding was provoked when trying to remove the clot indicating neovascularization. Most of the clot was removed and hemostasis was achieved using Surgicel Snow.

The patient was discharged from the hospital after 4 days. S-hCG decreased to 473.

Histology revealed trophoblastic tissue in the clot removed from the peritoneum.

Seven days later the patient was admitted to the hospital again with pain in the right lower quadrant of the abdomen. Vital signs were stable. S-hCG had decreased to 208. An insignificant amount of free fluid was found in the pouch of Douglass (2.5 cm × 1.5 cm). The patient was treated with 49 mg of Methotrexate (MTX) i.m. to eliminate potentially residual trophoblastic tissue and was discharged the same day in a state of well-being.

The patient had no complications following her last admission.

Twenty-one days after the discharge the S-hCG was undetectable.

3. Material and methods

A systematic literature review was conducted until January 2018 using PubMed and MEDLINE in order to identify all other case reports of reimplantation of trophoblastic tissue in the peritoneum/omentum following laparoscopic treatment of an ectopic pregnancy. No language restrictions. Search terms used included "secondary implantation of ectopic pregnancy", "ectopic pregnancy reimplantation", "peritoneal trophoblastic reimplantation", "omental trophoblastic reimplantation", "trophoblastic peritoneal reimplantation", "trophoblastic omental reimplantation", "peritoneal reimplantation of ectopic pregnancy". "omental reimplantation of ectopic pregnancy". An additional search on references was performed.

First, the articles were selected based on their title alone and subsequently on their abstract.

Only case reports concerning primary tubal pregnancy and those where laparoscopy was the primary intervention in treating the condition were included as references (in order to compare the case reports to our case). In all cases the diagnosis (reimplanted trophoblastic tissue) was made during reoperation (laparoscopy (LS) or laparotomy (LT)) and histologically verified.

Table 1
Summary of literature reports on reimplanted trophoblastic tissue after laparoscopic treatment of ectopic pregnancy.

Author	Year	No. of cases	Primary procedure	Localization of reimplanted tissue	Days after operation	Secondary procedure
Thatcher et al. [18]	1989	1	LS (salpingostomy)	Peritoneum, lig. sacrouterina	8	LT (salpingectomy)
Reich et al. [13]	1989	2	I: LS (salpingostomy) II: LS (salpingectomy)	I: Peritoneum, sigmoideum II: Peritoneum	I: 28 II: 35	I: LS II: LS
Cartwright et al. [4]	1991	8	LS (salpingostomy or salpingectomy)	Peritoneum and/or omentum (not specified)	Not reported	LS or LT (not specified)
Beck et al. [16]	1991	1	LS (salpingostomy)	Peritoneum	22	LS + MTX 20 mg × 1 daily for 5 days
Garcia-Padial [19]	1993	1	LS (salpingostomy)	Peritoneum	22	LT
Foulot et al. [8]	1994	2	I: LS (salpingostomy) II: LS (salpingectomy)	I: Peritoneum II: Peritoneum	I: 7 II: 14	I: LS (salpingectomy) + MTX 50 mg × 1 II: LS + 50 mg MTX × 2
Sjøgren + Hansen [9]	1996	1	LS (salpingectomy)	Peritoneum	51	LS
Giuliani et al. [7]	1998	1	LS (salpingostomy)	Peritoneum, sigmoideum, omentum	30	LT
Doss et al. [5]	1998	1	LS (salpingectomy)	Peritoneum, omentum	28	LT
Ben-Arie et al. [3]	2001	1	LS (salpingectomy)	Peritoneum, omentum, bowel	21	LS
Shamini et al. [12]	2002	1	LS (salpingectomy)	Omentum	23	LT + MTX 50 mg × 1
Pal et al. [11]	2003	1	LS (salpingostomy followed by LT and salpingectomy (due to bleeding))	Omentum	21	LT
Ali + Fitzgerald [20]	2006	1	LS (salpingectomy)	Omentum, peritoneum	14	LS
Bucella et al. [21]	2008	1	LS (salpingectomy)	Omentum	One week during surgical staging (cancer)	LS
Wu et al. [6]	2011	1	LS (salpingostomy)	Omentum	35	MTX LS converted to LT
Current case	2018	1	LS (salpingectomy)	Peritoneum	14	LS MTX 49 mg × 1 after 7 days

Abbreviations: LS = laparoscopy; LT = laparotomy; MTX = Methotrexate.

A total of 25 case reports have been published (including the current case that we present) in the period January 1989–January 2018. No reports were found before 1989.

To the best of our knowledge, all reported cases and available data are summarized in Table 1.

4. Results

In 8/25 cases (32%) salpingostomy was done as the primary treatment of EP. In 9/25 cases (36%) salpingectomy was performed as the primary intervention. The remaining 8 cases, presented by Cartwright et al. [4], do not discuss the use of salpingostomy vs. salpingectomy.

As in our case Doss et al. [5] fails the attempt to carry out a salpingostomy due to adherent tissue in the tube and performs a salpingectomy instead. The rest of the cases reporting salpingectomy as the primary procedure do not specify if salpingostomy was attempted initially and there are no reports on tubal ruptures during surgery in any of the cases.

In 10/25 cases (40%) laparoscopy was performed as the secondary procedure while laparotomy was performed as secondary surgery in 6/25 cases (24%) (Wu et al. [6] started with laparoscopy but converted into laparotomy due to bleeding). Cartwright et al. have not specified whether laparoscopy or laparotomy was performed as the second operation in the 8 cases they present.

The localization of the reimplanted trophoblastic tissue is distributed as follows: 11/25 (44%) was exclusively or partially placed in the peritoneum, 8/25 (32%) in the omentum, 3/25 (12%) on the bowel, 1/25 in the uterosacral ligament and 1/25 (4%) on the uterine body. The 8 cases presented by Cartwritght et al. the tissue was placed in peritoneum or omentum (not further specified).

Additional treatment with Methotrexate was given in 6/25 cases (24%) during or after the secondary operation.

5. Discussion

The frequency of reimplanted trophoblastic tissue in the peritoneum/omentum following surgical removal of an ectopic pregnancy is estimated to be 1–1.9% [4,7]. This includes both laparoscopy and laparotomy as the primary operation. Most likely this number is an underestimation as the majority of reimplanted trophoblastic tissue simply undergoes natural degeneration, or degenerates due to treatment with Methotrexate (MTX) following stagnating S-hCG values or insufficient decrease in S-hCG, without anyone knowing the exact anatomical localization of the hCG-producing tissue.

In this article we have chosen to exclusively include cases where the primary intervention is laparoscopy corresponding to the case that we present.

From the information in Table 1 there is an equal distribution between salpingostomy and salpingectomy as a primary intervention. The secondary procedure in the majority of the cases is laparoscopy.

Tubal rupture during surgery when performing a salpingectomy could be an explanation for reimplantation of trophoblastic tissue following this procedure, but the complication has not been reported in any of the 9 cases where salpingectomy is performed.

In 1989 Cartwright et al. sent out questionnaires to members of the American Association of Gynecologic Laparoscopists to determine the incidence of reimplantation of trophoblastic tissue in the abdomen following surgical treatment of EP. Out of 100 members, 25 replied and a total of 14 cases were presented. In all cases the diagnosis was made during reoperation and histologically verified. Eight of the 14 cases followed laparoscopic intervention. The remaining 6 cases occurred after laparotomy (these are not included in Table 1). A similar study has to date not yet been repeated which makes the frequency of reimplantation of trophoblastic tissue following surgical management of EP presented by Cartwright et al. (1.9%) [4] the closest we get to an actual estimate, even though the evidence in the survey can be discussed due to the study design and the sample size. Furthermore the study is performed in 1989 when MTX was not used routinely in the treatment of EP as today so the frequency of the complication could possibly be lower if reproducing the study today.

In the presented cases (Table 1) the symptoms vary from abdominal pain, vaginal bleeding to hemorrhagic shock. The time from primary operation until the patient returns to the hospital varies from 7 to 51 days [8,9], which indicates the importance of considering the possibility of persistent/reimplanted trophoblastic tissue in case of the above mentioned symptoms even though weeks have passed since the primary operation. The patient in our case is hospitalized 14 days after surgery due to intra-abdominal bleeding.

In case of an ectopic pregnancy the S-hCG is usually stagnating or insufficiently rising compared to a normally developing pregnancy where S-hCG doubles every other day until day 40 of gestation [1]. This is comparable with our case where S-hCG, prior to surgical intervention rises insufficiently from 8900 to 13,600 IU/L in 2 days.

Studies show that the S-hCG half-life time following salpingectomy is 15–19.4 h within the first 48 h after which the S-hCG declines more slowly [10]. Persistent trophoblastic tissue after surgical treatment of an EP causes the S-hCG to rise or decrease insufficiently. This emphasizes the importance of measuring the S-hCG after treatment of EP. In 6 of the 25 cases S-hCG is measured within the first 3 days after the primary surgery [3,6,8,11–13]. In the remaining cases information regarding S-hCG postoperatively is not available.

Primary medical treatment of EP using a single-dose Methotrexate (MTX) is an alternative to surgery [14]. MTX is a folic acid antagonist which inhibits the DNA synthesis and cell division, and causes the pregnancy to degenerate. The use of single-dose MTX in medical treatment of EP has a success rate (defined by no need for further intervention) of 88.1%. Afterwards the S-hCG level should be monitored until undetectable. In 15–20% of the cases a second dose of MTX is required [1].

The success rate is higher when treating an EP by performing a salpingostomy compared to a single-dose of MTX [14]. Treatment with MTX has a lower risk of complications but is not always an option, as in our case together with the cases in Table 1, where the condition of the patients required surgical intervention.

Post-surgical treatment using a single-dose MTX is recommended in cases where there is a potential risk of persistent tissue [14,15]. There is no evidence that repeated doses of MTX have a better effect than a single dose [1]. Marret et al. emphasize that there is no evidence for routine treatment of all patients undergoing surgical treatment for an EP with MTX [14]. None of the reported cases uses MTX following primary surgery. In 6 cases (reported in 1991–2018 including our case) treatment with MTX is conducted after the secondary procedure [6,8,12,16].

When laparoscopic treatment of EP, where pneumoperitoneum and the Trendelenburg position are used, fragments of trophoblastic tissue can be displaced increasing the risk of reimplantation of the tissue in the abdomen. As a precaution during surgery aspiration of all blood clots and tissue fragments together with an extensive irrigation of the peritoneal cavity should be done. Furthermore all trophoblastic tissue should be carefully extracted and the whole salpinx removed when performing a salpingectomy. Minimizing the use of the Trendelenburg position during surgery could possibly diminish the risk of displaced tissue [3,11].

The level of S-hCG postoperatively should be known to facilitate the diagnosis if reimplantation occurs. Several studies recommend that S-hCG is monitored until undetectable [1,3,7,17].

6. Conclusion

Reimplantation of trophoblastic tissue after laparoscopic removal of an ectopic pregnancy is rarely reported, but it is very likely an underestimated complication. More studies are required to get a realistic picture of the prevalence.

During surgery it is important to remove all pathologic tissue, blood clots etc. and the Trendelenburg position should be considered avoided. Besides, treatment with a single-dose Methotrexate should be used in cases with a potential risk of retaining tissue after surgery or where serum human chorionic gonadotropin is rising or insufficiently decreasing.

All patients treated for an ectopic pregnancy should be considered monitored until serum human chorionic gonadotropin is undetectable.

Disclosure statement

The authors declare that they have no competing interest.

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